

Draft for consultation

## Type 2 diabetes in adults: management (medicines update)

**[E2.2] Evidence reviews for initial pharmacological management of type 2 diabetes: appendices J and K**

*NICE guideline GID-NG10336*

*Evidence reviews underpinning recommendations 1.8.6-1.8.32, 1.8.34, 1.8.38-1.8.60 and recommendations for research in the NICE guideline*

*August 2025*

*Draft for Consultation*

*This evidence review was developed by NICE*



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# Appendices

## Appendix J Excluded studies

### J.1 Clinical studies

**Table 1: Studies not included in this review as they are included in review 1.2 subsequent pharmacological management of type 2 diabetes**

| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Abdul-Ghani, M., Migahid, O., Megahed, A. et al. (2020) Combination Therapy with Pioglitazone/Exenatide Improves Beta Cell Function and Produces Superior Glycemic Control Compared to Basal/Bolus Insulin in Poorly Controlled T2DM: 3-Year Follow-up of the Qatar Study.</a> Diabetes, obesity & metabolism                                           | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Abdul-Ghani, Muhammad, Migahid, Osama, Megahed, Ayman et al. (2017) Combination Therapy With Exenatide Plus Pioglitazone Versus Basal/Bolus Insulin in Patients With Poorly Controlled Type 2 Diabetes on Sulfonylurea Plus Metformin: The Qatar Study.</a> Diabetes care 40(3): 325-331                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Abreu, M., Tumyan, A., Elhassan, A. et al. (2019) A randomized trial comparing the efficacy and safety of treating patients with type 2 diabetes and highly elevated HbA1c levels with basal-bolus insulin or a glucagon-like peptide-1 receptor agonist plus basal-bolus insulin: the SIMPLE study.</a> Diabetes Obes Metab 21(9): 2133-2141           | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Adel, S. M. H., Jorfi, F., Mombeini, H. et al. (2022) Effect of a low dose of empagliflozin on short-term outcomes in type 2 diabetics with acute coronary syndrome after percutaneous coronary intervention.</a> Saudi Med J 43(5): 458-464                                                                                                            | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Ahmadi, S S, Filipsson, K, Dimenas, H et al. (2019) Effect of liraglutide on anthropometric measurements, sagittal abdominal diameter and adiponectin levels in people with type 2 diabetes treated with multiple daily insulin injections: evaluations from a randomized trial (MDI-liraglutide study 5).</a> Obesity science & practice 5(2): 130-140 | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| <a href="#">Ahmann, A., Rodbard, H. W., Rosenstock, J. et al. (2015) Efficacy and safety of liraglutide versus placebo added to basal insulin analogues (with or without metformin) in patients with type 2 diabetes: A randomized, placebo-controlled trial. Diab Obes Metab 17(11): 1056-64</a>                                                  | Included in 1.2 medicine/strategies for further treatment                                  |
| <a href="#">Ahmann, Andrew J, Capehorn, Matthew, Charpentier, Guillaume et al. (2018) Efficacy and Safety of Once-Weekly Semaglutide Versus Exenatide ER in Subjects With Type 2 Diabetes (SUSTAIN 3): A 56-Week, Open-Label, Randomized Clinical Trial. Diabetes care 41(2): 258-266</a>                                                          | Included in 1.2 medicine/strategies for further treatment<br><i>parent paper SUSTAIN 3</i> |
| <a href="#">Ahren, B., Johnson, S. L., Stewart, M. et al. (2014) HARMONY 3: 104-week randomized, double-blind, placebo- and active-controlled trial assessing the efficacy and safety of albiglutide compared with placebo, sitagliptin, and glimepiride in patients with type 2 diabetes taking metformin. Diabetes Care 37(8): 2141-8</a>        | Included in 1.2 medicine/strategies for further treatment                                  |
| <a href="#">Ahren, Bo, Pacini, Giovanni, Foley, James E et al. (2005) Improved meal-related beta-cell function and insulin sensitivity by the dipeptidyl peptidase-IV inhibitor vildagliptin in metformin-treated patients with type 2 diabetes over 1 year. Diabetes care 28(8): 1936-40</a>                                                      | Included in 1.2 medicine/strategies for further treatment                                  |
| <a href="#">Ahrén, B., Gomis, R., Standl, E. et al. (2004) Twelve- and 52-week efficacy of the dipeptidyl peptidase IV inhibitor LAF237 in metformin-treated patients with type 2 diabetes. Diabetes Care 27(12): 2874-80</a>                                                                                                                      | Included in 1.2 medicine/strategies for further treatment                                  |
| <a href="#">Ahrén, B., Leguizamo Dimas, A., Miossec, P. et al. (2013) Efficacy and safety of lixisenatide once-daily morning or evening injections in type 2 diabetes inadequately controlled on metformin (GetGoal-M). Diabetes Care 36(9): 2543-50</a>                                                                                           | Included in 1.2 medicine/strategies for further treatment                                  |
| <a href="#">Ahrén, B., Masmiquel, L., Kumar, H. et al. (2017) Efficacy and safety of once-weekly semaglutide versus once-daily sitagliptin as an add-on to metformin, thiazolidinediones, or both, in patients with type 2 diabetes (SUSTAIN 2): A 56-week, double-blind, phase 3a, randomised trial. Lancet Diabetes Endocrinol 5(5): 341-354</a> | Included in 1.2 medicine/strategies for further treatment                                  |

| Study                                                                                                                                                                                                                                                                                                                                                                                                   | Reason                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Ando, Y., Shigiyama, F., Hirose, T. et al. (2021) Simplification of complex insulin regimens using canagliflozin or liraglutide in patients with well-controlled type 2 diabetes: A 24-week randomized controlled trial. Journal of Diabetes Investigation 12(10): 1816-1826</a>                                                                                                            | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Araki, E., Inagaki, N., Tanizawa, Y. et al. (2015) Efficacy and safety of once-weekly dulaglutide in combination with sulphonylurea and/or biguanide compared with once-daily insulin glargine in Japanese patients with type 2 diabetes: a randomized, open-label, phase III, non-inferiority study. Diabetes Obes Metab 17(10): 994-1002</a>                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Araki, E., Tanizawa, Y., Tanaka, Y. et al. (2015) Long-term treatment with empagliflozin as add-on to oral antidiabetes therapy in Japanese patients with type 2 diabetes mellitus. Diabetes Obes Metab 17(7): 665-674</a>                                                                                                                                                                  | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Arechavaleta, R., Seck, T., Chen, Y. et al. (2011) Efficacy and safety of treatment with sitagliptin or glimepiride in patients with type 2 diabetes inadequately controlled on metformin monotherapy: a randomized, double-blind, non-inferiority trial. Diabetes Obes Metab 13(2): 160-8</a>                                                                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Aroda, V. R., Bain, S. C., Cariou, B. et al. (2017) Efficacy and safety of once-weekly semaglutide versus once-daily insulin glargine as add-on to metformin (with or without sulfonylureas) in insulin-naïve patients with type 2 diabetes (SUSTAIN 4): A randomised, open-label, parallel-group, multicentre, multinational, phase 3a trial. Lancet Diabetes Endocrinol 5(5): 355-366</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Aroda, V. R., Gonzalez-Galvez, G., Gron, R. et al. (2019) Durability of insulin degludec plus liraglutide versus insulin glargine U100 as initial injectable therapy in type 2 diabetes (DUAL VIII): a multicentre, open-label, phase 3b, randomised controlled trial. The Lancet Diabetes &amp; Endocrinology 7(8): 596-605</a>                                                            | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Aroda, Vanita R, Rosenstock, Julio, Wysham, Carol et al. (2016) Efficacy and Safety of LixiLan, a Titratable Fixed-Ratio Combination of Insulin Glargine Plus Lixisenatide in Type 2 Diabetes Inadequately Controlled on Basal</a>                                                                                                                                                          | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                      | Reason                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Insulin and Metformin: The LixiLan-L Randomized Trial.</a> Diabetes care 39(11): 1972-1980                                                                                                                                                                                                                                     |                                                           |
| <a href="#">Arturi, F., Succurro, E., Miceli, S. et al. (2017) Liraglutide improves cardiac function in patients with type 2 diabetes and chronic heart failure.</a> Endocrine 57(3): 464-473                                                                                                                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Aschner, P., Chan, J., Owens, D. R. et al. (2012) Insulin glargine versus sitagliptin in insulin-naïve patients with type 2 diabetes mellitus uncontrolled on metformin (EASIE): a multicentre, randomised open-label trial.</a> Lancet 379(9833): 2262-9                                                                      | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Avilés-Santa, L.; Sinding, J.; Raskin, P. (1999) Effects of metformin in patients with poorly controlled, insulin-treated type 2 diabetes mellitus. A randomized, double-blind, placebo-controlled trial.</a> Ann Intern Med 131(3): 182-8                                                                                     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Ba, J., Han, P., Yuan, G. et al. (2017) Randomized trial assessing the safety and efficacy of sitagliptin in Chinese patients with type 2 diabetes mellitus inadequately controlled on sulfonylurea alone or combined with metformin.</a> J Diabetes 9: 667-676                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Babar, M., Hussain, M., Ahmad, M. et al. (2021) Comparison Of Efficacy And Safety Profile Of Empagliflozin As A Combination Therapy In Obese Type 2 Diabetic Patients.</a> Journal of Ayub Medical College, Abbottabad: JAMC 33(2): 188-191                                                                                    | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bae, J., Huh, J. H., Lee, M. et al. (2021) Glycaemic control with add-on thiazolidinedione or a sodium-glucose co-transporter-2 inhibitor in patients with type 2 diabetes after the failure of an oral triple antidiabetic regimen: A 24-week, randomized controlled trial.</a> Diabetes, Obesity & Metabolism 23(2): 609-618 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bailey, C. J., Gross, J. L., Pieters, A. et al. (2010) Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial.</a> Lancet 375(9733): 2223-33                                                                      | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                      | Reason                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Bailey, Clifford J, Gross, Jorge L, Hennicken, Delphine et al. (2013) Dapagliflozin add-on to metformin in type 2 diabetes inadequately controlled with metformin: a randomized, double-blind, placebo-controlled 102-week trial. BMC medicine 11: 43</a>                                                      | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bailey, T. S., Takacs, R., Tinahones, F. J. et al. (2016) Efficacy and safety of switching from sitagliptin to liraglutide in subjects with type 2 diabetes (LIRA-SWITCH): a randomized, double-blind, double-dummy, active-controlled 26-week trial. Diabetes Obes Metab 18(12): 1191-1198</a>                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bain, Stephen C, Mosenzon, Ofri, Arechavaleta, Rosario et al. (2019) Cardiovascular safety of oral semaglutide in patients with type 2 diabetes: Rationale, design and patient baseline characteristics for the PIONEER 6 trial. Diabetes, obesity &amp; metabolism 21(3): 499-508</a>                         | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bajaj, M., Gilman, R., Patel, S. et al. (2014) Linagliptin improved glycaemic control without weight gain or hypoglycaemia in patients with Type 2 diabetes inadequately controlled by a combination of metformin and pioglitazone: A 24-week randomized, double-blind study. Diabet Med 31(12): 1505-1514</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Barnett, A. H., Charbonnel, B., Donovan, M. et al. (2012) Effect of saxagliptin as add-on therapy in patients with poorly controlled type 2 diabetes on insulin alone or insulin combined with metformin. Curr Med Res Opin 28(4): 513-23</a>                                                                  | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Barnett, A. H., Huisman, H., Jones, R. et al. (2013) Linagliptin for patients aged 70 years or older with type 2 diabetes inadequately controlled with common antidiabetes treatments: a randomised, double-blind, placebo-controlled trial. Lancet 382(9902): 1413-23</a>                                     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Barnett, A. H., Mithal, A., Manassie, J. et al. (2014) Efficacy and safety of empagliflozin added to existing antidiabetes treatment in patients with type 2 diabetes and chronic kidney disease: A randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol 2(5): 369-384</a>           | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                | Reason                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Barnett, Anthony H, Charbonnel, Bernard, Li, Jia et al. (2013) Saxagliptin add-on therapy to insulin with or without metformin for type 2 diabetes mellitus: 52-week safety and efficacy. Clinical drug investigation 33(10): 707-17</a>                                                 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bergenstal, R. M., Wysham, C., Macconell, L. et al. (2010) Efficacy and safety of exenatide once weekly versus sitagliptin or pioglitazone as an adjunct to metformin for treatment of type 2 diabetes (DURATION-2): a randomised trial. Lancet 376(9739): 431-9</a>                     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bergenstal, R., Lewin, A., Bailey, T. et al. (2009) Efficacy and safety of biphasic insulin aspart 70/30 versus exenatide in subjects with type 2 diabetes failing to achieve glycemic control with metformin and a sulfonylurea. Curr Med Res Opin 25(1): 65-75</a>                     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Berndt-Zipfel, C., Michelson, G., Dworak, M. et al. (2013) Vildagliptin in addition to metformin improves retinal blood flow and erythrocyte deformability in patients with type 2 diabetes mellitus - results from an exploratory study. Cardiovasc Diabetol 12(1): 59</a>              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Best, Jennie H, Rubin, Richard R, Peyrot, Mark et al. (2011) Weight-related quality of life, health utility, psychological well-being, and satisfaction with exenatide once weekly compared with sitagliptin or pioglitazone after 26 weeks of treatment. Diabetes care 34(2): 314-9</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bethel M, A, Engel S, S, Stevens S, R et al. (2019) Progression of glucose-lowering diabetes therapy in TECOS. Endocrinology, Diabetes and Metabolism 2(1): e00053</a>                                                                                                                   | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Betteridge, D J and Verges, B (2005) Long-term effects on lipids and lipoproteins of pioglitazone versus gliclazide addition to metformin and pioglitazone versus metformin addition to sulphonylurea in the treatment of type 2 diabetes. Diabetologia 48(12): 2477-81</a>              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Billings, Liana K, Doshi, Ankur, Gouet, Didier et al. (2018) Efficacy and Safety of IDegLira Versus Basal-Bolus Insulin Therapy in Patients With Type 2 Diabetes Uncontrolled on Metformin and Basal Insulin: The DUAL VII</a>                                                           | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                      | Reason                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Randomized Clinical Trial. Diabetes care 41(5): 1009-1016</a>                                                                                                                                                                                                                                  |                                                           |
| <a href="#">Bizino, M. B., Jazet, I. M., Westenberg, J. J. M. et al. (2019) Effect of liraglutide on cardiac function in patients with type 2 diabetes mellitus: randomized placebo-controlled trial. Cardiovasc Diabetol 18(1): 55</a>                                                                    | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Blonde, L., Belousova, L., Fainberg, U. et al. (2020) Liraglutide as add-on to sodium-glucose co-transporter-2 inhibitors in patients with inadequately controlled type 2 diabetes: LIRA-ADD2SGLT2i, a 26-week, randomized, double-blind, placebo-controlled trial. Diab Obes Metab</a>        | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Blonde, L., Jendle, J., Gross, J. et al. (2015) Once-weekly dulaglutide versus bedtime insulin glargine, both in combination with prandial insulin lispro, in patients with type 2 diabetes (AWARD-4): a randomised, open-label, phase 3, non-inferiority study. Lancet 385(9982): 2057-66</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bode, B., Stenlöf, K., Sullivan, D. et al. (2013) Efficacy and safety of canagliflozin treatment in older subjects with type 2 diabetes mellitus: a randomized trial. Hosp Pract (1995) 41(2): 72-84</a>                                                                                       | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bode, B., Stenlof, K., Harris, S et al. (2015) Long-term efficacy and safety of canagliflozin over 104 weeks in patients aged 55-80 years with type 2 diabetes. Diabetes, obesity &amp; metabolism 17(3): 294-303</a>                                                                          | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bolinder, J., Ljunggren, Ö, Kullberg, J. et al. (2012) Effects of dapagliflozin on body weight, total fat mass, and regional adipose tissue distribution in patients with type 2 diabetes mellitus with inadequate glycemic control on metformin. J Clin Endocrinol Metab 97(3): 1020-31</a>   | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Bolinder, J., Ljunggren, O, Johansson, L et al. (2014) Dapagliflozin maintains glycaemic control while reducing weight and body fat mass over 2 years in patients with type 2 diabetes mellitus inadequately controlled on metformin. Diabetes, obesity &amp; metabolism 16(2): 159-69</a>     | Included in 1.2 medicine/strategies for further treatment |



| Study                                                                                                                                                                                                                                                                                | Reason                                                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| <a href="#">Bolli, G. B., Munteanu, M., Dotsenko, S. et al. (2014) Efficacy and safety of lixisenatide once daily vs. placebo in people with Type 2 diabetes insufficiently controlled on metformin (GetGoal-F1). Diabetic Med 31(2): 176-184</a>                                    | Included in 1.2 medicine/strategies for further treatment  |
| <a href="#">Bolli, G., Dotta, F., Colin, L. et al. (2009) Comparison of vildagliptin and pioglitazone in patients with type 2 diabetes inadequately controlled with metformin. Diabetes Obes Metab 11(6): 589-95</a>                                                                 | Included in 1.2 medicine/strategies for further treatment  |
| <a href="#">Bolli, G, Dotta, F, Rochotte, E et al. (2008) Efficacy and tolerability of vildagliptin vs. pioglitazone when added to metformin: a 24-week, randomized, double-blind study. Diabetes, obesity &amp; metabolism 10(1): 82-90</a>                                         | Included in 1.2 medicine/strategies for further treatment  |
| <a href="#">Bosi, E., Camisasca, R. P., Collober, C. et al. (2007) Effects of vildagliptin on glucose control over 24 weeks in patients with type 2 diabetes inadequately controlled with metformin. Diabetes Care 30(4): 890-5</a>                                                  | Included in 1.2 medicine/strategies for further treatment  |
| <a href="#">Brown, A. J. M., Gandy, S., McCrimmon, R. et al. (2020) A randomized controlled trial of dapagliflozin on left ventricular hypertrophy in people with type two diabetes: the DAPA-LVH trial. European Heart Journal 41(36): 3421-3432</a>                                | Included in 1.2 medicine/strategies for further treatment  |
| <a href="#">Brown, Alexander J M, Lang, Chim, McCrimmon, Rory et al. (2017) Does dapagliflozin regress left ventricular hypertrophy in patients with type 2 diabetes? A prospective, double-blind, randomised, placebo-controlled study. BMC cardiovascular disorders 17(1): 229</a> | Included in 1.2 medicine/strategies for further treatment) |
| <a href="#">Bunck, M C, Eliasson, B, Corner, A et al. (2011) Exenatide treatment did not affect bone mineral density despite body weight reduction in patients with type 2 diabetes. Diabetes, obesity &amp; metabolism 13(4): 374-7</a>                                             | Included in 1.2 medicine/strategies for further treatment  |
| <a href="#">Bunck, M. C., Diamant, M., Cornér, A. et al. (2009) One-year treatment with exenatide improves beta-cell function, compared with insulin glargine, in metformin-treated type 2 diabetic patients: a randomized, controlled trial. Diabetes Care 32(5): 762-8</a>         | Included in 1.2 medicine/strategies for further treatment  |



| Study                                                                                                                                                                                                                                                                                                                                       | Reason                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Bunck, Mathijs C, Diamant, Michaela, Eliasson, Bjorn et al. (2010) Exenatide affects circulating cardiovascular risk biomarkers independently of changes in body composition. Diabetes care 33(8): 1734-7</a>                                                                                                                   | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Buse, J. B., Bergenstal, R. M., Glass, L. C. et al. (2011) Use of twice-daily exenatide in Basal insulin-treated patients with type 2 diabetes: a randomized, controlled trial. Ann Intern Med 154(2): 103-12</a>                                                                                                               | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Buse, J. B., Henry, R. R., Han, J. et al. (2004) Effects of exenatide (Exendin-4) on glycemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes. Diabetes Care 27(11): 2628-35</a>                                                                                                                    | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Buse, John B, Bode, Bruce W, Mertens, Ann et al. (2020) Long-term efficacy and safety of oral semaglutide and the effect of switching from sitagliptin to oral semaglutide in patients with type 2 diabetes: a 52-week, randomized, open-label extension of the PIONEER 7 trial. BMJ open diabetes research &amp; care 8(2)</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Buse, John B, Nauck, Michael, Forst, Thomas et al. (2013) Exenatide once weekly versus liraglutide once daily in patients with type 2 diabetes (DURATION-6): a randomised, open-label study. Lancet (London, England) 381(9861): 117-24</a>                                                                                     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Buse, John B, Rosenstock, Julio, Sesti, Giorgio et al. (2009) Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6). Lancet (London, England) 374(9683): 39-47</a>                                                            | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Buse, John B, Vilsboll, Tina, Thurman, Jerry et al. (2014) Contribution of liraglutide in the fixed-ratio combination of insulin degludec and liraglutide (IDegLira). Diabetes care 37(11): 2926-33</a>                                                                                                                         | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Butler, Javed, Zannad, Faiez, Fitchett, David et al. (2019) Empagliflozin Improves Kidney Outcomes in Patients With or Without Heart Failure. Circulation. Heart failure 12(6): e005875</a>                                                                                                                                     | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                           | Reason                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Cahn, Avivit, Raz, Itamar, Leiter, Lawrence A et al. (2021) Cardiovascular, Renal, and Metabolic Outcomes of Dapagliflozin Versus Placebo in a Primary Cardiovascular Prevention Cohort: Analyses From DECLARE-TIMI 58. Diabetes care 44(5): 1159-1167</a>                                                          | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Camerini-Davalos, R. A.; Velasco, C. A.; Reddi, A. S. (1994) Effect of insulin-glipizide combination on skeletal muscle capillary basement membrane width in diabetic patients. Clin Ther 16(6): 952-61</a>                                                                                                         | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Cannon Christopher, P, McGuire Darren, K, Pratley, Richard et al. (2018) Design and baseline characteristics of the eValuation of ERTugliflozin efficacy and Safety CardioVascular outcomes trial (VERTIS-CV). American heart journal 206: 11-23</a>                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Cannon Christopher, P, Pratley, Richard, Dagogo-Jack, Samuel et al. (2020) Cardiovascular Outcomes with Ertugliflozin in Type 2 Diabetes. The New England journal of medicine 383(15): 1425-1435</a>                                                                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Capehorn, M S, Catarig, A-M, Furberg, J K et al. (2020) Efficacy and safety of once-weekly semaglutide 1.0mg vs once-daily liraglutide 1.2mg as add-on to 1-3 oral antidiabetic drugs in subjects with type 2 diabetes (SUSTAIN 10). Diabetes &amp; metabolism 46(2): 100-109</a>                                   | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Cefalu, W. T., Leiter, L. A., de Bruin, T. W. et al. (2015) Dapagliflozin's effects on glycemia and cardiovascular risk factors in high-risk patients with type 2 diabetes: A 24-week, multicenter, randomized, double-blind, placebo-controlled study with a 28-week extension. Diabetes Care 38(7): 1218-1227</a> | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                         | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                        | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                      | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                              | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                   | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                     |
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| Study                                                                                                                                                                                                                                                                                              | Reason                                                    |
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| <a href="#">Addition to Standard Insulin Treatment in Patients with Type 2 Diabetes Mellitus Requiring Hemodialysis: Results from the PLOren Study.</a> Nephron extra 2(1): 104-14                                                                                                                 |                                                           |
| <a href="#">Gallwitz, B., Böhmer, M., Segiet, T. et al. (2011) Exenatide twice daily versus premixed insulin aspart 70/30 in metformin-treated patients with type 2 diabetes: a randomized 26-week study on glycemic control and hypoglycemia.</a> Diabetes Care 34(3): 604-6                      | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                 | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                             |
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| Study                                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                      |
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| Study                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                                    | Reason                                                    |
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| <a href="#">Haring, H. U., Merker, L., Seewaldt-Becker, E. et al. (2014) Empagliflozin as add-on to metformin in patients with type 2 diabetes: A 24-week, randomized, double-blind, placebo-controlled trial. Diabetes Care 37(6): 1650-1659</a>                                                                                                                                                        | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                       | Reason                                                    |
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| <a href="#">Heine, R. J., Gaal, L. F., Johns, D. et al. (2005) Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial.</a> Ann Intern Med 143(8): 559-69                                                                                                                                            | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Heise, T., Mari, A., DeVries, J. H. et al. (2022) Effects of subcutaneous tirzepatide versus placebo or semaglutide on pancreatic islet function and insulin sensitivity in adults with type 2 diabetes: a multicentre, randomised, double-blind, parallel-arm, phase 1 clinical trial.</a> The lancet. Diabetes & endocrinology 10(6): 418-429 | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                          | Reason                                                    |
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| <a href="#">patients with type 2 diabetes mellitus</a> . Diabetes & vascular disease research 8(2): 125-35                                                                                                                                                                                                                     |                                                           |
| <a href="#">Holman Rury, R, Bethel Mary, Angelyn, George, Jyothis et al. (2016) Rationale and design of the EXenatide Study of Cardiovascular Event Lowering (EXSCEL) trial</a> . American heart journal 174: 103-10                                                                                                           | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Ikonomidis, I., Pavlidis, G., Thymis, J. et al. (2020) Effects of Glucagon-Like Peptide-1 Receptor Agonists, Sodium-Glucose Cotransporter-2 Inhibitors, and Their Combination on Endothelial Glycocalyx, Arterial Function, and Myocardial Work Index in Patients With Type 2 Diabetes Mellitus After 12-Month</a> | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
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| <a href="#">Treatment</a> . Journal of the American Heart Association 9(9): e015716                                                                                                                                                                                                                                                                                                 |                                                           |
| <a href="#">Inagaki, N., Atsumi, Y., Oura, T. et al. (2012) Efficacy and safety profile of exenatide once weekly compared with insulin once daily in Japanese patients with type 2 diabetes treated with oral antidiabetes drug(s): results from a 26-week, randomized, open-label, parallel-group, multicenter, noninferiority study</a> . Clin Ther 34(9): 1892-908               | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Jabbour, S. A., Frias, J. P., Ahmed, A. et al. (2020) Efficacy and Safety Over 2 Years of Exenatide Plus Dapagliflozin in the DURATION-8 Study: A Multicenter, Double-Blind, Phase 3, Randomized Controlled Trial</a> . Diabetes Care 43(10): 2528-2536                                                                                                                 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Jabbour, S. A., Hardy, E., Sugg, J. et al. (2014) Dapagliflozin is effective as add-on therapy to sitagliptin with or without metformin: A 24-Week, multicenter, randomized, double-blind, placebo-controlled study</a> . Diabetes Care 37(3): 740-750                                                                                                                  | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Jabbour, Serge A, Frias, Juan P, Hardy, Elise et al. (2018) Safety and Efficacy of Exenatide Once Weekly Plus Dapagliflozin Once Daily Versus Exenatide or Dapagliflozin Alone in Patients With Type 2 Diabetes Inadequately Controlled With Metformin Monotherapy: 52-Week Results of the DURATION-8 Randomized Controlled Trial</a> . Diabetes care 41(10): 2136-2146 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Jardine, Meg J, Mahaffey, Kenneth W, Neal, Bruce et al. (2017) The Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) Study Rationale, Design, and Baseline</a>                                                                                                                                                  | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                        | Reason                                                    |
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| <a href="#">Characteristics</a> . American journal of nephrology 46(6): 462-472                                                                                                                                                                                                                                                                              |                                                           |
| <a href="#">Ji, L. N., Pan, C. Y., Lu, J. M. et al. (2016) Efficacy and safety of combination therapy with vildagliptin and metformin versus metformin uptitration in Chinese patients with type 2 diabetes inadequately controlled with metformin monotherapy: a randomized, open-label, prospective study (VISION). Diabetes Obes Metab 18(8): 775-782</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Ji, L., Dong, X., Li, Y. et al. (2021) Efficacy and safety of once-weekly semaglutide versus once-daily sitagliptin as add-on to metformin in patients with type 2 diabetes in SUSTAIN China: A 30-week, double-blind, phase 3a, randomized trial. Diabetes, Obesity &amp; Metabolism 23(2): 404-414</a>                                         | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Ji, Linong, Lu, Yibin, Li, Qifu et al. (2023) Efficacy and safety of empagliflozin in combination with insulin in Chinese patients with type 2 diabetes and insufficient glycaemic control: A phase III, randomized, double-blind, placebo-controlled, parallel study. Diabetes, obesity &amp; metabolism</a>                                    | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                | Reason                                                    |
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| <a href="#">Jonker, J T, Lamb, H J, van der Meer, R W et al. (2010) Pioglitazone compared with metformin increases pericardial fat volume in patients with type 2 diabetes mellitus.</a> The Journal of clinical endocrinology and metabolism 95(1): 456-60                                                                                          | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                    |
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| <a href="#">Kaku, K, Rasmussen, M F, Clauson, P et al. (2010) Improved glycaemic control with minimal hypoglycaemia and no weight change with the once-daily human glucagon-like peptide-1 analogue liraglutide as add-on to sulphonylurea in Japanese patients with type 2 diabetes. Diabetes, obesity &amp; metabolism 12(4): 341-7</a>                                                      | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                 | Reason                                                    |
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| <a href="#">Kesavadev, J., Pillai, P. B. S., Shankar, A. et al. (2017) Sitagliptin 100 mg vs glimepiride 1-3 mg as an add-on to insulin and metformin in type 2 diabetes (SWIM). Endocrine connections 6(8): 748-757</a>                                                                                                                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Khaloo, P., Asadi Komeleh, S., Alemi, H. et al. (2019) Sitagliptin vs. pioglitazone as add-on treatments in patients with uncontrolled type 2 diabetes on the maximal dose of metformin plus sulfonylurea. J Endocrinol Invest 42(7): 851-857</a>                                                                                                         | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Kinoshita, T., Shimoda, M., Nakashima, K. et al. (2020) Comparison of the effects of three kinds of glucose-lowering drugs on non-alcoholic fatty liver disease in patients with type 2 diabetes: a randomized, open-label, three-arm, active control study. J Diabetes Invest</a>                                                                        | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Kirkman, M Sue, Tripputi, Mark, Krause-Steinrauf, Heidi et al. (2024) Comparative</a>                                                                                                                                                                                                                                                                     | - Top-up search 2 (1.2 model 5)                           |

| Study                                                                                                                                                                                                                                                                                                            | Reason                                                    |
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| <a href="#">Effects of Randomized Second-line Therapy for Type 2 Diabetes on a Composite Outcome Incorporating Glycemic Control, Body Weight, and Hypoglycemia: An Analysis of Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE).</a> Diabetes care                           | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Kohan, D. E., Fioretto, P., Tang, W. et al. (2014) Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve glycemic control.</a> Kidney Int 85(4): 962-971                                    | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Kothny, W., Shao, Q., Groop, P-H et al. (2012) One-year safety, tolerability and efficacy of vildagliptin in patients with type 2 diabetes and moderate or severe renal impairment.</a> Diabetes, obesity & metabolism 14(11): 1032-9                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Kothny, Wolfgang, Lukashevich, Valentina, Foley, James E et al. (2015) Comparison of vildagliptin and sitagliptin in patients with type 2 diabetes and severe renal impairment: a randomised clinical trial.</a> Diabetologia 58(9): 2020-6                                                          | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Kovacs, C. S., Seshiah, V., Swallow, R. et al. (2014) Empagliflozin improves glycaemic and weight control as add-on therapy to pioglitazone or pioglitazone plus metformin in patients with type 2 diabetes: A 24-week, randomized, placebo-controlled trial.</a> Diabetes Obes Metab 16(2): 147-158 | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                     | Reason                                                    |
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| <a href="#">Kovacs, Christopher S, Seshiah, Veeraswamy, Merker, Ludwig et al. (2015) Empagliflozin as Add-on Therapy to Pioglitazone With or Without Metformin in Patients With Type 2 Diabetes Mellitus. Clinical therapeutics 37(8): 1773-88e1</a>                                                                                      | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Koyama, H., Tanaka, S., Monden, M. et al. (2014) Comparison of effects of pioglitazone and glimepiride on plasma soluble RAGE and RAGE expression in peripheral mononuclear cells in type 2 diabetes: Randomized controlled trial (PioRAGE). Atherosclerosis 234(2): 329-334</a>                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Krobot, Karl J, Ferrante, Shannon Allen, Davies, Michael J et al. (2012) Lower risk of hypoglycemia with sitagliptin compared to glipizide when either is added to metformin therapy: a pre-specified analysis adjusting for the most recently measured HbA(1c) value. Current medical research and opinion 28(8): 1281-7</a> | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                         | Reason                                                    |
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| <a href="#">Lee, H. W., Lee, H. C., Kim, B. W. et al. (2013) Effects of low dose pioglitazone on restenosis and coronary atherosclerosis in diabetic patients undergoing drug eluting stent implantation.</a> Yonsei Med J 54(6): 1313-1320                                                                                                   | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Leiter, L. A., Cefalu, W. T., De Bruin, T. W. A. et al. (2014) Dapagliflozin added to usual care in individuals with type 2 diabetes mellitus with preexisting cardiovascular disease: A 24-week, multicenter, randomized, double-blind, placebo-controlled study with a 28-week extension.</a> J Am Geriatr Soc 62(7): 1252-1262 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Leiter, Lawrence A, Yoon, Kun-Ho, Arias, Pablo et al. (2015) Canagliflozin provides durable glycemic improvements and body weight reduction over 104 weeks versus glimepiride in patients with type 2 diabetes on metformin: a randomized, double-blind, phase 3 study.</a> Diabetes care 38(3): 355-64                           | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Li, Chun-Jun, Liu, Xiao-Juan, Bai, Lian et al. (2014) Efficacy and safety of vildagliptin, Saxagliptin or Sitagliptin as add-on therapy in Chinese patients with type 2 diabetes inadequately controlled with dual combination of traditional oral hypoglycemic agents.</a> Diabetology & metabolic syndrome 6: 69                | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Lind, M., Hirsch, I. B., Tuomilehto, J. et al. (2015) Liraglutide in people treated for type 2</a>                                                                                                                                                                                                                                | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                 | Reason                                                    |
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| <a href="#">diabetes with multiple daily insulin injections: randomised clinical trial (MDI Liraglutide trial).</a> BMJ 351: h5364                                                                                                                                                                                                                    |                                                           |
| <a href="#">Lind, Marcus, Hirsch, Irl B, Tuomilehto, Jaakko et al. (2015) Design and methods of a randomised double-blind trial of adding liraglutide to control HbA1c in patients with type 2 diabetes with impaired glycaemic control treated with multiple daily insulin injections (MDI-Liraglutide trial).</a> Primary care diabetes 9(1): 15-22 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Lingvay, I., Catarig, A. M., Frias, J. P. et al. (2019) Efficacy and safety of once-weekly semaglutide versus daily canagliflozin as add-on to metformin in patients with type 2 diabetes (SUSTAIN 8): a double-blind, phase 3b, randomised controlled trial.</a> Lancet Diabetes Endocrinol 7(11): 834-844                               | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Lingvay, Ildiko, Perez Manghi, Federico, Garcia-Hernandez, Pedro et al. (2016) Effect of Insulin Glargine Up-titration vs Insulin Degludec/Liraglutide on Glycated Hemoglobin Levels in Patients With Uncontrolled Type 2 Diabetes: The DUAL V Randomized Clinical Trial.</a> JAMA 315(9): 898-907                                        | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Liu, S. C., Chien, K. L., Wang, C. H. et al. (2013) Efficacy and safety of adding pioglitazone or sitagliptin to patients with type 2 diabetes insufficiently controlled with metformin and a sulfonylurea.</a> Endocr Pract 19(6): 980-988                                                                                               | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Liu, S. C., Lee, C. C., Chuang, S. M. et al. (2021) Comparison of efficacy and safety of empagliflozin vs linagliptin added to premixed insulin in patients with uncontrolled type 2 diabetes: A randomized, open-label study.</a> Diabetes & Metabolism 47(3): 101184                                                                    | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Ljunggren, O, Bolinder, J, Johansson, L et al. (2012) Dapagliflozin has no effect on markers of bone formation and resorption or bone mineral density in patients with inadequately controlled</a>                                                                                                                                        | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                  | Reason                                                    |
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| <a href="#">type 2 diabetes mellitus on metformin.</a> Diabetes, obesity & metabolism 14(11): 990-9                                                                                                                                                                                                                    |                                                           |
| <a href="#">Ludvik, B., Frias, J. P., Tinahones, F. J. et al. (2018) Dulaglutide as add-on therapy to SGLT2 inhibitors in patients with inadequately controlled type 2 diabetes (AWARD-10): a 24-week, randomised, double-blind, placebo-controlled trial.</a> Lancet Diabetes Endocrinol 6(5): 370-381                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Ludvik, B., Giorgino, F., Jodar, E. et al. (2021) Once-weekly tirzepatide versus once-daily insulin degludec as add-on to metformin with or without SGLT2 inhibitors in patients with type 2 diabetes (SURPASS-3): a randomised, open-label, parallel-group, phase 3 trial.</a> Lancet 398(10300): 583-598 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Lukashevich, V., Schweizer, A., Shao, Q. et al. (2011) Safety and efficacy of vildagliptin versus placebo in patients with type 2 diabetes and moderate or severe renal impairment: a prospective 24-week randomized placebo-controlled trial.</a> Diabetes Obes Metab 13(10): 947-54                      | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Lukashevich, V., Del Prato, S., Araga, M et al. (2014) Efficacy and safety of vildagliptin in patients with type 2 diabetes mellitus inadequately controlled with dual combination of metformin and sulphonylurea.</a> Diabetes, obesity & metabolism 16(5): 403-9                                         | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Lundby Christensen, L., Almdal, T., Boesgaard, T et al. (2009) Study rationale and design of the CIMT trial: the Copenhagen Insulin and Metformin Therapy trial.</a> Diabetes, obesity & metabolism 11(4): 315-22                                                                                          | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Lundby-Christensen, L., Tarnow, L., Boesgaard, T. W. et al. (2016) Metformin versus placebo in combination with insulin analogues in patients with type 2 diabetes mellitus-the randomised, blinded Copenhagen Insulin and Metformin Therapy (CIMT) trial.</a> BMJ Open 6(2): e008376                      | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Macauley, M., Hollingsworth, K. G., Smith, F. E. et al. (2015) Effect of vildagliptin on hepatic steatosis.</a> J Clin Endocrinol Metabol 100(4): 1578-85                                                                                                                                                  | Included in 1.2 medicine/strategies for further treatment |



| Study                                                                                                                                                                                                                                                                                                                                    | Reason                                                    |
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| <a href="#">Mahaffey Kenneth, W, Neal, Bruce, Perkovic, Vlado et al. (2018) Canagliflozin for Primary and Secondary Prevention of Cardiovascular Events: Results From the CANVAS Program (Canagliflozin Cardiovascular Assessment Study).</a> Circulation 137(4): 323-334                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Mann, Johannes F E, Orsted, David D, Brown-Frandsen, Kirstine et al. (2017) Liraglutide and Renal Outcomes in Type 2 Diabetes.</a> The New England journal of medicine 377(9): 839-848                                                                                                                                       | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Marre, M., Shaw, J., Brändle, M. et al. (2009) Liraglutide, a once-daily human GLP-1 analogue, added to a sulphonylurea over 26 weeks produces greater improvements in glycaemic and weight control compared with adding rosiglitazone or placebo in subjects with Type 2 diabetes (LEAD-1 SU).</a> Diabet Med 26(3): 268-78 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Marso S, P, Baeres F, M.M, Bain S, C et al. (2020) Effects of Liraglutide on Cardiovascular Outcomes in Patients With Diabetes With or Without Heart Failure.</a> Journal of the American College of Cardiology 75(10): 1128-1141                                                                                            | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Marso Steven, P, Daniels Gilbert, H, Brown-Frandsen, Kirstine et al. (2016) Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes.</a> The New England journal of medicine 375(4): 311-22                                                                                                                               | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Marso, Steven P, Poulter, Neil R, Nissen, Steven E et al. (2013) Design of the liraglutide effect and action in diabetes: evaluation of cardiovascular outcome results (LEADER) trial.</a> American heart journal 166(5): 823-30e5                                                                                           | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Marx, Nikolaus, Rosenstock, Julio, Kahn, Steven E et al. (2015) Design and baseline characteristics of the CARdiovascular Outcome Trial of LINAgliptin Versus Glimepiride in Type 2 Diabetes (CAROLINA R).</a> Diabetes & vascular disease research 12(3): 164-74                                                            | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                          | Reason                                                    |
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| <a href="#">Mathieu, C., Herrera Marmolejo, M., Gonzalez Gonzalez, J. G. et al. (2016) Efficacy and safety of triple therapy with dapagliflozin add-on to saxagliptin plus metformin over 52 weeks in patients with type 2 diabetes.</a> Diabetes Obes Metab 18(11): 1134-1137 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Mathieu, C., Rodbard, H. W., Cariou, B. et al. (2014) A comparison of adding liraglutide versus a single daily dose of insulin aspart to insulin degludec in subjects with type 2 diabetes (BEGIN: VICTOZA ADD-ON).</a> Diabetes Obes Metab 16(7): 636-644         | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Mathieu, C., Shankar, R. R., Lorber, D. et al. (2015) A randomized clinical trial to evaluate the efficacy and safety of co-administration of sitagliptin with intensively titrated insulin glargine.</a> Diabetes Ther 6(2): 127-142                              | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                    | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                    | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                       | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                           | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                   | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                | Reason                                                    |
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| <a href="#">Papathanassiou, Katerina, Naka, Katerina K, Kazakos, Nikolaos et al. (2009) Pioglitazone vs glimepiride: Differential effects on vascular endothelial function in patients with type 2 diabetes</a> . Atherosclerosis 205(1): 221-6                                                                                                      | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Park, C. Y., Kang, J. G., Chon, S. et al. (2014) Comparison between the therapeutic effect of</a>                                                                                                                                                                                                                                        | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                | Reason                                                    |
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| <a href="#">metformin, glimepiride and their combination as an add-on treatment to insulin glargine in uncontrolled patients with type 2 diabetes.</a> PLoS ONE 9(3): e88779                                                                                                                                                                         |                                                           |
| <a href="#">Park, J. S., Cho, M. H., Nam, J. S. et al. (2011) Effect of pioglitazone on serum concentrations of osteoprotegerin in patients with type 2 diabetes mellitus.</a> Eur J Endocrinol 164(1): 69-74                                                                                                                                        | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Perkovic V, Tuttle KR, Rossing P, Mahaffey KW, Mann JFE, Bakris G, Baeres FMM, Idorn T, Bosch-Traber H, Lausvig NL PR and FLOW Trial Committees and Investigators. (2024) Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes.</a> N Engl J Med 391(2): 109-121                                            | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                  | Reason                                                    |
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| <a href="#">Petrica, L., Vlad, A., Petrica, M. et al. (2011) Pioglitazone delays proximal tubule dysfunction and improves cerebral vessel endothelial dysfunction in normoalbuminuric people with type 2 diabetes mellitus.</a> Diabetes Res Clin Pract 94(1): 22-32                                                                   | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Pfeffer Marc, A, Claggett, Brian, Diaz, Rafael et al. (2015) Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome.</a> The New England journal of medicine 373(23): 2247-57                                                                                                                           | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Pfützner, A., Marx, N., Lübken, G. et al. (2005) Improvement of cardiovascular risk markers by pioglitazone is independent from glycemic control: results from the pioneer study.</a> J Am Coll Cardiol 45(12): 1925-31                                                                                                    | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Philis-Tsimikas, A., Billings, L. K., Busch, R. et al. (2019) Superior efficacy of insulin degludec/liraglutide versus insulin glargine U100 as add-on to sodium-glucose co-transporter-2 inhibitor therapy: a randomized clinical trial in people with uncontrolled type 2 diabetes.</a> Diab Obes Metab 21(6): 1399-1408 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Philis-Tsimikas, A., Del Prato, S., Satman, I. et al. (2013) Effect of insulin degludec versus sitagliptin in patients with type 2 diabetes uncontrolled on oral antidiabetic agents.</a> Diabetes Obes Metab 15(8): 760-766                                                                                               | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Phrommintikul, A., Wongcharoen, W., Kumfu, S. et al. (2019) Effects of dapagliflozin vs vildagliptin on cardiometabolic parameters in diabetic patients with coronary artery disease: a randomised study.</a> Br J Clin Pharmacol 85(6): 1337-1347                                                                         | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
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| <a href="#">open-label, randomised, phase 3a trial.</a> Lancet Diabetes Endocrinol 7(7): 528-539                                                                                                                                                                                                                                                                                                    |                                                           |
| <a href="#">Pinget, M., Goldenberg, R., Niemoeller, E. et al. (2013) Efficacy and safety of lixisenatide once daily versus placebo in type 2 diabetes insufficiently controlled on pioglitazone (GetGoal-P).</a> Diabetes Obes Metab 15(11): 1000-1007                                                                                                                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Pollock, C., Stefansson, B., Reyner, D. et al. (2019) Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT): a randomised, double-blind, placebo-controlled trial.</a> Lancet Diabetes Endocrinol 7(6): 429-441 | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Pratley, R. E., Kipnes, M. S., Fleck, P. R. et al. (2009) Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes inadequately controlled by glyburide monotherapy.</a> Diabetes Obes Metab 11(2): 167-76                                                                                                                               | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Pratley, R. E., Reusch, J. E., Fleck, P. R. et al. (2009) Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin added to</a>                                                                                                                                                                                                                                           | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                                                 | Reason                                                    |
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| <a href="#">pioglitazone in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study.</a> Curr Med Res Opin 25(10): 2361-71                                                                                                                                                                                                                                |                                                           |
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| <a href="#">Rasouli, N, Younes, N, Ghosh, A et al. (2024) Longitudinal Effects of Glucose-Lowering Medications on <math>\beta</math>-Cell Responses and Insulin Sensitivity in Type 2 Diabetes: the GRADE Randomized Clinical Trial.</a> Diabetes care                                                                                                                                | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                                       | Reason                                                    |
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| <a href="#">Raz, I., Chen, Y., Wu, M. et al. (2008) Efficacy and safety of sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes. Curr Med Res Opin 24(2): 537-50</a>                                                                                                                                                                             | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                              | Reason                                                    |
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| <a href="#">Rosenstock, J., Allison, D., Birkenfeld, A. L. et al. (2019) Effect of additional oral semaglutide vs sitagliptin on glycated hemoglobin in adults with type 2 diabetes uncontrolled with metformin alone or with sulphonylurea: the PIONEER 3 randomized clinical trial. JAMA 321(15): 1466-1480</a>                                  | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                     | Reason                                                    |
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| <a href="#">peptidase-4 inhibitor sitagliptin added to ongoing pioglitazone therapy in patients with type 2 diabetes: a 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study.</a> Clin Ther 28(10): 1556-68                                                                                                           |                                                           |
| <a href="#">Rosenstock, J., Buse, J. B., Azeem, R. et al. (2018) Efficacy and Safety of ITCA 650, a Novel Drug-Device GLP-1 Receptor Agonist, in Type 2 Diabetes Uncontrolled With Oral Antidiabetes Drugs: the FREEDOM-1 Trial.</a> Diabetes Care 41(2): 333-340                                                                                         | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Rosenstock, J., Hansen, L., Zee, P. et al. (2015) Dual add-on therapy in type 2 diabetes poorly controlled with metformin monotherapy: a randomized double-blind trial of saxagliptin plus dapagliflozin addition versus single addition of saxagliptin or dapagliflozin to metformin.</a> Diabetes Care 38(3): 376-83                        | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                    | Reason                                                    |
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| <a href="#">Rosenstock, J., Vico, M., Wei, L. et al. (2012) Effects of dapagliflozin, an SGLT2 inhibitor, on HbA(1c), body weight, and hypoglycemia risk in patients with type 2 diabetes inadequately controlled on pioglitazone monotherapy. Diabetes Care 35(7): 1473-8</a>                                                                                           | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Rosenstock, Julio, Aronson, Ronnie, Grunberger, George et al. (2016) Benefits of LixiLan, a Titratable Fixed-Ratio Combination of Insulin Glargine Plus Lixisenatide, Versus Insulin Glargine and Lixisenatide Monocomponents in Type 2 Diabetes Inadequately Controlled on Oral Agents: The LixiLan-O Randomized Trial. Diabetes care 39(11): 2026-2035</a> | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Rosenstock, Julio, Frias, Juan P, Rodbard, Helena W et al. (2023) Tirzepatide vs Insulin Lispro Added to Basal Insulin in Type 2 Diabetes: The SURPASS-6 Randomized Clinical Trial. JAMA 330(17): 1631-1640</a>                                                                                                                                              | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                    |
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| <a href="#">Rosenstock, Julio, Kolkailah, Ahmed A, McGuire, Darren K et al. (2023) Incident and recurrent hypoglycaemia with linagliptin and glimepiride over a median of 6 years in the CAROLINA cardiovascular outcome trial. Diabetes, obesity &amp; metabolism 25(6): 1453-1463</a>                                                                                                                | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Rosenstock, Julio, Perkovic, Vlado, Alexander John, H et al. (2018) Rationale, design, and baseline characteristics of the CARdiovascular safety and Renal Microvascular outcomE study with LINAgliptin (CARMELINA R): a randomized, double-blind, placebo-controlled clinical trial in patients with type 2 diabetes and high cardio-renal risk. Cardiovascular diabetology 17(1): 39</a> | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                    |
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| <a href="#">sulfonylurea therapy in type 2 diabetes mellitus (LEAD-5 met+SU): a randomised controlled trial.</a> Diabetologia 52(10): 2046-55                                                                                                                                                                                                                                                 |                                                           |
| <a href="#">Sarraju, Ashish, Li, JingWei, Cannon, Christopher P et al. (2021) Effects of canagliflozin on cardiovascular, renal, and safety outcomes in participants with type 2 diabetes and chronic kidney disease according to history of heart failure: Results from the CRENDENCE trial.</a> American heart journal 233: 141-148                                                         | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Scott, R., Morgan, J., Zimmer, Z. et al. (2018) A randomized clinical trial of the efficacy and safety of sitagliptin compared with dapagliflozin in patients with type 2 diabetes mellitus and mild</a>                                                                                                                                                                          | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                                                                                 | Reason                                                    |
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| <a href="#">renal insufficiency: the CompoSIT-R study.</a> Diab Obes Metab 20(12): 2876-2884                                                                                                                                                                                                                                                          |                                                           |
| <a href="#">Seck, T., Nauck, M., Sheng, D. et al. (2010) Safety and efficacy of treatment with sitagliptin or glipizide in patients with type 2 diabetes inadequately controlled on metformin: a 2-year study.</a> Int J Clin Pract 64(5): 562-76                                                                                                     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Secnik Boye, Kristina, Matza, Louis S, Oglesby, Alan et al. (2006) Patient-reported outcomes in a trial of exenatide and insulin glargine for the treatment of type 2 diabetes.</a> Health and quality of life outcomes 4: 80                                                                                                             | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Seino, Y., Kaku, K., Kadowaki, T. et al. (2021) A randomized, placebo-controlled trial to assess the efficacy and safety of sitagliptin in Japanese patients with type 2 diabetes and inadequate glycaemic control on ipragliflozin.</a> Diabetes, Obesity & Metabolism 23(6): 1342-1350                                                  | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Sesti, G., Bardtrum, L., Dagdelen, S. et al. (2020) A greater proportion of participants with type 2 diabetes achieve treatment targets with IDegLira (insulin degludec/liraglutide) versus insulin glargine U100 at 26weeks: DUAL VIII a randomized trial designed to resemble clinical practice.</a> Diabetes, obesity & metabolism     | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                                             | Reason                                                    |
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| <a href="#">Shankar, R. R., Bao, Y., Han, P. et al. (2017) Sitagliptin added to stable insulin therapy with or without metformin in Chinese patients with type 2 diabetes. J Diabetes Invest 8(3): 321-329</a>                                                                                    | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Skrivanek, Z, Gaydos, B L, Chien, J Y et al. (2014) Dose-finding results in an adaptive, seamless, randomized trial of once-weekly dulaglutide combined with metformin in type 2 diabetes patients (AWARD-5). Diabetes, obesity &amp; metabolism 16(8): 748-56</a>                    | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Sridhar, S., Walia, R., Sachdeva, N. et al. (2013) Effect of pioglitazone on testosterone in eugonadal men with type 2 diabetes mellitus: a randomized double-blind placebo-controlled study. Clin Endocrinol 78(3): 454-9</a>                                                        | Included in 1.2 medicine/strategies for further treatment |
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| <a href="#">Strojek, K., Yoon, K. H., Hrubá, V. et al. (2011) Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with glimepiride: a randomized, 24-week, double-blind, placebo-controlled trial. Diabetes Obes Metab 13(10): 928-38</a>              | Included in 1.2 medicine/strategies for further treatment |



| Study                                                                                                                                                                                                                                                                                                                                                                                                 | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                                                                   | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                               | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                                              | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                       | Reason                                                    |
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| Study                                                                                                                                                                                                                                                               | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                          | Reason                                                    |
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| Study                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                    |
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| <a href="#">Yang, W., Xu, X., Lei, T. et al. (2021) Efficacy and safety of linagliptin as add-on therapy to insulin in Chinese patients with type 2 diabetes mellitus: A randomized, double-blind, placebo-controlled trial</a> . Diabetes, Obesity & Metabolism 23(2): 642-647                                                                                                | Included in 1.2 medicine/strategies for further treatment |
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| Study                                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                    |
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| <a href="#">Yuan, X., Guo, X., Zhang, J. et al. (2022) Improved glycaemic control and weight benefit with iGlarLixi versus insulin glargine 100 U/mL in Chinese people with type 2 diabetes advancing their therapy from basal insulin plus oral antihyperglycaemic drugs: Results from the LixiLan-L-CN randomized controlled trial. Diabetes, Obesity and Metabolism 24(11): 2182-2191</a> | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zang, L., Liu, Y., Geng, J. et al. (2016) Efficacy and safety of liraglutide versus sitagliptin, both in combination with metformin, in Chinese patients with type 2 diabetes: a 26-week, open-label, randomized, active comparator clinical trial. Diabetes Obes Metab 18(8): 803-11</a>                                                                                        | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zannad, Faiez, Cannon Christopher, P, Cushman William, C et al. (2015) Heart failure and mortality outcomes in patients with type 2 diabetes taking alogliptin versus placebo in EXAMINE: a multicentre, randomised, double-blind trial. Lancet (London, England) 385(9982): 2067-76</a>                                                                                         | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zelniker T, A, Bonaca M, P, Furtado R, H.M et al. (2020) Effect of dapagliflozin on atrial fibrillation in patients with type 2 diabetes mellitus: Insights from the DECLARE-TIMI 58 Trial. Circulation: 1227-1234</a>                                                                                                                                                           | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zelniker, Thomas A, Raz, Itamar, Mosenzon, Ofri et al. (2021) Effect of Dapagliflozin on Cardiovascular Outcomes According to Baseline Kidney Function and Albuminuria Status in Patients With Type 2 Diabetes: A Prespecified Secondary Analysis of a Randomized Clinical Trial. JAMA cardiology 6(7): 801-810</a>                                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zhang, J., Xian, T. Z., Wu, M. X. et al. (2020) Comparison of the effects of twice-daily exenatide and insulin on carotid intima-media thickness in type 2 diabetes mellitus patients: a 52-week randomized, open-label, controlled trial. Cardiovascular Diabetology 19(1): 48</a>                                                                                              | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zhao, Lijie; Sun, Tingli; Wang, Lina (2017) Chitosan oligosaccharide improves the therapeutic efficacy of sitagliptin for the therapy of Chinese elderly patients with type 2 diabetes mellitus. Therapeutics and clinical risk management 13: 739-750</a>                                                                                                                       | Included in 1.2 medicine/strategies for further treatment |

| Study                                                                                                                                                                                                                                                                             | Reason                                                    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| <a href="#">Zhou, Z, Lindley R, I, Radholm, K et al. (2019) Canagliflozin and Stroke in Type 2 Diabetes Mellitus: Results from the Randomized CANVAS Program Trials.</a> Stroke 50(2): 396-404                                                                                    | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zinman, B., Aroda, V. R., Buse, J. B. et al. (2019) Efficacy, Safety, and Tolerability of Oral Semaglutide Versus Placebo Added to Insulin With or Without Metformin in Patients With Type 2 Diabetes: The PIONEER 8 Trial.</a> Diabetes Care 42(12): 2262-2271       | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zinman, B., Bhosekar, V., Busch, R. et al. (2019) Semaglutide once weekly as add-on to SGLT-2 inhibitor therapy in type 2 diabetes (SUSTAIN 9): a randomised, placebo-controlled trial.</a> Lancet Diabetes Endocrinol 7(5): 356-367                                  | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zinman, B., Gerich, J., Buse, J. B. et al. (2009) Efficacy and safety of the human glucagon-like peptide-1 analog liraglutide in combination with metformin and thiazolidinedione in patients with type 2 diabetes (LEAD-4 Met+TZD).</a> Diabetes Care 32(7): 1224-30 | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zinman, Bernard, Inzucchi, Silvio E, Lachin, John M et al. (2014) Rationale, design, and baseline characteristics of a randomized, placebo-controlled cardiovascular outcome trial of empagliflozin (EMPA-REG OUTCOME TM).</a> Cardiovascular diabetology 13: 102     | Included in 1.2 medicine/strategies for further treatment |
| <a href="#">Zinman, Bernard, Wanner, Christoph, Lachin John, M et al. (2015) Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes.</a> The New England journal of medicine 373(22): 2117-28                                                                   | Included in 1.2 medicine/strategies for further treatment |

**Table 2: Studies to be included at a future date (these studies have been agreed to be unlikely to significantly change the results at this time)**

| Study                                                                                                                                                                                                                                                                                           | Reason                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| <a href="#">Aashish, Mondal, Arindam, Naskar, Siddiqi, Sheelu Shafiq et al. (2024) Efficacy and safety of fixed dose combination of Sitagliptin, metformin, and pioglitazone in type 2 Diabetes (IMPACT study): a randomized controlled trial.</a> Clinical diabetes and endocrinology 10(1): 3 | - Top-up search 2 (1.2 model 5) |

| Study                                                                                                                                                                                                                                                                                                                                                    | Reason                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| <a href="#">Akyay, O.Z., Selek, A., Tarkun, I. et al. (2023) Evaluation of Exenatide Versus Insulin Glargine Treatment's Impact on Brown Adipose Tissue Markers and Epicardial Adipose Tissue. Medical Journal of Bakirkoy 19(3): 276-282</a>                                                                                                            | - Top-up search 2 (1.2 model 5) |
| <a href="#">Attaran, Fereshte, Emami, Sepideh, Sohrabi, Masoudreza et al. (2023) Effect of Empagliflozin and Pioglitazone on left ventricular function in patients with type two diabetes and nonalcoholic fatty liver disease without established cardiovascular disease: a randomized single-blind clinical trial. BMC gastroenterology 23(1): 327</a> | - Top-up search (1.2 model 5)   |
| <a href="#">Dwibedi, Chinmay, Ekstrom, Ola, Brandt, Jasmine et al. (2024) Randomized open-label trial of semaglutide and dapagliflozin in patients with type 2 diabetes of different pathophysiology. Nature metabolism 6(1): 50-60</a>                                                                                                                  | - Top-up search 2 (1.2 model 5) |
| <a href="#">Frias, Juan P, Hsia, Stanley, Eyde, Sarah et al. (2023) Efficacy and safety of oral orforglipron in patients with type 2 diabetes: a multicentre, randomised, dose-response, phase 2 study. Lancet (London, England) 402(10400): 472-483</a>                                                                                                 | - Top-up search (1.2 model 5)   |
| <a href="#">Fu, Qianyu, Zhou, Longhua, Fan, Yugin et al. (2023) Effect of SGLT-2 inhibitor, dapagliflozin, on left ventricular remodeling in patients with type 2 diabetes and HFrEF. BMC cardiovascular disorders 23(1): 544</a>                                                                                                                        | - Top-up search 2 (1.2 model 1) |
| <a href="#">Galindo, Rodolfo J, Moazzami, Bobak, Scioscia, Maria F et al. (2023) A Randomized Controlled Trial Comparing the Efficacy and Safety of IDegLira Versus Basal-Bolus in Patients With Poorly Controlled Type 2 Diabetes and Very High HbA1c &gt;=9-15%: DUAL HIGH Trial. Diabetes care 46(9): 1640-1645</a>                                   | - Top-up search (1.2 model 5)   |
| <a href="#">Gao, Leili, Lee, Byung Wan, Chawla, Manoj et al. (2023) Tirzepatide versus insulin glargine as second-line or third-line therapy in type 2 diabetes in the Asia-Pacific region: the SURPASS-AP-Combo trial. Nature medicine 29(6): 1500-1510</a>                                                                                             | - Top-up search (1.2 model 5)   |
| <a href="#">Garvey, W Timothy, Frias, Juan P, Jastreboff, Ania M et al. (2023) Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind,</a>                                                                                                                                                     | - Top-up search (1.2 model 5)   |

| Study                                                                                                                                                                                                                                                                                                                                                             | Reason                            |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|
| <a href="#">randomised, multicentre, placebo-controlled, phase 3 trial.</a> Lancet (London, England) 402(10402): 613-626                                                                                                                                                                                                                                          |                                   |
| <a href="#">Heo, Ji Hye, Han, Kyung Ah, Hong, Jun Hwa et al. (2024) Pioglitazone as Add-on THERAPY in Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Dapagliflozin and Metformin: Double-Blind, Randomized, Placebo-Controlled Trial.</a> Diabetes & metabolism journal                                                                      | - Top-up search 2 (1.2 model 5)   |
| <a href="#">Hong, Jun Hwa, Moon, Jun Sung, Seong, Kayeon et al. (2023) Comparison of therapeutic efficacy and safety of sitagliptin, dapagliflozin, or lobeglitazone adjunct therapy in patients with type 2 diabetes mellitus inadequately controlled on sulfonylurea and metformin: Third agent study.</a> Diabetes research and clinical practice 203: 110872  | - Top-up search (1.2 model 5)     |
| <a href="#">Hooshmand Gharabagh, Laya, Shargh, Ali, Mohammad Hosseini Azar, Mohammad Reza et al. (2024) Comparison between the effect of Empagliflozin and Pioglitazone added to metformin in patients with type 2 diabetes and nonalcoholic fatty liver disease.</a> Clinics and research in hepatology and gastroenterology 48(3): 102279                       | - Top-up search 2 (1.2 model 5)   |
| <a href="#">Iijima, Takahiro, Shibuya, Makoto, Ito, Yuzuru et al. (2023) Effects of switching from liraglutide to semaglutide or dulaglutide in patients with type 2 diabetes: A randomized controlled trial.</a> Journal of diabetes investigation 14(6): 774-781                                                                                                | - Top-up search (1.2 model 5)     |
| <a href="#">Kimura, Tomohiko, Katakura, Yukino, Shimoda, Masashi et al. (2023) Comparison of clinical efficacy and safety of weekly glucagon-like peptide-1 receptor agonists dulaglutide and semaglutide in Japanese patients with type 2 diabetes: Randomized, parallel-group, multicentre, open-label trial (COMING study).</a> Diabetes, obesity & metabolism | - Top-up search (1.2 model 3 CKD) |
| <a href="#">Lee, B-W, Cho, YM, Kim, SG et al. (2024) Efficacy and Safety of Once-Weekly Semaglutide Versus Once-Daily Sitagliptin as Metformin Add-on in a Korean Population with Type 2 Diabetes.</a> Diabetes therapy                                                                                                                                           | - Top-up search 2 (1.2 model 5)   |
| <a href="#">Lim, Soo, Lee, Seung-Hwan, Min, Kyung-Wan et al. (2024) A multicentre, double-blind, placebo-controlled, randomized, parallel</a>                                                                                                                                                                                                                     | - Top-up search 2 (1.2 model 5)   |



| Study                                                                                                                                                                                                                                                                                                                                                                         | Reason                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| <a href="#">comparison, phase 3 trial to evaluate the efficacy and safety of pioglitazone add-on therapy in type 2 diabetic patients treated with metformin and dapagliflozin.</a> Diabetes, obesity & metabolism                                                                                                                                                             |                                 |
| <a href="#">Omachi, Takemasa, Ohara, Makoto, Fujikawa, Tomoki et al. (2024) Comparison of Effects of Injectable Semaglutide and Dulaglutide on Oxidative Stress and Glucose Variability in Patients with Type 2 Diabetes Mellitus: A Prospective Preliminary Study.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 15(1): 111-126 | - Top-up search 2 (1.2 model 5) |
| <a href="#">Park, Hyeong Kyu, Kim, Kyoung-Ah, Min, Kyung-Wan et al. (2023) Effects of dapagliflozin compared with glimepiride on body composition in Asian patients with type 2 diabetes inadequately controlled with metformin: The BEYOND study.</a> Diabetes, obesity & metabolism                                                                                         | - Top-up search (1.2 model 5)   |
| <a href="#">Simonson, Donald C, Testa, Marcia A, Ekholm, Ella et al. (2024) Continuous Glucose Monitoring Profiles and Health Outcomes after Dapagliflozin Plus Saxagliptin vs Insulin Glargine.</a> The Journal of clinical endocrinology and metabolism                                                                                                                     | - Top-up search 2 (1.2 model 5) |
| <a href="#">Sivalingam, Suvanjaa, Wasehuus, Victor Soendergaard, Rotbain Curovic, Viktor et al. (2023) Albuminuria-lowering effect of adding semaglutide on top of empagliflozin in individuals with type 2 diabetes: A randomized and placebo-controlled study.</a> Diabetes, obesity & metabolism                                                                           | - Top-up search (1.2 model 5)   |
| <a href="#">Wang, Wei, Guo, Xiaohui, Zhang, Cheng et al. (2024) Prusogliptin (DBPR108) monotherapy in treatment-naïve patients with type 2 diabetes: A randomized, double-blind, active and placebo-controlled, phase 3 study.</a> Diabetes, obesity & metabolism 26(4): 1321-1332                                                                                            | - Top-up search 2 (1.1 model 5) |
| <a href="#">Wang, Weimin, Yan, Xin, Cheng, Zhifeng et al. (2023) Efficacy and safety of adding once-weekly dulaglutide to basal insulin for inadequately controlled type 2 diabetes in Chinese patients (AWARD-CHN3): A randomized, double-blind, placebo-controlled, phase III trial.</a> Diabetes, obesity & metabolism                                                     | - Top-up search (1.2 model 5)   |

| Study                                                                                                                                                                                                                                                                                                                                                   | Reason                                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| <a href="#">Xu, Mingtong, Sun, Kan, Xu, Wenjie et al. (2023) Fotagliptin monotherapy with alogliptin as an active comparator in patients with uncontrolled type 2 diabetes mellitus: a randomized, multicenter, double-blind, placebo-controlled, phase 3 trial. BMC medicine 21(1): 388</a>                                                            | - Top-up search 2 (1.1 model 5)                                    |
| <a href="#">Yabe, Daisuke, Shiki, Kosuke, Homma, Gosuke et al. (2023) Efficacy and safety of the sodium-glucose co-transporter-2 inhibitor empagliflozin in elderly Japanese adults (&gt;=65 years) with type 2 diabetes: A randomized, double-blind, placebo-controlled, 52-week clinical trial (EMPA-ELDERLY). Diabetes, obesity &amp; metabolism</a> | - Top-up search (1.2 model 5)                                      |
| <a href="#">Yoshihara, Fumiki, Imazu, Miki, Sakuma, Ichiro et al. (2023) DAPagliflozin for the attenuation of albuminuria in Patients with hEaRt failure and type 2 diabetes (DAPPER study): a multicentre, randomised, open-label, parallel-group, standard treatment-controlled trial. EClinicalMedicine 66: 102334</a>                               | - Top-up search 2 (1.2 model 1)<br>- Top-up search 2 (1.2 model 2) |

**Table 3: Studies excluded from the clinical review**

| Study                                                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                                                                                                                                                        |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">(2015) SGLT2 inhibition in type 2 diabetes. New study data for reducing cardiovascular risk. MMW Fortschritte der Medizin 157(18): 86-87</a>                                                                                                                                                                                                                                                       | - Study not reported in English                                                                                                                                                                                                                                                                                               |
| <a href="#">Abdul-Ghani, M A, Puckett, C, Triplitt, C et al. (2015) Initial combination therapy with metformin, pioglitazone and exenatide is more effective than sequential add-on therapy in subjects with new-onset diabetes. Results from the Efficacy and Durability of Initial Combination Therapy for Type 2 Diabetes (EDICT): a randomized trial. Diabetes, obesity &amp; metabolism 17(3): 268-75</a> | - Comparator in study does not match that specified in this review protocol<br><i>At 24 months in the conventional treatment arm - 19% of people took metformin alone, 53% took metformin and glipizide, 28% took metformin, glipizide and glargine. Therefore, cannot stratify this treatment into a group for analysis.</i> |
| <a href="#">Abdul-Ghani, Muhammad, Migahid, Osama, Megahed, Ayman et al. (2020) Combination therapy with pioglitazone/exenatide improves beta-cell function and produces superior glycaemic control compared with basal/bolus insulin in poorly controlled type 2 diabetes: A 3-year follow-up of the Qatar study. Diabetes, obesity &amp; metabolism 22(12): 2287-2294</a>                                    | - Duplicate reference                                                                                                                                                                                                                                                                                                         |

| Study                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                                                                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">Abdul-Ghani, Muhammad, Puckett, Curtiss, Adams, John et al. (2021) Durability of Triple Combination Therapy Versus Stepwise Addition Therapy in Patients With New-Onset T2DM: 3-Year Follow-up of EDICT.</a> Diabetes care 44(2): 433-439                                          | - Comparator in study does not match that specified in this review protocol<br><br><i>At 24 months in the conventional treatment arm - 19% of people took metformin alone, 53% took metformin and glipizide, 28% took metformin, glipizide and glargine. Therefore, cannot stratify this treatment into a group for analysis.</i> |
| <a href="#">Abdullaev, S. and Sharapov, O. (2023) EFFECT OF DAPAGLIFLOZIN ON ALBUMINURIA IN PATIENTS WITH TYPE 2 DIABETES AND CKD.</a> Nephrology Dialysis Transplantation 38(supplement1): i685-i686                                                                                          | - Conference abstract                                                                                                                                                                                                                                                                                                             |
| <a href="#">Abdullah, F., Sattar, A., Shaukat, K. et al. (2021) To compare the efficacy of dapagliflozin &amp; metformin vs sitagliptin &amp; metformin in newly diagnosed type 2 diabetic patients.</a> Pakistan Journal of Medical and Health Sciences 15(1): 85-86                          | - Data not reported in an extractable format or a format that can be analysed<br><br><i>Reported HbA1c as the number of people achieving a certain HbA1c value at a certain time which was not specified as relevant in the protocol</i>                                                                                          |
| <a href="#">Abe, M., Higuchi, T., Moriuchi, M. et al. (2016) Efficacy and safety of saxagliptin, a dipeptidyl peptidase-4 inhibitor, in hemodialysis patients with diabetic nephropathy: A randomized open-label prospective trial.</a> Diabetes Res Clin Pract 116: 244-252                   | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares to usual care which could include a range of different medications with no specified comparator drug</i>                                                                                                                           |
| <a href="#">Abe, M., Okada, K., Maruyama, T. et al. (2010) Clinical effectiveness and safety evaluation of long-term pioglitazone treatment for erythropoietin responsiveness and insulin resistance in type 2 diabetic patients on hemodialysis.</a> Expert Opin Pharmacother 11(10): 1611-20 | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares to usual care which could include a range of different medications with no specified comparator drug</i>                                                                                                                           |
| <a href="#">Abe, M, Okada, K, Kikuchi, F et al. (2008) Clinical investigation of the effects of pioglitazone on the improvement of insulin resistance and blood pressure in type 2-diabetic patients undergoing hemodialysis.</a> Clinical nephrology 70(3): 220-8                             | - Comparator in study does not match that specified in this review protocol<br><br><i>Comparator group was conventional antidiabetic medication (95% of this group were on medications no longer used in the UK)</i>                                                                                                              |
| <a href="#">Abe, T, Matsubayashi, Y, Yoshida, A et al. (2018) Predictors of the response of HbA1c and body weight after SGLT2 inhibition.</a> Diabetes & metabolism 44(2): 172-174                                                                                                             | - Study design not relevant to this review protocol<br><br><i>Pooled analysis of TOFO phase 2 and 3 studies</i>                                                                                                                                                                                                                   |
| <a href="#">Abrilla, Aedrian A; Pajes, A Nico Nahar I; Jimeno, Cecilia A (2021) Metformin extended-</a>                                                                                                                                                                                        | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                             |

| Study                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                                                         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">release versus metformin immediate-release for adults with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials</a> . Diabetes research and clinical practice 178: 108824                                                                                                                    |                                                                                                                                                                                                                                |
| <a href="#">Adamou, Anastasia, Chlorogiannis, David Dimitris, Kyriakoulis, Ioannis G et al. (2024) Sodium-glucose cotransporter-2 inhibitors in heart failure patients across the range of body mass index: a systematic review and meta-analysis of randomized controlled trials</a> . Internal and emergency medicine 19(2): 565-573              | - Systematic review used as source of primary studies                                                                                                                                                                          |
| <a href="#">Adji, A.S., Billah, A., Baraja, A. et al. (2022) A Systematic Review and Meta-analysis of Randomized Placebo-controlled Trials 1 Year after Starting Sodium-glucose Transporter-2 Inhibitors in Heart Failure Patients with Reduced Ventricular Ejection Fraction</a> . Open Access Macedonian Journal of Medical Sciences 10: 1-6      | - Population not relevant to this review protocol<br><i>People with or without diabetes</i>                                                                                                                                    |
| <a href="#">Afshani, Mohammad Reza, Torfi, Ekhlash, Akiash, Nehzat et al. (2024) Effect of empagliflozin on left ventricular volumes in type 2 diabetes or prediabetes heart failure patients with reduced ejection fraction</a> . Acta cardiologica: 796-802                                                                                       | - Population not relevant to this review protocol<br><i>Population includes people with type 2 diabetes and pre-diabetes and does not report the proportions of each population included in the trial.</i>                     |
| <a href="#">Ahmad, Ehtasham, Arsenyadis, Franciskos, Almaghaw, Abdullah et al. (2023) Impact of novel glucose-lowering therapies on physical function in people with type 2 diabetes; a systematic review and meta-analysis of randomised placebo-controlled trials</a> . Diabetic medicine : a journal of the British Diabetic Association: e15083 | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>Systematic review included RCTs &lt;24 weeks</i>                                                                                                 |
| <a href="#">Ahmad, Ehtasham, Waller, Helen L, Sargeant, Jack A et al. (2021) Effects of liraglutide versus sitagliptin on circulating cardiovascular biomarkers, including circulating progenitor cells, in individuals with type 2 diabetes and obesity: Analyses from the LYDIA trial</a> . Diabetes, obesity & metabolism 23(6): 1409-1414       | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                         |
| <a href="#">Ahmed, I, Ali, Z, Afridi, MAR et al. (2021) A COMPARATIVE STUDY TO ASSESS SAFETY AND EFFICACY OF VILDAGLIPTIN AND METFORMIN WITH GLIMEPIRIDE AND METFORMIN AMONG TYPE 2 DIABETES</a>                                                                                                                                                    | - Methodology unclear<br><i>Error in printing where introduction is printed in the introduction and methodology section so it is unclear what the methods are for this study (including the dose of medication and whether</i> |

| Study                                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| <a href="#">PATIENTS</a> . Journal of postgraduate medical institute 35(3): 136-142                                                                                                                                                                                                                                                                                                                 | <i>concomitant treatments were used before the study).</i>                                             |
| <a href="#">Ahn, C. H., Han, K. A., Yu, J. M. et al. (2017) Efficacy and safety of gemigliptin, a dipeptidyl peptidase-4 inhibitor, in patients with type 2 diabetes mellitus inadequately controlled with combination treatment of metformin and sulphonylurea: A 24-week, multicentre, randomized, double-blind, placebo-controlled study (TROICA study)</a> . Diabetes Obes Metab 19(5): 635-643 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Ahn, K.J.; Eun, J.J.; In-Kyung, J. (2023) Clinical Factors Affecting Dapagliflozin Response For Glycemic Control And Body Weight Reduction: Post-hoc Analysis Of BEYOND Study</a> . Journal of the Endocrine Society 7(supplement1): a370                                                                                                                                               | - Conference abstract                                                                                  |
| <a href="#">Ahren, Bo, Foley, James E, Ferrannini, Ele et al. (2010) Changes in prandial glucagon levels after a 2-year treatment with vildagliptin or glimepiride in patients with type 2 diabetes inadequately controlled with metformin monotherapy</a> . Diabetes care 33(4): 730-2                                                                                                             | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Akhtar, F., Hamid, S., Abbas, A. et al. (2022) Physio Biochemical Effects of Metformin in Association with Non Insulin Dependent Type 2 Diabetic Patients</a> . Pakistan Journal of Medical and Health Sciences 16(12): 487-489                                                                                                                                                         | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Akshay, D., Dinesh, K., Parveen, S. et al. (2021) To Compare the Safety of Saxagliptin vs Glimepiride as add on Therapy to Metformin in Patients of Type 2 Diabetes Mellitus</a> . Indian Journal of Pharmacology 53(7supplement1): 443                                                                                                                                                 | - Conference abstract                                                                                  |
| <a href="#">Al-Sadawi, M., Aslam, F., Aleem, S. et al. (2022) THE EFFECT OF GLP-1 AGONISTS IN PATIENTS WITH TYPE 2 DIABETES ON ALL-CAUSE MORTALITY AND CARDIOVASCULAR MORTALITY: AN UPDATED META-ANALYSIS OF 44 RANDOMIZED CONTROLLED TRIALS</a> . Journal of the American College of Cardiology 79(9supplement): 1542                                                                              | - Conference abstract                                                                                  |
| <a href="#">Aladel, Alanoud; Aljaouni, Jamilah; Basaad, Reem (2023) Effect of Liraglutide on Fat Mass Percentage Among Overweight and Obese Adults with Type 2 Diabetes: A Systematic</a>                                                                                                                                                                                                           | - Study design not relevant to this review protocol<br><i>SR that included observational studies</i>   |

| Study                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">Review</a> . Diabetes, metabolic syndrome and obesity : targets and therapy 16: 3381-3391                                                                                                                                                                                                                                              |                                                                                                                                   |
| <a href="#">Alatawi, A.M. (2024) Metformin versus sodium glucose co-transporters inhibitors as first-line for atherosclerotic cardiovascular disease: A meta-analysis</a> . Pakistan Journal of Medical Sciences 40(1): 209-213                                                                                                                    | - Study design not relevant to this review protocol                                                                               |
| <a href="#">Alexander, Jason T, Staab, Erin M, Wan, Wen et al. (2022) Longer-term Benefits and Risks of Sodium-Glucose Cotransporter-2 Inhibitors in Type 2 Diabetes: a Systematic Review and Meta-analysis</a> . Journal of general internal medicine 37(2): 439-448                                                                              | - Systematic review used as source of primary studies                                                                             |
| <a href="#">Alexander, Jason T, Staab, Erin M, Wan, Wen et al. (2022) The Longer-Term Benefits and Harms of Glucagon-Like Peptide-1 Receptor Agonists: a Systematic Review and Meta-Analysis</a> . Journal of general internal medicine 37(2): 415-438                                                                                             | - Systematic review used as source of primary studies                                                                             |
| <a href="#">Alfayez, Osamah M, Al Yami, Majed S, Alshibani, Mohannad et al. (2019) Network meta-analysis of nine large cardiovascular outcome trials of new antidiabetic drugs</a> . Primary care diabetes 13(3): 204-211                                                                                                                          | - Systematic review used as source of primary studies                                                                             |
| <a href="#">Alfayez, Osamah M, Almutairi, Abdulaali R, Aldosari, Ali et al. (2019) Update on Cardiovascular Safety of Incretin-Based Therapy in Adults With Type 2 Diabetes Mellitus: A Meta-Analysis of Cardiovascular Outcome Trials</a> . Canadian journal of diabetes 43(7): 538-545e2                                                         | - Systematic review used as source of primary studies                                                                             |
| <a href="#">Alhindi, Yousef and Avery, Amanda (2022) The efficacy and safety of oral semaglutide for glycaemic management in adults with type 2 diabetes compared to subcutaneous semaglutide, placebo, and other GLP-1 RA comparators: A systematic review and network meta-analysis</a> . Contemporary clinical trials communications 28: 100944 | - Study design not relevant to this review protocol<br><br><i>Systematic review, includes studies of 20 week duration or more</i> |
| <a href="#">Ali, Ali Muhammed, Martinez, Robert, Al-Jobori, Hussein et al. (2020) Combination Therapy With Canagliflozin Plus Liraglutide Exerts Additive Effect on Weight Loss, but Not on HbA1c, in Patients With Type 2 Diabetes</a> . Diabetes care 43(6): 1234-1241                                                                           | - Trial that has a treatment and follow up period of less than 24 weeks                                                           |



| Study                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                                                                                     |
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| <a href="#">Ali, Muhammad Usman, Mancini, G B John, Fitzpatrick-Lewis, Donna et al. (2024) The effectiveness of sodium-glucose co-transporter 2 inhibitors on cardiorenal outcomes: an updated systematic review and meta-analysis. Cardiovascular diabetology 23(1): 72</a>                                                  | - Population not relevant to this review protocol                                                                                                                                                                                          |
| <a href="#">Ali, Muhammad Usman, Mancini, G B John, Fitzpatrick-Lewis, Donna et al. (2022) The Effectiveness of Sodium-Glucose Cotransporter 2 Inhibitors and Glucagon-like Peptide-1 Receptor Agonists on Cardiorenal Outcomes: Systematic Review and Meta-analysis. The Canadian journal of cardiology 38(8): 1201-1210</a> | - Systematic review used as source of primary studies                                                                                                                                                                                      |
| <a href="#">Aljohani, H., Alrubaish, F.S., Alghamdi, W. et al. (2022) Safety of Linagliptin in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Drug Safety 45(10): 1162-1163</a>                                                                                                               | - Conference abstract                                                                                                                                                                                                                      |
| <a href="#">Allas, S, Delale, T, Ngo, N et al. (2016) Safety, tolerability, pharmacokinetics and pharmacodynamics of AZP-531, a first-in-class analogue of unacylated ghrelin, in healthy and overweight/obese subjects and subjects with type 2 diabetes. Diabetes, obesity &amp; metabolism 18(9): 868-74</a>               | - Study does not contain an intervention relevant to this review protocol                                                                                                                                                                  |
| <a href="#">Allegretti, A. S., Zhang, W., Zhou, W. et al. (2019) Safety and effectiveness of bexagliflozin in patients with type 2 diabetes mellitus and stage 3a/3b CKD. Am J Kidney Dis 74(3): 328-337</a>                                                                                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                              |
| <a href="#">Altuntas, Y, Ozen, B, Ozturk, B et al. (2003) Comparison of additional metformin or NPH insulin to mealtime insulin lispro therapy with mealtime human insulin therapy in secondary OAD failure. Diabetes, obesity &amp; metabolism 5(6): 371-8</a>                                                               | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares people receiving metformin and insulin with people receiving insulin. Everyone in the study receives insulin so not a valid comparison.</i> |
| <a href="#">Alvarsson, M., Sundkvist, G., Lager, I. et al. (2003) Beneficial effects of insulin versus sulphonylurea on insulin secretion and metabolic control in recently diagnosed type 2 diabetic patients. Diabetes Care 26(8): 2231-7</a>                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                              |
| <a href="#">Ametov, AS and Gusenbekova, DG (2014) Effect of dipeptidyl peptidase-4 inhibitors on lipid metabolism in patients with type 2 diabetes mellitus. Terapevticheskii arkhiv 86(8): 85-89</a>                                                                                                                         | - Study not reported in English                                                                                                                                                                                                            |



| Study                                                                                                                                                                                                                                                                                                                                                                     | Reason                                                                                              |
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| <a href="#">Amjad, Waseem, Malik, Adnan, Qureshi, Waqas et al. (2022) Sodium-glucose cotransporter-2 inhibitors improve liver enzymes in patients with co-existing non-alcoholic fatty liver disease: a systematic review and meta-analysis. Przegląd gastroenterologiczny 17(4): 288-300</a>                                                                             | - Population not relevant to this review protocol                                                   |
| <a href="#">Anderson, John E; Wright, Eugene E Jr; Shaefer, Charles F Jr (2017) Empagliflozin: Role in Treatment Options for Patients with Type 2 Diabetes Mellitus. Diabetes therapy : research, treatment and education of diabetes and related disorders 8(1): 33-53</a>                                                                                               | - Commentary only<br><i>Narrative review</i>                                                        |
| <a href="#">Anholm, Christian, Kumarathurai, Preman, Pedersen, Lene Rorholm et al. (2019) Liraglutide in combination with metformin may improve the atherogenic lipid profile and decrease C-reactive protein level in statin treated obese patients with coronary artery disease and newly diagnosed type 2 diabetes: A randomized trial. Atherosclerosis 288: 60-66</a> | - Trial that has a treatment and follow up period of less than 24 weeks                             |
| <a href="#">Anker, Stefan D, Butler, Javed, Filippatos, Gerasimos et al. (2021) Effect of Empagliflozin on Cardiovascular and Renal Outcomes in Patients With Heart Failure by Baseline Diabetes Status: Results From the EMPEROR-Reduced Trial. Circulation 143(4): 337-349</a>                                                                                          | - Population not relevant to this review protocol                                                   |
| <a href="#">Anker, Stefan D, Butler, Javed, Filippatos, Gerasimos et al. (2020) Baseline characteristics of patients with heart failure with preserved ejection fraction in the EMPEROR-Preserved trial. European journal of heart failure 22(12): 2383-2392</a>                                                                                                          | - Population not relevant to this review protocol<br><i>People with and without type 2 diabetes</i> |
| <a href="#">Anonymous (1998) Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet (London, England) 352(9131): 854-65</a>                                                                                                                | - Study does not contain an intervention relevant to this review protocol                           |
| <a href="#">Anonymous (1998) United Kingdom Prospective Diabetes Study 24: a 6-year, randomized, controlled trial comparing sulfonylurea, insulin, and metformin therapy in patients with newly diagnosed type 2 diabetes that could not be controlled with diet therapy. United Kingdom Prospective Diabetes Study Group. Annals of internal medicine 128(3): 165-75</a> | - Study does not contain an intervention relevant to this review protocol                           |

| Study                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                                                                                                                                                                                                                          |
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| <a href="#">Anonymous (2019) Lack of Durable Improvements in beta-Cell Function Following Withdrawal of Pharmacological Interventions in Adults With Impaired Glucose Tolerance or Recently Diagnosed Type 2 Diabetes.</a> Diabetes care 42(9): 1742-1751                                                           | - Population not relevant to this review protocol<br><i>Impaired glucose tolerance (IGT) and type 2 diabetes mixed population. Over 70% IGT. No separate reporting of data for study participants with type 2 diabetes.</i>                                                                                                                                                                     |
| <a href="#">Anonymous (1985) U.K. prospective diabetes study. II. Reduction in HbA1c with basal insulin supplement, sulfonylurea, or biguanide therapy in maturity-onset diabetes. A multicenter study.</a> Diabetes 34(8): 793-8                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK<br><i>4 arms: 1. diet only 2. insulin 3. chlorpropamide and 4. glibenclamide 5 arms in obese group: 1. diet only 2. insulin 3. chlorpropamide and 4. glibenclamide 5. metformin Results from obese population, metformin / insulin groups are not reported in sufficient detail to be useful.</i> |
| <a href="#">Anonymous (2019) Long-term Effects of Metformin on Diabetes Prevention: Identification of Subgroups That Benefited Most in the Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study.</a> Diabetes care 42(4): 601-608                                                             | - Population not relevant to this review protocol<br><i>At risk of developing diabetes (impaired glucose tolerance, elevated fasting blood glucose, higher BMI)</i>                                                                                                                                                                                                                             |
| <a href="#">Anonymous (2022) Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials.</a> Lancet (London, England) 400(10365): 1788-1801                                                                 | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                           |
| <a href="#">Anonymous (2015) Predictors of nonsevere and severe hypoglycemia during glucose-lowering treatment with insulin glargine or standard drugs in the ORIGIN trial.</a> Diabetes care 38(1): 22-8                                                                                                           | - Comparator in study does not match that specified in this review protocol<br><i>Compares adding insulin to usual care</i>                                                                                                                                                                                                                                                                     |
| <a href="#">Anonymous (2005) PROactive study shows reduced heart attacks and strokes in type 2 diabetics on pioglitazone HCl (Actos) therapy.</a> Cardiovascular journal of South Africa : official journal for Southern Africa Cardiac Society [and] South African Society of Cardiac Practitioners 16(5): 286-287 | - Commentary only                                                                                                                                                                                                                                                                                                                                                                               |
| <a href="#">Anonymous (2023) Corrigendum to Effects of switching from liraglutide to semaglutide or dulaglutide in patients with type 2 diabetes: A randomized controlled trial.</a> Journal of diabetes investigation                                                                                              | - Commentary only                                                                                                                                                                                                                                                                                                                                                                               |
| <a href="#">Anonymous (2016) Glucose Variability in a 26-Week Randomized Comparison of Mealtime</a>                                                                                                                                                                                                                 | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                                                                                                                                     |

| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                                                     |
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| <a href="#">Treatment With Rapid-Acting Insulin Versus GLP-1 Agonist in Participants With Type 2 Diabetes at High Cardiovascular Risk.</a> Diabetes care 39(6): 973-81                                                                                                                                                       | <i>Compares exenatide plus insulin to insulin, which ultimately means comparing exenatide to no treatment. Not relevant to our review protocol.</i>                                        |
| <a href="#">Anonymous (2023) Correction to: Efpeglenatide and Clinical Outcomes With and Without Concomitant Sodium-Glucose Cotransporter-2 Inhibition Use in Type 2 Diabetes: Exploratory Analysis of the AMPLITUDE-O Trial.</a> Circulation 147(23): e720                                                                  | - Commentary only                                                                                                                                                                          |
| <a href="#">Anonymous (2024) Impact of primary kidney disease on the effects of empagliflozin in patients with chronic kidney disease: secondary analyses of the EMPA-KIDNEY trial.</a> The lancet. Diabetes & endocrinology 12(1): 51-60                                                                                    | - Subgroup analysis of a trial that was not relevant for inclusion                                                                                                                         |
| <a href="#">Anonymous. (2023) In type 2 diabetes, glargine and liraglutide each improved glycemic outcomes at 5 y vs. glimepiride or sitagliptin.</a> Annals of Internal Medicine 176(1): jc8-jc9                                                                                                                            | - Commentary only                                                                                                                                                                          |
| <a href="#">Anonymous. (2013) Corrigendum to A comparison of efficacy and safety of vildagliptin and gliclazide in combination with metformin in patients with Type 2 diabetes inadequately controlled with metformin alone: A 52-week, randomized study [Diabet. Med., 27 (2010) 318-326].</a> Diabetic Medicine 30(5): 632 | - Study design not relevant to this review protocol<br><i>Suggests correction</i>                                                                                                          |
| <a href="#">Anonymous. (2010) Saxagliptin (Onglyza) for type 2 diabetes.</a> Obstetrics and Gynecology 115(5): 1081-1083                                                                                                                                                                                                     | - Study design not relevant to this review protocol<br><i>Medical letter</i>                                                                                                               |
| <a href="#">Apovian, C. M., Bergenstal, R. M., Cuddihy, R. M. et al. (2010) Effects of exenatide combined with lifestyle modification in patients with type 2 diabetes.</a> Am J Med 123(5): 468.e9-17                                                                                                                       | - Additional outcomes relevant to living guideline work                                                                                                                                    |
| <a href="#">Araki, Eiichi, Unno, Yuriko, Tanaka, Yuko et al. (2019) Long-Term Efficacy and Safety of Linagliptin in a Japanese Population with Type 2 Diabetes Aged &gt;= 60 Years Treated with Basal Insulin: A Randomised Trial.</a> Advances in therapy 36(10): 2697-2711                                                 | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Reports 52-week extension data only for Japanese subgroup of Ledesma 2019</i> |
| <a href="#">Armstrong, M.J., Houlihan, D.D., Rowe, I.A. et al. (2013) Safety and efficacy of liraglutide in patients with type 2 diabetes with elevated liver enzymes: Individual patient data meta-analysis</a>                                                                                                             | - Conference abstract                                                                                                                                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                |
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| <a href="#">of the LEAD programme.</a> The Lancet 381(suppl1): 20                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                       |
| <a href="#">Armstrong, Matthew James, Gaunt, Piers, Aithal, Guruprasad P et al. (2016) Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study.</a> Lancet (London, England) 387(10019): 679-690                                                                   | - Population not relevant to this review protocol<br><i>Only 35% of the population had type 2 diabetes</i>                                                                                                            |
| <a href="#">Arnetz, Lisa, Hage, Camilla, Ekberg, Neda Rajamand et al. (2015) Improved glycemic control due to sitagliptin is not related to cortisol or the surrogate marker IGFBP-1 for hepatic insulin sensitivity.</a> Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society 25(6): 298-303 | - Population not relevant to this review protocol<br><i>Less than 35% participants are with T2DM</i><br><br>- Trial that has a treatment and follow up period of less than 24 weeks<br><i>12 weeks follow up time</i> |
| <a href="#">Arnott, C, Neuen B, L, Heerspink H, J.L et al. (2020) The effects of combination canagliflozin and glucagon-like peptide-1 receptor agonist therapy on intermediate markers of cardiovascular risk in the CANVAS program.</a> International Journal of Cardiology 318: 126-129                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                |
| <a href="#">Aroda, V. R., Bailey, T. S., Cariou, B. et al. (2016) Effect of adding insulin degludec to treatment in patients with type 2 diabetes inadequately controlled with metformin and liraglutide: a double-blind randomized controlled trial (BEGIN: ADD TO GLP-1 Study).</a> Diab Obes Metab 18(7): 663-670                                                        | - Comparator in study does not match that specified in this review protocol<br><i>Compares insulin to placebo (with liraglutide provided to both study arms)</i>                                                      |
| <a href="#">Aroda, V.R., Bain, S.C., Cariou, B. et al. (2017) Efficacy and safety of once-weekly semaglutide vs once-daily insulin glargine in insulin-naïve subjects with Type 2 diabetes (SUSTAIN 4).</a> Diabetic Medicine 34(supplement1): 146                                                                                                                          | - Conference abstract                                                                                                                                                                                                 |
| <a href="#">Aroda, V.R., Rosenstock, J., Terauchi, Y. et al. (2019) PIONEER 1: Randomized Clinical Trial Comparing the Efficacy and Safety of Oral Semaglutide Monotherapy with Placebo in Patients with Type 2 Diabetes.</a> Diabetes care                                                                                                                                 | - Duplicate reference                                                                                                                                                                                                 |
| <a href="#">Aroda, Vanita R, Capehorn, Matthew S, Chaykin, Louis et al. (2020) Impact of baseline characteristics and beta-cell function on the efficacy and safety of subcutaneous once-weekly semaglutide: A patient-level, pooled</a>                                                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                |

| Study                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                                                                                                  |
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| <a href="#">analysis of the SUSTAIN 1-5 trials</a> . Diabetes, obesity & metabolism 22(3): 303-314                                                                                                                                                                                             |                                                                                                                                                                                                                                                                         |
| <a href="#">Aroda, Vanita R, Edelstein, Sharon L, Goldberg, Ronald B et al. (2016) Long-term Metformin Use and Vitamin B12 Deficiency in the Diabetes Prevention Program Outcomes Study</a> . The Journal of clinical endocrinology and metabolism 101(4): 1754-61                             | - Population not relevant to this review protocol<br><i>Impaired glucose tolerance</i>                                                                                                                                                                                  |
| <a href="#">Aroda, Vanita R, Erhan, Umut, Jelles, Peter et al. (2023) Safety and tolerability of semaglutide across the SUSTAIN and PIONEER phase IIIa clinical trial programmes</a> . Diabetes, obesity & metabolism                                                                          | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                  |
| <a href="#">Aronson, Ronnie, Frias, Juan, Goldman, Allison et al. (2018) Long-term efficacy and safety of ertugliflozin monotherapy in patients with inadequately controlled T2DM despite diet and exercise: VERTIS MONO extension study</a> . Diabetes, obesity & metabolism 20(6): 1453-1460 | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2                                                                                                |
| <a href="#">Aso, Y., Jojima, T., Iijima, T. et al. (2019) Effects of dapagliflozin, an SGLT2 inhibitor, on hepatic steatosis and fibrosis evaluated by transient elastography in patients with type 2 diabetes and nonalcoholic fatty liver disease</a> . Diabetes 68(supplement1)             | - Conference abstract                                                                                                                                                                                                                                                   |
| <a href="#">Aso, Y., Kato, K., Sakurai, S. et al. (2019) Impact of dapagliflozin, an SGLT2 inhibitor, on serum levels of soluble dipeptidyl peptidase-4 in patients with type 2 diabetes and non-alcoholic fatty liver disease</a> . International Journal of Clinical Practice 73(5): e13335  | - Comparator in study does not match that specified in this review protocol<br><i>No specific comparator listed (reports a usual care comparator which could include a range of pharmacological treatments but no specific agent that can be used for the analysis)</i> |
| <a href="#">Aso, Y., Takebayashi, K., Inukai, T. et al. (2011) Pioglitazone and cardiovascular events in type 2 diabetes: Effects of pioglitazone on cardiovascular outcomes in Japanese patients with type 2 diabetes in higashi-saitama (EPOCH Trial)</a> . Diabetes 60(suppl1): a557        | - Conference abstract                                                                                                                                                                                                                                                   |
| <a href="#">Aso, Yoshimasa, Takada, Yoshihisa, Tomotsune, Ken et al. (2021) Comparison of insulin degludec (IDeg)/insulin Aspart (IAsp) co-formulation therapy twice-daily with free combination of GLP-1 receptor agonist liraglutide plus insulin degludec in Tochigi:</a>                   | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                             |

| Study                                                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                                                                      |
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| <a href="#">IDEAL Trial</a> . International journal of clinical practice 75(4): e13734                                                                                                                                                                                                                                                                   |                                                                                                                                                                                             |
| <a href="#">Augusto, Gustavo A, Cassola, Nicolle, Dualib, Patricia M et al. (2021) Sodium-glucose cotransporter-2 inhibitors for type 2 diabetes mellitus in adults: An overview of 46 systematic reviews</a> . Diabetes, obesity & metabolism 23(10): 2289-2302                                                                                         | - Systematic review used as source of primary studies                                                                                                                                       |
| <a href="#">Ayers, Dieter, Kanters, Steve, Goldgrub, Rachel et al. (2017) Network meta-analysis of liraglutide versus dipeptidyl peptidase-4 inhibitors for the treatment of type 2 diabetes in Japanese patients</a> . Current medical research and opinion 33(9): 1653-1661                                                                            | - Study design not relevant to this review protocol<br><i>Includes studies of 1 week duration or more</i>                                                                                   |
| <a href="#">Azar, S T, Ectay, A, Wan Bebakar, W M et al. (2016) Efficacy and safety of liraglutide compared to sulphonylurea during Ramadan in patients with type 2 diabetes (LIRA-Ramadan): a randomized trial</a> . Diabetes, obesity & metabolism 18(10): 1025-33                                                                                     | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>Treatment duration was variable. Potentially some participants received treatment for less than 24 weeks.</i> |
| <a href="#">Azharuddin, M. and Sharma, M. (2022) A meta-analytic synthesis of DPP4 inhibitors compared to sulfonylureas as add-on therapy to metformin and risk of fractures in patients with type 2 diabetes: Evidence from randomized controlled trials</a> . Osteoporosis International 32(suppl1): 387                                               | - Conference abstract                                                                                                                                                                       |
| <a href="#">Bachmann, W., Petzinna, D., Raptis, S. A. et al. (2003) Long-term improvement of metabolic control by acarbose in type 2 diabetes patients poorly controlled with maximum sulfonylurea therapy</a> . Clin Drug Invest 23(10): 679-86                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                               |
| <a href="#">Badjatiya, Anish, Merrill, Peter, Buse John, B et al. (2019) Clinical Outcomes in Patients With Type 2 Diabetes Mellitus and Peripheral Artery Disease: Results From the EXSCEL Trial</a> . Circulation. Cardiovascular interventions 12(12): e008018                                                                                        | - Post-hoc analysis of included study                                                                                                                                                       |
| <a href="#">Bae, Jae Hyun, Park, Eun-Gee, Kim, Sunhee et al. (2021) Comparative Renal Effects of Dipeptidyl Peptidase-4 Inhibitors and Sodium-Glucose Cotransporter 2 Inhibitors on Individual Outcomes in Patients with Type 2 Diabetes: A Systematic Review and Network Meta-Analysis</a> . Endocrinology and metabolism (Seoul, Korea) 36(2): 388-400 | - Systematic review used as source of primary studies<br><i>Identified in the rerun search. No additional studies to add.</i>                                                               |



| Study                                                                                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                            |
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| <a href="#">Bae, Ji Cheol, Min, Kyung Wan, Kim, Yong Hyun et al. (2019) Efficacy and safety of fixed-dose combination therapy with gemigliptin (50 mg) and rosuvastatin compared with monotherapy in patients with type 2 diabetes and dyslipidaemia (BALANCE): A multicentre, randomized, double-blind, controlled, phase 3 trial. Diabetes, obesity &amp; metabolism 21(1): 103-111</a> | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                     |
| <a href="#">Bailey, C J, Morales Villegas, E C, Woo, V et al. (2015) Efficacy and safety of dapagliflozin monotherapy in people with Type 2 diabetes: a randomized double-blind placebo-controlled 102-week trial. Diabetic medicine : a journal of the British Diabetic Association 32(4): 531-41</a>                                                                                    | - Study design                                                                                                                                                    |
| <a href="#">Bain, S.C., Desouza, C.V., Gondolf, T. et al. (2019) The effect of once-weekly semaglutide on MACE, blood pressure and lipids by race and ethnicity: a SUSTAIN 6 post hoc analysis. Diabetologia 62(supplement1): 365</a>                                                                                                                                                     | - Conference abstract                                                                                                                                             |
| <a href="#">Bain, S.C.; Stella, P.; Cao, A. (2010) Significantly reduced body mass index with liraglutide 1.2 mg treatment versus glimepiride may have an impact on cardiovascular risk in patients with type 2 diabetes. Diabetic Medicine 27(2suppl1): 79</a>                                                                                                                           | - Conference abstract                                                                                                                                             |
| <a href="#">Bajaj, Harpreet S, Raz, Itamar, Mosenzon, Ofri et al. (2020) Cardiovascular and renal benefits of dapagliflozin in patients with short and long-standing type 2 diabetes: Analysis from the DECLARE-TIMI 58 trial. Diabetes, obesity &amp; metabolism 22(7): 1122-1131</a>                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis, nothing additional to add</i> |
| <a href="#">Bajaj, M., Gilman, R., Patel, S. et al. (2013) Linagliptin improved glycemic control without weight gain or hypoglycemia in patients with type 2 diabetes inadequately controlled by a combination of metformin and pioglitazone. Diabetes 62(suppl1): a283</a>                                                                                                               | - Conference abstract                                                                                                                                             |
| <a href="#">Bakris, G. L., Agarwal, R., Anker, S. D. et al. (2020) Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. New England Journal of Medicine 383(23): 2219-2229</a>                                                                                                                                                                                     | - Study does not contain an intervention relevant to this review protocol                                                                                         |
| <a href="#">Bakris, G. L., Ruilope, L. M., McMorn, S. O. et al. (2006) Rosiglitazone reduces</a>                                                                                                                                                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                     |



| Study                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                               |
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| <a href="#">microalbuminuria and blood pressure independently of glycemia in type 2 diabetes patients with microalbuminuria.</a> J Hypertens 24(10): 2047-55                                                                                                                                             |                                                                                                                                                      |
| <a href="#">Banerjee, M., Pal, R., Nair, K. et al. (2023) SGLT2 inhibitors and cardiovascular outcomes in heart failure with mildly reduced and preserved ejection fraction: A systematic review and meta-analysis.</a> Indian Heart Journal                                                             | - Study design not relevant to this review protocol<br><br><i>Systematic review that includes RCTs and post-hoc analyses of RCTs to find results</i> |
| <a href="#">Banerjee, Mainak; Maisnam, Indira; Mukhopadhyay, Satinath (2023) Impact of Heart Failure History at Baseline on Cardiovascular Effects of GLP-1 Receptor Agonists in Type 2 Diabetes: a Meta-analysis.</a> Cardiovascular drugs and therapy                                                  | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Banerjee, Mainak, Pal, Rimesh, Maisnam, Indira et al. (2023) Serum uric acid lowering and effects of sodium-glucose cotransporter-2 inhibitors on gout: A meta-analysis and meta-regression of randomized controlled trials.</a> Diabetes, obesity & metabolism                              | - Population not relevant to this review protocol                                                                                                    |
| <a href="#">Banerjee, Mainak, Pal, Rimesh, Maisnam, Indira et al. (2024) GLP-1 receptor agonists, SGLT2 inhibitors and noncardiovascular mortality in type 2 diabetes: Insights from a meta-analysis.</a> Diabetes & metabolic syndrome 18(1): 102943                                                    | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Banerjee, Mainak, Pal, Rimesh, Mukhopadhyay, Satinath et al. (2023) GLP-1 Receptor Agonists and Risk of Adverse Cerebrovascular Outcomes in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.</a> The Journal of clinical endocrinology and metabolism | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Bardi, L., Paolillo, S., Bruzzese, D. et al. (2021) Effects of sodium-glucose co-transporter 2 (SGLT2) inhibitors on major cardiovascular events in Type 2 diabetic patients: A meta-analysis of randomized controlled trials.</a> European Heart Journal, Supplement 23(supplg): g102       | - Conference abstract                                                                                                                                |
| <a href="#">Barnett, A. H., Grant, P. J., Hitman, G. A. et al. (2003) Rosiglitazone in Type 2 diabetes mellitus: an evaluation in British Indo-Asian patients.</a> Diabetic Med 20(5): 387-93                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |

| Study                                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                                                                                                                                                                                                        |
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| <a href="#">Barracough, Jennifer Y, Yu, Jie, Figtree, Gemma A et al. (2022) Cardiovascular and renal outcomes with canagliflozin in patients with peripheral arterial disease: Data from the CANVAS Program and CREDENCE trial.</a> Diabetes, obesity & metabolism 24(6): 1072-1083                                                       | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                                                        |
| <a href="#">Barritt, A Sidney 4th; Marshman, Emma; Nouredin, Mazen (2022) Review article: role of glucagon-like peptide-1 receptor agonists in non-alcoholic steatohepatitis, obesity and diabetes-what hepatologists need to know.</a> Alimentary pharmacology & therapeutics 55(8): 944-959                                             | - Review article but not a systematic review                                                                                                                                                                                                                                                                                                  |
| <a href="#">Bastyr, E J 3rd, Johnson, M E, Trautmann, M E et al. (1999) Insulin lispro in the treatment of patients with type 2 diabetes mellitus after oral agent failure.</a> Clinical therapeutics 21(10): 1703-14                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                                 |
| <a href="#">Battelino, T., Johnson, J., Katz, M. et al. (2023) The Effect of Tirzepatide vs. Insulin Degludec on Post-meal Glucose Control in Patients with Type 2 Diabetes (SURPASS-3 CGM).</a> Diabetes 72(supplement1)                                                                                                                 | - Conference abstract                                                                                                                                                                                                                                                                                                                         |
| <a href="#">Bayrasheva, V. K., Pchelin, I. Y., Dobronravov, V. A. et al. (2020) Short-term renal and metabolic effects of low dose vildagliptin treatment added-on insulin therapy in non-proteinuric patients with type 2 diabetes: open-label randomized prospective study.</a> Archives of endocrinology and metabolism 64(4): 418-426 | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                                                                                   |
| <a href="#">Bebakar, W.M.W., Chow, C.C., Kadir, K.A. et al. (2007) Adding biphasic insulin aspart 30 once or twice daily is more efficacious than optimizing oral antidiabetic treatment in patients with type 2 diabetes.</a> Diabetes, Obesity and Metabolism 9(5): 724-732                                                             | - Study does not contain an intervention relevant to this review protocol                                                                                                                                                                                                                                                                     |
| <a href="#">Bechlioulis, Aris, Markozannes, Georgios, Chionidi, Ifigeneia et al. (2023) The effect of SGLT2 inhibitors, GLP1 agonists, and their sequential combination on cardiometabolic parameters: A randomized, prospective, intervention study.</a> Journal of diabetes and its complications 37(4): 108436                         | - Population not relevant to this review protocol<br><br><i>2 arm trial: empagliflozin for 3 months, then empagliflozin + liraglutide for 6 months vs. liraglutide for 3 months, then liraglutide + empagliflozin for 6 months. Initial treatment duration is too short (&lt;24 weeks) and the second treatment is the same in both arms.</i> |

| Study                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                                                                                           |
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| <a href="#">Beernink, Jelle M, Persson, Frederik, Jongs, Niels et al. (2023) Efficacy of Dapagliflozin by Baseline Diabetes Medications: A Prespecified Analysis From the DAPA-CKD Study.</a> Diabetes care 46(3): 602-607                                                                                           | - Population not relevant to this review protocol                                                                                                                                                                                                |
| <a href="#">Belcher, G and Schernthaner, G (2005) Changes in liver tests during 1-year treatment of patients with Type 2 diabetes with pioglitazone, metformin or gliclazide.</a> Diabetic medicine : a journal of the British Diabetic Association 22(8): 973-9                                                     | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Reports liver outcomes from 4 studies already identified: Schernthaner 2004, Charbonnel 2005, Hanefeld 2004, Matthews 2005.</i> |
| <a href="#">Benham, Jamie L, Booth, Jane E, Sigal, Ronald J et al. (2021) Systematic review and meta-analysis: SGLT2 inhibitors, blood pressure and cardiovascular outcomes.</a> International journal of cardiology. Heart & vasculature 33: 100725                                                                 | - Systematic review used as source of primary studies                                                                                                                                                                                            |
| <a href="#">Bentley-Lewis, Rhonda, Aguilar, David, Riddle, Matthew C et al. (2015) Rationale, design, and baseline characteristics in Evaluation of LIXisenatide in Acute Coronary Syndrome, a long-term cardiovascular end point trial of lixisenatide versus placebo.</a> American heart journal 169(5): 631-638e7 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                           |
| <a href="#">Berberoglu, Z.; Yazici, A. C.; Demirag, N. G. (2010) Effects of rosiglitazone on bone mineral density and remodelling parameters in postmenopausal diabetic women: a 2-year follow-up study.</a> Clin Endocrinol 73(3): 305-12                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                    |
| <a href="#">Berg, David D, Wiviott, Stephen D, Scirica, Benjamin M et al. (2021) A Biomarker-Based Score for Risk of Hospitalization for Heart Failure in Patients With Diabetes.</a> Diabetes care 44(11): 2573-2581                                                                                                | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Uses data from the placebo arms of SAVOR-TIMI 53 and DECLARE-TIMI 58</i>                                                        |
| <a href="#">Bergental, R.M., Calabro, P., Lutomirsky, M.M. et al. (2016) Effect of empagliflozin on nephropathy in subgroups by age: Results from empa-reg outcome.</a> Diabetes 65(supplement1): a314                                                                                                               | - Conference abstract                                                                                                                                                                                                                            |
| <a href="#">Bergmark, BA, Bhatt, DL, McGuire, DK et al. (2019) Metformin Use and Clinical Outcomes among Patients with Diabetes with or without Heart Failure or Kidney Dysfunction:</a>                                                                                                                             | - Study design not relevant to this review protocol<br><br><i>Posthoc analysis</i>                                                                                                                                                               |

| Study                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                              |
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| <a href="#">observations from the SAVOR-TIMI 53 Trial.</a><br>Circulation                                                                                                                                                                                                                    | - Duplicate reference<br><br>- Secondary publication of an included study that does not provide any additional relevant information                                 |
| <a href="#">Bergmark, Brian A, Bhatt, Deepak L, McGuire, Darren K et al. (2019) Metformin Use and Clinical Outcomes Among Patients With Diabetes Mellitus With or Without Heart Failure or Kidney Dysfunction: Observations From the SAVOR-TIMI 53 Trial.</a> Circulation 140(12): 1004-1014 | - Duplicate reference<br><br>- Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis</i> |
| <a href="#">Bertrand, O. F., Poirier, P., Rodés-Cabau, J. et al. (2010) Cardiometabolic effects of rosiglitazone in patients with type 2 diabetes and coronary artery bypass grafts: A randomized placebo-controlled clinical trial.</a> Atherosclerosis 211(2): 565-73                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                       |
| <a href="#">Bethel M, Angelyn, Engel Samuel, S, Green Jennifer, B et al. (2017) Assessing the Safety of Sitagliptin in Older Participants in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS).</a> Diabetes care 40(4): 494-501                                         | - Secondary publication of an included study that does not provide any additional relevant information                                                              |
| <a href="#">Bethel, M A, Green, J B, Milton, J et al. (2015) Regional, age and sex differences in baseline characteristics of patients enrolled in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS).</a> Diabetes, obesity & metabolism 17(4): 395-402                  | - Secondary publication of an included study that does not provide any additional relevant information                                                              |
| <a href="#">Bethel, M Angelyn, Stevens, Susanna R, Buse, John B et al. (2020) Exploring the Possible Impact of Unbalanced Open-Label Drop-In of Glucose-Lowering Medications on EXSCEL Outcomes.</a> Circulation 141(17): 1360-1370                                                          | - Secondary publication of an included study that does not provide any additional relevant information                                                              |
| <a href="#">Bhansali, A and Masoodi, SR (2005) Efficacy of once- or twice-daily extended release metformin compared with thrice-daily immediate release metformin in type 2 diabetes mellitus.</a> Journal of the Association of Physicians of India 53: 441-445                             | - Study design not relevant to this review protocol                                                                                                                 |

| Study                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                                  |
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| <a href="#">Bhansali, Shipra, Bhansali, Anil, Dutta, Pinaki et al. (2020) Metformin upregulates mitophagy in patients with T2DM: A randomized placebo-controlled study.</a> Journal of cellular and molecular medicine 24(5): 2832-2846                                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                 |
| <a href="#">Bhatia, K., Jain, V., Gupta, K. et al. (2021) Prevention of Heart Failure Events with SGLT-2 Inhibitors Across a Spectrum of Cardio-Renal-Metabolic Risk.</a> European journal of heart failure                                                                                               | - Population not relevant to this review protocol                                                                                                                       |
| <a href="#">Bhatia, Kirtipal, Jain, Vardhmaan, Gupta, Kartik et al. (2021) Prevention of heart failure events with sodium-glucose co-transporter 2 inhibitors across a spectrum of cardio-renal-metabolic risk.</a> European journal of heart failure 23(6): 1002-1008                                    | - Population not relevant to this review protocol<br><i>Systematic review investigating prevention of heart failure that is not just in people with type 2 diabetes</i> |
| <a href="#">Bhatt, Ankeet S, Luo, Nancy, Solomon, Nicole et al. (2019) International variation in characteristics and clinical outcomes of patients with type 2 diabetes and heart failure: Insights from TECOS.</a> American heart journal 218: 57-65                                                    | - Study design not relevant to this review protocol<br><i>Posthoc analysis by region where people participated in the trial</i>                                         |
| <a href="#">Bhatt, D. L., Szarek, M., Pitt, B. et al. (2021) Sotagliflozin in Patients with Diabetes and Chronic Kidney Disease.</a> New England Journal of Medicine 384(2): 129-139                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                           |
| <a href="#">Bhatt, D. L., Szarek, M., Steg, P. G. et al. (2021) Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure.</a> New England Journal of Medicine 384(2): 117-128                                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                           |
| <a href="#">Bhattarai, Mukul, Salih, Mohsin, Regmi, Manjari et al. (2022) Association of Sodium-Glucose Cotransporter 2 Inhibitors With Cardiovascular Outcomes in Patients With Type 2 Diabetes and Other Risk Factors for Cardiovascular Disease: A Meta-analysis.</a> JAMA network open 5(1): e2142078 | - Population not relevant to this review protocol                                                                                                                       |
| <a href="#">Bi, Y., Lu, S., Tang, J. et al. (2024) Efficacy and Safety of Tirzepatide in Patients with Type 2 Diabetes: Analysis of SURPASS-AP-Combo by Different Subgroups.</a> Diabetes Therapy                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                                                  |
| <a href="#">Bica, Ioana-Cristina, Stoica, Roxana Adriana, Salmen, Teodor et al. (2023) The Effects of Sodium-Glucose Cotransporter 2-Inhibitors on Steatosis and Fibrosis in Patients with Non-</a>                                                                                                       | - Systematic review used as source of primary studies                                                                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                  |
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| <a href="#">Alcoholic Fatty Liver Disease or Steatohepatitis and Type 2 Diabetes: A Systematic Review of Randomized Controlled Trials.</a> Medicina (Kaunas, Lithuania) 59(6)                                                                                                                                                                     |                                                                                                                         |
| <a href="#">Biessels Geert, Jan, Verhagen, Chloe, Janssen, Jolien et al. (2019) Effect of Linagliptin on Cognitive Performance in Patients With Type 2 Diabetes and Cardiorenal Comorbidities: The CARMELINA Randomized Trial.</a> Diabetes care 42(10): 1930-1938                                                                                | - Secondary publication of an included study that does not provide any additional relevant information                  |
| <a href="#">Biessels, Geert Jan, Verhagen, Chloe, Janssen, Jolien et al. (2021) Effects of linagliptin vs glimepiride on cognitive performance in type 2 diabetes: results of the randomised double-blind, active-controlled CAROLINA-COGNITION study.</a> Diabetologia 64(6): 1235-1245                                                          | - Secondary publication of an included study that does not provide any additional relevant information                  |
| <a href="#">Bilal, A., Yi, F., Gonzalez, G.R. et al. (2023) Effects of newer antidiabetic agents on cardiovascular outcomes in older adults: systematic review and meta-analysis.</a> Postgraduate Medicine 135(supplement2): 7-8                                                                                                                 | - Conference abstract                                                                                                   |
| <a href="#">Bilezikian, John P, Watts, Nelson B, Usiskin, Keith et al. (2016) Evaluation of Bone Mineral Density and Bone Biomarkers in Patients With Type 2 Diabetes Treated With Canagliflozin.</a> The Journal of clinical endocrinology and metabolism 101(1): 44-51                                                                          | - Secondary publication of an included study that does not provide any additional relevant information                  |
| <a href="#">Billings, Liana K, Agner, Bue F Ross, Altuntas, Yuksel et al. (2021) The Benefit of Insulin Degludec/Liraglutide (IDegLira) Compared With Basal-Bolus Insulin Therapy is Consistent Across Participant Subgroups With Type 2 Diabetes in the DUAL VII Randomized Trial.</a> Journal of diabetes science and technology 15(3): 636-645 | - Secondary publication of an included study that does not provide any additional relevant information                  |
| <a href="#">Birkeland, K. I., Hanssen, K. F., Urdal, P. et al. (1994) A long-term, randomized, comparative study of insulin versus sulfonylurea therapy in type 2 diabetes.</a> J Intern Med 236(3): 305-13                                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                           |
| <a href="#">Bizino, Maurice B, Jazet, Ingrid M, van Eyk, Huub J et al. (2021) Efficacy of liraglutide on glycemic endpoints in people of Western European and South Asian descent with T2DM using multiple daily insulin injections: results of the MAGNA VICTORIA studies.</a> Acta diabetologica 58(4): 485-493                                 | - Post-hoc analysis of included study<br><br><i>Secondary pooled analysis of data from Bizino 2019 and van Eyk 2019</i> |



| Study                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                            |
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| <a href="#">Bjorner, Jakob Bue, Larsen, Sara, Lubker, Christopher et al. (2023) The improved health utility of once-weekly subcutaneous semaglutide 2.4 mg compared with placebo in the STEP 1-4 obesity trials.</a> Diabetes, obesity & metabolism                                                                         | - Population not relevant to this review protocol                                                                 |
| <a href="#">Blevins, Thomas, Zhang, Qianyi, Frias, Juan P et al. (2020) Randomized Double-Blind Clinical Trial Comparing Ultra Rapid Lispro With Lispro in a Basal-Bolus Regimen in Patients With Type 2 Diabetes: PRONTO-T2D.</a> Diabetes care 43(12): 2991-2998                                                          | - Comparator in study does not match that specified in this review protocol<br><i>Insulin compared to insulin</i> |
| <a href="#">Blonde, L., Belousova, L., Fainberg, U. et al. (2019) Liraglutide as Add-on to SGLT2 Inhibitors in Patients with Inadequately Controlled Type 2 Diabetes (LIRA-ADD2SGLT2i): A 26- Week, Randomized, Double-Blind, Placebo-Controlled Trial.</a> Journal of the Endocrine Society 3(supplement1)                 | - Conference abstract                                                                                             |
| <a href="#">Blonde, L., Belousova, L., Fainberg, U. et al. (2020) Liraglutide as add-on to SGLT2 inhibitors in patients with inadequately controlled type 2 diabetes: LIRA-ADD2SGLT2i, a 26-week, randomized, double-blind, placebo-controlled trial.</a> Diabetes, obesity & metabolism                                    | - Conference abstract                                                                                             |
| <a href="#">Blonde, L., Rosenstock, J., Del Prato, S. et al. (2019) Switching to iGlarLixi vs continuation of glucagon-like peptide-1 receptor agonist in inadequately controlled type 2 diabetes: the randomised LixiLan-G trial.</a> Diabetologia 62(supplement1): 427                                                    | - Conference abstract                                                                                             |
| <a href="#">Blonde, Lawrence, Fainberg, Udi, Kaltoft, Margit S et al. (2021) Efficacy of liraglutide added to sodium-glucose cotransporter-2 inhibitors in type 2 diabetes, stratified by baseline characteristics: Post-hoc analysis of LIRA-ADD2SGLT2i.</a> Diabetes, obesity & metabolism 23(10): 2234-2241              | - Secondary publication of an included study that does not provide any additional relevant information            |
| <a href="#">Blonde, Lawrence, Rosenstock, Julio, Del Prato, Stefano et al. (2019) Switching to iGlarLixi Versus Continuing Daily or Weekly GLP-1 RA in Type 2 Diabetes Inadequately Controlled by GLP-1 RA and Oral Antihyperglycemic Therapy: The LixiLan-G Randomized Clinical Trial.</a> Diabetes care 42(11): 2108-2116 | - Comparator in study does not match that specified in this review protocol                                       |



| Study                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                   |
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| <a href="#">Bluher, Matthias, Rosenstock, Julio, Hoefler, Josef et al. (2024) Dose-response effects on HbA1c and bodyweight reduction of survodutide, a dual glucagon/GLP-1 receptor agonist, compared with placebo and open-label semaglutide in people with type 2 diabetes: a randomised clinical trial. Diabetologia 67(3): 470-482</a> | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                  |
| <a href="#">Bode, B W, Testa, M A, Magwire, M et al. (2010) Patient-reported outcomes following treatment with the human GLP-1 analogue liraglutide or glimepiride in monotherapy: results from a randomized controlled trial in patients with type 2 diabetes. Diabetes, obesity &amp; metabolism 12(7): 604-12</a>                        | - Secondary publication of an included study that does not provide any additional relevant information                                                   |
| <a href="#">Bohm, M, Slawik, J, Brueckmann, M et al. (2020) Efficacy of empagliflozin on heart failure and renal outcomes in patients with atrial fibrillation: data from the EMPA-REG OUTCOME trial. European Journal of Heart Failure 22(1): 126-135</a>                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information                                                   |
| <a href="#">Bohra, M., Neerjesh, Rajvaidya, D. et al. (2023) EFFECT OF SITAGLIPTIN ALONE AS MONOTHERAPY VS SITAGLIPTIN + METFORMIN IN COMBINATION ON THE BETA CELL FUNCTION IN RECENTLY DIAGNOSED TYPE 2 DIABETICS: A COMPARATIVE STUDY. Journal of Cardiovascular Disease Research 14(5): 2167-2175</a>                                    | - No relevant outcomes reported                                                                                                                          |
| <a href="#">Bonaca M, P, Wiviott S, D, Zelniker T, A et al. (2020) Dapagliflozin and Cardiac, Kidney, and Limb Outcomes in Patients with and without Peripheral Artery Disease in DECLARE-TIMI 58. Circulation: 734-747</a>                                                                                                                 | - Additional outcomes relevant to living guideline work                                                                                                  |
| <a href="#">Bonadonna, R C, Giaccari, A, Buzzetti, R et al. (2019) Italian Titration Approach Study (ITAS) with insulin glargine 300 U/mL in insulin-naïve type 2 diabetes: Design and population. Nutrition, metabolism, and cardiovascular diseases : NMCD 29(5): 496-503</a>                                                             | - Study design<br><i>Study design and baseline characteristics only</i><br><br>- Study does not contain an intervention relevant to this review protocol |
| <a href="#">Bonadonna, Riccardo C, Yale, Jean-Francois, Brulle-Wohlhueter, Claire et al. (2019) Hypoglycaemia as a function of HbA1c in type 2 diabetes: Insulin glargine 300 U/mL in a patient-</a>                                                                                                                                        | - Study does not contain an intervention relevant to this review protocol                                                                                |

| Study                                                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                        |
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| <a href="#">level pooled analysis of EDITION 1, 2 and 3.</a><br>Diabetes, obesity & metabolism 21(3): 715-719                                                                                                                                                                                                                                                                                                    |                                                                                               |
| <a href="#">Borges, J. L., Bilezikian, J. P., Jones-Leone, A. R. et al. (2011) A randomized, parallel group, double-blind, multicentre study comparing the efficacy and safety of Avandamet (rosiglitazone/metformin) and metformin on long-term glycaemic control and bone mineral density after 80 weeks of treatment in drug-naïve type 2 diabetes mellitus patients.</a> Diabetes Obes Metab 13(11): 1036-46 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Borisov, Angel N, Kutz, Alexander, Christ, Emanuel R et al. (2023) Canagliflozin and Metabolic Associated Fatty Liver Disease in Patients with Diabetes Mellitus: New Insights from CANVAS.</a> The Journal of clinical endocrinology and metabolism                                                                                                                                                 | - Post-hoc analysis of included study                                                         |
| <a href="#">Bosi, E., Ellis, G. C., Wilson, C. A. et al. (2011) Alogliptin as a third oral antidiabetic drug in patients with type 2 diabetes and inadequate glycaemic control on metformin and pioglitazone: a 52-week, randomized, double-blind, active-controlled, parallel-group study.</a> Diabetes Obes Metab 13(12): 1088-96                                                                              | - Comparator in study does not match that specified in this review protocol                   |
| <a href="#">Bouchi, R., Nakano, Y., Fukuda, T. et al. (2017) Reduction of visceral fat by liraglutide is associated with ameliorations of hepatic steatosis, albuminuria, and microinflammation in type 2 diabetic patients with insulin treatment: a randomized controlled trial.</a> Diabetes 66: A287                                                                                                         | - Duplicate reference                                                                         |
| <a href="#">Bouchi, Ryotaro, Nakano, Yujiro, Fukuda, Tatsuya et al. (2017) Reduction of visceral fat by liraglutide is associated with ameliorations of hepatic steatosis, albuminuria, and micro-inflammation in type 2 diabetic patients with insulin treatment: a randomized control trial.</a> Endocrine journal 64(3): 269-281                                                                              | - Comparator in study does not match that specified in this review protocol                   |
| <a href="#">Boye, K., Sapin, H., Poon, J.-L. et al. (2023) Tirzepatide improves health-related quality of life vs insulin lispro in poorly controlled basal insulin-treated adults with type 2 diabetes (SURPASS-6).</a> Diabetologia 66(supplement1): 314                                                                                                                                                       | - Conference abstract                                                                         |
| <a href="#">Boye, K.S., Yu, M., Van Brunt, K. et al. (2014) Patient-reported outcomes with once weekly dulaglutide 1.5 mg versus once daily liraglutide</a>                                                                                                                                                                                                                                                      | - Conference abstract                                                                         |

| Study                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                 |
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| <a href="#">1.8 mg (AWARD-6)</a> . Diabetologia 57(1suppl1): 369-s370                                                                                                                                                                                                                                                                                      |                                                                                                        |
| <a href="#">Boye, Kristina S, Thieu, Vivian Thuyanh, Sapin, Helene et al. (2023) Patient-Reported Outcomes in People with Type 2 Diabetes Receiving Tirzepatide in the SURPASS Clinical Trial Programme</a> . Diabetes therapy : research, treatment and education of diabetes and related disorders                                                       | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Br?nden, A, Christensen, MB, Glintborg, D et al. (2023) Effects of DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, and sulfonylureas on mortality, cardiovascular and renal outcomes in type 2 diabetes: a network meta-analyses-driven approach</a> . Diabetic medicine : a journal of the British Diabetic Association: e15157 | - Duplicate reference                                                                                  |
| <a href="#">Branch, Kelley R H, Dagenais, Gilles R, Avezum, Alvaro et al. (2022) Dulaglutide and cardiovascular and heart failure outcomes in patients with and without heart failure: a post-hoc analysis from the REWIND randomized trial</a> . European journal of heart failure 24(10): 1805-1812                                                      | - Study design not relevant to this review protocol<br><i>Post-hoc analysis</i>                        |
| <a href="#">Braun, D.; Schonherr, U.; Mitzkat, H. J. (1996) Efficacy of acarbose monotherapy in patients with type 2 diabetes: A double-blind study conducted in general practice</a> . Endocrinol Metab 3(4): 275-80                                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Bretzel, R. G., Nuber, U., Landgraf, W. et al. (2008) Once-daily basal insulin glargine versus thrice-daily prandial insulin lispro in people with type 2 diabetes on oral hypoglycaemic agents (APOLLO): an open randomised controlled trial</a> . Lancet 371(9618): 1073-84                                                                  | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Brice, R., Hassan, S.W., Spencer, W. et al. (2016) A comparison of empagliflozin vs glimepiride, based on Quality and Outcomes Framework (QOF) targets, weight control and hypoglycaemic adverse events: Post hoc analysis of a head-to-head study (NCT01167881)</a> . Diabetic Medicine 33(suppl1): 189-190                                   | - Conference abstract                                                                                  |
| <a href="#">Brockmeyer, Maximilian, Parco, Claudio, Vargas, Kris Gregory et al. (2024) Absolute treatment effects of novel antidiabetic drugs on</a>                                                                                                                                                                                                       | - Study design not relevant to this review protocol                                                    |

| Study                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                            |
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| <a href="#">a composite renal outcome: meta-analysis of digitalized individual patient data.</a> Journal of nephrology                                                                                                                                                                                                                                                       |                                                                                                                   |
| <a href="#">Bronden, Andreas, Christensen, Mikkel Bring, Glinborg, Dorte et al. (2023) Effects of DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors and sulphonylureas on mortality, cardiovascular and renal outcomes in type 2 diabetes: A network meta-analyses-driven approach.</a> Diabetic medicine : a journal of the British Diabetic Association: e15157 | - Systematic review used as source of primary studies                                                             |
| <a href="#">Brown, JB and Pedula, KL (1999) Metformin as secondary therapy in a defined population with Type 2 Diabetes.</a> Clinical therapeutics 21(10): 1678-1687                                                                                                                                                                                                         | - Study does not contain an intervention relevant to this review protocol                                         |
| <a href="#">Brown-Frandsen, Kirstine, Emerson, Scott S, McGuire, Darren K et al. (2019) Lower rates of cardiovascular events and mortality associated with liraglutide use in patients treated with basal insulin: A DEVOTE subanalysis (DEVOTE 10).</a> Diabetes, obesity & metabolism 21(6): 1437-1444                                                                     | - Comparator in study does not match that specified in this review protocol<br><i>Compares insulin to insulin</i> |
| <a href="#">Bryson, A., Jennings, P. E., Deak, L. et al. (2016) The efficacy and safety of teneligliptin added to ongoing metformin monotherapy in patients with type 2 diabetes: a randomized study with open label extension.</a> Expert Opin Pharmacother 17(10): 1309-16                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                     |
| <a href="#">Budoff, Matthew J, Davis, Timothy M E, Palmer, Alexandra G et al. (2021) Efficacy and Safety of Ertugliflozin in Patients with Type 2 Diabetes Inadequately Controlled by Metformin and Sulfonylurea: A Sub-Study of VERTIS CV.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 12(5): 1279-1297                      | - Trial that has a treatment and follow up period of less than 24 weeks                                           |
| <a href="#">Bunck, Mathijs C, Poelma, Marieke, Eekhoff, E Marelise et al. (2012) Effects of vildagliptin on postprandial markers of bone resorption and calcium homeostasis in recently diagnosed, well-controlled type 2 diabetes patients.</a> Journal of diabetes 4(2): 181-5                                                                                             | - Secondary publication of an included study that does not provide any additional relevant information            |
| <a href="#">Burggraaf, Benjamin, Pouw, Nadine M C, Fernandez Arroyo, Salvador et al. (2022) Effects of dapagliflozin on postprandial lipid metabolism</a>                                                                                                                                                                                                                    | - Trial that has a treatment and follow up period of less than 24 weeks                                           |

| Study                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                                              |
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| <a href="#">in type 2 diabetes mellitus</a> . European journal of endocrinology 186(5): 597-605                                                                                                                                             |                                                                                                                                                                                                                                                     |
| <a href="#">Buse John, B, Bethel M, Angelyn, Green Jennifer, B et al. (2017) Pancreatic Safety of Sitagliptin in the TECOS Study</a> . Diabetes care 40(2): 164-170                                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                              |
| <a href="#">Buse, John B, Bain, Stephen C, Mann, Johannes F E et al. (2020) Cardiovascular Risk Reduction With Liraglutide: An Exploratory Mediation Analysis of the LEADER Trial</a> . Diabetes care 43(7): 1546-1552                      | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                              |
| <a href="#">Butt, Jawad H, Dewan, Pooja, DeFilippis, Ersilia M et al. (2022) Effects of Dapagliflozin According to the Heart Failure Collaboratory Medical Therapy Score: Insights From DAPA-HF</a> . JACC. Heart failure 10(8): 543-555    | - Post-hoc analysis of included study<br>- Population not relevant to this review protocol                                                                                                                                                          |
| <a href="#">Buysschaert, M (2019) Canagliflozin (Invokana®) associated with exemplary nephro- and cardioprotection in Type 2 diabetes Synopsis of the CREDENCE study</a> . Louvain medical 139(5): 255-260                                  | - Study not reported in English                                                                                                                                                                                                                     |
| <a href="#">Buzzetti, R, Pozzilli, P, Frederich, R et al. (2016) Saxagliptin improves glycaemic control and C-peptide secretion in latent autoimmune diabetes in adults (LADA)</a> . Diabetes/metabolism research and reviews 32(3): 289-96 | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Pooled analysis of 5 RCTS, which have been identified by our search. The subgroup analysis is not relevant to the review protocol.</i> |
| <a href="#">Cabral, BV; Fernando, R; Villegas Cinco, A (1985) Place of Gliclazide in the treatment of early diabetic retinopathy</a> . Therapie 40(4): 231-233                                                                              | - Study not reported in English                                                                                                                                                                                                                     |
| <a href="#">Cahn, A., Wiviott, S.D., Mosenzon, O. et al. (2021) The cardiovascular and renal benefits of dapagliflozin are independent of baseline HbA1c: Analyses from DECLARE-TIMI 58</a> . Diabetes 70(suppl1)                           | - Conference abstract                                                                                                                                                                                                                               |
| <a href="#">Cahn, A, Raz, I, Bonaca, M et al. (2020) Safety of dapagliflozin in a broad population of patients with type 2 diabetes: Analyses from the DECLARE-TIMI 58 study</a> . Diabetes, Obesity and Metabolism 22(8): 1357-1368        | - Additional outcomes relevant to living guideline work                                                                                                                                                                                             |

| Study                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                               |
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| <a href="#">Cahn, Avivit, Mosenzon, Ofri, Wiviott Stephen, D et al. (2020) Efficacy and Safety of Dapagliflozin in the Elderly: Analysis From the DECLARE-TIMI 58 Study.</a> Diabetes care 43(2): 468-475                                                                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                               |
| <a href="#">Cahn, Avivit, Wiviott, Stephen D, Mosenzon, Ofri et al. (2022) Association of Baseline HbA1c With Cardiovascular and Renal Outcomes: Analyses From DECLARE-TIMI 58.</a> Diabetes care 45(4): 938-946                                                                                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information                                               |
| <a href="#">Cahn, Avivit, Wiviott, Stephen D, Mosenzon, Ofri et al. (2021) Cardiorenal outcomes with dapagliflozin by baseline glucose-lowering agents: Post hoc analyses from DECLARE-TIMI 58.</a> Diabetes, obesity & metabolism 23(1): 29-38                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                               |
| <a href="#">Cai, Ru-Ping; Xu, Yu-Li; Su, Qiang (2021) Dapagliflozin in Patients with Chronic Heart Failure: A Systematic Review and Meta-Analysis.</a> Cardiology research and practice 2021: 6657380                                                                                                                                                             | - Population not relevant to this review protocol<br><i>People with heart failure, not just people with type 2 diabetes</i>                          |
| <a href="#">Cai, T. T., Li, H. Q., Jiang, L. L. et al. (2021) Effects of GLP-1 Receptor Agonists on Bone Mineral Density in Patients with Type 2 Diabetes Mellitus: A 52-Week Clinical Study.</a> BioMed Research International 2021: 3361309                                                                                                                     | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Camerini-Davalos, R. A., Velasco, C. A., Reddi, A. S. et al. (1988) Delay of progression of diabetic microangiopathy.</a> Metabolism 37(2suppl1): 10-8                                                                                                                                                                                                | - Duplicate reference                                                                                                                                |
| <a href="#">Cannon, C.P., McGuire, D., Pratley, R. et al. (2018) Design and baseline characteristics of the evaluation of ertugliflozin efficacy and safety cardiovascular outcomes trial (VERTIS-CV).</a> Journal of the American College of Cardiology 71(11supplement1)                                                                                        | - Conference abstract                                                                                                                                |
| <a href="#">Cannon, Christopher P, Perkovic, Vlado, Agarwal, Rajiv et al. (2020) Evaluating the Effects of Canagliflozin on Cardiovascular and Renal Events in Patients With Type 2 Diabetes Mellitus and Chronic Kidney Disease According to Baseline HbA1c, Including Those With HbA1c &lt;7%: Results From the CREDENCE Trial.</a> Circulation 141(5): 407-410 | - Not a peer-reviewed publication                                                                                                                    |



| Study                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| <a href="#">Cao, Haiyan, Liu, Youxia, Tian, Zhixia et al. (2021) Sodium-glucose cotransporter 2 inhibitors benefit to kidney and cardiovascular outcomes for patients with type 2 diabetes mellitus and chronic kidney disease 3b-4: A systematic review and meta-analysis of randomized clinical trials.</a> Diabetes research and clinical practice 180: 109033 | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                     |
| <a href="#">Caparrotta, Thomas M, Greenhalgh, Andrew M, Osinski, Karen et al. (2021) Sodium-Glucose Co-Transporter 2 Inhibitors (SGLT2i) Exposure and Outcomes in Type 2 Diabetes: A Systematic Review of Population-Based Observational Studies.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 12(4): 991-1028      | - Study design not relevant to this review protocol<br><i>Systematic review of observational studies</i>                                                                                                                                                                                                                                                                                                                                                  |
| <a href="#">Carlson, A. L., Mullen, D. M., Mazze, R. et al. (2019) EVALUATION OF INSULIN GLARGINE AND EXENATIDE ALONE AND IN COMBINATION: a RANDOMIZED CLINICAL TRIAL WITH CONTINUOUS GLUCOSE MONITORING AND AMBULATORY GLUCOSE PROFILE ANALYSIS.</a> Endocrine practice 25(4): 306-314                                                                           | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>While 32 weeks in total - 16 weeks were spent in the randomised groups, but then therapy was optimised after that point which included putting some people in the individual treatment arms onto the combined treatment (meaning that the comparison of combined treatments and individual treatments while maintaining appropriate randomisation is only for 16 weeks)</i> |
| <a href="#">Caruso, Irene, Cignarelli, Angelo, Sorice, Gian Pio et al. (2022) Cardiovascular and Renal Effectiveness of GLP-1 Receptor Agonists vs. Other Glucose-Lowering Drugs in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Real-World Studies.</a> Metabolites 12(2)                                                                           | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                     |
| <a href="#">Caruso, Irene, Di Gioia, Ludovico, Di Molfetta, Sergio et al. (2023) Glucometabolic outcomes of GLP-1 receptor agonist-based therapies in patients with type 2 diabetes: a systematic review and network meta-analysis.</a> EClinicalMedicine 64: 102181                                                                                              | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                     |
| <a href="#">Caruso, Paola, Maiorino, Maria Ida, Longo, Miriam et al. (2024) Liraglutide for Lower Limb Perfusion in People With Type 2 Diabetes and Peripheral Artery Disease: The STARDUST Randomized Clinical Trial.</a> JAMA network open 7(3): e241545                                                                                                        | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                                                                                                                                                                                               |



| Study                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                 |
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| <a href="#">Casner, P. R. (1988) Insulin-glyburide combination therapy for non-insulin-dependent diabetes mellitus: a long-term double-blind, placebo-controlled trial.</a> Clin Pharmacol Ther 44(5): 594-603                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Cavender Matthew, A, Scirica Benjamin, M, Raz, Itamar et al. (2016) Cardiovascular Outcomes of Patients in SAVOR-TIMI 53 by Baseline Hemoglobin A1c.</a> The American journal of medicine 129(3): 340e1-8                                                                                                                            | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Cavender Matthew, A, White William, B, Jarolim, Petr et al. (2017) Serial Measurement of High-Sensitivity Troponin I and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus in the EXAMINE Trial (Examination of Cardiovascular Outcomes With Alogliptin Versus Standard of Care).</a> Circulation 135(20): 1911-1921 | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Cavender, Matthew A, White, William B, Liu, Yuyin et al. (2018) Total cardiovascular events analysis of the EXAMINE trial in patients with type 2 diabetes and recent acute coronary syndrome.</a> Clinical cardiology 41(8): 1022-1027                                                                                              | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Cefalu, W.T., Bell-Farrow, A., Wang, Z.Q. et al. (1998) Effect of glipizide GITS on insulin sensitivity, glycemic indices, and abdominal fat composition in NIDDM.</a> Drug Development Research 44(1): 1-7                                                                                                                          | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Cefalu, W.T., Leiter, L.A., Debruin, T.W. et al. (2012) Dapagliflozin treatment for type 2 diabetes mellitus patients with comorbid cardiovascular disease and hypertension.</a> Diabetes 61(suppl1): a271                                                                                                                           | - Conference abstract                                                                                  |
| <a href="#">Cefalu, William T, Schneider, David J, Carlson, Harold E et al. (2002) Effect of combination glipizide GITS/metformin on fibrinolytic and metabolic parameters in poorly controlled type 2 diabetic subjects.</a> Diabetes care 25(12): 2123-8                                                                                       | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Ceriello, A, Ofstad A, P, Zwiener, I et al. (2020) Empagliflozin reduced long-term HbA1c variability and cardiovascular death: insights from the EMPA-REG OUTCOME trial.</a> Cardiovascular Diabetology 19(1): 176                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information |

| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                                                        |
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| <a href="#">Cha, Ashley S, Chen, Yilin, Fazioli, Katherine et al. (2021) Microvascular Benefits of New Antidiabetic Agents: A Systematic Review and Network Meta-Analysis of Kidney Outcomes.</a><br>The Journal of clinical endocrinology and metabolism 106(4): 1225-1234                                                  | - Systematic review used as source of primary studies                                                                                                                                         |
| <a href="#">Chacra, A R, Tan, G H, Apanovitch, A et al. (2009) Saxagliptin added to a submaximal dose of sulphonylurea improves glycaemic control compared with uptitration of sulphonylurea in patients with type 2 diabetes: a randomised controlled trial.</a> International journal of clinical practice 63(9): 1395-406 | - Comparator in study does not match that specified in this review protocol                                                                                                                   |
| <a href="#">Chacra, A., Gantz, I., Mendizabal, G. et al. (2017) A randomised, double-blind, trial of the safety and efficacy of omarigliptin (a once-weekly DPP-4 inhibitor) in subjects with type 2 diabetes and renal impairment.</a> Int J Clin Pract 71(6): e12955                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                 |
| <a href="#">Chai, Shangyu, Zhang, Ruya, Carr, Richard David et al. (2023) Impact of dipeptidyl peptidase-4 inhibitors on glucose-dependent insulintropic polypeptide in type 2 diabetes mellitus: a systematic review and meta-analysis.</a> Frontiers in endocrinology 14: 1203187                                          | - No relevant outcomes reported                                                                                                                                                               |
| <a href="#">Chai, Shangyu, Zhang, Ruya, Zhang, Ye et al. (2022) Effect of dipeptidyl peptidase-4 inhibitors on postprandial glucagon level in patients with type 2 diabetes mellitus: A systemic review and meta-analysis.</a> Frontiers in endocrinology 13: 994944                                                         | - Study design not relevant to this review protocol<br><i>Systematic review. Treatment period for inclusion not specified.</i>                                                                |
| <a href="#">Chalhoub, J.M., Grantham, T., Andrawes, S.A. et al. (2023) EFFICACY AND SAFETY OF SEMAGLUTIDE IN NONALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW.</a> Gastroenterology 164(6supplement): 1055                                                                                                              | - Conference abstract                                                                                                                                                                         |
| <a href="#">Chalmers, J., Marre, M., De Galan, B. et al. (2009) The efficacy of lowering HbA1c with a gliclazide modified release-based intensive glucose lowering regimen in the advance trial.</a> Diabetologia 52(s1): 354                                                                                                | - Comparator in study does not match that specified in this review protocol<br><i>Compares to usual care which is not a comparator specified in the protocol</i><br><br>- Conference abstract |

| Study                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                               |
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| <a href="#">Chalmoukou, Konstantina, Polyzos, Dimitris, Manta, Eleni et al. (2022) Renal outcomes associated with glucose-lowering agents: Systematic review and meta-analysis of randomized outcome trials.</a> European journal of internal medicine 97: 78-85                                            | - Population not relevant to this review protocol                                                                                                    |
| <a href="#">Chan, J C N, Scott, R, Arjona Ferreira, J C et al. (2008) Safety and efficacy of sitagliptin in patients with type 2 diabetes and chronic renal insufficiency.</a> Diabetes, obesity & metabolism 10(7): 545-55                                                                                 | - Comparator in study does not match that specified in this review protocol                                                                          |
| <a href="#">Chan, J. C., Chan, K. W., Ho, L. L. et al. (1998) An Asian multicenter clinical trial to assess the efficacy and tolerability of acarbose compared with placebo in type 2 diabetic patients previously treated with diet.</a> Asian Acarbose Study Group. Diabetes Care 21(7): 1058-61          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Chan, Juliana C N, Paldanius, Paivi M, Mathieu, Chantal et al. (2021) Early combination therapy delayed treatment escalation in newly diagnosed young-onset type 2 diabetes: A subanalysis of the VERIFY study.</a> Diabetes, obesity & metabolism 23(1): 245-251                               | - Comparator in study does not match that specified in this review protocol                                                                          |
| <a href="#">Charbonnel, Bernard, DeFronzo, Ralph, Davidson, Jaime et al. (2010) Pioglitazone use in combination with insulin in the prospective pioglitazone clinical trial in macrovascular events study (PROactive19).</a> The Journal of clinical endocrinology and metabolism 95(5): 2163-71            | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                                                                       |
| <a href="#">Chavez, A.O., Guardado-Mendoza, R., Varvel, S. et al. (2015) Differential effect of pioglitazone, exenatide, and combination of pioglitazone and exenatide on plasma metabolites in type 2 diabetes.</a> Diabetes 64(suppl1): a529                                                              | - Conference abstract                                                                                                                                |
| <a href="#">Chehrehgosha, H., Sohrabi, M. R., Ismail-Beigi, F. et al. (2021) Empagliflozin Improves Liver Steatosis and Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease and Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial.</a> Diabetes Therapy 12(3): 843-861 | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Chen, Chengcong, Peng, Hong, Li, Mingzhu et al. (2021) Patients With Type 2 Diabetes Mellitus and Heart Failure Benefit More From</a>                                                                                                                                                           | - Systematic review used as source of primary studies                                                                                                |

| Study                                                                                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                 |
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| <a href="#">Sodium-Glucose Cotransporter 2 Inhibitor: A Systematic Review and Meta-Analysis.</a> Frontiers in endocrinology 12: 664533                                                                                                                                                                                                                                                                      |                                                                                                        |
| <a href="#">Chen, Han, Li, Xin-Zhu, Chen, Jia-Qing et al. (2023) Comparative efficacy and safety of glucagon-like peptide 1 receptor agonists for the treatment of type 2 diabetes: A network meta-analysis.</a> Medicine 102(27): e34122                                                                                                                                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Chen, Kuanlin, Zhuo, Tiejun, Wang, Jian et al. (2018) Saxagliptin Upregulates Nesfatin-1 Secretion and Ameliorates Insulin Resistance and Metabolic Profiles in Type 2 Diabetes Mellitus.</a> Metabolic syndrome and related disorders 16(7): 336-341                                                                                                                                           | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Chen, Mao-Bing, Wang, Hua, Cui, Wei-Yan et al. (2021) Effect of SGLT inhibitors on weight and lipid metabolism at 24 weeks of treatment in patients with diabetes mellitus: A systematic review and network meta-analysis.</a> Medicine 100(6): e24593                                                                                                                                          | - Systematic review used as source of primary studies                                                  |
| <a href="#">Chen, S. and Li, T. (2023) Meta-Analysis on the Effect and Safety of Dapagliflozin on Blood Sugar Fluctuation in Patients with Type 2 Diabetes Mellitus.</a> Latin American Journal of Pharmacy 42(12): 2600-2604                                                                                                                                                                               | - SR - does not match PICO<br><i>Appears that the follow-up times were between 8 and 24 weeks only</i> |
| <a href="#">Chen, X., Wang, J., Huang, X. et al. (2015) Effects of vildagliptin vs. saxagliptin on daily acute glucose fluctuation in chinese type 2 diabetics inadequately controlled with dual combination of metformin and sulphonylurea.</a> Diabetes 64(suppl1): a318                                                                                                                                  | - Conference abstract                                                                                  |
| <a href="#">Chen, Xi, Xu, Yongping, Zhang, Jianhua et al. (2021) Exenatide Twice Daily Plus Glargine Versus Aspart 70/30 Twice Daily in Patients With Type 2 Diabetes With Inadequate Glycemic Control on Premixed Human Insulin and Metformin.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 27(8): 790-797 | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Chen, Xiutian, Wang, Jiali, Lin, Yongda et al. (2023) Cardiovascular outcomes and safety of SGLT2 inhibitors in chronic kidney disease patients.</a> Frontiers in endocrinology 14: 1236404                                                                                                                                                                                                     | - Population not relevant to this review protocol                                                      |

| Study                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                        |
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| <a href="#">Chen, Y., Ning, G., Wang, C. et al. (2013) Efficacy and safety of linagliptin monotherapy in Asian patients with inadequately controlled type 2 diabetes mellitus: A 24-Week, randomized, phase III clinical trial.</a> Diabetes 62(suppl1): a302                                                                                  | - Conference abstract                                                                         |
| <a href="#">Chen, Yu-Hsin; Tarng, Der-Cherng; Chen, Harn-Shen (2016) Renal Outcomes of Pioglitazone Compared with Acarbose in Diabetic Patients: A Randomized Controlled Study.</a> PloS one 11(11): e0165750                                                                                                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Chenchula, Santenna; Varthya, Shoban Babu; Padmavathi, R (2022) Rationality, Efficacy, Tolerability of Empagliflozin Plus Linagliptin Combination for the Management of Type 2 Diabetes Mellitus: A Systematic Review of Randomized Controlled Trials and Observational Studies.</a> Current diabetes reviews 18(4): e100921196392 | - Systematic review used as source of primary studies                                         |
| <a href="#">Cheng, A., Sloan, L., Carlson, A. et al. (2023) COMPARISON OF SECOND-GENERATION BASAL INSULIN ANALOGS GLARGINE 300 U/ML AND DEGLUDEC 100 U/ML IN INSULIN-NAIVE PEOPLE WITH T2DM AND RENAL IMPAIRMENT: TRENT CLINICAL TRIAL DESIGN.</a> Diabetes Technology and Therapeutics 25(supplement2): a131                                  | - Conference abstract                                                                         |
| <a href="#">Cheng, Haiyan, Zhang, Zhou, Zhang, Bing et al. (2022) Enhancement of Impaired Olfactory Neural Activation and Cognitive Capacity by Liraglutide, but Not Dapagliflozin or Acarbose, in Patients With Type 2 Diabetes: A 16-Week Randomized Parallel Comparative Study.</a> Diabetes care 45(5): 1201-1210                          | - Trial that has a treatment and follow up period of less than 24 weeks                       |
| <a href="#">Cheng, P.-C., Hsu, S.-R., Kuo, J.-F. et al. (2019) Comparing the effect of dipeptidyl-peptidase 4 inhibitors and sulfonylureas on albuminuria in patients with newly diagnosed type 2 diabetes mellitus: A prospective open-label study.</a> Journal of Clinical Medicine 8(10): 1715                                              | - Study design not relevant to this review protocol                                           |
| <a href="#">Cheng, Qian, Zou, Shupeng, Feng, Chengyang et al. (2023) Effect of ertugliflozin on renal function and cardiovascular outcomes in patients with type 2 diabetes mellitus: A systematic review and meta-analysis.</a> Medicine 102(10): e33198                                                                                      | - Systematic review used as source of primary studies                                         |

| Study                                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                 |
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| <a href="#">Cherney David Z, I, Zinman, Bernard, Inzucchi Silvio, E et al. (2017) Effects of empagliflozin on the urinary albumin-to-creatinine ratio in patients with type 2 diabetes and established cardiovascular disease: an exploratory analysis from the EMPA-REG OUTCOME randomised, placebo-controlled trial. The lancet. Diabetes &amp; endocrinology 5(8): 610-621</a> | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Cherney, D. Z. I., Ferrannini, E., Umpierrez, G. E. et al. (2021) Efficacy and safety of sotagliflozin in patients with type 2 diabetes and severe renal impairment. Diabetes Obes Metab 23(12): 2632-2642</a>                                                                                                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Cherney, D., Charbonnel, B., Cosentino, F. et al. (2021) POS-354 WORSENING KIDNEY DISEASE INFLUENCES THE EFFICACY OF ERTUGLIFLOZIN ON GLUCOSURIA-MEDIATED ENDPOINTS BUT DOES NOT INFLUENCE THE EFFICACY ON NATRIURESIS-RELATED ENDPOINTS: PRESPECIFIED ANALYSES FROM VERTIS CV. Kidney International Reports 6(4supplement): 154-s155</a>                             | - Conference abstract                                                                                  |
| <a href="#">Cherney, D.Z.I., Segar, M., Pandey, A. et al. (2021) Mediators of the effect of ertugliflozin on a composite kidney outcome in patients with type 2 diabetes and atherosclerotic cardiovascular disease: Analyses from VERTIS CV. European Heart Journal 42(suppl1): 2925</a>                                                                                         | - Conference abstract                                                                                  |
| <a href="#">Cherney, David Z I, Cosentino, Francesco, Dagogo-Jack, Samuel et al. (2021) Ertugliflozin and Slope of Chronic eGFR: Prespecified Analyses from the Randomized VERTIS CV Trial. Clinical journal of the American Society of Nephrology : CJASN 16(9): 1345-1354</a>                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Cherney, David Z I, Dagogo-Jack, Samuel, Cosentino, Francesco et al. (2022) Heart and Kidney Outcomes With Ertugliflozin in People with Non-albuminuric Diabetic Kidney Disease: A post hoc Analysis from the Randomized VERTIS CV Trial. Kidney international reports 7(8): 1782-1792</a>                                                                            | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                         |
| <a href="#">Cherney, David, Lund, Soren S, Perkins, Bruce A et al. (2016) The effect of sodium glucose cotransporter 2 inhibition with empagliflozin on microalbuminuria and macroalbuminuria in</a>                                                                                                                                                                              | - Review article but not a systematic review<br><i>Pooled analysis of multiple RCTs</i>                |



| Study                                                                                                                                                                                                                                                    | Reason                                                                                                                                                                                                                                  |
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| <a href="#">patients with type 2 diabetes.</a> Diabetologia 59(9): 1860-70                                                                                                                                                                               |                                                                                                                                                                                                                                         |
| <a href="#">Cherrington, Andrea L, Krause-Steinrauf, Heidi, Bebu, Ionut et al. (2021) Study of emotional distress in a comparative effectiveness trial of diabetes treatments: Rationale and design.</a> Contemporary clinical trials 107: 106366        | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                  |
| <a href="#">Chertow, G., Vart, P., Jongs, N. et al. (2021) The effect of dapagliflozin in patients with eGFR &lt;30 mL/min/1.73m2: Findings from the DAPA-CKD trial.</a> Nephrology 26(suppl2): 33-34                                                    | - Conference abstract<br><br>- Duplicate reference                                                                                                                                                                                      |
| <a href="#">Chertow, G.M., Vart, P., Jongs, N. et al. (2021) POS-831 THE EFFECT OF DAPAGLIFLOZIN IN PATIENTS WITH eGFR &lt;30 mL/min/1.73m2: FINDINGS FROM THE DAPA-CKD TRIAL.</a> Kidney International Reports 6(4supplement): 361-s362                 | - Conference abstract                                                                                                                                                                                                                   |
| <a href="#">Chertow, Glenn M, Vart, Priya, Jongs, Niels et al. (2022) Quetelet (body mass) index and effects of dapagliflozin in chronic kidney disease.</a> Diabetes, obesity & metabolism 24(5): 827-837                                               | - Population not relevant to this review protocol<br><br><i>People with and without type 2 diabetes</i>                                                                                                                                 |
| <a href="#">Chiang, B; Chew, D P; De Pasquale, C G (2022) Outcome trial data on sodium glucose cotransporter-2 inhibitors: Putting clinical benefits and risks in perspective.</a> International journal of cardiology 349: 96-98                        | - Study design not relevant to this review protocol                                                                                                                                                                                     |
| <a href="#">Chiasson, J. L., Josse, R. G., Hunt, J. A. et al. (1994) The efficacy of acarbose in the treatment of patients with non-insulin-dependent diabetes mellitus. A multicenter controlled clinical trial.</a> Ann Intern Med 121(12): 928-35     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                           |
| <a href="#">Chien, M. N., Lee, C. C., Chen, W. C. et al. (2011) Effect of sitagliptin as add-on therapy in elderly type 2 diabetes patients with inadequate glycemic control in Taiwan.</a> Int J Gerontol 5(2): 103-6                                   | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares to usual care (which includes a range of antihyperglycaemic drugs but no specified treatment that can be specified for the analysis)</i> |
| <a href="#">Chilton, Robert, Tikkanen, Ilkka, Hehnke, Uwe et al. (2017) Impact of empagliflozin on blood pressure in dipper and non-dipper patients with type 2 diabetes mellitus and hypertension.</a> Diabetes, obesity & metabolism 19(11): 1620-1624 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                  |



| Study                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                 |
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| <a href="#">Chiquette, Elaine, Toth, Peter P, Ramirez, Gilbert et al. (2012) Treatment with exenatide once weekly or twice daily for 30 weeks is associated with changes in several cardiovascular risk markers.</a> Vascular health and risk management 8: 621-9              | - Comparator in study does not match that specified in this review protocol                                                                                                            |
| <a href="#">Cho, Kyu Yong, Nakamura, Akinobu, Omori, Kazuno et al. (2021) Favorable effect of sodium-glucose cotransporter 2 inhibitor, dapagliflozin, on non-alcoholic fatty liver disease compared with pioglitazone.</a> Journal of diabetes investigation 12(7): 1272-1277 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                 |
| <a href="#">Cho, Y. M., Deerochanawong, C., Seekaew, S. et al. (2020) Efficacy and safety of gemigliptin as add-on therapy to insulin, with or without metformin, in patients with type 2 diabetes mellitus (ZEUS II study).</a> Diabetes Obes Metab 22(1): 123-127            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                          |
| <a href="#">Choe, EY, Cho, Y, Choi, Y et al. (2014) The Effect of DPP-4 Inhibitors on Metabolic Parameters in Patients with Type 2 Diabetes.</a> Diabetes & metabolism journal 38(3): 211-219                                                                                  | - Study design not relevant to this review protocol<br><i>retrospective, non randomised observational study design</i>                                                                 |
| <a href="#">Choi, D., Kim, S. K., Choi, S. H. et al. (2004) Preventative effects of rosiglitazone on restenosis after coronary stent implantation in patients with type 2 diabetes.</a> Diabetes Care 27(11): 2654-60                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                          |
| <a href="#">Chou, H. S., Palmer, J. P., Jones, A. R. et al. (2008) Initial treatment with fixed-dose combination rosiglitazone/glimepiride in patients with previously untreated type 2 diabetes.</a> Diabetes Obes Metab 10(8): 626-37                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                          |
| <a href="#">Christensen, Mette M H, Brasch-Andersen, Charlotte, Green, Henrik et al. (2011) The pharmacogenetics of metformin and its impact on plasma metformin steady-state levels and glycosylated hemoglobin A1c.</a> Pharmacogenetics and genomics 21(12): 837-50         | - Secondary publication of an included study that does not provide any additional relevant information                                                                                 |
| <a href="#">Chuang, S. M., Wang, C. H., Liu, S. C. et al. (2020) Efficacy of combination of insulin glargine with either metformin or sulfonylurea in patients with poorly controlled type 2 diabetes.</a>                                                                     | - Comparator in study does not match that specified in this review protocol<br><i>A specific sulfonylurea is not specified in the control arm therefore, this cannot be put into a</i> |

| Study                                                                                                                                                                                                                                                                                                                                 | Reason                                                                                                 |
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| International Journal of Gerontology 14(2): 138-141                                                                                                                                                                                                                                                                                   | <i>group for the analysis and therefore is not included</i>                                            |
| <a href="#">Chung, S.M., Moon, J.S., Hong, J.H. et al. (2023) Comparison of the effects of gemigliptin versus glimepiride on cardiac function in patients with type 2 diabetes uncontrolled with metformin: The gemi-heart study.</a> Diabetes, Obesity and Metabolism                                                                | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Cinti, Francesca, Leccisotti, Lucia, Sorice, Gian Pio et al. (2023) Dapagliflozin treatment is associated with a reduction of epicardial adipose tissue thickness and epicardial glucose uptake in human type 2 diabetes.</a> Cardiovascular diabetology 22(1): 349                                                       | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Cintra, Riobaldo M, Nogueira, Ana Claudia, Bonilha, Isabella et al. (2021) Glucose-lowering Drugs and Hospitalization for Heart Failure: A Systematic Review and Additive-effects Network Meta-analysis With More Than 500 000 Patient-years.</a> The Journal of clinical endocrinology and metabolism 106(10): 3060-3067 | - Population not relevant to this review protocol                                                      |
| <a href="#">Clegg Lindsay, E, Penland Robert, C, Bachina, Srinivas et al. (2019) Effects of exenatide and open-label SGLT2 inhibitor treatment, given in parallel or sequentially, on mortality and cardiovascular and renal outcomes in type 2 diabetes: insights from the EXSCEL trial.</a> Cardiovascular diabetology 18(1): 138   | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Coelho, C., Dobbie, L.J., Crane, J. et al. (2023) The Impact of the Combination of the GLP-1 Analogue Liraglutide (Victoza) and Laparoscopic Adjustable Gastric Banding (LAGB) on Diabetes Control: A Pilot Randomised Double-Blind Placebo-Controlled Trial (GLIDE).</a> Obesity Facts 16(supplement1): 241              | - Study does not contain an intervention relevant to this review protocol                              |
| <a href="#">Coelho, Francisca Dos Santos, Borges-Canha, Marta, von Hafe, Madalena et al. (2021) Effects of sodium-glucose co-transporter 2 inhibitors on liver parameters and steatosis: A meta-analysis of randomized clinical trials.</a> Diabetes/metabolism research and reviews 37(6): e3413                                     | - Systematic review used as source of primary studies                                                  |
| <a href="#">Coniff, R. F.; Shapiro, J. A.; Seaton, T. B. (1994) Long-term efficacy and safety of acarbose in the treatment of obese subjects with non-insulin-</a>                                                                                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                            |
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| <a href="#">dependent diabetes mellitus</a> . Arch Intern Med 154(21): 2442-8                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                   |
| <a href="#">Coniff, R. F., Shapiro, J. A., Seaton, T. B. et al. (1995) Multicenter, placebo-controlled trial comparing acarbose (BAY g 5421) with placebo, tolbutamide, and tolbutamide-plus-acarbose in non-insulin-dependent diabetes mellitus</a> . Am J Med 98(5): 443-51                                                                                                                       | - Data not reported in an extractable format or a format that can be analysed                                                                                                                     |
| <a href="#">Coniff, R. F., Shapiro, J. A., Seaton, T. B. et al. (1995) A double-blind placebo-controlled trial evaluating the safety and efficacy of acarbose for the treatment of patients with insulin-requiring type II diabetes</a> . Diabetes Care 18(7): 928-32                                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                     |
| <a href="#">Cooper M, E, Rosenstock, J, Kadowaki, T et al. (2020) Cardiovascular and kidney outcomes of linagliptin treatment in older people with type 2 diabetes and established cardiovascular disease and/or kidney disease: A prespecified subgroup analysis of the randomized, placebo-controlled CARMELINA trial</a> . Diabetes, Obesity and Metabolism 22(7): 1062-1073                     | - Secondary publication of an included study that does not provide any additional relevant information                                                                                            |
| <a href="#">Cooper, Mark E, Perkovic, Vlado, McGill, Janet B et al. (2015) Kidney Disease End Points in a Pooled Analysis of Individual Patient-Level Data From a Large Clinical Trials Program of the Dipeptidyl Peptidase 4 Inhibitor Linagliptin in Type 2 Diabetes</a> . American journal of kidney diseases : the official journal of the National Kidney Foundation 66(3): 441-9              | - Study design<br><i>IPD using pooled data from 12 RCTs. Study periods ranged from 12 to 72 weeks (5 studies were &lt; 24 weeks). Unclear if systematic search for relevant studies was done.</i> |
| <a href="#">Corbin, K.D., Dagogo-Jack, S., Cannon, C.P. et al. (2021) Long-term effects of ertugliflozin (ERTU) on liver enzymes and indices in patients with type 2 diabetes: Analyses from VERTIS CV</a> . Diabetologia 64(supplement1): 218-s219                                                                                                                                                 | - Conference abstract                                                                                                                                                                             |
| <a href="#">Corbin, Karen D, Dagogo-Jack, Samuel, Cannon, Christopher P et al. (2023) Cardiorenal outcomes by indices of liver steatosis and fibrosis in individuals with type 2 diabetes and atherosclerotic cardiovascular disease: Analyses from VERTIS CV, a randomized trial of the sodium-glucose cotransporter-2 inhibitor ertugliflozin</a> . Diabetes, obesity & metabolism 25(3): 758-766 | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Post-hoc analysis</i>                                                                |
| <a href="#">Cosentino, F., Cherney, D.Z.I., Dagogo-Jack, S. et al. (2023) Effect of ertugliflozin on body</a>                                                                                                                                                                                                                                                                                       | - Conference abstract                                                                                                                                                                             |

| Study                                                                                                                                                                                                                                                                                                       | Reason                                                                                                 |
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| <a href="#">weight and HbA1c by baseline BMI: observations from VERTIS CV</a> . Diabetologia 66(supplement1): 349                                                                                                                                                                                           |                                                                                                        |
| <a href="#">Coskun, T., Rosenstock, J., Frias, J. et al. (2023) Retatrutide, a triple GIP/GLP-1/glucagon receptor agonist, provides robust HbA1c and body weight reductions to people with type 2 diabetes: a 36-week, phase 2 study</a> . Diabetologia 66(supplement1): 31                                 | - Conference abstract                                                                                  |
| <a href="#">Costa, B. and Piñol, C. (1997) Acarbose in ambulatory treatment of non-insulin-dependent diabetes mellitus associated to imminent sulfonylurea failure: a randomised-multicentric trial in primary health-care</a> . Diabetes and Acarbose Research Group. Diabetes Res Clin Pract 38(1): 33-40 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Coward, Kevin and Carris, Nicholas W (2021) Evaluation of cardiovascular and renal outcomes with ertugliflozin: what is the VERdict from the VERTIS-CV trial?</a> . Expert opinion on pharmacotherapy 22(2): 163-165                                                                            | - Review article but not a systematic review                                                           |
| <a href="#">Cukierman-Yaffe, Tali, Gerstein Hertz, C., Colhoun Helen, M et al. (2020) Effect of dulaglutide on cognitive impairment in type 2 diabetes: an exploratory analysis of the REWIND trial</a> . The Lancet. Neurology 19(7): 582-590                                                              | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">D'Emden, M., Udell, J., Zinman, B. et al. (2019) Qualifying Event Proximity, Cardiovascular Risk, and Benefit of Empagliflozin in Patients with Type 2 Diabetes and Stable Atherosclerosis in the EMPA-REG OUTCOME Trial</a> . Heart Lung and Circulation 28(supplement4): 314                  | - Conference abstract                                                                                  |
| <a href="#">Da Porto, Andrea, Casarsa, Viviana, Colussi, Gianluca et al. (2020) Dulaglutide reduces binge episodes in type 2 diabetic patients with binge eating disorder: A pilot study</a> . Diabetes & metabolic syndrome 14(4): 289-292                                                                 | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Dagenais, Gilles R, Ryden, Lars, Leiter, Lawrence A et al. (2020) Total cardiovascular or fatal events in people with type 2 diabetes and cardiovascular risk factors treated with dulaglutide in the REWIND trial: a post hoc analysis</a> . Cardiovascular diabetology 19(1): 199             | - Secondary publication of an included study that does not provide any additional relevant information |

| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                                                                                                                   |
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| <a href="#">Dagogo-Jack, S., Pratley, R.E., Cherney, D. et al. (2021) Glycemic efficacy and safety of ertugliflozin (ERTU) in patients with type 2 diabetes (T2D) and chronic kidney disease stage 3 (CKD 3): An analysis from VERTIS CV. Diabetes 70(suppl1)</a>                                                            | - Conference abstract                                                                                                                                                                                                                                    |
| <a href="#">Dagogo-Jack, S., Cannon, CP, Cherney, DZI et al. (2022) Cardiorenal outcomes with ertugliflozin by baseline glucose-lowering agent: an analysis from VERTIS CV. Diabetes, obesity &amp; metabolism</a>                                                                                                           | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                   |
| <a href="#">Dagogo-Jack, Samuel, Pratley, Richard E, Cherney, David Z I et al. (2021) Glycemic efficacy and safety of the SGLT2 inhibitor ertugliflozin in patients with type 2 diabetes and stage 3 chronic kidney disease: an analysis from the VERTIS CV randomized trial. BMJ open diabetes research &amp; care 9(1)</a> | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                   |
| <a href="#">Dahlqvist, Sofia, Ahlen, Elsa, Filipsson, Karin et al. (2018) Variables associated with HbA1c and weight reductions when adding liraglutide to multiple daily insulin injections in persons with type 2 diabetes (MDI Liraglutide trial 3). BMJ open diabetes research &amp; care 6(1): e000464</a>              | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                   |
| <a href="#">Dailey, G. E., Noor, M. A., Park, J. S. et al. (2004) Glycemic control with glyburide/metformin tablets in combination with rosiglitazone in patients with type 2 diabetes: a randomized, double-blind trial. Am J Med 116(4): 223-9</a>                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                            |
| <a href="#">Dailey, George E, Dex, Terry A, Roberts, Michelle et al. (2019) Efficacy and safety of lixisenatide as add-on therapy to basal insulin in older adults with type 2 diabetes in the GetGoal-O Study. Journal of diabetes 11(12): 971-981</a>                                                                      | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis based on whether or T2DM was controlled with basal insulin (with our without other oral antidiabetic medication).</i> |
| <a href="#">Dailey, George, Bajaj, Harpreet S, Dex, Terry et al. (2019) Post hoc efficacy and safety analysis of insulin glargine/lixisenatide fixed- ratio combination in North American patients compared with the rest of world. BMJ open diabetes research &amp; care 7(1): e000581</a>                                  | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                 |
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| <a href="#">Daniels, G H, Hegedus, L, Marso, S P et al. (2015) LEADER 2: baseline calcitonin in 9340 people with type 2 diabetes enrolled in the Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results (LEADER) trial: preliminary observations. Diabetes, obesity &amp; metabolism 17(5): 477-86</a>                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Dargie, H. J., Hildebrandt, P. R., Riegger, G. A. et al. (2007) A randomized, placebo-controlled trial assessing the effects of rosiglitazone on echocardiographic function and cardiac status in type 2 diabetic patients with New York Heart Association Functional Class I or II Heart Failure. J Am Coll Cardiol 49(16): 1696-704</a>                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Davidson, J. A., McMorn, S. O., Waterhouse, B. R. et al. (2007) A 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study of the efficacy and tolerability of combination therapy with rosiglitazone and sulfonylurea in African American and Hispanic American patients with type 2 diabetes inadequately controlled with sulfonylurea monotherapy. Clin Ther 29(9): 1900-14</a> | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Davidson, Jaime A, Manghi, Federico Perez, Yu, Maria et al. (2016) EFFICACY AND SAFETY OF DULAGLUTIDE IN HISPANIC/LATINO PATIENTS WITH TYPE 2 DIABETES IN THE AWARD CLINICAL PROGRAM. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 22(12): 1406-1414</a>                                                               | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                         |
| <a href="#">Davidson, Michael H, Beam, Craig A, Haffner, Steven et al. (2010) Pioglitazone versus glimepiride on coronary artery calcium progression in patients with type 2 diabetes mellitus: a secondary end point of the CHICAGO study. Arteriosclerosis, thrombosis, and vascular biology 30(9): 1873-6</a>                                                                                                               | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Davies, M., Bode, B.W., Kushner, R.F. et al. (2014) Liraglutide 3.0 mg for weight management in obese/overweight adults with type 2 diabetes: Results from the Scale<sup>TM</sup> diabetes 56-week randomized, double-blind, placebo-controlled trial. Diabetes 63(suppl1): a26</a>                                                                                                                                | - Conference abstract                                                                                  |



| Study                                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                 |
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| <a href="#">Davies, M., Faerch, L., Goldman, B. et al. (2022) Associations between weight loss and glycaemic control with onceweekly semaglutide 1.0 mg and 2.4 mg in the STEP 2 trial.</a> Diabetologia 65(supplement1): 254-s255                                                                                                                                                | - Conference abstract                                                                                  |
| <a href="#">Davies, M., Faerch, L., Jeppesen, O.K. et al. (2021) Efficacy and Safety of Semaglutide 2.4 MG Once- Weekly in Adults With Overweight or Obesity and Type 2 Diabetes (STEP 2).</a> Journal of the Endocrine Society 5(supplement1): a10-a11                                                                                                                           | - Conference abstract                                                                                  |
| <a href="#">Davies, M.J.; Bergenstal, R.; Bode, B. (2016) Erratum: NN8022-1922 Study Group. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE Diabetes randomized clinical trial (JAMA - Journal of the American Medical Association (2015) 314:7 (687-699)).</a> JAMA - Journal of the American Medical Association 315(1): 90              | - Study design not relevant to this review protocol<br><i>Erratum only</i>                             |
| <a href="#">Davies, M.J., Donnelly, R.D., Barnett, A.H. et al. (2009) Exenatide compared with long acting insulin to achieve glycaemic control with minimal weight gain in patients with Type 2 diabetes mellitus (T2D): Results of the Helping Evaluate Exenatide in patients with diabetes compared to long-acting insulin (HEELA) study.</a> Diabetic Medicine 26(suppl1): 4-5 | - Conference abstract                                                                                  |
| <a href="#">Davies, Melanie J, Russell-Jones, David, Barber, Thomas M et al. (2019) Glycaemic benefit of iGlarLixi in insulin-naïve type 2 diabetes patients with high HbA1c or those with inadequate glycaemic control on two oral antihyperglycaemic drugs in the LixiLan-O randomized trial.</a> Diabetes, obesity & metabolism 21(8): 1967-1972                               | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Davis, Stephen N (2014) Canagliflozin versus glimepiride treatment in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU trial).</a> Expert review of clinical pharmacology 7(1): 21-3                                                                                                                                                  | - Commentary only                                                                                      |
| <a href="#">Davis, T.M.E., Maxwell, S., Chan, C. et al. (2024) The effect of empagliflozin and fenofibrate therapies, alone and in combination, on the serum urate concentration in hyperuricaemic type 2 diabetes.</a> Diabetes, Obesity and Metabolism 26(1): 385-388                                                                                                           | - No relevant outcomes reported                                                                        |



| Study                                                                                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                         |
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| <a href="#">Davis, Timothy M E, Giczewska, Anna, Lokhnygina, Yuliya et al. (2022) Effect of race on cardiometabolic responses to once-weekly exenatide: insights from the Exenatide Study of Cardiovascular Event Lowering (EXSCEL).</a> Cardiovascular diabetology 21(1): 116                                                                                                                                                                   | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i> |
| <a href="#">De Almeida, V.F., Pratley, R.E., Aroda, V.R. et al. (2019) Efficacy and safety of semaglutide 0.5 MG vs dulaglutide 1.5 MG once weekly in type 2 diabetes: A post HOC analysis of sustain 7.</a> Diabetology and Metabolic Syndrome 11(supplement1)                                                                                                                                                                                  | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i> |
| <a href="#">De Block, Christophe E M, Dirinck, Eveline, Verhaegen, Ann et al. (2022) Efficacy and safety of high-dose glucagon-like peptide-1, glucagon-like peptide-1/glucose-dependent insulinotropic peptide, and glucagon-like peptide-1/glucagon receptor agonists in type 2 diabetes.</a> Diabetes, obesity & metabolism 24(5): 788-805                                                                                                    | - Systematic review used as source of primary studies                          |
| <a href="#">De Buitelir, C, O' Connor, E, Satti, M M et al. (2021) Efficacy and safety of a sodium-glucose co-transporter-2 inhibitor versus placebo as an add-on therapy for people with type 2 diabetes inadequately treated with metformin and a dipeptidyl peptidase-4 inhibitor: a systematic review and meta-analysis of randomised controlled trials.</a> Diabetic medicine : a journal of the British Diabetic Association 38(2): e14409 | - Systematic review used as source of primary studies                          |
| <a href="#">de Carvalho, Luiz Sergio Fernandes, Nogueira, Ana Claudia Cavalcante, Bonilha, Isabella et al. (2022) Glucose-Lowering and the Risk of Cardiovascular Events With Antidiabetic Therapies: A Systematic Review and Additive-Effects Network Meta-Analysis.</a> Frontiers in cardiovascular medicine 9: 876795                                                                                                                         | - Systematic review used as source of primary studies                          |
| <a href="#">De Ferrari, Gaetano M, Stevens, Susanna R, Ambrosio, Giuseppe et al. (2020) Low-density lipoprotein cholesterol treatment and outcomes in patients with type 2 diabetes and established cardiovascular disease: Insights from TECOS.</a> American heart journal 220: 82-88                                                                                                                                                           | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i> |
| <a href="#">de Jager, Jolien, Kooy, Adriaan, Lehert, Philippe et al. (2010) Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo</a>                                                                                                                                                                                                                                      | - No relevant outcomes reported                                                |

| Study                                                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                              |
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| <a href="#">controlled trial</a> . BMJ (Clinical research ed.) 340: c2181                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                     |
| <a href="#">de Mesquita, Yasmin Luz Lima, Pera Calvi, Izabela, Reis Marques, Isabela et al. (2023) Efficacy and safety of the dual GIP and GLP-1 receptor agonist tirzepatide for weight loss: a meta-analysis of randomized controlled trials</a> . International journal of obesity (2005) 47(10): 883-892                                                                                                 | - Systematic review used as source of primary studies                                                                                                               |
| <a href="#">de Ranitz-Greven, Wendela Lucia, Beulens, Joline Wilhelma Johanna, Hoeks, Lette Birgit Elisabeth Anne et al. (2014) Patients with type 2 diabetes mellitus failing on oral agents and starting once daily insulin regimen; a small randomized study investigating effects of adding vildagliptin</a> . BMC research notes 7: 579                                                                 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                             |
| <a href="#">de Wit, H. M., Vervoort, G. M., Jansen, H. J. et al. (2014) Liraglutide reverses pronounced insulin-associated weight gain, improves glycaemic control and decreases insulin dose in patients with type 2 diabetes: a 26 week, randomised clinical trial (ELEGANT)</a> . Diabetologia 57(9): 1812-9                                                                                              | - Comparator in study does not match that specified in this review protocol<br><i>Compares to usual care which is not specified as a comparison in the protocol</i> |
| <a href="#">DeFronzo, R., Burant, C., Fleck, P. et al. (2009) Effect of alogliptin combined with pioglitazone on glycaemic control in metformin-treated patients with type 2 diabetes</a> . Diabetologia 52(s1): 295                                                                                                                                                                                         | - Conference abstract                                                                                                                                               |
| <a href="#">Dei Cas, A., Spigoni, V., Cito, M. et al. (2017) Vildagliptin, but not glibenclamide, increases circulating endothelial progenitor cell number: A 12-month randomized controlled trial in patients with type 2 diabetes</a> . Cardiovasc Diabetol 16(1): 27                                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                       |
| <a href="#">Dekkers, Ilona A, Bizino, Maurice B, Paiman, Elisabeth H M et al. (2021) The Effect of Glycemic Control on Renal Triglyceride Content Assessed by Proton Spectroscopy in Patients With Type 2 Diabetes Mellitus: A Single-Center Parallel-Group Trial</a> . Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation 31(6): 611-619 | - Secondary publication of an included study that does not provide any additional relevant information<br><br>- Post-hoc analysis of included study                 |
| <a href="#">Del Parigi, Angelo, Tang, Wenbo, Liu, Dacheng et al. (2019) Machine Learning to Identify Predictors of Glycemic Control in Type 2</a>                                                                                                                                                                                                                                                            | - Study design not relevant to this review protocol                                                                                                                 |

| Study                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                           |
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| <a href="#">Diabetes: An Analysis of Target HbA1c Reduction Using Empagliflozin/Linagliptin Data.</a><br>Pharmaceutical medicine 33(3): 209-217                                                                                                                                                                                  | <i>Pooled data from 2 studies and applied machine learning to identify factors that predict glycaemic control</i>                                                |
| <a href="#">Del Prato, S., Camisasca, R., Wilson, C. et al. (2013) Durability of the efficacy and safety of alogliptin compared to glipizide over 2 years when used in combination with metformin.</a><br>Diabetologia 56(suppl1): 52-s53                                                                                        | - Conference abstract<br><br>- Study design not relevant to this review protocol                                                                                 |
| <a href="#">Del Prato, S., Kahn, S.E., Pavo, I. et al. (2022) Efficacy and Safety of Tirzepatide versus Insulin Glargine in Patients with Type 2 Diabetes and Increased Cardiovascular Risk (SURPASS-4).</a><br>Diabetologie und Stoffwechsel 17(supplement1): 20-s21                                                            | - Conference abstract                                                                                                                                            |
| <a href="#">Delivanis, DA and Montori, VM (2015) In type 2 diabetes, saxagliptin increased HF hospitalizations, regardless of history of HF or CKD.</a> ACP journal club 162(8): 1-1                                                                                                                                             | - Commentary only                                                                                                                                                |
| <a href="#">Della Pepa, Giuseppe, Russo, Marco, Vitale, Marilena et al. (2021) Pioglitazone even at low dosage improves NAFLD in type 2 diabetes: clinical and pathophysiological insights from a subgroup of the TOSCA.IT randomised trial.</a><br>Diabetes research and clinical practice 178: 108984                          | - Comparator in study does not match that specified in this review protocol                                                                                      |
| <a href="#">Deng, Manjun, Wen, Yonghao, Yan, JingXin et al. (2023) Comparative effectiveness of multiple different treatment regimens for nonalcoholic fatty liver disease with type 2 diabetes mellitus: a systematic review and Bayesian network meta-analysis of randomised controlled trials.</a><br>BMC medicine 21(1): 447 | - Population not relevant to this review protocol                                                                                                                |
| <a href="#">Deng, Rui, Mei, Kaibo, Song, Tiangang et al. (2024) First-line treatment with sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide-1 receptor agonists in type 2 diabetic population at low risk of cardiovascular disease: a meta-analysis.</a> Frontiers in endocrinology 15: 1289643               | - Systematic review used as source of primary studies                                                                                                            |
| <a href="#">Deng, X. L., Ma, R., Zhu, H. X. et al. (2017) Short article: a randomized-controlled study of sitagliptin for treating diabetes mellitus complicated by nonalcoholic fatty liver disease.</a><br>Eur J Gastroenterol Hepatol 29(3): 297-301                                                                          | - Comparator in study does not match that specified in this review protocol<br><br><i>Diet and exercise which was not stated as a comparator in the protocol</i> |

| Study                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                 |
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| <a href="#">Derosa, G., Cicero, A. F. G., Franzetti, I. G. et al. (2013) Effects of exenatide and metformin in combination on some adipocytokine levels: A comparison with metformin monotherapy. Can J Physiol Pharmacol 91(9): 724-732</a>                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Derosa, G., Cicero, A. F., Gaddi, A. V. et al. (2005) Long-term effects of glimepiride or rosiglitazone in combination with metformin on blood pressure control in type 2 diabetic patients affected by the metabolic syndrome: a 12-month, double-blind, randomized clinical trial. Clin Ther 27(9): 1383-91</a> | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Derosa, G., D'Angelo, A., Fogari, E. et al. (2007) Effects of nateglinide and glibenclamide on prothrombotic factors in naive type 2 diabetic patients treated with metformin: a 1-year, double-blind, randomized clinical trial. Intern Med 46(22): 1837-1846</a>                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Derosa, G., D'Angelo, A., Salvadeo, S. A. et al. (2009) Modulation of adipokines and vascular remodelling markers during OGTT with acarbose or pioglitazone treatment. Biomed Pharmacother 63(10): 723-33</a>                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Derosa, G., Maffioli, P., D'Angelo, A. et al. (2011) Acarbose on insulin resistance after an oral fat load: a double-blind, placebo controlled study. J Diabetes Complications 25(4): 258-66</a>                                                                                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Derosa, G., Maffioli, P., Salvadeo, S. A. et al. (2010) Exenatide versus glibenclamide in patients with diabetes. Diabetes Technol Ther 12(3): 233-40</a>                                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Derosa, G., Mugellini, A., Ciccarelli, L. et al. (2003) Comparison of glycaemic control and cardiovascular risk profile in patients with type 2 diabetes during treatment with either repaglinide or metformin. Diabetes Res Clin Pract 60(3): 161-9</a>                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Derosa, G., Mugellini, A., Ciccarelli, L. et al. (2003) Comparison between repaglinide and glimepiride in patients with type 2 diabetes mellitus: a one-year, randomized, double-blind assessment of metabolic parameters and cardiovascular risk factors. Clin Ther 25(2): 472-84</a>                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                 |
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| <a href="#">Derosa, Giuseppe, Franzetti, Ivano G, Querci, Fabrizio et al. (2013) Variation in inflammatory markers and glycemic parameters after 12 months of exenatide plus metformin treatment compared with metformin alone: a randomized placebo-controlled trial. Pharmacotherapy 33(8): 817-26</a>                                                            | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Derosa, Giuseppe, Ragonesi, Pietro D, Carbone, Anna et al. (2013) RETRACTED: Evaluation of the positive effects on insulin-resistance and beta-cell measurements of vildagliptin in addition to metformin in type 2 diabetic patients. Pharmacological research 73: 20-6</a>                                                                            | - Not a peer-reviewed publication                                                                      |
| <a href="#">Desai, M., Merton, K., Davies, M.J. et al. (2016) Canagliflozin provides greater improvement in risk factors of metabolic syndrome (MetS) versus glimepiride in patients with type 2 diabetes and MetS on background metformin. Diabetologia 59(1supplement1): 340-s341</a>                                                                             | - Conference abstract                                                                                  |
| <a href="#">Deshmukh, V., Blonde, L., Belousova, L. et al. (2019) Liraglutide as add-on to sodium-glucose cotransporter-2 inhibitors in patients with inadequately controlled type 2 diabetes (LIRA-ADD2SGLT2i): A 26-week, randomized, double-blind, placebo-controlled trial. Indian Journal of Endocrinology and Metabolism 23(7supplement): 16-s17</a>          | - Conference abstract                                                                                  |
| <a href="#">Deshmukh, Vaishali, Sathyanarayana, Srikanta, Menon, Shalini et al. (2015) Safety and efficacy of initial combination of linagliptin and metformin in patients with type 2 diabetes: A subgroup analysis of Indian patients from a randomized, double-blind, placebo-controlled study. Indian journal of endocrinology and metabolism 19(2): 256-61</a> | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Deshpande, Radhika, Patel, Raj, Regmi, Manjari R et al. (2023) Safety outcomes of sodium-glucose cotransporter-2 inhibitors in patients with type 2 diabetes and other risk factors for cardiovascular disease: a systematic review and meta-analysis. Cardiovascular endocrinology &amp; metabolism 12(2): e0284</a>                                   | - Systematic review used as source of primary studies                                                  |
| <a href="#">DeVries, J Hans, Desouza, Cyrus, Bellary, Srikanth et al. (2018) Achieving glycaemic control without weight gain, hypoglycaemia, or gastrointestinal adverse events in type 2</a>                                                                                                                                                                       | - Secondary publication of an included study that does not provide any additional relevant information |

| Study                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                           |
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| <a href="#">diabetes in the SUSTAIN clinical trial programme</a> . Diabetes, obesity & metabolism 20(10): 2426-2434                                                                                                                                                                                               |                                                                                                                                                  |
| <a href="#">DeVries, J. H., Bain, S. C., Rodbard, H. W. et al. (2012) Sequential intensification of metformin treatment in type 2 diabetes with liraglutide followed by randomized addition of basal insulin prompted by A1C targets</a> . Diabetes Care 35(7): 1446-54                                           | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares insulin to the same treatment without insulin</i> |
| <a href="#">Dhatariya, K., Bain, S.C., Pratley, R.E. et al. (2017) Exploring the impact of liraglutide on diabetic foot ulcers on subjects with type 2 diabetes and increased risk of cardiovascular events: Results from the LEADER trial</a> . Diabetologia 60(1supplement1): 465                               | - Conference abstract                                                                                                                            |
| <a href="#">Dhatariya, Ketan, Bain Stephen, C, Buse John, B et al. (2018) The Impact of Liraglutide on Diabetes-Related Foot Ulceration and Associated Complications in Patients With Type 2 Diabetes at High Risk for Cardiovascular Events: Results From the LEADER Trial</a> . Diabetes care 41(10): 2229-2235 | - Additional outcomes relevant to living guideline work                                                                                          |
| <a href="#">Diallo, A, Carlos-Bolumbu, M, Renard, E et al. (2022) Large Effect Size in Composite Kidney Outcomes than in Majors Cardiovascular Events of SGLT2 inhibitors compared with GLP-1 RAs: A Pooled Analysis of Type 2 Diabetes Trials</a> . Diabetes, obesity & metabolism                               | - Systematic review used as source of primary studies                                                                                            |
| <a href="#">Diallo, Alhassane; Carlos-Bolumbu, Miguel; Galtier, Florence (2022) Age, sex, race, BMI, and duration of diabetes differences in cardiovascular outcomes with glucose lowering drugs in type 2 diabetes: A systematic review and meta-analysis</a> . EClinicalMedicine 54: 101697                     | - Systematic review used as source of primary studies                                                                                            |
| <a href="#">Diallo, Alhassane; Carlos-Bolumbu, Miguel; Galtier, Florence (2023) Blood pressure-lowering effects of SGLT2 inhibitors and GLP-1 receptor agonists for preventing of cardiovascular events and death in type 2 diabetes: a systematic review and meta-analysis</a> . Acta diabetologica              | - Systematic review used as source of primary studies                                                                                            |
| <a href="#">Ding, Y, Liu, Y, Qu, Y et al. (2022) Efficacy and safety of combination therapy with vildagliptin and metformin vs. metformin monotherapy for Type 2 Diabetes Mellitus therapy: a meta-</a>                                                                                                           | - Systematic review used as source of primary studies                                                                                            |



| Study                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                     |
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| <a href="#">analysis</a> . European review for medical and pharmacological sciences 26(8): 2802-2817                                                                                                                                                                                                                                              |                                                                                                                                                                            |
| <a href="#">Ding, Yanan, Shi, Yufei, Guan, Ruifang et al. (2024) Evaluation and comparison of efficacy and safety of tirzepatide and semaglutide in patients with type 2 diabetes mellitus: A Bayesian network meta-analysis.</a> Pharmacological research 199: 107031                                                                            | - Systematic review used as source of primary studies                                                                                                                      |
| <a href="#">Distiller, L. A., Nortje, H., Wellmann, H. et al. (2014) A 24-week, prospective, randomized, open-label, treat-to-target pilot study of obese type 2 diabetes patients with severe insulin resistance to assess the addition of exenatide on the efficacy of U-500 regular insulin plus metformin.</a> Endocr Pract 20(11): 1143-1150 | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares exenatide to usual care (both groups receive metformin and insulin)</i>     |
| <a href="#">Dobrecky-Mery, Idit and Sommer, Adir (2021) Vildagliptin vs. insulin treatment alone in diabetic acute coronary syndrome patients.</a> Coronary artery disease 32(1): 4-9                                                                                                                                                             | - Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>2 days</i>                                                                               |
| <a href="#">Docherty, Kieran F, Jhund, Pardeep S, Bengtsson, Olof et al. (2020) Effect of Dapagliflozin in DAPA-HF According to Background Glucose-Lowering Therapy.</a> Diabetes care 43(11): 2878-2881                                                                                                                                          | - Subgroup analysis of a trial that was not relevant for inclusion<br><br><i>The original trial was conducted with people who did not necessarily have type 2 diabetes</i> |
| <a href="#">Doehner, Wolfram, Erdmann, Erland, Cairns, Richard et al. (2012) Inverse relation of body weight and weight change with mortality and morbidity in patients with type 2 diabetes and cardiovascular co-morbidity: an analysis of the PROactive study population.</a> International journal of cardiology 162(1): 20-6                 | - Post-hoc analysis of included study                                                                                                                                      |
| <a href="#">Doni, Katharina, Buhn, Stefanie, Weise, Alina et al. (2022) Safety of dipeptidyl peptidase-4 inhibitors in older adults with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials.</a> Therapeutic advances in drug safety 13: 20420986211072383                                                    | - Systematic review used as source of primary studies                                                                                                                      |
| <a href="#">Dou, J., Ma, J., Liu, J. et al. (2017) Efficacy and safety of saxagliptin plus metformin as initial therapy in patients with type 2 diabetes.</a> Diabetes 66(supplement1): a327                                                                                                                                                      | - Conference abstract                                                                                                                                                      |
| <a href="#">Drent, M. L., Tollefsen, A. T., Heusden, F. H. et al. (2002) Dose-dependent efficacy of miglitol.</a>                                                                                                                                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                              |



| Study                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                       |
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| <a href="#">an alpha-glucosidase inhibitor, in type 2 diabetic patients on diet alone: results of a 24-week double-blind placebo-controlled study</a> . Diab Nutr Metab 15(3): 152-9                                                                                                                                                |                                                                                                                                                              |
| <a href="#">Du, J., Liang, L., Fang, H. et al. (2017) Efficacy and safety of saxagliptin compared with acarbose in Chinese patients with type 2 diabetes mellitus uncontrolled on metformin monotherapy: results of a Phase IV open-label randomized controlled study (the SMART study)</a> . Diabetes Obes Metab 19(11): 1513-1520 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                |
| <a href="#">Duan, Kaixin, Yan, Xiaolu, Gao, Zhe et al. (2022) Effect of glucagon-like peptide-1 receptor agonists on fat distribution in patients with type 2 diabetes: A systematic review and meta-analysis</a> . Journal of diabetes investigation 13(7): 1149-1160                                                              | - Study design not relevant to this review protocol<br><i>Systematic review excluded due to not matching protocol (no minimum study duration specified).</i> |
| <a href="#">Dungan, K.M.; Povedano, S.T.; Forst, T. (2014) Erratum: Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial (Lancet (2014) 384 (1349-1357))</a> . The Lancet 384(9951): 1348                   | - Study design not relevant to this review protocol<br><i>Erratum only</i>                                                                                   |
| <a href="#">Duo, Yanbei, Gao, Junxiang, Yuan, Tao et al. (2023) Effect of sodium-glucose cotransporter 2 inhibitors on the rate of decline in kidney function: A systematic review and meta-analysis</a> . Journal of diabetes 15(1): 58-70                                                                                         | - Study design not relevant to this review protocol<br><i>Systematic review nit matching protocol (minimum trial duration 12 weeks).</i>                     |
| <a href="#">Duran-Garcia, S, Lee, J, Yki-Jarvinen, H et al. (2016) Efficacy and safety of linagliptin as add-on therapy to basal insulin and metformin in people with Type 2 diabetes</a> . Diabetic medicine : a journal of the British Diabetic Association 33(7): 926-33                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                                       |
| <a href="#">Dutta, Deep, Harish, B G, Anne, Beatrice et al. (2023) Role of novel sodium glucose co-transporter-2 inhibitor enavogliflozin in type-2 diabetes: A systematic review and meta-analysis</a> . Diabetes & metabolic syndrome 17(8): 102816                                                                               | - Study does not contain an intervention relevant to this review protocol                                                                                    |
| <a href="#">Dutta, Deep, Surana, Vineet, Singla, Rajiv et al. (2021) Efficacy and safety of novel twincretin tirzepatide a dual GIP and GLP-1 receptor agonist in the management of type-2 diabetes:</a>                                                                                                                            | - Systematic review used as source of primary studies                                                                                                        |

| Study                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                                                                                                     |
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| <a href="#">A Cochrane meta-analysis</a> . Indian journal of endocrinology and metabolism 25(6): 475-489                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                            |
| <a href="#">Ebato, C., Shimizu, T., Arakawa, M. et al. (2009) Effect of sulfonylureas on switching to insulin therapy (twice-daily biphasic insulin aspart 30): comparison of twice-daily biphasic insulin aspart 30 with or without glimepiride in type 2 diabetic patients poorly controlled with sub-maximal glimepiride</a> . Diabetes Res Clin Pract 86(1): 31-6          | - Comparator in study does not match that specified in this review protocol<br><br><i>Comparison not possible on a drug level (drugs available to both arms include metformin and alpha glucosidase inhibitors but doesn't specify which ones are provided and to who)</i> |
| <a href="#">Eeley, E A, Stratton, I M, Hadden, D R et al. (1996) UKPDS 18: estimated dietary intake in type 2 diabetic patients randomly allocated to diet, sulphonylurea or insulin therapy. UK Prospective Diabetes Study Group</a> . Diabetic medicine : a journal of the British Diabetic Association 13(7): 656-62                                                        | - Study design not relevant to this review protocol                                                                                                                                                                                                                        |
| <a href="#">Eghbali, Maryam, Alaei-Shahmiri, Fariba, Hashemi-Madani, Nahid et al. (2024) Glucagon-Like Peptide 1 (GLP-1) Receptor Variants and Glycemic Response to Liraglutide: A Pharmacogenetics Study in Iranian People with Type 2 Diabetes Mellitus</a> . Advances in therapy 41(2): 826-836                                                                             | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                |
| <a href="#">Ejiri, K., Miyoshi, T., Kihara, H. et al. (2020) Effect of Luseogliflozin on Heart Failure With Preserved Ejection Fraction in Patients With Diabetes Mellitus</a> . J Am Heart Assoc 9(16): e015103                                                                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                              |
| <a href="#">Ekholm, Ella, Hansen, Lars, Johnsson, Eva et al. (2017) COMBINED TREATMENT WITH SAXAGLIPTIN PLUS DAPAGLIFLOZIN REDUCES INSULIN LEVELS BY INCREASED INSULIN CLEARANCE AND IMPROVES beta-CELL FUNCTION</a> . Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 23(3): 258-265 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                     |
| <a href="#">El-Naggar, Abdel Rahman, Zaafar, Dalia, Elyamany, Mohammed et al. (2019) The Role of Vildagliptin in Treating Hypertension Through Modulating Serum VEGF in Diabetic Hypertensive Patients</a> . Journal of cardiovascular pharmacology and therapeutics 24(3): 254-261                                                                                            | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2                                                                                                                       |
| <a href="#">Eldor, Roy, Francis, Bruce H, Fleming, Alexander et al. (2023) Oral insulin (ORMD-0801) in type 2 diabetes mellitus: A dose-finding</a>                                                                                                                                                                                                                            | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                   |
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| <a href="#">12-week randomized placebo-controlled study.</a><br>Diabetes, obesity & metabolism 25(4): 943-952                                                                                                                                                                                                                                                        |                                                                                                                                                                          |
| <a href="#">Elharram, M, Sharma, A, White, W et al. (2020) Timing of randomization after an acute coronary syndrome in patients with type 2 diabetes mellitus.</a> American Heart Journal 229: 40-51                                                                                                                                                                 | - Post-hoc analysis of included study                                                                                                                                    |
| <a href="#">Elhini, Sahar Hossam, Hussien, Amal K, Omran, Ahmed Abd Elsamie et al. (2021) Efficacy and safety profile of sitagliptin, vildagliptin, and metformin in newly diagnosed type 2 diabetic subjects.</a> Clinical and experimental pharmacology & physiology 48(12): 1589-1602                                                                             | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Eliashewitz, Freddy G, Calvo, Cesar, Valbuena, Humberto et al. (2006) Therapy in type 2 diabetes: insulin glargine vs. NPH insulin both in combination with glimepiride.</a> Archives of medical research 37(4): 495-501                                                                                                                                 | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Elrakaybi, A., Laubner, K., Zhou, Q. et al. (2022) Mechanistic insights into the effects of empagliflozin in patients with type 2 diabetes and heart failure.</a> Diabetologia 65(supplement1): 24                                                                                                                                                       | - Conference abstract                                                                                                                                                    |
| <a href="#">Emara, A.N., Wadie, M., Mansour, N.O. et al. (2023) The clinical outcomes of dapagliflozin in patients with acute heart failure: A randomized controlled trial (DAPA-RESPONSE-AHF).</a> European Journal of Pharmacology 961: 176179                                                                                                                     | - Population not relevant to this review protocol                                                                                                                        |
| <a href="#">Emery, Alexandra, Ye, Chang, Choi, Haysook et al. (2019) INTERMITTENT INTENSIVE INSULIN THERAPY FOR TYPE 2 DIABETES: EFFECTS ON HYPOGLYCEMIA, WEIGHT GAIN, AND QUALITY OF LIFE OVER 2 YEARS.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 25(9): 899-907 | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Engelbrechtsen, L., Iepsen, E. P. W., Andersson, E. A. et al. (2016) Weight loss and weight maintenance obtained with or without GLP-1 analogue treatment decrease branched chain amino acid levels.</a> Metabolomics 12(12): 181                                                                                                                        | - Comparator in study does not match that specified in this review protocol<br><i>Usual care (weight loss intervention)</i>                                              |

| Study                                                                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                    |
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| <a href="#">Erdmann, Erland, Charbonnel, Bernard, Wilcox Robert, G et al. (2007) Pioglitazone use and heart failure in patients with type 2 diabetes and preexisting cardiovascular disease: data from the PROactive study (PROactive 08).</a> Diabetes care 30(11): 2773-8                                                                                               | - Secondary publication of an included study that does not provide any additional relevant information                    |
| <a href="#">Erdmann, Erland, Dormandy John, A, Charbonnel, Bernard et al. (2007) The effect of pioglitazone on recurrent myocardial infarction in 2,445 patients with type 2 diabetes and previous myocardial infarction: results from the PROactive (PROactive 05) Study.</a> Journal of the American College of Cardiology 49(17): 1772-80                              | - Secondary publication of an included study that does not provide any additional relevant information                    |
| <a href="#">Erdmann, Erland, Spanheimer, Robert, Charbonnel, Bernard et al. (2010) Pioglitazone and the risk of cardiovascular events in patients with Type 2 diabetes receiving concomitant treatment with nitrates, renin-angiotensin system blockers, or insulin: results from the PROactive study (PROactive 20).</a> Journal of diabetes 2(3): 212-20                | - Secondary publication of an included study that does not provide any additional relevant information                    |
| <a href="#">Escobar, Carlos, Barrios, Vivencio, Cosin, Juan et al. (2021) SGLT2 inhibitors and GLP1 agonists administered without metformin compared to other glucose-lowering drugs in patients with type 2 diabetes mellitus to prevent cardiovascular events: A systematic review.</a> Diabetic medicine : a journal of the British Diabetic Association 38(3): e14502 | - Trial that has a treatment and follow up period of less than 24 weeks                                                   |
| <a href="#">Espeland M, A, Pratley R, E, Rosenstock, J et al. (2020) Cardiovascular outcomes and safety with linagliptin, a dipeptidyl peptidase-4 inhibitor, compared with the sulphonylurea glimepiride in older people with type 2 diabetes: a subgroup analysis of the randomized CAROLINA trial.</a> Diabetes, obesity & metabolism                                  | - Secondary publication of an included study that does not provide any additional relevant information                    |
| <a href="#">Esposito, K., Giugliano, D., Nappo, F. et al. (2004) Regression of carotid atherosclerosis by control of postprandial hyperglycemia in type 2 diabetes mellitus.</a> Circulation 110(2): 214-9                                                                                                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Esposito, Katherine, Ciotola, Miryam, Maiorino, Maria Ida et al. (2008) Addition of neutral protamine lispro insulin or insulin glargine to oral type 2 diabetes regimens for patients with suboptimal glycemic control: a randomized trial.</a> Annals of internal medicine 149(8): 531-9                                                                    | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i> |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                            |
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| <a href="#">Esteghamati, Alireza, Zamanzadeh, Mehran, Malek, Mojtaba et al. (2023) Efficacy and Safety of a Biosimilar Liraglutide (Melitide R) Versus the Reference Liraglutide (Victoza R) in People with Type 2 Diabetes Mellitus: A Randomized, Double-Blind, Noninferiority Clinical Trial.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders                                    | - Comparator in study does not match that specified in this review protocol                                       |
| <a href="#">Eurich, Dean T, Tsuyuki, Ross T, Majumdar, Sumit R et al. (2009) Metformin treatment in diabetes and heart failure: when academic equipoise meets clinical reality.</a> Trials 10: 12                                                                                                                                                                                                                              | - No relevant outcomes reported                                                                                   |
| <a href="#">Evans, Marc, Kuodi, Paul, Akunna, Chisom Joyqueenet et al. (2023) Cardiovascular and renal outcomes of GLP-1 receptor agonists vs. DPP-4 inhibitors and basal insulin in type 2 diabetes mellitus: A systematic review and meta-analysis.</a> Diabetes & vascular disease research 20(6): 14791641231221740                                                                                                        | - Study design not relevant to this review protocol                                                               |
| <a href="#">Fanghanel, G, Sanchez-Reyes, L, Trujillo, C et al. (1996) Metformin's effects on glucose and lipid metabolism in patients with secondary failure to sulfonylureas.</a> Diabetes care 19(11): 1185-9                                                                                                                                                                                                                | - Trial that has a treatment and follow up period of less than 24 weeks                                           |
| <a href="#">Farcasiu, Eugenia, Ivanyi, Tibor, Mozejko-Pastewka, Barbara et al. (2011) Efficacy and safety of prandial premixed therapy using insulin lispro mix 50/50 3 times daily compared with progressive titration of insulin lispro mix 75/25 or biphasic insulin aspart 70/30 twice daily in patients with type 2 diabetes mellitus: a randomized, 16-week, open-label study.</a> Clinical therapeutics 33(11): 1682-93 | - Comparator in study does not match that specified in this review protocol<br><i>Insulin compared to insulin</i> |
| <a href="#">Farrash, S., Aleisa, L., Alhazmi, N. et al. (2023) Investigating Semaglutide in Adult Patients on Body Weight Compared with Other GLP-1 Drugs.</a> International Journal of Pharmaceutical Research and Allied Sciences 12(4): 95-103                                                                                                                                                                              | - Systematic review used as source of primary studies                                                             |
| <a href="#">Feng, Kent Y, Li, JingWei, Ianus, Juliana et al. (2021) Reasons for hospitalizations in patients with type 2 diabetes in the CANVAS programme: A secondary analysis.</a> Diabetes, obesity & metabolism 23(12): 2707-2715                                                                                                                                                                                          | - Study design not relevant to this review protocol<br><i>Post hoc</i>                                            |
| <a href="#">Feng, X., Gu, Q., Gao, G. et al. (2020) The plasma levels of atrial natriuretic peptide and</a>                                                                                                                                                                                                                                                                                                                    | - Study does not contain an intervention relevant to this review protocol                                         |

| Study                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                               |
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| <a href="#">brain natriuretic peptide in type 2 diabetes treated with sodium-glucose cotransporter-2 inhibitor.</a> Annales d Endocrinologie 81(5): 476-481                                                                                                                                                              | <i>Class level rather than drug level interventions</i>                                                              |
| <a href="#">Ferdinand, Keith C, Dunn, Julia, Nicolay, Claudia et al. (2023) Weight-dependent and weight-independent effects of dulaglutide on blood pressure in patients with type 2 diabetes.</a> Cardiovascular diabetology 22(1): 49                                                                                  | - Review article but not a systematic review<br><i>Pooled analysis of five trials already included in the review</i> |
| <a href="#">Ferdinand, Keith C; Seman, Leo; Salsali, Afshin (2018) Design of a 24-week trial of empagliflozin once daily in hypertensive black/African American patients with type 2 diabetes mellitus.</a> Current medical research and opinion 34(2): 361-367                                                          | - Study design not relevant to this review protocol<br><i>Protocol only</i>                                          |
| <a href="#">Ferrannini, E., Boss, A., Dex, T. et al. (2021) Fixed-ratio combination of insulin glargine plus lixisenatide (iGlarLixi) improves beta cell function in people with type 2 diabetes.</a> Diabetologia 64(supplement1): 261-s262                                                                             | - Conference abstract                                                                                                |
| <a href="#">Ferrannini, E, Betteridge D, J, Dormandy J, A et al. (2011) High-density lipoprotein-cholesterol and not HbA1c was directly related to cardiovascular outcome in PROactive.</a> Diabetes, obesity & metabolism 13(8): 759-64                                                                                 | - Secondary publication of an included study that does not provide any additional relevant information               |
| <a href="#">Ferrannini, Ele, Baldi, Simona, Scozzaro, Tiziana et al. (2022) Fasting Substrate Concentrations Predict Cardiovascular Outcomes in the CANagliflozin cardioVascular Assessment Study (CANVAS).</a> Diabetes care 45(8): 1893-1899                                                                           | - Secondary publication of an included study that does not provide any additional relevant information               |
| <a href="#">Ferrannini, G., Fortin, E., Mellbin, L. et al. (2023) Empagliflozin improves insulin sensitivity in patients with a recent coronary syndrome and newly detected dysglycaemia.</a> Diabetologia 66(supplement1): 243-s244                                                                                     | - Conference abstract                                                                                                |
| <a href="#">Ferrannini, Giulia, Gerstein, Hertznel, Colhoun, Helen Martina et al. (2021) Similar cardiovascular outcomes in patients with diabetes and established or high risk for coronary vascular disease treated with dulaglutide with and without baseline metformin.</a> European heart journal 42(26): 2565-2573 | - Secondary publication of an included study that does not provide any additional relevant information               |



| Study                                                                                                                                                                                                                                                                                                          | Reason                                                                                                     |
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| <a href="#">Ferrari, Filipe, Martins, Vitor M, Scheffel, Rafael S et al. (2021) The Role of Sodium-Glucose Cotransporter-2 Inhibitors in Patients With Heart Failure, Regardless of Diabetes Status: Focus on Cardiovascular Disease. The Annals of pharmacotherapy 55(10): 1267-1275</a>                      | - Study design not relevant to this review protocol<br><i>Post hoc analysis</i>                            |
| <a href="#">Ferreira J, P, Mehta, C, Sharma, A et al. (2020) Alogliptin after acute coronary syndrome in patients with type 2 diabetes: A renal function stratified analysis of the EXAMINE trial. BMC Medicine 18(1): 165</a>                                                                                 | - Secondary publication of an included study that does not provide any additional relevant information     |
| <a href="#">Ferreira, Joao Pedro, Fitchett, David, Ofstad, Anne Pernille et al. (2020) Empagliflozin for Patients With Presumed Resistant Hypertension: A Post Hoc Analysis of the EMPA-REG OUTCOME Trial. American journal of hypertension 33(12): 1092-1101</a>                                              | - Secondary publication of an included study that does not provide any additional relevant information     |
| <a href="#">Ferreira, Joao Pedro, Kraus, Bettina Johanna, Zwiener, Isabella et al. (2021) Cardio/Kidney Composite End Points: A Post Hoc Analysis of the EMPA-REG OUTCOME Trial. Journal of the American Heart Association 10(7): e020053</a>                                                                  | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                             |
| <a href="#">Ferreira, Joao Pedro, Oliveira, Ana Cristina, Saraiva, Francisca A et al. (2021) Sodium-glucose co-transporter inhibitors in insulin-treated diabetes: a meta-analysis. European journal of endocrinology 184(6): 783-790</a>                                                                      | - Study design not relevant to this review protocol<br><i>Meta-analysis. Trial duration not specified.</i> |
| <a href="#">Ferreira, Joao Pedro, Rossignol, Patrick, Bakris, George et al. (2021) Body weight changes in patients with type 2 diabetes and a recent acute coronary syndrome: an analysis from the EXAMINE trial. Cardiovascular diabetology 20(1): 187</a>                                                    | - Secondary publication of an included study that does not provide any additional relevant information     |
| <a href="#">Ferreira, Joao Pedro, Saraiva, Francisca, Sharma, Abhinav et al. (2023) Glucagon-like peptide 1 receptor agonists in patients with type 2 diabetes with and without chronic heart failure: A meta-analysis of randomized placebo-controlled outcome trials. Diabetes, obesity &amp; metabolism</a> | - Systematic review used as source of primary studies                                                      |
| <a href="#">Ferreira, Joao Pedro, Verma, Subodh, Fitchett, David et al. (2020) Metabolic syndrome in patients with type 2 diabetes and atherosclerotic cardiovascular disease: a post hoc analyses of</a>                                                                                                      | - Secondary publication of an included study that does not provide any additional relevant information     |



| Study                                                                                                                                                                                                                                                                                                          | Reason                                                                                                 |
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| <a href="#">the EMPA-REG OUTCOME trial.</a> Cardiovascular diabetology 19(1): 200                                                                                                                                                                                                                              |                                                                                                        |
| <a href="#">Ferreira-Hermosillo, Aldo, Molina-Ayala, Mario Antonio, Molina-Guerrero, Diana et al. (2020) Efficacy of the treatment with dapagliflozin and metformin compared to metformin monotherapy for weight loss in patients with class III obesity: a randomized controlled trial.</a> Trials 21(1): 186 | - Study design not relevant to this review protocol<br><i>Protocol only</i>                            |
| <a href="#">Figtree, G., Radholm, K., Barrett, T.D. et al. (2019) EFFECTS OF CANAGLIFLOZIN ON HEART FAILURE OUTCOMES WITH AND WITHOUT PRESERVED EJECTION FRACTION IN TYPE 2 DIABETES: RESULTS FROM THE CANVAS PROGRAM.</a> Journal of the American College of Cardiology 73(9supplement1): 685                 | - Conference abstract                                                                                  |
| <a href="#">Figtree, Gemma A, Radholm, Karin, Barrett, Terrance D et al. (2019) Effects of Canagliflozin on Heart Failure Outcomes Associated With Preserved and Reduced Ejection Fraction in Type 2 Diabetes Mellitus.</a> Circulation 139(22): 2591-2593                                                     | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Filippatos, Gerasimos, Butler, Javed, Farmakis, Dimitrios et al. (2022) Empagliflozin for Heart Failure With Preserved Left Ventricular Ejection Fraction With and Without Diabetes.</a> Circulation 146(9): 676-686                                                                               | - Population not relevant to this review protocol                                                      |
| <a href="#">Finn, A. V., Oh, J. S., Hendricks, M. et al. (2009) Predictive factors for in-stent late loss and coronary lesion progression in patients with type 2 diabetes mellitus randomized to rosiglitazone or placebo.</a> Am Heart J 157(2): 383.e1-8                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Fioretto, P., Del Prato, S., Goldenberg, R. et al. (2018) Efficacy and safety of dapagliflozin in patients with type 2 diabetes and moderate renal impairment (chronic kidney disease Stage 3A): The DERIVE Study.</a> Endocrine Reviews 39(2supplement1)                                          | - Conference abstract                                                                                  |
| <a href="#">Fischer, S., Hanefeld, M., Spengler, M. et al. (1998) European study on dose-response relationship of acarbose as a first-line drug in non-insulin-dependent diabetes mellitus: efficacy and safety of low and high doses.</a> Acta Diabetologica 35(1): 34-40                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                             | Reason                                                                                                 |
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| <a href="#">Fitchett, D., Inzucchi, S., Lachin, J.M. et al. (2016) Effect of empagliflozin on mortality and causes of death in patients with type 2 diabetes at high cardiovascular risk. Canadian Journal of Cardiology 32(10supplement1): 122-s123</a>                                          | - Conference abstract                                                                                  |
| <a href="#">Fitchett, D, Zinman, B, Wanner, C et al. (2016) Heart failure outcomes with empagliflozin in patients with type 2 diabetes at high cardiovascular risk: Results of the EMPA-REG OUTCOME trial. European Heart Journal 37(19): 1526-1534</a>                                           | - Post-hoc analysis of included study                                                                  |
| <a href="#">Fitchett, David, Butler, Javed, van de Borne, Philippe et al. (2018) Effects of empagliflozin on risk for cardiovascular death and heart failure hospitalization across the spectrum of heart failure risk in the EMPA-REG OUTCOME R trial. European heart journal 39(5): 363-370</a> | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Fitchett, David, Inzucchi, Silvio E, Cannon, Christopher P et al. (2019) Empagliflozin Reduced Mortality and Hospitalization for Heart Failure Across the Spectrum of Cardiovascular Risk in the EMPA-REG OUTCOME Trial. Circulation 139(11): 1384-1395</a>                           | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Flint, A., Andersen, G., Hockings, P. et al. (2020) Semaglutide treatment in subjects with NAFLD: Effects assessed by magnetic resonance elastography and magnetic resonance imaging proton density fat fraction. Hepatology 72(1suppl): 1036a</a>                                    | - Conference abstract                                                                                  |
| <a href="#">Fonseca, V., Grunberger, G., Gupta, S. et al. (2003) Addition of nateglinide to rosiglitazone monotherapy suppresses mealtime hyperglycemia and improves overall glycemic control. Diabetes Care 26(6): 1685-90</a>                                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Fonseca, V., Rosenstock, J., Patwardhan, R. et al. (2000) Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus: a randomized controlled trial. JAMA 283(13): 1695-702</a>                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Forst, T., Eriksson, J. W., Strotmann, H. J. et al. (2003) Metabolic effects of mealtime insulin lispro in comparison to glibenclamide in early type 2 diabetes. Exp Clin Endocrinol Diabetes 111(2): 97-103</a>                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                 |
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| <a href="#">Forst, T, Dworak, M, Berndt-Zipfel, C et al. (2013) Effect of vildagliptin compared to glimepiride on postprandial proinsulin processing in the beta cell of patients with type 2 diabetes mellitus.</a> Diabetes, obesity & metabolism 15(6): 576-9                                                                                                 | - Data not reported in an extractable format or a format that can be analysed                          |
| <a href="#">Forst, T, Uhlig-Laske, B, Ring, A et al. (2010) Linagliptin (BI 1356), a potent and selective DPP-4 inhibitor, is safe and efficacious in combination with metformin in patients with inadequately controlled Type 2 diabetes.</a> Diabetic medicine : a journal of the British Diabetic Association 27(12): 1409-19                                 | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Franek, Edward, Gerstein, Hertz C, Riddle, Matthew C et al. (2022) Efficacy and safety outcomes of dulaglutide by baseline HbA1c: A post hoc analysis of the REWIND trial.</a> Diabetes, obesity & metabolism 24(9): 1753-1761                                                                                                                       | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Frias, J. P., Choi, J., Rosenstock, J. et al. (2022) Efficacy and Safety of Once-Weekly Epeglenatide Monotherapy Versus Placebo in Type 2 Diabetes: the AMPLITUDE-M Randomized Controlled Trial.</a> Diabetes care 45(7): 1592-1600                                                                                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Frias, J.P., Rosenstock, J., Rodbard, H.W. et al. (2023) "Surpass(ing)" an era of basal-bolus insulin therapy: tirzepatide vs insulin lispro tid added-on to poorly controlled basal insulintreated type 2 diabetes.</a> Diabetologia 66(supplement1): 5-s6                                                                                          | - Conference abstract                                                                                  |
| <a href="#">Frias, Juan P, Deenadayalan, Srikanth, Erichsen, Lars et al. (2023) Efficacy and safety of co-administered once-weekly cagrilintide 2.4 mg with once-weekly semaglutide 2.4 mg in type 2 diabetes: a multicentre, randomised, double-blind, active-controlled, phase 2 trial.</a> Lancet (London, England) 402(10403): 720-730                       | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Frias, Juan P, Hardy, Elise, Ahmed, Azazuddin et al. (2018) Effects of exenatide once weekly plus dapagliflozin, exenatide once weekly alone, or dapagliflozin alone added to metformin monotherapy in subgroups of patients with type 2 diabetes in the DURATION-8 randomized controlled trial.</a> Diabetes, obesity & metabolism 20(6): 1520-1525 | - Secondary publication of an included study that does not provide any additional relevant information |

| Study                                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                   |
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| <a href="#">Frias, Juan P, Zimmer, Zachary, Lam, Raymond L H et al. (2019) Double-blind, randomized clinical trial assessing the efficacy and safety of early initiation of sitagliptin during metformin uptitration in the treatment of patients with type 2 diabetes: The CompoSIT-M study. Diabetes, obesity &amp; metabolism 21(5): 1128-1135</a>                                         | - Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>20 weeks</i>                                                                           |
| <a href="#">Fritsche, A, Larbig, M, Owens, D et al. (2010) Comparison between a basal-bolus and a premixed insulin regimen in individuals with type 2 diabetes-results of the GINGER study. Diabetes, obesity &amp; metabolism 12(2): 115-23</a>                                                                                                                                              | - Study does not contain an intervention relevant to this review protocol<br><br><i>Includes insulin compared to other types of insulin</i>                              |
| <a href="#">Fuchigami, A., Shigiyama, F., Hirose, T. et al. (2019) Comparing the effects of dapagliflozin and sitagliptin on glucose variability using FGMin patients with type 2 diabetes: the DIVERSITYCVR study. Diabetologia 62(supplement1): 345</a>                                                                                                                                     | - Conference abstract                                                                                                                                                    |
| <a href="#">Fuchigami, A., Shigiyama, F., Kitazawa, T. et al. (2020) Efficacy of dapagliflozin versus sitagliptin on cardiometabolic risk factors in Japanese patients with type 2 diabetes: a prospective, randomized study (DIVERSITY-CVR). Cardiovasc Diabetol 19(1)</a>                                                                                                                   | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Fujioka, K, Brazg, R L, Raz, I et al. (2005) Efficacy, dose-response relationship and safety of once-daily extended-release metformin (Glucophage XR) in type 2 diabetic patients with inadequate glycaemic control despite prior treatment with diet and exercise: results from two double-blind, placebo-controlled studies. Diabetes, obesity &amp; metabolism 7(1): 28-39</a> | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Fukui, Kensuke, Kawahito, Hiroyuki, Wakana, Noriyuki et al. (2015) Dipeptidyl peptidase-4 inhibitor sitagliptin improves pancreatic beta-cell function in hypertensive diabetic patients treated with angiotensin receptor blockers. Journal of the renin-angiotensin-aldosterone system : JRAAS 16(4): 1001-9</a>                                                                | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Fulcher, G., Davies, M., Tsoukas, M. et al. (2018) Effects of canagliflozin on HbA1c and changes in antihyperglycaemic agents in the CANVAS Programme. Diabetologia 61(supplement1): 320-s321</a>                                                                                                                                                                                 | - Conference abstract                                                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                                   |
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| <a href="#">Fulcher, G, Matthews D, R, Perkovic, V et al. (2016) Efficacy and safety of canagliflozin when used in conjunction with incretin-mimetic therapy in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 18(1): 82-91                                                                                                                               | - Post-hoc analysis of included study                                                                                                                                    |
| <a href="#">Fulcher, G, Matthews D, R, Perkovic, V et al. (2015) Efficacy and Safety of Canagliflozin Used in Conjunction with Sulfonylurea in Patients with Type 2 Diabetes Mellitus: A Randomized, Controlled Trial.</a> Diabetes Therapy 6(3): 289-302                                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Furtado Remo H, M, Bonaca Marc, P, Raz, Itamar et al. (2019) Dapagliflozin and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Previous Myocardial Infarction.</a> Circulation 139(22): 2516-2527                                                                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Furtado, Remo H M, Raz, Itamar, Goodrich, Erica L et al. (2022) Efficacy and Safety of Dapagliflozin in Type 2 Diabetes According to Baseline Blood Pressure: Observations From DECLARE-TIMI 58 Trial.</a> Circulation 145(21): 1581-1591                                                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Furumoto, T., Oba, K., Tsutsui, H. et al. (2016) A randomized controlled trial comparing the effects of sitagliptin and glimepiride on endothelial function and metabolic parameters: Sapporo athero-incretin study 1 (SAIS1).</a> PLoS ONE 11(10): e0164255                                                                                                     | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Furusawa, Sho, Nomoto, Hiroshi, Yokoyama, Hiroki et al. (2024) Glycaemic control efficacy of switching from dipeptidyl peptidase-4 inhibitors to oral semaglutide in subjects with type 2 diabetes: A multicentre, prospective, randomized, open-label, parallel-group comparison study (SWITCH-SEMA 2 study).</a> Diabetes, obesity & metabolism 26(3): 961-970 | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Gaal, L., Maislos, M., Schernthaner, G. et al. (2001) Miglitol combined with metformin improves glycaemic control in type 2 diabetes.</a> Diabetes Obes Metab 3(5): 326-31                                                                                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Gager, GM, Gelbenegger, G, Jilma, B et al. (2021) Cardiovascular Outcome in Patients Treated With SGLT2 Inhibitors for Heart Failure: A Meta-Analysis.</a> Frontiers in cardiovascular medicine 8: 691907                                                                                                                                                        | - Population not relevant to this review protocol<br><i>People with heart failure, not just people with type 2 diabetes</i>                                              |

| Study                                                                                                                                                                                                                                                                                                | Reason                                                                                                 |
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| <a href="#">Galeone, F; Fiore, G; Mannucci, E (1999) Medium-term hypoglycaemic effects of two different oral formulations of gliclazide.</a> Diabetic medicine 16(7): 618-619                                                                                                                        | - Commentary only                                                                                      |
| <a href="#">Gallo, S., Charbonnel, B., Goldman, A. et al. (2019) Long-term efficacy and safety of ertugliflozin in patients with type 2 diabetes mellitus inadequately controlled with metformin monotherapy: 104-week VERTIS MET trial.</a> Diabetes, Obesity and Metabolism 21(4): 1027-1036       | - Study design                                                                                         |
| <a href="#">Gallwitz, B, Rosenstock, J, Emser, A et al. (2013) Linagliptin is more effective than glimepiride at achieving a composite outcome of target HbA1c &lt; 7% with no hypoglycaemia and no weight gain over 2 years.</a> International journal of clinical practice 67(4): 317-21           | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Gantz, I., Chen, M., Suryawanshi, S. et al. (2017) A randomized, placebo-controlled study of the cardiovascular safety of the once-weekly DPP-4 inhibitor omarigliptin in patients with type 2 diabetes mellitus.</a> Cardiovasc Diabetol 16(1): 112                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Gantz, I., Okamoto, T., Ito, Y. et al. (2017) A Randomized, Placebo-Controlled Trial Evaluating the Safety and Efficacy of Adding Omarigliptin to Antihyperglycemic Therapies in Japanese Patients with Type 2 Diabetes and Inadequate Glycemic Control.</a> Diabetes Ther 8(4): 793-810 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Gantz, I., Sokolova, L., Jain, L. et al. (2017) Use of Prohibited Medication, a Potentially Overlooked Confounder in Clinical Trials: omarigliptin (Once-weekly DPP-4 Inhibitor) Monotherapy Trial in 18- to 45-year-olds.</a> Clin Ther 39(10): 2024-2037                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Gao, F., Lv, X., Mo, Z. et al. (2020) Efficacy and safety of polyethylene glycol loxenatide as add-on to metformin in patients with type 2 diabetes: A multicentre, randomized, double-blind, placebo-controlled, phase 3b trial.</a> Diabetes, Obesity & Metabolism 22(12): 2375-2383   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Gao, Y., Gao, L., Peng, Y. et al. (2020) Therapeutic effects of the combination of linagliptin and metformin on the treatment of</a>                                                                                                                                                     | - Trial that has a treatment and follow up period of less than 24 weeks                                |



| Study                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                                                                                                      |
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| <a href="#">elderly type 2 diabetes mellitus and influences on serum uric acid, insulin resistance and insulin A cell functions.</a> Acta Medica Mediterranea 36(1): 421-425                                                                                                                                                         |                                                                                                                                                                                                                                                             |
| <a href="#">Garber, A. J., Foley, J. E., Banerji, M. A. et al. (2008) Effects of vildagliptin on glucose control in patients with type 2 diabetes inadequately controlled with a sulphonylurea.</a> Diabetes Obes Metab 10(11): 1047-56                                                                                              | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                     |
| <a href="#">Garber, A. J., Schweizer, A., Baron, M. A. et al. (2007) Vildagliptin in combination with pioglitazone improves glycaemic control in patients with type 2 diabetes failing thiazolidinedione monotherapy: a randomized, placebo-controlled study.</a> Diabetes Obes Metab 9(2): 166-74                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                     |
| <a href="#">Garber, A., Klein, E., Bruce, S. et al. (2006) Metformin-glibenclamide versus metformin plus rosiglitazone in patients with type 2 diabetes inadequately controlled on metformin monotherapy.</a> Diabetes Obes Metab 8(2): 156-63                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                               |
| <a href="#">Garber, A, Henry, R R, Ratner, R et al. (2011) Liraglutide, a once-daily human glucagon-like peptide 1 analogue, provides sustained improvements in glycaemic control and weight for 2 years as monotherapy compared with glimepiride in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 13(4): 348-56 | - Data not reported in an extractable format or a format that can be analysed<br><br><i>102 week extension to Garber 2009. Population comprises treatment naïve (36.5%) and switched from previous treatment (63.5%) - results not reported separately.</i> |
| <a href="#">Garcia-Perez, L.-E., Maldonado, J.M., Ranta, K.T. et al. (2021) Effect of once weekly dulaglutide 3.0 and 4.5 mg in patients with different baseline renal function: Post hoc analysis from the AWARD-11 trial.</a> Diabetologia 64(supplement1): 235                                                                    | - Study design not relevant to this review protocol<br><br><i>Posthoc analysis</i>                                                                                                                                                                          |
| <a href="#">García-Hernández, P, Arechavaleta-Granell Mdel, R, Yamamoto, J et al. (2010) Liraglutide and glimepiride on glycaemic control in type 2 diabetes in the Mexican cohort (LEAD 3).</a> Revista medica del Instituto Mexicano del Seguro Social 48(5): 543-548                                                              | - Study not reported in English                                                                                                                                                                                                                             |
| <a href="#">Garvey, W Timothy, Cohen, Robert M, Butera, Nicole M et al. (2024) Association of Baseline Factors With Glycemic Outcomes in GRADE: A Comparative Effectiveness Randomized Clinical Trial.</a> Diabetes care                                                                                                             | - Data not reported in an extractable format or a format that can be analysed                                                                                                                                                                               |



| Study                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                     |
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| <a href="#">Garvey, W Timothy, Van Gaal, Luc, Leiter, Lawrence A et al. (2018) Effects of canagliflozin versus glimepiride on adipokines and inflammatory biomarkers in type 2 diabetes. Metabolism: clinical and experimental 85: 32-37</a>                                                                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information                                                                                     |
| <a href="#">Gastaldelli, A.; Brodows, R. G.; D'Alessio, D. (2014) The effect of chronic twice daily exenatide treatment on beta-cell function in new onset type 2 diabetes. Clin Endocrinol 80(4): 545-553</a>                                                                                                                                                                      | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Moretto 2008. No relevant outcomes reported.</i>                              |
| <a href="#">Gastaldelli, A., Cusi, K., Lando, L.F. et al. (2023) Effect of Tirzepatide Versus Insulin Degludec on Liver Fat Content and Abdominal Adipose Tissue in Patients with Type 2 Diabetes (SURPASS-3 MRI). Diabetologie und Stoffwechsel 18(supplement1): 17-s18</a>                                                                                                        | - Conference abstract                                                                                                                                                                      |
| <a href="#">Gastaldelli, Amalia, Cusi, Kenneth, Fernandez Lando, Laura et al. (2022) Effect of tirzepatide versus insulin degludec on liver fat content and abdominal adipose tissue in people with type 2 diabetes (SURPASS-3 MRI): a substudy of the randomised, open-label, parallel-group, phase 3 SURPASS-3 trial. The lancet. Diabetes &amp; endocrinology 10(6): 393-406</a> | - Secondary publication of an included study that does not provide any additional relevant information                                                                                     |
| <a href="#">Gautier, J F, Monguillon, P, Verier-Mine, O et al. (2016) Which oral antidiabetic drug to combine with metformin to minimize the risk of hypoglycemia when initiating basal insulin?: A randomized controlled trial of a DPP4 inhibitor versus insulin secretagogues. Diabetes research and clinical practice 116: 26-8</a>                                             | - Study does not contain an intervention relevant to this review protocol<br><i>Included sulfonylureas as a class rather than individual sulfonylureasm that could be compared between</i> |
| <a href="#">Gautier, Thibault, Umpierrez, Guillermo, Renard, Eric et al. (2021) The Differential and Combined Action of Insulin Glargine and Lixisenatide on the Fasting and Postprandial Components of Glucose Control. Journal of diabetes science and technology 15(2): 371-376</a>                                                                                              | - Post-hoc analysis of included study                                                                                                                                                      |
| <a href="#">Gebrie, Desye; Getnet, Desalegn; Manyazewal, Tsegahun (2021) Cardiovascular safety and efficacy of metformin-SGLT2i versus metformin-sulfonylureas in type 2 diabetes: systematic review and meta-analysis of randomized controlled trials. Scientific reports 11(1): 137</a>                                                                                           | - Systematic review used as source of primary studies                                                                                                                                      |
| <a href="#">Geng, Qiang, Hou, Fangjie, Zhang, Yonghuan et al. (2022) Effects of different doses of</a>                                                                                                                                                                                                                                                                              | - Study design not relevant to this review protocol                                                                                                                                        |

| Study                                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                      |
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| <a href="#">canagliflozin on blood pressure and lipids in patients with type 2 diabetes: a meta-analysis.</a> Journal of hypertension 40(5): 996-1001                                                                                                                                                                                                                             | <i>Meta analysis. Minimum duration for included trials is 18 weeks.</i>                                                                     |
| <a href="#">Gentile, S., Turco, S., Guarino, G. et al. (2001) Effect of treatment with acarbose and insulin in patients with non-insulin-dependent diabetes mellitus associated with non-alcoholic liver cirrhosis.</a> Diabetes Obes Metab 3(1): 33-40                                                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                               |
| <a href="#">Gentilella, Raffaella, Romera, Irene, Nicolay, Claudia et al. (2019) Change in HbA1c Across the Baseline HbA1c Range in Type 2 Diabetes Patients Receiving Once-Weekly Dulaglutide Versus Other Incretin Agents.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 10(3): 1113-1125                                          | - Secondary publication of an included study that does not provide any additional relevant information                                      |
| <a href="#">Gentilella, Raffaella, Sesti, Giorgio, Vazquez, Luis et al. (2019) Dulaglutide is an effective treatment for lowering HbA1c in patients with type 2 diabetes regardless of body mass index.</a> Diabetes, obesity & metabolism 21(12): 2660-2666                                                                                                                      | - Study design not relevant to this review protocol<br><i>Pooled analysis of 8 AWARD studies</i>                                            |
| <a href="#">Georgiou, Petros, Shi, Wangpan, Serhiyenia, Tatsiana et al. (2021) Cardiovascular Benefit of Sodium-Glucose Cotransporter-2 (SGLT-2) Inhibitors in Type 2 Diabetes: A Systematic Review.</a> Cureus 13(10): e18485                                                                                                                                                    | - Study design not relevant to this review protocol<br><i>Systematic review. No minimum trial duration specified.</i>                       |
| <a href="#">Gerardo Gonzalez-Gonzalez, Jose, Cesar Solis, Ricardo, Diaz Gonzalez-Colmenero, Alejandro et al. (2022) Effect of metformin on microvascular outcomes in patients with type 2 diabetes: A systematic review and meta-analysis.</a> Diabetes research and clinical practice 186: 109821                                                                                | - Systematic review used as source of primary studies                                                                                       |
| <a href="#">Gerich, J., Raskin, P., Jean-Louis, L. et al. (2005) PRESERVE-beta: two-year efficacy and safety of initial combination therapy with nateglinide or glyburide plus metformin.</a> Diabetes Care 28(9): 2093-9                                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                               |
| <a href="#">Gerstein, H C, Yale, J-F, Harris, S B et al. (2006) A randomized trial of adding insulin glargine vs. avoidance of insulin in people with Type 2 diabetes on either no oral glucose-lowering agents or submaximal doses of metformin and/or sulphonylureas. The Canadian INSIGHT (Implementing New Strategies with Insulin Glargine for Hyperglycaemia Treatment)</a> | - Comparator in study does not match that specified in this review protocol<br><i>Does not outline the drugs for 'conventional therapy'</i> |

| Study                                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                    |
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| <a href="#">Study</a> . Diabetic medicine : a journal of the British Diabetic Association 23(7): 736-42                                                                                                                                                                                                                                                                                        |                                                                                                                                                                           |
| <a href="#">Gerstein, H. C., Ratner, R. E., Cannon, C. P. et al. (2010) Effect of rosiglitazone on progression of coronary atherosclerosis in patients with type 2 diabetes mellitus and coronary artery disease: the assessment on the prevention of progression by rosiglitazone on atherosclerosis in diabetes patients with cardiovascular history trial.</a> Circulation 121(10): 1176-87 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                             |
| <a href="#">Gerstein, H. C., Sattar, N., Rosenstock, J. et al. (2021) Cardiovascular and Renal Outcomes with Efpeglenatide in Type 2 Diabetes.</a> New England Journal of Medicine 385(10): 896-907                                                                                                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                             |
| <a href="#">Gerstein, Hertz C, Hart, Robert, Colhoun, Helen M et al. (2020) The effect of dulaglutide on stroke: an exploratory analysis of the REWIND trial.</a> The lancet. Diabetes & endocrinology 8(2): 106-114                                                                                                                                                                           | - Secondary publication of an included study that does not provide any additional relevant information                                                                    |
| <a href="#">Ghanbari, S., Gohari, S., Reshadmanesh, T. et al. (2024) Empagliflozin improves left ventricular ejection fraction and end systolic volume in patients with type 2 diabetes mellitus and coronary artery disease: a post-hoc analysis of EMPA-CARD trial.</a> Journal of Diabetes and Metabolic Disorders                                                                          | - No relevant outcomes reported                                                                                                                                           |
| <a href="#">Ghosal, Samit and Sinha, Binayak (2023) Exploring the comparative cardiovascular death benefits of sodium-glucose cotransporter 2 inhibitors in type 2 diabetes: a frequentist and Bayesian network meta-analysis-based scoring.</a> Frontiers in endocrinology 14: 1168755                                                                                                        | - Systematic review used as source of primary studies                                                                                                                     |
| <a href="#">Ghosh, Sujoy, Mukhopadhyay, Pradip, Pandey, Prabhakar et al. (2020) Cardiovascular safety of Glimepiride: An indirect comparison from CAROLINA and CARMELINA.</a> Diabetes & vascular disease research 17(6): 1479164120973653                                                                                                                                                     | - Study design not relevant to this review protocol<br><i>Indirect treatment comparison between two trials using a pooled analysis that is non-systematic in approach</i> |
| <a href="#">Gilbert, M., Bain, S., Franek, E. et al. (2018) Effect of liraglutide on cardiovascular outcomes in elderly patients in the leader trial.</a> Journal of the American College of Cardiology 71(11supplement1)                                                                                                                                                                      | - Conference abstract                                                                                                                                                     |

| Study                                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                        |
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| <a href="#">Gilbert, Matthew P, Marre, Michel, Holst, Jens Juul et al. (2016) COMPARISON OF THE LONG-TERM EFFECTS OF LIRAGLUTIDE AND GLIMEPIRIDE MONOTHERAPY ON BONE MINERAL DENSITY IN PATIENTS WITH TYPE 2 DIABETES.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 22(4): 406-11 | - Secondary publication of an included study that does not provide any additional relevant information                                                                        |
| <a href="#">Giles, T. D., Miller, A. B., Elkayam, U. et al. (2008) Pioglitazone and heart failure: results from a controlled study in patients with type 2 diabetes mellitus and systolic dysfunction.</a> J Card Fail 14(6): 445-52                                                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                 |
| <a href="#">Gillani, Syed Wasif, Ghayedi, Nahal, Roosta, Pardis et al. (2021) Effect of Metformin on Lipid Profiles of Type 2 Diabetes Mellitus: A Meta-analysis of Randomized Controlled Trials.</a> Journal of pharmacy & bioallied sciences 13(1): 76-82                                                                                                                       | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                       |
| <a href="#">Giorgino, Francesco, Shaunik, Alka, Liu, Minzhi et al. (2019) Achievement of glycaemic control is associated with improvements in lipid profile with iGlarLixi versus iGlar: A post hoc analysis of the LixiLan-L trial.</a> Diabetes, obesity & metabolism 21(12): 2712-2717                                                                                         | - Additional outcomes relevant to living guideline work                                                                                                                       |
| <a href="#">Giorgino, Francesco, Yu, Maria, Haupt, Axel et al. (2019) Effect of once-weekly dulaglutide versus insulin glargine in people with type 2 diabetes and different baseline glycaemic patterns: A post hoc analysis of the AWARD-2 clinical trial.</a> Diabetes, obesity & metabolism 21(11): 2570-2575                                                                 | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis that was not prespecified.</i>             |
| <a href="#">Gitt, A K, Bramlage, P, Binz, C et al. (2013) Prognostic implications of DPP-4 inhibitor vs. sulfonylurea use on top of metformin in a real world setting - results of the 1 year follow-up of the prospective DiaRegis registry.</a> International journal of clinical practice 67(10): 1005-14                                                                      | - Study design not relevant to this review protocol<br><br><i>Observational registry data</i>                                                                                 |
| <a href="#">Giugliano, D., Longo, M., Caruso, P. et al. (2021) Feasibility of Simplification From a Basal-Bolus Insulin Regimen to a Fixed-Ratio Formulation of Basal Insulin Plus a GLP-1RA or to Basal Insulin Plus an SGLT2 Inhibitor: BEYOND, a Randomized, Pragmatic Trial.</a> Diabetes Care 44(6): 1353-1360                                                               | - Study does not contain an intervention relevant to this review protocol<br><br><i>Specific GLP-1 or SGLT-2 used not specified therefore cannot be used in this analysis</i> |

| Study                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                                                  |
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| <a href="#">Giugliano, D., Longo, M., Caruso, P. et al. (2021) SGLT-2 inhibitors for prevention of cardiorenal outcomes in type 2 diabetes: an updated meta-analysis.</a> Diabetes, obesity & metabolism                                                                                                          | - Systematic review used as source of primary studies                                                                                                                                                   |
| <a href="#">Giugliano, Dario, Longo, Miriam, Caruso, Paola et al. (2021) Sodium-glucose co-transporter-2 inhibitors for the prevention of cardiorenal outcomes in type 2 diabetes: An updated meta-analysis.</a> Diabetes, obesity & metabolism 23(7): 1672-1676                                                  | - Systematic review used as source of primary studies                                                                                                                                                   |
| <a href="#">Giugliano, Dario, Longo, Miriam, Scappaticcio, Lorenzo et al. (2024) BEYOND 2 years: durability of metabolic benefits by simplification of complex insulin regimens in type 2 diabetes.</a> Endocrine 83(2): 399-404                                                                                  | - Study does not contain an intervention relevant to this review protocol                                                                                                                               |
| <a href="#">Giugliano, Dario, Longo, Miriam, Signoriello, Simona et al. (2022) The effect of DPP-4 inhibitors, GLP-1 receptor agonists and SGLT-2 inhibitors on cardiorenal outcomes: a network meta-analysis of 23 CVOTs.</a> Cardiovascular diabetology 21(1): 42                                               | - Study design not relevant to this review protocol<br><i>Network meta-analysis. Includes people with and without type 2 diabetes.</i>                                                                  |
| <a href="#">Giugliano, Dario, Scappaticcio, Lorenzo, Longo, Miriam et al. (2021) GLP-1 receptor agonists and cardiorenal outcomes in type 2 diabetes: an updated meta-analysis of eight CVOTs.</a> Cardiovascular diabetology 20(1): 189                                                                          | - Study design not relevant to this review protocol<br><i>Meta-analysis. Minimum trial duration not specified.</i>                                                                                      |
| <a href="#">Glasziou, Paul, Alexander, Jan, Beller, Elaine et al. (2007) Which health-related quality of life score? A comparison of alternative utility measures in patients with Type 2 diabetes in the ADVANCE trial.</a> Health and quality of life outcomes 5: 21                                            | - Study does not contain an intervention relevant to this review protocol<br><i>Intervention arm = intensive glucose control (gliclazide modified release, then adding OADs / insulin as required).</i> |
| <a href="#">Gohari, Sepehr, Reshadmanesh, Tara, Khodabandehloo, Hadi et al. (2021) Study rationale and design of a study of EMPAgliflozin's effects in patients with type 2 diabetes mellitus and Coronary ARtery disease: the EMPA-CARD randomized controlled trial.</a> BMC cardiovascular disorders 21(1): 318 | - No relevant outcomes reported                                                                                                                                                                         |
| <a href="#">Goldenberg, R.M., Pratley, R.E., Bauer, R. et al. (2020) 56 - Effect of Oral Semaglutide With or Without Background SGLT2i in Patients With T2D: Subgroup Analysis of PIONEER 4.</a>                                                                                                                  | - Conference abstract                                                                                                                                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                                   |
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| Canadian Journal of Diabetes 44(7supplement): 24                                                                                                                                                                                                                                                                                        |                                                                                                                                                                          |
| <a href="#">Gomez, M.R., Lawitz, E., Ravi Shankar, R. et al. (2023) A Phase 2a, randomized, active-comparator-controlled, openlabel study to evaluate the efficacy and safety of efinopegdutide in individuals with non-alcoholic fatty liver disease. Journal of Hepatology 78(supplement1): 53</a>                                    | - Study does not contain an intervention relevant to this review protocol                                                                                                |
| <a href="#">Gomis, R., Espadero, R. M., Jones, R. et al. (2011) Efficacy and safety of initial combination therapy with linagliptin and pioglitazone in patients with inadequately controlled type 2 diabetes: a randomized, double-blind, placebo-controlled study. Diabetes Obes Metab 13(7): 653-61</a>                              | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Gong, Chen, Shen, Shi-Chun, Zhang, Ke et al. (2022) Association of sodium-glucose cotransporter 2 inhibitors with cardiovascular outcome and safety events: A meta-analysis of randomized controlled clinical trials. Frontiers in cardiovascular medicine 9: 926979</a>                                                    | - Study design not relevant to this review protocol<br><i>Meta-analysis. Includes trials with populations other than type 2 diabetes.</i>                                |
| <a href="#">Gonzales, K. and Gandhi, G.Y. (2016) In type 2 diabetes treated with high-dose insulin, liraglutide reduced HbA1c. Annals of Internal Medicine 165(8): jc40</a>                                                                                                                                                             | - Commentary only<br><i>Summary and commentary of Vanderheiden 2016</i>                                                                                                  |
| <a href="#">Gonzalez, Jeffrey S, Bebu, Ionut, Krause-Steinrauf, Heidi et al. (2024) Differential Effects of Type 2 Diabetes Treatment Regimens on Diabetes Distress and Depressive Symptoms in the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE): A Randomized Clinical Trial. Diabetes care</a> | - Additional outcomes relevant to living guideline work                                                                                                                  |
| <a href="#">Goudswaard, Alex N, Stolk, Ronald P, Zuithoff, Peter et al. (2004) Starting insulin in type 2 diabetes: continue oral hypoglycemic agents? A randomized trial in primary care. The Journal of family practice 53(5): 393-9</a>                                                                                              | - Study does not contain an intervention relevant to this review protocol                                                                                                |
| <a href="#">Gower, Emily W, Lovato, James F, Ambrosius, Walter T et al. (2018) Lack of Longitudinal Association Between Thiazolidinediones and Incidence and Progression of Diabetic Eye Disease: The ACCORD Eye Study. American journal of ophthalmology 187: 138-147</a>                                                              | - Study does not contain an intervention relevant to this review protocol                                                                                                |



| Study                                                                                                                                                                                                                                                                                                                                                                                                                 | Reason                                                                                                                                                                             |
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| <a href="#">Grant, Paul; Lipscomb, David; Quin, John (2011) Psychological and quality of life changes in patients using GLP-1 analogues. Journal of diabetes and its complications 25(4): 244-6</a>                                                                                                                                                                                                                   | - Study design not relevant to this review protocol<br><i>Non-randomised study</i>                                                                                                 |
| <a href="#">Green, JB, Merrill, P, Lokhnygina, Y et al. (2023) Sex differences in complications, care, and clinical outcomes of patients with type 2 diabetes in the Exenatide Study of Cardiovascular Event Lowering (EXSCEL). Diabetes, obesity &amp; metabolism</a>                                                                                                                                                | - Duplicate reference                                                                                                                                                              |
| <a href="#">Green, Jennifer B, Merrill, Peter, Lokhnygina, Yuliya et al. (2023) Sex differences in the complications, care and clinical outcomes of patients with type 2 diabetes in the Exenatide Study of Cardiovascular Event Lowering (EXSCEL). Diabetes, obesity &amp; metabolism</a>                                                                                                                            | - Secondary publication of an included study that does not provide any additional relevant information                                                                             |
| <a href="#">Green, Jennifer B, Mottl, Amy K, Bakris, George et al. (2023) Design of the COMbination effect of FInerenone and EmpaglifloziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint study (CONFIDENCE). Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 38(4): 894-903</a> | - Comparator in study does not match that specified in this review protocol                                                                                                        |
| <a href="#">Gregorio, F, Ambrosi, F, Angelici, F et al. (1989) Body mass index, blood lactate and therapeutic effectiveness of metformin in type II diabetes mellitus. Medicina (Florence, Italy) 9(2): 200-204</a>                                                                                                                                                                                                   | - Study not reported in English                                                                                                                                                    |
| <a href="#">Gregorio, F, Ambrosi, F, Manfrini, S et al. (1999) Poorly controlled elderly Type 2 diabetic patients: the effects of increasing sulphonylurea dosages or adding metformin. Diabetic medicine : a journal of the British Diabetic Association 16(12): 1016-24</a>                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK<br><i>Sulphonylureas included glibenclamide (not used in the UK) and gliclazide.</i> |
| <a href="#">Grewal, Simran, Zaman, Ninad, Borgatta, Louis et al. (2021) Usefulness of Glucagon-Like Peptide-1 Receptor Agonists to Reduce Adverse Cardiovascular Disease Events in Patients with Type 2 Diabetes Mellitus. The American journal of cardiology 154: 48-53</a>                                                                                                                                          | - Systematic review used as source of primary studies                                                                                                                              |
| <a href="#">Grunberger, G, Chen, L, Rodriguez, A et al. (2016) A randomized clinical trial of basal insulin peglispro vs NPH in insulin-naïve patients with</a>                                                                                                                                                                                                                                                       | - Comparator in study does not match that specified in this review protocol                                                                                                        |



| Study                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                               |
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| <a href="#">type 2 diabetes: the IMAGINE 6 trial</a> . Diabetes, obesity & metabolism 18suppl2: 34-42                                                                                                                                                                                                                                                                        | <i>Compares different types of insulin delivered at different times</i>                                                                              |
| <a href="#">Gu, Shuyan, Hu, Xiaogian, Shi, Lizheng et al. (2022) Choice of Glucose-Lowering Drugs as Initial Monotherapy for Type 2 Diabetes Patients with Contraindications or Intolerance to Metformin: A Systematic Review and Meta-Analysis</a> . Journal of clinical medicine 11(23)                                                                                    | - Comparator in study does not match that specified in this review protocol                                                                          |
| <a href="#">Guardado-Mendoza, Rodolfo, Salazar-Lopez, Sara Stephania, Alvarez-Canales, Mildred et al. (2020) The combination of linagliptin, metformin and lifestyle modification to prevent type 2 diabetes (PRELLIM). A randomized clinical trial</a> . Metabolism: clinical and experimental 104: 154054                                                                  | - Population not relevant to this review protocol<br><i>Prediabetes</i>                                                                              |
| <a href="#">Gudipaty, L., Rosenfeld, N. K., Fuller, C. S. et al. (2014) Effect of exenatide, sitagliptin, or glimepiride on beta-cell secretory capacity in early type 2 diabetes</a> . Diabetes Care 37(9): 2451-2458                                                                                                                                                       | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Guerci, Bruno, Trautmann, Michael E, Lin, Tim et al. (2019) Predictive factors associated with three years of response to HbA1c goals with exenatide QW or insulin glargine: Post-hoc analysis of the DURATION-3 study</a> . Diabetes, obesity & metabolism 21(4): 1049-1053                                                                                     | - Study design not relevant to this review protocol<br><i>post hoc analysis</i>                                                                      |
| <a href="#">Guimaraes, Patricia O, Peterson, Eric D, Stevens, Susanna R et al. (2019) Antithrombotic treatment gap among patients with atrial fibrillation and type 2 diabetes</a> . International journal of cardiology 289: 58-62                                                                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Post hoc analysis</i>                   |
| <a href="#">Gullaksen, S., Hald, L.V., Sorensen, S.S. et al. (2023) Effects of 32 weeks' treatment with semaglutide, empagliflozin or the combination on retinal oxygenation, vessel diameter and central retinal thickness</a> . Diabetologia 66(supplement1): 458                                                                                                          | - Conference abstract                                                                                                                                |
| <a href="#">Gullaksen, Soren, Vernstrom, Liv, Sorensen, Steffen Skovgaard et al. (2023) Effects of semaglutide and empagliflozin on oxygenation, vascular autoregulation, and central thickness of the retina in people with type 2 diabetes: A prespecified secondary analysis of a randomised clinical trial</a> . Journal of diabetes and its complications 37(5): 108472 | - Secondary publication of an included study that does not provide any additional relevant information                                               |

| Study                                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                            |
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| <a href="#">Guo, Li-Xin, Liu, Guo-En, Chen, Li et al. (2021) Comparison of Clinical Efficacy and Safety of Metformin Sustained-Release Tablet (II) (Dulening) and Metformin Tablet (Glucophage) in Treatment of Type 2 Diabetes Mellitus. Frontiers in endocrinology 12: 712200</a>                                                                    | - Trial that has a treatment and follow up period of less than 24 weeks                                           |
| <a href="#">Guo, Nuojin, Shi, Hekai, Zhang, Hao et al. (2023) Comparison of the efficacy and safety of hypoglycemic treatments in patients with non-alcoholic fatty liver disease and type-2 diabetes: a systematic review and Bayesian network analysis. European journal of clinical pharmacology</a>                                                | - Systematic review used as source of primary studies                                                             |
| <a href="#">Guo, Xueyuan, Sang, Caihua, Tang, Ribo et al. (2023) Effects of glucagon-like peptide-1 receptor agonists on major coronary events in patients with type 2 diabetes. Diabetes, obesity &amp; metabolism</a>                                                                                                                                | - Study design not relevant to this review protocol<br><i>Meta-analysis. No minimum trial duration specified.</i> |
| <a href="#">Gupta, Sunil, Shaikh, Shehla, Joshi, Pooja et al. (2017) Long-Term Efficacy and Safety of Empagliflozin Monotherapy in Drug-Naive Patients with Type 2 Diabetes in Indian Subgroup: Results from a 76-week Extension Trial of Phase III, Double-Blind, Randomized Study. Indian journal of endocrinology and metabolism 21(2): 286-292</a> | - Secondary publication of an included study that does not provide any additional relevant information            |
| <a href="#">Guthrie, Robert (2016) Empagliflozin reduces cardiovascular events and mortality in type 2 diabetes. Postgraduate medicine 128(4): 335-7</a>                                                                                                                                                                                               | - Study design not relevant to this review protocol<br><i>Post hoc analysis</i>                                   |
| <a href="#">Gutierrez, Jorge Antonio, Scirica, Benjamin M, Bonaca, Marc P et al. (2019) Prevalence and Outcomes of Polyvascular (Coronary, Peripheral, or Cerebrovascular) Disease in Patients With Diabetes Mellitus (From the SAVOR-TIMI 53 Trial). The American journal of cardiology 123(1): 145-152</a>                                           | - Secondary publication of an included study that does not provide any additional relevant information            |
| <a href="#">Gutniak, M.; Karlander, S. G.; Efendi, S. (1987) Glyburide decreases insulin requirement, increases beta-cell response to mixed meal, and does not affect insulin sensitivity: effects of short- and long-term combined treatment in secondary failure to sulfonylurea. Diabetes Care 10(5): 545-54</a>                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                     |

| Study                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                           |
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| <a href="#">Gómez-Perez, F. J., Fanghanel-Salmón, G., Antonio Barbosa, J. et al. (2002) Efficacy and safety of rosiglitazone plus metformin in Mexicans with type 2 diabetes.</a> Diabetes Metab Res Rev 18(2): 127-34                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                    |
| <a href="#">Göke, B. (2002) Improved glycemic control and lipid profile in a randomized study of pioglitazone compared with acarbose in patients with type 2 diabetes mellitus.</a> Treat Endocrinol 1(5): 329-36                                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                    |
| <a href="#">Güvener, N. and Gedik, O. (1999) Effects of combination of insulin and acarbose compared with insulin and gliclazide in type 2 diabetic patients.</a> Acta Diabetol 36(12): 93-7                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                    |
| <a href="#">Hadjadj, S., Thomas, M.C., Cooper, M.E. et al. (2017) Empagliflozin (EMPA) and incidence of rapid decline in egfr in patients with type 2 diabetes (T2D) and established cardiovascular disease (CVD): An exploratory analysis from the Empa-Reg outcome trial.</a> Journal of the American Society of Nephrology 28: 10 | - Conference abstract                                                                                                            |
| <a href="#">Haedersdal, Sofie, Lund, Asger, Nielsen-Hannerup, Elisabeth et al. (2020) The Role of Glucagon in the Acute Therapeutic Effects of SGLT2 Inhibition.</a> Diabetes 69(12): 2619-2629                                                                                                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                                          |
| <a href="#">Hage, Camilla, Brismar, Kerstin, Lundman, Pia et al. (2014) The DPP-4 inhibitor sitagliptin and endothelial function in patients with acute coronary syndromes and newly detected glucose perturbations: A report from the BEGAMI study.</a> Diabetes & vascular disease research 11(4): 290-293                         | - Population not relevant to this review protocol<br><i>Around 70% of people had impaired glucose tolerance rather than T2DM</i> |
| <a href="#">Halalau, Alexandra; Fuller, William; Wheeler, Stephanie (2021) Canagliflozin Reduces the Risk of Kidney Failure in Patients with Type 2 Diabetes Mellitus and Nephropathy: The CREDENCE Randomized Trial.</a> Journal of general internal medicine                                                                       | - Commentary only                                                                                                                |
| <a href="#">Halimi, S.; Berre, M. A.; Grangé, V. (2000) Efficacy and safety of acarbose add-on therapy in the treatment of overweight patients with Type 2 diabetes inadequately controlled with metformin: a double-blind, placebo-controlled study.</a> Diabetes Res Clin Pract 50(1): 49-56                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                    |

| Study                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                    |
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| <a href="#">Halvorsen, Y. C., Walford, GA, Massaro, J et al. (2019) A 96-week, multinational, randomized, double-blind, parallel-group, clinical trial evaluating the safety and effectiveness of bexagliflozin as a monotherapy for adults with type 2 diabetes. Diab Obes Metab 21(11): 2496-2504</a>                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Halvorsen, Yuan-Di, Lock, John P., Zhou, Wenjiong et al. (2019) A 24-week, randomized, double-blind, active-controlled clinical trial comparing bexagliflozin with sitagliptin as an adjunct to metformin for the treatment of type 2 diabetes in adults. Diabetes, obesity &amp; metabolism 21(10): 2248-2256</a>     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Hamal, Chandani, Velugoti, Lakshmi Sai Deepak Reddy, Tabowei, Godfrey et al. (2022) Metformin for the Improvement of Comorbid Depression Symptoms in Diabetic Patients: A Systematic Review. Cureus 14(8): e28609</a>                                                                                                  | - Study design not relevant to this review protocol<br><br><i>Systematic review which includes observational studies.</i> |
| <a href="#">Han, E., Huh, J. H., Lee, E. Y. et al. (2022) Efficacy and safety of evogliptin in patients with type 2 diabetes and non-alcoholic fatty liver disease: a multicentre, double-blind, randomized, comparative trial. Diabetes, obesity &amp; metabolism 24(4): 752-756</a>                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Han, E., Lee, Y. H., Lee, B. W. et al. (2020) Ipragliflozin additively ameliorates non-alcoholic fatty liver disease in patients with type 2 diabetes controlled with metformin and pioglitazone: A 24-week randomized controlled trial. Journal of Clinical Medicine 9(1)</a>                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Han, K. A., Chon, S., Chung, C. H. et al. (2018) Efficacy and safety of ipragliflozin as an add-on therapy to sitagliptin and metformin in Korean patients with inadequately controlled type 2 diabetes mellitus: a randomized controlled trial. Diab Obes Metab 20(10): 2408-2415</a>                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Handelsman, Y., Lauring, B., Gantz, I. et al. (2017) A randomized, double-blind, non-inferiority trial evaluating the efficacy and safety of omarigliptin, a once-weekly DPP-4 inhibitor, or glimepiride in patients with type 2 diabetes inadequately controlled on metformin monotherapy. Curr Med Res Opin: 1-8</a> | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |

| Study                                                                                                                                                                                                                                                                                                                                    | Reason                                                                                        |
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| <a href="#">Haneda, M., Seino, Y., Inagaki, N. et al. (2016) Influence of renal function on the 52-week efficacy and safety of the sodium glucose cotransporter 2 inhibitor luseogliflozin in Japanese patients with type 2 diabetes mellitus. Clin Ther 38(1): 88e66-88e120</a>                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Hanefeld, M., Fischer, S., Schulze, J. et al. (1991) Therapeutic potentials of acarbose as first-line drug in NIDDM insufficiently treated with diet alone. Diabetes Care 14(8): 732-7</a>                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Hanefeld, M.; Patwardhan, R.; Jones, N. P. (2007) A one-year study comparing the efficacy and safety of rosiglitazone and glibenclamide in the treatment of type 2 diabetes. Nutr Metab Cardiovasc Dis 17(1): 13-23</a>                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Hankosky, Emily R, Wang, Hui, Neff, Lisa M et al. (2024) Tirzepatide reduces the predicted risk of atherosclerotic cardiovascular disease and improves cardiometabolic risk factors in adults with obesity or overweight: SURMOUNT-1 post hoc analysis. Diabetes, obesity &amp; metabolism 26(1): 319-328</a>                | - Population not relevant to this review protocol                                             |
| <a href="#">Hansen, Christian Stevns, Lundby-Christiansen, Louise, Tarnow, Lise et al. (2020) Metformin may adversely affect orthostatic blood pressure recovery in patients with type 2 diabetes: substudy from the placebo-controlled Copenhagen Insulin and Metformin Therapy (CIMT) trial. Cardiovascular diabetology 19(1): 150</a> | - Additional outcomes relevant to living guideline work                                       |
| <a href="#">Hansen, T., Rasmussen, I., Zobel, E. et al. (2021) Liraglutide reduces cardiac adipose tissue in type 2 diabetes: Results from the LiraFlame randomised controlled trial. Diabetologia 64(supplement1): 99</a>                                                                                                               | - Conference abstract                                                                         |
| <a href="#">Hao, Q and Guyatt, G (2021) Efficacy and safety of dapagliflozin were similar in patients with type 2 DM and atherosclerotic CVD, regardless of PAD. Annals of internal medicine 174(1): jc10</a>                                                                                                                            | - Commentary only                                                                             |
| <a href="#">Harashima, S-I, Ogura, M, Tanaka, D et al. (2012) Sitagliptin add-on to low dosage sulphonylureas: efficacy and safety of combination therapy on glycaemic control and insulin secretion capacity in type 2 diabetes.</a>                                                                                                    | - Study design not relevant to this review protocol<br><i>Non-randomised</i>                  |

| Study                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                               |
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| International journal of clinical practice 66(5): 465-476                                                                                                                                                                                                                                                                  |                                                                                                                                                      |
| <a href="#">Harris, Stewart B, Kocsis, Gyoza, Prager, Rudolf et al. (2017) Safety and efficacy of IDeqLira titrated once weekly versus twice weekly in patients with type 2 diabetes uncontrolled on oral antidiabetic drugs: DUAL VI randomized clinical trial. Diabetes, obesity &amp; metabolism 19(6): 858-865</a>     | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares once weekly dosing to twice weekly dosing</i>         |
| <a href="#">Harrower, A D and Wong, C (1990) Comparison of secondary failure rate between three second generation sulphonylureas. Diabetes research (Edinburgh, Scotland) 13(1): 19-21</a>                                                                                                                                 | - No relevant outcomes reported                                                                                                                      |
| <a href="#">Hartman, M., Loomba, R., Sanyal, A.J. et al. (2019) Effects of tirzepatide, a novel dual gip and glp-1 receptor agonist, on biomarkers of non-alcoholic steatohepatitis (NASH) in probable NASH subgroups of patients with type 2 diabetes (T2D). Hepatology v70 suppl.1 2019 70(supplement1): 1270a-1271a</a> | - Conference abstract                                                                                                                                |
| <a href="#">Hartman, Mark L, Sanyal, Arun J, Loomba, Rohit et al. (2020) Effects of Novel Dual GLP and GLP-1 Receptor Agonist Tirzepatide on Biomarkers of Nonalcoholic Steatohepatitis in Patients With Type 2 Diabetes. Diabetes care 43(6): 1352-1355</a>                                                               | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis of Frias 2018</i> |
| <a href="#">Hasche, H., Mertes, G., Bruns, C. et al. (1999) Effects of acarbose treatment in Type 2 diabetic patients under dietary training: a multicentre, double-blind, placebo-controlled, 2-year study. Diabetes Nutr Metab 12(4): 277-85</a>                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Hasebe, Masashi, Yoshiji, Satoshi, Keidai, Yamato et al. (2023) Efficacy of antihyperglycemic therapies on cardiovascular and heart failure outcomes: an updated meta-analysis and meta-regression analysis of 35 randomized cardiovascular outcome trials. Cardiovascular diabetology 22(1): 62</a>           | - Population not relevant to this review protocol<br><br><i>People with type 2 diabetes or prediabetes</i>                                           |
| <a href="#">Hassan Adel, SM, Fazeli, S, Jorfi, F et al. (2022) The effect of empagliflozin administration on lipid profile in diabetic patients with acute coronary syndrome after PCI. Tehran university medical journal 80(3): 206-216</a>                                                                               | - Study not reported in English                                                                                                                      |



| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                               |
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| <a href="#">Hattori, A., Takemoto, M., Tokuyama, H. et al. (2017) Sitagliptin but not alpha glucosidase inhibitor reduced the serum soluble CD163, a marker for activated macrophage, in individuals with type 2 diabetes mellitus.</a> Diabetes Res Clin Pract 126: 138-143                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Hattori, S. (2021) Ten-year follow-up of sitagliptin treatment in patients with type 2 diabetes mellitus.</a> Diabetology and Metabolic Syndrome 13(1)                                                                                                                                                           | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Haupt, A., Sanyal, A., Loomba, R. et al. (2019) Effects of tirzepatide (TZP), a novel dual GIP and GLP-1 receptor agonist, on biomarkers of non-alcoholic steatohepatitis (NASH) in patients with type 2 diabetes.</a> Diabetologia 62(supplement1): 91                                                          | - Conference abstract                                                                                                                                |
| <a href="#">Hazra, M. (2022) A Comparative Pharmacovigilance Analytical Research Study on the Glycaemic Stabilisation Rate and Safety Levels, Between Metformin Monotherapy and Combination Therapies, Among Type II Diabetic Patients.</a> International Journal of Toxicological and Pharmacological Research 12(3): 35-43 | - Comparator in study does not match that specified in this review protocol                                                                          |
| <a href="#">He, Fengling, Chen, Wei, Xu, Wenlong et al. (2023) Safety and efficacy of liraglutide on reducing visceral and ectopic fat in adults with or without type 2 diabetes mellitus: A systematic review and meta-analysis.</a> Diabetes, obesity & metabolism 25(3): 664-674                                          | - Population not relevant to this review protocol<br><i>People with or without type 2 diabetes</i>                                                   |
| <a href="#">He, L., Wang, J., Yang, N. et al. (2022) Dipeptidyl peptidase-4 inhibitors and gallbladder or biliary disease in type 2 diabetes: Systematic review and meta-analysis of randomised controlled trials.</a> Diabetologia 65(supplement1): 311                                                                     | - Conference abstract                                                                                                                                |
| <a href="#">Hedblad, B., Zambanini, A., Nilsson, P. et al. (2007) Rosiglitazone and carotid IMT progression rate in a mixed cohort of patients with type 2 diabetes and the insulin resistance syndrome: main results from the Rosiglitazone Atherosclerosis Study.</a> J Intern Med 261: 293-305                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Heerspink, H.J., Friedman, A.N., Bjornstad, P. et al. (2023) Effect of Tirzepatide on Kidney Function in People with Excess Body Weight: A</a>                                                                                                                                                                   | - Conference abstract                                                                                                                                |



| Study                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                                  |
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| <a href="#">Post Hoc Analysis of the SURMOUNT-1 Trial.</a><br>Journal of the American Society of Nephrology<br>34: 41                                                                                                                                                                                                                |                                                                                                                                                                                         |
| <a href="#">Heerspink, H.J.L., Chertow, G., Jongs, N. et al. (2022) Effects of Dapagliflozin in Patients Without Diabetes and Microalbuminuria: An Exploratory Analysis From the DAPA-CKD Trial.</a><br>Journal of the American Society of Nephrology<br>33: 847-848                                                                 | - Conference abstract                                                                                                                                                                   |
| <a href="#">Heerspink, H.J.L., Desai, M., Jardine, M. et al. (2016) Canagliflozin slows progression of renal function decline independent of glycaemic effects.</a> Diabetologia 59(1supplement1): 28                                                                                                                                | - Conference abstract                                                                                                                                                                   |
| <a href="#">Heerspink, H.J.L., Jongs, N., Chertow, G.M. et al. (2021) Correlates and consequences of an acute decline in estimated glomerular filtration rate in response to the SGLT-2 inhibitor dapagliflozin.</a> Journal of the American Society of Nephrology 32: 726                                                           | - Conference abstract                                                                                                                                                                   |
| <a href="#">Heerspink, H.J.L., Oshima, M., Zhang, H. et al. (2021) Canagliflozin Reduces Kidney-Related Adverse Events in Type 2 Diabetes and CKD: Findings From the Randomized CREDENCE Trial.</a> American journal of kidney diseases : the official journal of the National Kidney Foundation                                     | - Post-hoc analysis of included study                                                                                                                                                   |
| <a href="#">Heerspink, H.J.L., Zhang, H., Mahaffey, K.W. et al. (2019) Canagliflozin and renal-related adverse events in type 2 diabetes and CKD: Results from credence.</a> Journal of the American Society of Nephrology 30: 101                                                                                                   | - Conference abstract                                                                                                                                                                   |
| <a href="#">Heerspink, Hidde J L, Cherney, David, Postmus, Douwe et al. (2022) A pre-specified analysis of the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) randomized controlled trial on the incidence of abrupt declines in kidney function.</a><br>Kidney international 101(1): 174-184 | - Population not relevant to this review protocol<br><br><i>Main trial population is a mixture of people with and without type 2 diabetes - analysis does not separate these people</i> |
| <a href="#">Heerspink, Hidde J L, Desai, Mehul, Jardine, Meg et al. (2017) Canagliflozin Slows Progression of Renal Function Decline Independently of Glycemic Effects.</a> Journal of the American Society of Nephrology : JASN<br>28(1): 368-375                                                                                   | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis</i>                                                                                                     |

| Study                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                            |
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| <a href="#">Heerspink, Hiddo J L, Oshima, Megumi, Zhang, Hong et al. (2022) Canagliflozin and Kidney-Related Adverse Events in Type 2 Diabetes and CKD: Findings From the Randomized CREDENCE Trial.</a> American journal of kidney diseases : the official journal of the National Kidney Foundation 79(2): 244-256e1         | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Post hoc analysis</i>                |
| <a href="#">Hegele, R. A., Connelly, P. W., Palmason, C. et al. (1995) Differential response of plasma lipoprotein(a) and apolipoprotein B in NIDDM subjects treated with acarbose.</a> Diabetes Care 18(2): 272-3                                                                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                     |
| <a href="#">Hehnke, U, Tamminen, I, Thiemann, S et al. (2016) Efficacy and safety of linagliptin in Japanese type 2 diabetes patients with moderate to severe renal impairment: subgroup analysis of 52-week randomized, double-blind, international clinical study.</a> Japanese pharmacology and therapeutics 44(4): 571-582 | - Study not reported in English                                                                                                                   |
| <a href="#">Heine, RJ, Scheen, A, Van Gaal, L et al. (1995) Efficacy of bedtime NPH insulin alone, as compared to combination with metformin and/or glipizide in NIDDM patients with secondary failure on oral hypoglycaemic agents.</a> Netherlands journal of medicine 47: A59-A60                                           | - Conference abstract                                                                                                                             |
| <a href="#">Heise, Tim, Tack, Cees J, Cuddihy, Robert et al. (2011) A new-generation ultra-long-acting basal insulin with a bolus boost compared with insulin glargine in insulin-naïve people with type 2 diabetes: a randomized, controlled trial.</a> Diabetes care 34(3): 669-74                                           | - Study does not contain an intervention relevant to this review protocol<br><i>Includes insulin being compared to different types of insulin</i> |
| <a href="#">Heliövaara, M. K., Herz, M., Teppo, A. M. et al. (2007) Pioglitazone has anti-inflammatory effects in patients with Type 2 diabetes.</a> J Endocrinol Invest 30(4): 292-7                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                     |
| <a href="#">Henry, Robert R, Frias, Juan P, Walsh, Brandon et al. (2018) Improved glycemic control with minimal systemic metformin exposure: Effects of Metformin Delayed-Release (Metformin DR) targeting the lower bowel over 16 weeks in a randomized trial in subjects with type 2 diabetes.</a> PloS one 13(9): e0203946  | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>16 weeks</i>                                                        |
| <a href="#">Hermann, L. S., Ranstam, J., Vaaler, S. et al. (1999) Effects of antihyperglycaemic therapies on proinsulin and relation between proinsulin</a>                                                                                                                                                                    | - Comparator in study does not match that specified in this review protocol                                                                       |

| Study                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                                                                     |
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| <a href="#">and cardiovascular risk factors in type 2 diabetes.</a> Diabetes Obes Metab 1(4): 227-32                                                                                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK<br><i>Glibenclamide</i>                                                                                      |
| <a href="#">Hermans, Michel P, Delibasi, Tuncay, Farmer, Ian et al. (2012) Effects of saxagliptin added to sub-maximal doses of metformin compared with uptitration of metformin in type 2 diabetes: the PROMPT study.</a> Current medical research and opinion 28(10): 1635-45 | - Comparator in study does not match that specified in this review protocol                                                                                                                                |
| <a href="#">Herrington, W.G.; Zhu, D.; Haynes, R. (2019) In high-risk T2DM, canagliflozin reduced CV events regardless of baseline renal function.</a> Annals of Internal Medicine 170(4): jc15                                                                                 | - Commentary only                                                                                                                                                                                          |
| <a href="#">Herrington, William G, Staplin, Natalie, Wanner, Christoph et al. (2023) Empagliflozin in Patients with Chronic Kidney Disease.</a> The New England journal of medicine 388(2): 117-127                                                                             | - Population not relevant to this review protocol<br><i>Only 46% of people previously had diabetes. No outcomes relevant to the protocol are reported that purely examine people with type 2 diabetes.</i> |
| <a href="#">Hiralal, Rajesh; Koo, Karen K Y; Gerstein, Hertz C (2006) Does pioglitazone prevent macrovascular events in patients with type 2 diabetes?.</a> CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 174(8): 1090-1           | - Study design not relevant to this review protocol<br><i>Report only</i>                                                                                                                                  |
| <a href="#">Hiramatsu, T., Ito, H., Okumura, S. et al. (2020) Impact of glucagon like peptide-1 receptor agonist and sodium glucose cotransporter 2 inhibitors on type 2 diabetes patients with renal impairment.</a> Diabetes and Vascular Disease Research 17(6)              | - Study design not relevant to this review protocol<br><i>Prospective cohort study, not randomised.</i>                                                                                                    |
| <a href="#">Hirano, M., Nakamura, T., Kitta, Y. et al. (2009) Rapid improvement of carotid plaque echogenicity within 1 month of pioglitazone treatment in patients with acute coronary syndrome.</a> Atherosclerosis 203(2): 483-8                                             | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2                                   |
| <a href="#">Hirano, M., Nakamura, T., Obata, J. E. et al. (2012) Early improvement in carotid plaque echogenicity by acarbose in patients with acute coronary syndromes.</a> Circ J 76(6): 1452-60                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                                                                                                               |
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| <a href="#">Hirsch, I B (1999) Metformin added to insulin therapy in poorly controlled type 2 diabetes. Diabetes care 22(5): 854</a>                                                                                                                                                                                    | - Not a peer-reviewed publication                                                                                                                                                                                                                    |
| <a href="#">Hirukawa, H., Hashiramoto, M., Tanizawa, Y. et al. (2018) Remission of hyperglycemia after withdrawal of oral antidiabetic drugs in Japanese patients with early-stage type 2 diabetes. J Diabetes Invest 9(5): 1119-1127</a>                                                                               | - Comparator in study does not match that specified in this review protocol<br><br><i>The type of sulfonylurea was mixed, therefore cannot be included in the analysis. Includes a usual care comparison which is not specified in the protocol.</i> |
| <a href="#">Hoffmann, J. and Spengler, M. (1994) Efficacy of 24-week monotherapy with acarbose, glibenclamide, or placebo in NIDDM patients. The Essen Study. Diabetes Care 17(6): 561-6</a>                                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                        |
| <a href="#">Hohberg, C, Pflutzner, A, Forst, T et al. (2009) Successful switch from insulin therapy to treatment with pioglitazone in type 2 diabetes patients with residual beta-cell function: results from the PioSwitch Study. Diabetes, obesity &amp; metabolism 11(5): 464-471</a>                                | - Study design not relevant to this review protocol                                                                                                                                                                                                  |
| <a href="#">Hollander, P., Liu, J., Hill, J. et al. (2018) Safety and efficacy of ertugliflozin compared with glimepiride after 104 weeks in patients with type 2 diabetes inadequately controlled on metformin: VERTIS SU extension. Diabetologia 61(supplement1): 304-s305</a>                                        | - Conference abstract                                                                                                                                                                                                                                |
| <a href="#">Hollander, P.; Yu, D.; Chou, H. S. (2007) Low-dose rosiglitazone in patients with insulin-requiring type 2 diabetes. Arch Intern Med 167(12): 1284-90</a>                                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                        |
| <a href="#">Hollander, P, King, A B, Del Prato, S et al. (2015) Insulin degludec improves long-term glycaemic control similarly to insulin glargine but with fewer hypoglycaemic episodes in patients with advanced type 2 diabetes on basal-bolus insulin therapy. Diabetes, obesity &amp; metabolism 17(2): 202-6</a> | - Comparator in study does not match that specified in this review protocol<br><br><i>Comparing different types of insulin</i>                                                                                                                       |
| <a href="#">Hollander, P, Raslova, K, Skjoth, T V et al. (2011) Efficacy and safety of insulin detemir once daily in combination with sitagliptin and metformin: the TRANSITION randomized controlled trial. Diabetes, obesity &amp; metabolism 13(3): 268-75</a>                                                       | - Study does not contain an intervention relevant to this review protocol                                                                                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                                                                                    |
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| <a href="#">Holman, R. R.; Cull, C. A.; Turner, R. C. (1999) A randomized double-blind trial of acarbose in type 2 diabetes shows improved glycemic control over 3 years (U.K. Prospective Diabetes Study 44). Diabetes Care 22(6): 960-4</a>                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                             |
| <a href="#">Holman, R. R., Paul, S. K., Bethel, M. A. et al. (2008) 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 359(15): 1577-89</a>                                                                                                                                                                        | - Comparator in study does not match that specified in this review protocol<br><i>UKPDS study - comparing intensive therapy to conventional therapy which is not a comparison specified in the protocol</i>               |
| <a href="#">Holman, R. R., Thorne, K. I., Farmer, A. J. et al. (2007) Addition of biphasic, prandial, or basal insulin to oral therapy in type 2 diabetes. N Engl J Med 357(17): 1716-30</a>                                                                                                                                                    | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin to each other</i>                                                                                   |
| <a href="#">Home, P. D., Pocock, S. J., Beck-Nielsen, H. et al. (2009) Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial. Lancet 373(9681): 2125-35</a>                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                             |
| <a href="#">Home, P., Shankar, R. R., Gantz, I. et al. (2018) A randomized, double-blind trial evaluating the efficacy and safety of monotherapy with the once-weekly dipeptidyl peptidase-4 inhibitor omarigliptin in people with type 2 diabetes. Diabetes Res Clin Pract 138: 253-261</a>                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                             |
| <a href="#">Hong, A Ram, Lee, Jeun, Ku, Eu Jeong et al. (2015) Comparison of vildagliptin as an add-on therapy and sulfonylurea dose-increasing therapy in patients with inadequately controlled type 2 diabetes using metformin and sulfonylurea (VISUAL study): A randomized trial. Diabetes research and clinical practice 109(1): 141-8</a> | - Comparator in study does not match that specified in this review protocol<br><i>The control arm is sulfonylurea as a class rather than a specific sulfonylurea and so cannot be used in the analysis for the review</i> |
| <a href="#">Hong, J., Zhang, Y., Lai, S. et al. (2013) Effects of metformin versus glipizide on cardiovascular outcomes in patients with type 2 diabetes and coronary artery disease. Diabetes Care 36(5): 1304-11</a>                                                                                                                          | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2                                                                      |
| <a href="#">Hong, S. J., Choi, S. C., Cho, J. Y. et al. (2015) Pioglitazone increases circulating microRNA-24 with decrease in coronary neointimal hyperplasia in type 2 diabetic patients- optical</a>                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK<br><i>Usual care control that is not specified in the protocol</i>                                                          |

| Study                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                         |
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| <a href="#">coherence tomography analysis</a> . Circ J 79(4): 880-8                                                                                                                                                                                                                                                            |                                                                                                                                                |
| <a href="#">Hong, S., Park, C. Y., Han, K. A. et al. (2016) Efficacy and safety of teneligliptin, a novel dipeptidyl peptidase-4 inhibitor, in Korean patients with type 2 diabetes mellitus: A 24-week multicentre, randomized, double-blind, placebo-controlled phase III trial</a> . Diabetes Obes Metab 18(5): 528-532     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |
| <a href="#">Hong, Sang-Mo, Park, Cheol-Young, Hwang, Dong-Min et al. (2017) Efficacy and safety of adding evogliptin versus sitagliptin for metformin-treated patients with type 2 diabetes: A 24-week randomized, controlled trial with open label extension</a> . Diabetes, obesity & metabolism 19(5): 654-663              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |
| <a href="#">Horibe, Kayo, Morino, Katsutaro, Miyazawa, Itsuko et al. (2022) Metabolic changes induced by dapagliflozin, an SGLT2 inhibitor, in Japanese patients with type 2 diabetes treated by oral anti-diabetic agents: A randomized, clinical trial</a> . Diabetes research and clinical practice 186: 109781             | - Comparator in study does not match that specified in this review protocol<br><i>Usual care control that is not specified in the protocol</i> |
| <a href="#">Horowitz, M, Vilsboll, T, Zdravkovic, M et al. (2008) Patient-reported rating of gastrointestinal adverse effects during treatment of type 2 diabetes with the once-daily human GLP-1 analogue, liraglutide</a> . Diabetes, obesity & metabolism 10(7): 593-6                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                                                        |
| <a href="#">Hoshika, Yu, Kubota, Yoshiaki, Mozawa, Kosuke et al. (2022) Effect of Empagliflozin Versus Placebo on Body Fluid Balance in Patients With Acute Myocardial Infarction and Type 2 Diabetes Mellitus: Subgroup Analysis of the EMBODY Trial</a> . Journal of cardiac failure 28(1): 56-64                            | - Subgroup analysis of a trial that was not relevant for inclusion                                                                             |
| <a href="#">Hoshika, Yu, Kubota, Yoshiaki, Mozawa, Kosuke et al. (2021) Effect of Empagliflozin Versus Placebo on Plasma Volume Status in Patients with Acute Myocardial Infarction and Type 2 Diabetes Mellitus</a> . Diabetes therapy : research, treatment and education of diabetes and related disorders 12(8): 2241-2248 | - Subgroup analysis of a trial that was not relevant for inclusion                                                                             |
| <a href="#">Hotta, N., Kakuta, H., Sano, T. et al. (1993) Long-term effect of acarbose on glycaemic control in non-insulin-dependent diabetes</a>                                                                                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |



| Study                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                                                |
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| <a href="#">mellitus: a placebo-controlled double-blind study.</a> Diabetic Med 10(2): 134-8                                                                                                                                                                                                                   |                                                                                                                                                                                                                       |
| <a href="#">Hsieh, S. H., Shih, K. C., Chou, C. W. et al. (2011) Evaluation of the efficacy and tolerability of miglitol in Chinese patients with type 2 diabetes mellitus inadequately controlled by diet and sulfonylureas.</a> Acta Diabetologica 48(1): 71-7                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                         |
| <a href="#">Hu, C., Qu, T., Li, L. et al. (2023) Therapeutic outcome of dapagliflozin in patients with type 2 diabetes and non-alcoholic fatty liver disease: a meta-analysis of randomized controlled trials.</a> African Health Sciences 23(2): 416-421                                                      | - Systematic review used as source of primary studies                                                                                                                                                                 |
| <a href="#">Hu, Jing and Chen, Liyun (2021) Comparison of glucagons like peptide-1 receptor agonists and dipeptidyl peptide-4 inhibitors regarding cardiovascular safety and mortality in type 2 diabetes mellitus: A network meta-analysis.</a> Primary care diabetes 15(2): 227-233                          | - Study design not relevant to this review protocol<br><i>NMA with minimum trial duration of 12 weeks.</i>                                                                                                            |
| <a href="#">Hu, S., Lin, C., Cai, X. et al. (2022) Disparities in efficacy and safety of sodium-glucose cotransporter 2 inhibitor among patients with different extents of renal dysfunction: A systematic review and meta-analysis of randomized controlled trials.</a> Frontiers in Pharmacology 13: 1018720 | - Population not relevant to this review protocol<br><i>Investigates the use of SGLT-2 inhibitors for people with different extents of renal dysfunction rather than for people with type 2 diabetes specifically</i> |
| <a href="#">Hu, Shanshan; Su, Xiaorong; Fan, Guorong (2023) Efficacy and tolerability of the Subcutaneous Semaglutide for type 2 Diabetes patients: an updated systematic review and meta-analysis.</a> Diabetology & metabolic syndrome 15(1): 218                                                            | - Systematic review used as source of primary studies                                                                                                                                                                 |
| <a href="#">Hu, Xiaodong, Yang, Yue, Hu, Xiaona et al. (2022) Effects of sodium-glucose cotransporter 2 inhibitors on serum uric acid in patients with type 2 diabetes mellitus: A systematic review and network meta-analysis.</a> Diabetes, obesity & metabolism 24(2): 228-238                              | - Comparator in study does not match that specified in this review protocol                                                                                                                                           |
| <a href="#">Huang, Chen-Yu and Lee, Jen-Kuang (2020) Sodium-glucose co-transporter-2 inhibitors and major adverse limb events: A trial-level meta-analysis including 51 713 individuals.</a> Diabetes, obesity & metabolism 22(12): 2348-2355                                                                  | - Systematic review used as source of primary studies                                                                                                                                                                 |

| Study                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                        |
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| <a href="#">Huang, Chi-Jung, Wang, Wei-Ting, Sung, Shih-Hsien et al. (2022) Revisiting 'intensive' blood glucose control: A causal directed acyclic graph-guided systematic review of randomized controlled trials.</a> Diabetes, obesity & metabolism 24(12): 2341-2352                                                                      | - Systematic review used as source of primary studies                                         |
| <a href="#">Huang, Yun, Fang, Chongbo, Zhang, YuYu et al. (2023) Effectiveness and safety of angiotensin receptor-neprilysin inhibitor and sodium-glucose cotransporter-2 inhibitors for patients with heart failure with reduced ejection fraction: a meta-analysis.</a> Journal of cardiovascular medicine (Hagerstown, Md.) 24(2): 123-131 | - Systematic review used as source of primary studies                                         |
| <a href="#">Hung, Wei-Tse, Chen, Yuan-Jung, Cheng, Chun-Yu et al. (2022) Metformin plus a low hypoglycemic risk antidiabetic drug vs. metformin monotherapy for untreated type 2 diabetes mellitus: A meta-analysis of randomized controlled trials.</a> Diabetes research and clinical practice 189: 109937                                  | - Systematic review used as source of primary studies                                         |
| <a href="#">Hussain, Mazhar, Atif, Moazzam, Babar, Muhammad et al. (2021) Comparison Of Efficacy And Safety Profile Of Empagliflozin Versus Dapagliflozin As Add On Therapy In Type 2 Diabetic Patients.</a> Journal of Ayub Medical College, Abbottabad : JAMC 33(4): 593-597                                                                | - Trial that has a treatment and follow up period of less than 24 weeks                       |
| <a href="#">Hussein, M.A.M. and Jabbar, L. (2020) Study of anti-inflammatory effects of dapagliflozin as add on treatment versus metformin with placebo among diabetic patients in Thi-Qar city, South of Iraq.</a> International Journal of Pharmaceutical Research 12(supplementary2): 4573-4578                                            | - No relevant outcomes reported                                                               |
| <a href="#">Hwang, Y. C., Lee, E. Y., Lee, W. J. et al. (2008) Effects of rosiglitazone on body fat distribution and insulin sensitivity in Korean type 2 diabetes mellitus patients.</a> Metab Clin Experiment 57(4): 479-87                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Hygum, K., Harslof, T., Jorgensen, N. R. et al. (2020) Bone resorption is unchanged by liraglutide in type 2 diabetes patients: a randomised controlled trial.</a> Bone 132                                                                                                                                                       | - Population not relevant to this review protocol                                             |
| <a href="#">Ibrahim, Ayman, Ghaleb, Ramadan, Mansour, Hossam et al. (2020) Safety and Efficacy of</a>                                                                                                                                                                                                                                         | - Comparator in study does not match that specified in this review protocol                   |

| Study                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                                                                                                                                                                                                                                                          |
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| <a href="#">Adding Dapagliflozin to Furosemide in Type 2 Diabetic Patients With Decompensated Heart Failure and Reduced Ejection Fraction.</a><br>Frontiers in cardiovascular medicine 7: 602251                                                                                                                     | <i>Compares the addition of dapagliflozin to furosemide to furosemide alone for the management of decompensated heart failure in people with type 2 diabetes</i><br><br>- Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>Does not state the follow up length. Measures final outcomes till the 'discharge of patients'. But measure urinary output after 24hrs till 4 days</i> |
| <a href="#">Ikonomidis, I., Pavlidis, G., Lambadiari, V. et al. (2018) Effects of the glucagon like peptide-1 receptor agonist on arterial stiffness, LV myocardial deformation and oxidative stress in newly diagnosed type 2 diabetes after 6-month treatment.</a> European Heart Journal 39(supplement1): 868-869 | - Conference abstract                                                                                                                                                                                                                                                                                                                                                                                           |
| <a href="#">Inagaki, N, Yang, W, Watada, H et al. (2020) Linagliptin and cardiorenal outcomes in Asians with type 2 diabetes mellitus and established cardiovascular and/or kidney disease: subgroup analysis of the randomized CARMELINA trial.</a> Diabetology International 11(2): 129-141                        | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                                                                                                                          |
| <a href="#">Ingelgard, A., Grandy, S., Langkilde, A. et al. (2012) Health-related quality of life (EQ-5D) among type 2 diabetes mellitus patients treated with dapagliflozin for 24 weeks.</a> Diabetologia 55(suppl1): 320                                                                                          | - Conference abstract                                                                                                                                                                                                                                                                                                                                                                                           |
| <a href="#">Inoue, H., Morino, K., Ugi, S. et al. (2019) Ipragliflozin, a sodium-glucose cotransporter 2 inhibitor, reduces bodyweight and fat mass, but not muscle mass, in Japanese type 2 diabetes patients treated with insulin: a randomized clinical trial.</a> J Diabetes Invest 10(4): 1012-1021             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                                                                                                   |
| <a href="#">Inzucchi S, E, Fitchett, D, Jurisic-Erzen, D et al. (2020) Are the cardiovascular and kidney benefits of empagliflozin influenced by baseline glucose-lowering therapy?.</a> Diabetes, Obesity and Metabolism 22(4): 631-639                                                                             | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                                                                                                                          |
| <a href="#">Inzucchi, S.E., Davies, M., Khunti, K. et al. (2020) Association of Baseline Cardio-Metabolic Parameters on the Treatment Effects of Empagliflozin When Added to Metformin in</a>                                                                                                                        | - Conference abstract                                                                                                                                                                                                                                                                                                                                                                                           |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                 |
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| <a href="#">Patients with T2D.</a> Journal of the Endocrine Society 4(supplement1): a209                                                                                                                                                                                                                                                                                                                                   |                                                                                                        |
| <a href="#">Inzucchi, S.E., Wanner, C., Fitchett, D. et al. (2021) Empagliflozin reduced the total burden of events leading to or prolonging hospitalisation in EMPA-REG OUTCOME.</a> Diabetologia 64(supplement1): 255-s256                                                                                                                                                                                               | - Conference abstract                                                                                  |
| <a href="#">Inzucchi, S.E., Zinman, B., Wanner, C. et al. (2020) Empagliflozin reduces the total burden of all-cause hospitalizations (ACH) and mortality in Empa-Reg outcome.</a> Diabetes 69(supplement1)                                                                                                                                                                                                                | - Conference abstract                                                                                  |
| <a href="#">Inzucchi, Silvio E, Claggett, Brian L, Vaduganathan, Muthiah et al. (2022) Efficacy and safety of dapagliflozin in patients with heart failure with mildly reduced or preserved ejection fraction by baseline glycaemic status (DELIVER): a subgroup analysis from an international, multicentre, double-blind, randomised, placebo-controlled trial.</a> The lancet. Diabetes & endocrinology 10(12): 869-881 | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                         |
| <a href="#">Inzucchi, Silvio E, Davies, Melanie J, Khunti, Kamlesh et al. (2021) Empagliflozin treatment effects across categories of baseline HbA1c, body weight and blood pressure as an add-on to metformin in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 23(2): 425-433                                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Inzucchi, Silvio E, Khunti, Kamlesh, Fitchett, David H et al. (2020) Cardiovascular Benefit of Empagliflozin Across the Spectrum of Cardiovascular Risk Factor Control in the EMPA-REG OUTCOME Trial.</a> The Journal of clinical endocrinology and metabolism 105(9)                                                                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Inzucchi, Silvio E, Zinman, Bernard, Fitchett, David et al. (2018) How Does Empagliflozin Reduce Cardiovascular Mortality? Insights From a Mediation Analysis of the EMPA-REG OUTCOME Trial.</a> Diabetes care 41(2): 356-363                                                                                                                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Irfan, Hamza (2024) Obesity, Cardiovascular Disease, and the Promising Role of Semaglutide: Insights from the SELECT Trial.</a> Current problems in cardiology 49(1pta): 102060                                                                                                                                                                                                                                | - Commentary only                                                                                      |
| <a href="#">Irie, Yoko, Katakami, Naoto, Mita, Tomoya et al. (2018) Evaluation of the Effect of Alogliptin on</a>                                                                                                                                                                                                                                                                                                          | - Subgroup analysis of a trial that was not relevant for inclusion                                     |

| Study                                                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                                                                                                          |
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| <a href="#">Tissue Characteristics of the Carotid Wall: Subanalysis of the SPEAD-A Trial.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 9(1): 317-329                                                                                                                                                                                 |                                                                                                                                                                                                                                 |
| <a href="#">Ishii, H., Nakajima, H., Kamei, N. et al. (2020) Quality-of-Life Comparison of Dapagliflozin Versus Dipeptidyl Peptidase 4 Inhibitors in Patients with Type 2 Diabetes Mellitus: A Randomized Controlled Trial (J-BOND Study).</a> Diabetes Therapy 11(12): 2959-2977                                                                                                  | - Comparator in study does not match that specified in this review protocol<br><br><i>The type of DPP4 inhibitor was not specific to a certain drug and therefore could not be classified for the analysis</i>                  |
| <a href="#">Ishii, Hitoshi, Hansen, Brian B, Langer, Jakob et al. (2021) Effect of Orally Administered Semaglutide Versus Dulaglutide on Diabetes-Related Quality of Life in Japanese Patients with Type 2 Diabetes: The PIONEER 10 Randomized, Active-Controlled Trial.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 12(2): 613-623 | - Additional outcomes relevant to living guideline work<br><br><i>Reports additional HR-QoL data (Diabetes Therapy-Related Quality of Life questionnaire). Original trial article (Yabe 2020) reports SF-36v2 (acute) data.</i> |
| <a href="#">Ishii, Hitoshi, Onishi, Yukiko, Oura, Tomonori et al. (2020) Once-Weekly Dulaglutide with Insulin Therapy for Type 2 Diabetes: Efficacy and Safety Results from a Phase 4, Randomized, Placebo-Controlled Study.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 11(1): 133-145                                             | - Study design not relevant to this review protocol                                                                                                                                                                             |
| <a href="#">Ishii, Hitoshi; Oura, Tomonori; Takeuchi, Masakazu (2023) Treatment Satisfaction and Quality of Life with Tirzepatide Versus Dulaglutide Among Japanese Patients with Type 2 Diabetes: Exploratory Evaluation of the SURPASS J-mono Trial.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 14(12): 2173-2183                | - No relevant outcomes reported                                                                                                                                                                                                 |
| <a href="#">Ishikawa, Shinji, Shimano, Masayuki, Watarai, Masato et al. (2014) Impact of sitagliptin on carotid intima-media thickness in patients with coronary artery disease and impaired glucose tolerance or mild diabetes mellitus.</a> The American journal of cardiology 114(3): 384-8                                                                                     | - Population not relevant to this review protocol                                                                                                                                                                               |
| <a href="#">Ishtiaque, A., Khan, S.M., Azhar, S. et al. (2022) A Comparison of the Efficacy of Dapagliflozin Metformin Versus Sitagliptin Metformin: in Newly Diagnosed Type 2 Diabetes.</a> Pakistan Journal of Medical and Health Sciences 16(10): 459-461                                                                                                                       | - Population not relevant to this review protocol                                                                                                                                                                               |
| <a href="#">Ito, D., Shimizu, S., Inoue, K. et al. (2017) Comparison of ipragliflozin and pioglitazone</a>                                                                                                                                                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                                                 | Reason                                                                                                                                               |
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| <a href="#">effects on nonalcoholic fatty liver disease in patients with type 2 diabetes: A randomized, 24-week, open-label, active-controlled trial.</a> Diabetes Care 40(10): 1364-1372                                                                                                                                                                             |                                                                                                                                                      |
| <a href="#">Ito, Daisuke, Inoue, Kazuyuki, Saito, Daigo et al. (2021) Effects of Dapagliflozin Compared with Sitagliptin and Metformin in Drug-Naive Japanese Patients with Type 2 Diabetes: A 12-Week, Open-Label, Randomized, Active-Controlled Trial.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 12(12): 3201-3215 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                              |
| <a href="#">Ito, M., Abe, M., Okada, K. et al. (2011) The dipeptidyl peptidase-4 (DPP-4) inhibitor vildagliptin improves glycemic control in type 2 diabetic patients undergoing hemodialysis.</a> Endocrine J 58(11): 979-87                                                                                                                                         | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>   |
| <a href="#">Ito, S., Kashihara, N., Shikata, K. et al. (2020) Esaxerenone (CS-3150) in Patients with Type 2 Diabetes and Microalbuminuria (ESAX-DN): phase 3 Randomized Controlled Clinical Trial.</a> Clinical journal of the American Society of Nephrology 15(12): 1715-1727                                                                                       | - Study does not contain an intervention relevant to this review protocol<br><i>Intervention not specified in the protocol</i>                       |
| <a href="#">Iwase, M., Asano, T., Sasaki, N et al. (2010) Withdrawal of pioglitazone in patients with type 2 diabetes mellitus.</a> Journal of clinical pharmacy and therapeutics 35(4): 401-8                                                                                                                                                                        | - Trial that has a treatment and follow up period of less than 24 weeks                                                                              |
| <a href="#">Jackson, R A, Hawa, M I, Jaspan, J B et al. (1987) Mechanism of metformin action in non-insulin-dependent diabetes.</a> Diabetes 36(5): 632-40                                                                                                                                                                                                            | - Trial that has a treatment and follow up period of less than 24 weeks                                                                              |
| <a href="#">Jacob, A. N., Salinas, K., Adams-Huet, B. et al. (2007) Weight gain in type 2 diabetes mellitus.</a> Diabetes Obes Metab 9(3): 386-93                                                                                                                                                                                                                     | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Jain, R., Osei, K., Kupfer, S. et al. (2006) Long-term safety of pioglitazone versus glyburide in patients with recently diagnosed type 2 diabetes mellitus.</a> Pharmacotherapy 26(10): 1388-95                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Jameshorani, Maryam, Sayari, Saba, Kiahashemi, Narjes et al. (2017) Comparative Study on Adding Pioglitazone or Sitagliptin to Patients with Type 2 Diabetes Mellitus Insufficiently Controlled With Metformin.</a> Open                                                                                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>12 weeks</i>                                                           |



| Study                                                                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                    |
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| access Macedonian journal of medical sciences 5(7): 955-962                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                           |
| <a href="#">Jammah, Anwar Ali (2021) Indirect comparison of efficacy and safety of insulin glargine/lixisenatide and insulin degludec/insulin aspart in type 2 diabetes patients not controlled on basal insulin. Primary care diabetes 15(1): 132-137</a>                                                                                                                           | - Study design not relevant to this review protocol                                                                                                       |
| <a href="#">Janani, Leila, Bamehr, Hadi, Tanha, Kiarash et al. (2021) Effects of Sitagliptin as Monotherapy and Add-On to Metformin on Weight Loss among Overweight and Obese Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis. Drug research 71(9): 477-488</a>                                                                                                 | - Study design not relevant to this review protocol<br><br><i>Systematic review and meta-analysis, includes trials with minimum duration of 2 months.</i> |
| <a href="#">Janez, Andrej, Orsy, Petra, Stachlewska, Karolina et al. (2020) Benefits of insulin degludec/liraglutide are maintained even in patients discontinuing sulphonylureas or dipeptidyl peptidase-4 inhibitors upon initiation of degludec/liraglutide therapy: A post hoc analysis of the DUAL II and DUAL IX trials. Diabetes, obesity &amp; metabolism 22(4): 658-668</a> | - Secondary publication of an included study that does not provide any additional relevant information                                                    |
| <a href="#">Janka, Hans U, Plewe, Gerd, Riddle, Matthew C et al. (2005) Comparison of basal insulin added to oral agents versus twice-daily premixed insulin as initial insulin therapy for type 2 diabetes. Diabetes care 28(2): 254-9</a>                                                                                                                                          | - Study does not contain an intervention relevant to this review protocol                                                                                 |
| <a href="#">Januzzi, James L Jr, Butler, Javed, Jarolim, Petr et al. (2017) Effects of Canagliflozin on Cardiovascular Biomarkers in Older Adults With Type 2 Diabetes. Journal of the American College of Cardiology 70(6): 704-712</a>                                                                                                                                             | - Secondary publication of an included study that does not provide any additional relevant information                                                    |
| <a href="#">Januzzi, James L Jr, Liu, Yuxi, Sattar, Naveed et al. (2024) Vascular endothelial growth factors and risk of cardio-renal events: Results from the CRENCE trial. American heart journal 271: 38-47</a>                                                                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                                    |
| <a href="#">Januzzi, James L Jr, Xu, Jialin, Li, JingWei et al. (2020) Effects of Canagliflozin on Amino-Terminal Pro-B-Type Natriuretic Peptide: Implications for Cardiovascular Risk Reduction. Journal of the American College of Cardiology 76(18): 2076-2085</a>                                                                                                                | - Secondary publication of an included study that does not provide any additional relevant information                                                    |

| Study                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                   |
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| <a href="#">Jardine, M.J., Mahaffey, K.W., Agarwal, R. et al. (2019) Renal, cardiovascular, and safety outcomes of canagliflozin (CANA) according to baseline kidney function: A credence secondary analysis.</a> Journal of the American Society of Nephrology 30: 100-101                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Jardine, Meg J, Zhou, Zien, Mahaffey, Kenneth W et al. (2020) Renal, Cardiovascular, and Safety Outcomes of Canagliflozin by Baseline Kidney Function: A Secondary Analysis of the CREDENCE Randomized Trial.</a> Journal of the American Society of Nephrology : JASN 31(5): 1128-1139                           | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Jarnert, C., Landstedt-Hallin, L., Malmberg, K. et al. (2009) A randomized trial of the impact of strict glycaemic control on myocardial diastolic function and perfusion reserve: A report from the DADD (Diabetes mellitus and Diastolic Dysfunction) study.</a> European Journal of Heart Failure 11(1): 39-47 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Jarolim, Petr, White, William B, Cannon, Christopher P et al. (2018) Serial Measurement of Natriuretic Peptides and Cardiovascular Outcomes in Patients With Type 2 Diabetes in the EXAMINE Trial.</a> Diabetes care 41(7): 1510-1515                                                                             | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Jecht, M (2019) Adjunctive liraglutide treatment in patients with persistent or recurrent type 2 diabetes after bariatric surgery: the GRAVITAS trial.</a> Diabetologie 15(8): 740-743                                                                                                                            | - Study not reported in English                                                                                                                                          |
| <a href="#">Jendle, Johan, Birkenfeld, Andreas L, Polonsky, William H et al. (2019) Improved treatment satisfaction in patients with type 2 diabetes treated with once-weekly semaglutide in the SUSTAIN trials.</a> Diabetes, obesity & metabolism 21(10): 2315-2326                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Jensen, J., Omar, M., Kistorp, C. et al. (2021) Metabolic Effects of Empagliflozin in Heart Failure : A Randomized, Double-Blind, and Placebo-Controlled Trial (Empire HF Metabolic).</a> Circulation 143(22): 2208-2210                                                                                          | - Population not relevant to this review protocol                                                                                                                        |
| <a href="#">Jensen, Jacob K, Zobel, Emilie H, von Scholten, Bernt J et al. (2021) Effect of 26 Weeks of Liraglutide Treatment on Coronary Artery Inflammation in Type 2 Diabetes Quantified by</a>                                                                                                                            | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |

| Study                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                               |
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| <a href="#">[64Cu]Cu-DOTATATE PET/CT: Results from the LIRAFLAME Trial.</a> Frontiers in endocrinology 12: 790405                                                                                                                                                                                            |                                                                                                                                                      |
| <a href="#">Jensen, Troels M; Saha, Kishore; Steinberg, William M (2015) Is there a link between liraglutide and pancreatitis? A post hoc review of pooled and patient-level data from completed liraglutide type 2 diabetes clinical trials.</a> Diabetes care 38(6): 1058-66                               | - Secondary publication of an included study that does not provide any additional relevant information                                               |
| <a href="#">Jeon, H. J. and Oh, T. K. (2011) Comparison of vildagliptin-metformin and glimepiride-metformin treatments in type 2 diabetic patients.</a> Diabetes Metab J 35(5): 529-35                                                                                                                       | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Jeon, HJ; Ku, EJ; Oh, TK (2018) Dapagliflozin improves blood glucose in diabetes on triple oral hypoglycemic agents having inadequate glucose control.</a> Diabetes research and clinical practice 142(pp188194)                                                                                 | - Study design not relevant to this review protocol                                                                                                  |
| <a href="#">Jeon, Won Kyeong, Kang, Jeehoon, Kim, Hyo-Soo et al. (2022) Correction to: "Cardiovascular Outcomes Comparison of Dipeptidyl Peptidase-4 Inhibitors Versus Sulfonylurea as Add-on Therapy for Type 2 Diabetes Mellitus: A Meta-Analysis".</a> Journal of lipid and atherosclerosis 11(1): 89-101 | - Study design not relevant to this review protocol<br><i>Correction only</i>                                                                        |
| <a href="#">Jeon, Won Kyeong, Kang, Jeehoon, Kim, Hyo-Soo et al. (2021) Cardiovascular Outcomes Comparison of Dipeptidyl Peptidase-4 Inhibitors versus Sulfonylurea as Add-on Therapy for Type 2 Diabetes Mellitus: a Meta-Analysis.</a> Journal of lipid and atherosclerosis 10(2): 210-222                 | - Article retracted                                                                                                                                  |
| <a href="#">Jerums, G., Murray, R. M., Seeman, E. et al. (1987) Lack of effect of gliclazide on early diabetic nephropathy and retinopathy: a two-year controlled study.</a> Diabetes Res Clin Pract 3(2): 71-80                                                                                             | - Population not relevant to this review protocol                                                                                                    |
| <a href="#">Jha, V. (2020) Reducing risk of kidney failure in people with diabetes.</a> National Medical Journal of India 33(1): 31-32                                                                                                                                                                       | - Commentary only                                                                                                                                    |
| <a href="#">Jhund, Pardeep S, Solomon, Scott D, Docherty, Kieran F et al. (2021) Efficacy of Dapagliflozin on Renal Function and Outcomes in Patients With Heart Failure With Reduced Ejection</a>                                                                                                           | - Population not relevant to this review protocol                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                        |
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| <a href="#">Fraction: Results of DAPA-HF</a> . Circulation 143(4): 298-309                                                                                                                                                                                                                                                              |                                                                                               |
| <a href="#">Ji, L., Bian, F., Pan, T. et al. (2023) HSK7653, a Novel Ultralong-Acting DPP-4 Inhibitor, as Monotherapy in Patients With Type 2 Diabetes- A Randomized, Double-Blind, Placebo-Controlled Phase III Trial</a> . Diabetes 72(supplement1)                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Ji, L., Dong, X., Li, Y. et al. (2020) Efficacy and safety of once-weekly semaglutide vs once-daily sitagliptin as add-on to metformin in patients with type 2 diabetes (SUSTAIN China): a 30-week double-blind, phase 3a, randomised trial</a> . Diabetes, obesity & metabolism                                            | - Duplicate reference                                                                         |
| <a href="#">Ji, L., Li, L., Ma, J. et al. (2021) Efficacy and safety of teneligliptin added to metformin in Chinese patients with type 2 diabetes mellitus inadequately controlled with metformin: A phase 3, randomized, double-blind, placebo-controlled study</a> . Endocrinology, and Diabetes & Metabolism 4(2): e00222            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Ji, L., Lu, Y., Li, Q. et al. (2023) Efficacy and safety of empagliflozin in combination with insulin in Chinese patients with type 2 diabetes and insufficient glycaemic control: A Phase III, randomised, double-blind, placebo-controlled, parallel study</a> . Diabetes, obesity & metabolism                           | - Duplicate reference                                                                         |
| <a href="#">Ji, L., Ma, J., Lu, W. et al. (2021) Phase III, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of teneligliptin monotherapy in Chinese patients with type 2 diabetes mellitus inadequately controlled with diet and exercise</a> . Journal of Diabetes Investigation 12(4): 537-545 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Ji, Linong, Liu, Jie, Xu, Zhi Jin et al. (2023) Efficacy and Safety of Ertugliflozin Added to Metformin: A Pooled Population from Asia with Type 2 Diabetes and Overweight or Obesity</a> . Diabetes therapy : research, treatment and education of diabetes and related disorders 14(2): 319-334                           | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                |
| <a href="#">Ji, Linong, Lu, Jinmiao, Gao, Leili et al. (2023) A randomized, double-blind, placebo controlled, phase 3 trial to evaluate the efficacy and safety of cetagliptin added to ongoing metformin therapy in patients with uncontrolled type 2</a>                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                                                                                                                             |
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| <a href="#">diabetes with metformin monotherapy.</a> Diabetes, obesity & metabolism                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                    |
| <a href="#">Ji, Linong, Lu, Jinmiao, Gao, Leili et al. (2023) Efficacy and safety of cetagliptin as monotherapy in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled phase 3 trial.</a> Diabetes, obesity & metabolism                                                                                                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                      |
| <a href="#">Ji, Linong, Zinman, Bernard, Patel, Sanjay et al. (2015) Efficacy and safety of linagliptin co-administered with low-dose metformin once daily versus high-dose metformin twice daily in treatment-naïve patients with type 2 diabetes: a double-blind randomized trial.</a> Advances in therapy 32(3): 201-15                                                                                                                       | - Trial that has a treatment and follow up period of less than 24 weeks<br><br>14 weeks                                                                                                                                                                            |
| <a href="#">Ji, Ming, Xia, Libin, Cao, Jingzhu et al. (2016) Sitagliptin/Metformin Versus Insulin Glargine Combined With Metformin in Obese Subjects With Newly Diagnosed Type 2 Diabetes.</a> Medicine 95(11): e2961                                                                                                                                                                                                                            | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares to insulin glargine + metformin, which is not a comparator specified in the protocol (specifies comparison to insulin but not insulin combined with metformin).</i> |
| <a href="#">Jia, Shubing, Wang, Zhiying, Han, Ruobing et al. (2021) Incretin mimetics and sodium-glucose co-transporter 2 inhibitors as monotherapy or add-on to metformin for treatment of type 2 diabetes: a systematic review and network meta-analysis.</a> Acta diabetologica 58(1): 5-18                                                                                                                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                            |
| <a href="#">Jia, Weiping, Xiao, Xinhua, Ji, Qiuhe et al. (2015) Comparison of thrice-daily premixed insulin (insulin lispro premix) with basal-bolus (insulin glargine once-daily plus thrice-daily prandial insulin lispro) therapy in east Asian patients with type 2 diabetes insufficiently controlled with twice-daily premixed insulin: an open-label, randomised, controlled trial.</a> The lancet. Diabetes & endocrinology 3(4): 254-62 | - Conference abstract                                                                                                                                                                                                                                              |
| <a href="#">Jian, X., Yang, Q. L., Xiao, S. et al. (2018) The effects of a sodium-glucose cotransporter 2 inhibitor on diabetic nephropathy and serum oxidized low-density lipoprotein levels.</a> Eur Rev Med Pharmacol Sci 22(12): 3994-3999                                                                                                                                                                                                   | - No relevant outcomes reported                                                                                                                                                                                                                                    |
| <a href="#">Jiang, Lili, Jia, Yanyan, Wang, Xiaoyu et al. (2023) Insights into efficacy and safety of dapagliflozin treatment for the management in older adults with type 2 diabetes: a systematic</a>                                                                                                                                                                                                                                          | - Study design not relevant to this review protocol<br><br><i>Systematic review/meta-analysis. Minimum treatment period = 3 months.</i>                                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                               |
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| <a href="#">review and meta-analysis</a> . Expert opinion on drug safety: 1-10                                                                                                                                                                                                                                                                  |                                                                                                                                                      |
| <a href="#">Jiang, Meng, Liu, Qiaoshu, Jiang, Tiejian et al. (2021) Adding Sodium-Glucose Co-Transporter 2 Inhibitors to Sulfonylureas and Risk of Hypoglycemia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials</a> . <i>Frontiers in endocrinology</i> 12: 713192                                                       | - Study design not relevant to this review protocol<br><br><i>Systematic review/meta-analysis. Includes trials &lt; 24 weeks duration.</i>           |
| <a href="#">Jiang, Xiaojie, Shi, Tingting, Han, Dan et al. (2024) Exenatide and Metformin Improve Serum Indices and Intestinal Flora in patients with Type 2 Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease</a> . <i>JPM. The Journal of the Pakistan Medical Association</i> 74(1): 138-140                                           | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Jiang, Yu, Yang, Pingping, Fu, Linghua et al. (2022) Comparative Cardiovascular Outcomes of SGLT2 Inhibitors in Type 2 Diabetes Mellitus: A Network Meta-Analysis of Randomized Controlled Trials</a> . <i>Frontiers in endocrinology</i> 13: 802992                                                                                | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Jibrán, R., Suliman, M. I., Qureshi, F. et al. (2006) Safety and efficacy of repaglinide compared with glibenclamide in the management of type 2 diabetic Pakistani patients</a> . <i>Pak J Med Sci</i> 22(4): 385-90                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Jin, S-M, Park, S W, Yoon, K-H et al. (2015) Anagliptin and sitagliptin as add-ons to metformin for patients with type 2 diabetes: a 24-week, multicentre, randomized, double-blind, active-controlled, phase III clinical trial with a 28-week extension</a> . <i>Diabetes, obesity &amp; metabolism</i> 17(5): 511-5              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Jin, Zijie, Yuan, Yan, Zheng, Chen et al. (2023) Effects of sodium-glucose co-transporter 2 inhibitors on liver fibrosis in non-alcoholic fatty liver disease patients with type 2 diabetes mellitus: An updated meta-analysis of randomized controlled trials</a> . <i>Journal of diabetes and its complications</i> 37(8): 108558 | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Jodar, E., Dib, A., Bray, R. et al. (2023) IDF2022-0540 Impact of weight on Time in Range, Time in Tight Range, and Glycemic Variability as measured using CGM (SURPASS-3 CGM)</a> . <i>Diabetes Research and Clinical Practice</i> 197(supplement1): 110312                                                                        | - Secondary publication of an included study that does not provide any additional relevant information                                               |



| Study                                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                         |
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| <a href="#">Jodar, E., Michelsen, M., Polonsky, W.H. et al. (2020) Semaglutide improves health-related quality of life vs placebo when added to standard of care in patients with type 2 diabetes at high cardiovascular risk (SUSTAIN 6).</a> Diabetes, obesity & metabolism                                                                                           | - Duplicate reference                                                                                                                          |
| <a href="#">Johansson, Lars, Hockings, Paul D, Johnsson, Eva et al. (2020) Dapagliflozin plus saxagliptin add-on to metformin reduces liver fat and adipose tissue volume in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 22(7): 1094-1101                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                         |
| <a href="#">Johnston, P. S., Feig, P. U., Coniff, R. F. et al. (1998) Long-term titrated-dose alpha-glucosidase inhibition in non-insulin-requiring Hispanic NIDDM patients.</a> Diabetes Care 21(3): 409-15                                                                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |
| <a href="#">Johnston, P. S., Feig, P. U., Coniff, R. F. et al. (1998) Chronic treatment of African-American type 2 diabetic patients with alpha-glucosidase inhibition.</a> Diabetes Care 21(3): 416-22                                                                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |
| <a href="#">Johnston, P. S., Lebovitz, H. E., Coniff, R. F. et al. (1998) Advantages of alpha-glucosidase inhibition as monotherapy in elderly type 2 diabetic patients.</a> J Clin Endocrinol Metab 83(5): 1515-22                                                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |
| <a href="#">Jorsal, Anders, Kistorp, Caroline, Holmager, Pernille et al. (2017) Effect of liraglutide, a glucagon-like peptide-1 analogue, on left ventricular function in stable chronic heart failure patients with and without diabetes (LIVE)-a multicentre, double-blind, randomised, placebo-controlled trial.</a> European journal of heart failure 19(1): 69-77 | - Population not relevant to this review protocol<br><i>includes population with and without diabetes. Results are not reported separately</i> |
| <a href="#">Joshi, Shashank R, Rajput, Rajesh, Chowdhury, Subhankar et al. (2022) The role of oral semaglutide in managing type 2 diabetes in Indian clinical settings: Addressing the unmet needs.</a> Diabetes & metabolic syndrome 16(6): 102508                                                                                                                     | - Study design not relevant to this review protocol<br><i>No minimum trial duration specified.</i>                                             |
| <a href="#">Josse, R. G., Chiasson, J. L., Ryan, E. A. et al. (2003) Acarbose in the treatment of elderly patients with type 2 diabetes.</a> Diabetes Res Clin Pract 59(1): 37-42                                                                                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                  |

| Study                                                                                                                                                                                                                                                                                                     | Reason                                                                                                 |
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| <a href="#">Josse, Robert G, Majumdar, Sumit R, Zheng, Yinggan et al. (2017) Sitagliptin and risk of fractures in type 2 diabetes: Results from the TECOS trial.</a> Diabetes, obesity & metabolism 19(1): 78-86                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Joubert, M., Opigez, V., Pavlikova, B. et al. (2020) Efficacy and safety of Exenatide as add-on therapy for type 2 diabetes patients with intensive insulin regimen: a randomized double-blind trial.</a> Diabetes, obesity & metabolism                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Jovanovic, L., Dailey, G., Huang, W. C. et al. (2000) Repaglinide in type 2 diabetes: a 24-week, fixed-dose efficacy and safety study.</a> J Clin Pharm 40(1): 49-57                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Jovanovic, L., Hassman, D. R., Gooch, B. et al. (2004) Treatment of type 2 diabetes with a combination regimen of repaglinide plus pioglitazone.</a> Diabetes Res Clin Pract 63(2): 127-34                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Jung, H. S., Youn, B. S., Cho, Y. M. et al. (2005) The effects of rosiglitazone and metformin on the plasma concentrations of resistin in patients with type 2 diabetes mellitus.</a> Metabol Clin Exper 54(3): 314-20                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Jurgens, Mikkel, Schou, Morten, Hasbak, Philip et al. (2019) Design of a randomised controlled trial of the effects of empagliflozin on myocardial perfusion, function and metabolism in type 2 diabetes patients at high cardiovascular risk (the SIMPLE trial).</a> BMJ open 9(11): e029098 | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Jurisic-Erzen, D., Johansen, O.E., George, J. et al. (2017) Effect of empagliflozin when added to insulin in patients with type 2 diabetes and established cardiovascular disease: Results from the EMPA-REG OUTCOME trial.</a> Diabetologie und Stoffwechsel 12(supplement1)                 | - Conference abstract                                                                                  |
| <a href="#">Juurinen, L., Tiikkainen, M., Saltevo, J. et al. (2009) Nateglinide combination therapy with basal insulin and metformin in patients with Type 2 diabetes.</a> Diabetic Med 26(4): 409-15                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Jyotsna, F, Mahfooz, K, Patel, T et al. (2023) A Systematic Review and Meta-Analysis on the Efficacy and Safety of Finerenone Therapy in</a>                                                                                                                                                  | - Study does not contain an intervention relevant to this review protocol<br><br><i>Finerenone</i>     |

| Study                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                 |
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| <a href="#">Patients with Cardiovascular and Chronic Kidney Diseases in Type 2 Diabetes Mellitus.</a> Cureus 15(7): e41746                                                                                                                                                                                                                  |                                                                                                        |
| <a href="#">Kadoglou, N. P., Iliadis, F., Angelopoulou, N. et al. (2008) Beneficial effects of rosiglitazone on novel cardiovascular risk factors in patients with Type 2 diabetes mellitus.</a> Diabet Med 25(3): 333-40                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kadoglou, N. P., Iliadis, F., Liapis, C. D. et al. (2007) Beneficial effects of combined treatment with rosiglitazone and exercise on cardiovascular risk factors in patients with type 2 diabetes.</a> Diabetes Care 30(9): 2242-4                                                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kadoglou, N. P., Kapelouzou, A., Tsanikidis, H. et al. (2011) Effects of rosiglitazone/metformin fixed-dose combination therapy and metformin monotherapy on serum vaspin, adiponectin and IL-6 levels in drug-naïve patients with type 2 diabetes.</a> Exp Clin Endocrinol Diabetes 119(2): 63-8                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kadowaki, T., Inagaki, N., Kondo, K. et al. (2018) Efficacy and safety of teneligliptin added to canagliflozin monotherapy in Japanese patients with type 2 diabetes mellitus: a multicentre, randomized, double-blind, placebo-controlled, parallel-group comparative study.</a> Diab Obes Metab 20(2): 453-457                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kadowaki, T., Isendahl, J., Khalid, U. et al. (2022) Semaglutide once a week in adults with overweight or obesity, with or without type 2 diabetes in an east Asian population (STEP 6): a randomised, double-blind, double-dummy, placebo-controlled, phase 3a trial.</a> The Lancet Diabetes and Endocrinology 10(3): 193-206 | - Population not relevant to this review protocol                                                      |
| <a href="#">Kadowaki, T., Wang, G., Rosenstock, J et al. (2020) Effect of linagliptin, a dipeptidyl peptidase-4 inhibitor, compared with the sulfonylurea glimepiride on cardiovascular outcomes in Asians with type 2 diabetes: subgroup analysis of the randomized CAROLINA trial.</a> Diabetology International                          | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Kadowaki, Takashi, Chin, Rina, Ozeki, Akichika et al. (2022) Safety and efficacy of tirzepatide as an add-on to single oral antihyperglycaemic medication in patients with type 2 diabetes in Japan (SURPASS J-combo): a multicentre,</a>                                                                                       | - Comparator in study does not match that specified in this review protocol                            |

| Study                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                                                                                                                                 |
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| <a href="#">randomised, open-label, parallel-group, phase 3 trial</a> . The lancet. Diabetes & endocrinology 10(9): 634-644                                                                                                                                                                     |                                                                                                                                                                                                                                                                        |
| <a href="#">Kadowaki, Takashi, Haneda, Masakazu, Inagaki, Nobuya et al. (2015) Efficacy and safety of empagliflozin monotherapy for 52 weeks in Japanese patients with type 2 diabetes: a randomized, double-blind, parallel-group study</a> . Advances in therapy 32(4): 306-18                | - Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>12 weeks comparison of empagliflozin 5, 10, 25 or 50mg or placebo followed by 40 weeks of extension. 5, 50 and placebo were assigned to 10 and 25 mg during the extension period</i> |
| <a href="#">Kadowaki, Takashi, Nangaku, Masaomi, Hantel, Stefan et al. (2019) Empagliflozin and kidney outcomes in Asian patients with type 2 diabetes and established cardiovascular disease: Results from the EMPA-REG OUTCOME R trial</a> . Journal of diabetes investigation 10(3): 760-770 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                 |
| <a href="#">Kadro, W., Al Turkmani, M., Kadro, K. et al. (2020) The effect of SGLT2 inhibitors on silent myocardial ischemia</a> . European Heart Journal 41(suppl2): 1446                                                                                                                      | - Conference abstract                                                                                                                                                                                                                                                  |
| <a href="#">Kahl, S., Gancheva, S., Strassburger, K. et al. (2019) Effects of empagliflozin on liver fat content in type 2 diabetes: The emlifa001 trial</a> . Diabetes 68(supplement1)                                                                                                         | - Conference abstract                                                                                                                                                                                                                                                  |
| <a href="#">Kahn, S. E., Haffner, S. M., Heise, M. A. et al. (2006) Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy</a> . N Engl J Med 355(23): 2427-43                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                          |
| <a href="#">Kahn, S., Perkovic, V., Erik Johansen, O. et al. (2019) Baseline Characteristics and Effects on CV and Kidney Outcomes with Linagliptin Versus Placebo, Across GFR Categories in CARMELINA</a> . Journal of the Endocrine Society 3(supplement1)                                    | - Conference abstract                                                                                                                                                                                                                                                  |
| <a href="#">Kahn, S., Varkonyi, T., Pavo, I. et al. (2023) IDF2022-0918 Tirzepatide reduces serum triglyceride irrespective of fibrate use in people with T2D at high CV risk (SURPASS-4)</a> . Diabetes Research and Clinical Practice 197(supplement1): 110401                                | - Post-hoc analysis of included study                                                                                                                                                                                                                                  |
| <a href="#">Kaku, K., Araki, E., Tanizawa, Y. et al. (2019) Superior efficacy with the fixed-ratio combination of insulin degludec and liraglutide (IDegLira) compared with insulin degludec and</a>                                                                                            | - Duplicate reference                                                                                                                                                                                                                                                  |

| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                  |
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| <a href="#">liraglutide in insulin-naive Japanese subjects with type 2 diabetes in a phase 3, open-label, randomised trial.</a> Diabetes, obesity & metabolism                                                                                                                                                                                                      |                                                                                                                                                         |
| <a href="#">Kaku, K., Daida, H., Kashiwagi, A. et al. (2009) Long-term effects of pioglitazone in Japanese patients with type 2 diabetes without a recent history of macrovascular morbidity.</a> Curr Med Res Opin 25(12): 2925-32                                                                                                                                 | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparison which is not specified in the protocol.</i> |
| <a href="#">Kaku, K., Kadowaki, T., Seino, Y. et al. (2021) Efficacy and safety of ipragliflozin in Japanese patients with type 2 diabetes and inadequate glycaemic control on sitagliptin.</a> Diabetes, Obesity & Metabolism 23(9): 2099-2108                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                           |
| <a href="#">Kaku, K., Rasmussen, M. F., Nishida, T. et al. (2011) Fifty-two-week, randomized, multicenter trial to compare the safety and efficacy of the novel glucagon-like peptide-1 analog liraglutide vs glibenclamide in patients with type2 diabetes.</a> J Diabetes Invest 2(6): 441-7                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                           |
| <a href="#">Kaku, K., Sumino, S., Katou, M. et al. (2017) Randomized, double-blind, phase III study to evaluate the efficacy and safety of once-daily treatment with alogliptin and metformin hydrochloride in Japanese patients with type 2 diabetes.</a> Diabetes Obes Metab 19(3): 463-467                                                                       | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>  |
| <a href="#">Kaku, K., Watada, H., Iwamoto, Y. et al. (2014) Efficacy and safety of monotherapy with the novel sodium/glucose cotransporter-2 inhibitor tofogliflozin in Japanese patients with type 2 diabetes mellitus: A combined Phase 2 and 3 randomized, placebo-controlled, double-blind, parallel-group comparative study.</a> Cardiovasc Diabetol 13(1): 65 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                           |
| <a href="#">Kaku, Kohei, Kiyosue, Arihiro, Ono, Yuri et al. (2016) Liraglutide is effective and well tolerated in combination with an oral antidiabetic drug in Japanese patients with type 2 diabetes: A randomized, 52-week, open-label, parallel-group trial.</a> Journal of diabetes investigation 7(1): 76-84                                                  | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>  |
| <a href="#">Kaku, Kohei, Lee, Jisoo, Mattheus, Michaela et al. (2017) Empagliflozin and Cardiovascular Outcomes in Asian Patients With Type 2 Diabetes and Established Cardiovascular Disease - Results From EMPA-REG OUTCOME</a>                                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                                  |

| Study                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                 |
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| <a href="#">R. Circulation journal : official journal of the Japanese Circulation Society 81(2): 227-234</a>                                                                                                                                                                                                                                                   |                                                                                                        |
| <a href="#">Kaku, Kohei, Wanner, Christoph, Anker, Stefan D et al. (2022) The effect of empagliflozin on the total burden of cardiovascular and hospitalization events in the Asian and non-Asian populations of the EMPA-REG OUTCOME trial of patients with type 2 diabetes and cardiovascular disease. Diabetes, obesity &amp; metabolism 24(4): 662-674</a> | - Study design not relevant to this review protocol<br><i>Post hoc analysis</i>                        |
| <a href="#">Kaku, Kohei, Yamada, Yuichiro, Watada, Hirotaka et al. (2018) Safety and efficacy of once-weekly semaglutide vs additional oral antidiabetic drugs in Japanese people with inadequately controlled type 2 diabetes: A randomized trial. Diabetes, obesity &amp; metabolism 20(5): 1202-1212</a>                                                    | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Kalluri, Sahithi Reddy, Bhutta, Tinaz H, Hannoodde, Hanan et al. (2021) Do SGLT2 Inhibitors Improve Cardio-Renal Outcomes in Patients With Type II Diabetes Mellitus: A Systematic Review. Cureus 13(9): e17668</a>                                                                                                                                | - Study design                                                                                         |
| <a href="#">Kan, Chengxia, Zhang, Yang, Han, Fang et al. (2021) Mortality Risk of Antidiabetic Agents for Type 2 Diabetes With COVID-19: A Systematic Review and Meta-Analysis. Frontiers in endocrinology 12: 708494</a>                                                                                                                                      | - Study design not relevant to this review protocol<br><i>Minimum trial duration not specified.</i>    |
| <a href="#">Kan, Mengfan, Fu, Hui, Xu, Yunsheng et al. (2023) Effects of once-weekly glucagon-like peptide-1 receptor agonists on type 2 diabetes mellitus complicated with coronary artery disease: Potential role of the renin-angiotensin system. Diabetes, obesity &amp; metabolism</a>                                                                    | - Systematic review used as source of primary studies                                                  |
| <a href="#">Kanazawa, I., Yamamoto, M., Yamaguchi, T. et al. (2011) Effects of metformin and pioglitazone on serum pentosidine levels in type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes 119(6): 362-5</a>                                                                                                                                              | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Kanazawa, Ippei, Tanaka, Ken-Ichiro, Notsu, Masakazu et al. (2017) Long-term efficacy and safety of vildagliptin add-on therapy in type 2 diabetes mellitus with insulin treatment. Diabetes research and clinical practice 123: 9-17</a>                                                                                                          | - Comparator in study does not match that specified in this review protocol                            |



| Study                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                 |
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| <a href="#">Kaneko, Shizuka, Chow, Francis, Choi, Dong Seop et al. (2015) Insulin degludec/insulin aspart versus biphasic insulin aspart 30 in Asian patients with type 2 diabetes inadequately controlled on basal or pre-/self-mixed insulin: a 26-week, randomised, treat-to-target trial. Diabetes research and clinical practice 107(1): 139-47</a>                      | - Study does not contain an intervention relevant to this review protocol                              |
| <a href="#">Kaneko, Shizuka, Nishijima, Keiji, Bosch-Traberg, Heidrun et al. (2018) Efficacy and safety of adding liraglutide to existing insulin regimens in Japanese patients with type 2 diabetes mellitus: A post-hoc analysis of a phase 3 randomized clinical trial. Journal of diabetes investigation 9(4): 840-849</a>                                                | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Kaneko, Shizuka, Oura, Tomonori, Matsui, Akiko et al. (2017) Efficacy and safety of subgroup analysis stratified by baseline HbA1c in a Japanese phase 3 study of dulaglutide 0.75 mg compared with insulin glargine in patients with type 2 diabetes. Endocrine journal 64(12): 1165-1172</a>                                                                    | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Kaneko, Shizuka; Ueda, Youhei; Tahara, Yumiko (2018) GLP1 Receptor Agonist Liraglutide Is an Effective Therapeutic Option for Perioperative Glycemic Control in Type 2 Diabetes within Enhanced Recovery After Surgery (ERAS) Protocols. European surgical research. Europäische chirurgische Forschung. Recherches chirurgicales europeennes 59(56): 349-360</a> | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Kaneko, T, Sakamoto, N, Toyota, T et al. (1997) Clinical Evaluation of Glimepiride (HOE490) in Non-Insulin-Dependent Diabetes Mellitus: a Double-Blind Study versus Gliclazide (Phase III Additional Study). Rinsho iyaku (journal of clinical therapeutics and medicines) 13(17): 4479-4511</a>                                                                  | - Study not reported in English                                                                        |
| <a href="#">Kang, Seon Mee, Yun, Han Mi, Sohn, Minji et al. (2023) Vascular and metabolic effects of ipragliflozin versus sitagliptin (IVS) in type 2 diabetes treated with sulphonylurea and metformin: IVS study. Diabetes, obesity &amp; metabolism 25(7): 1922-1931</a>                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kanie, Takayoshi, Mizuno, Atsushi, Takaoka, Yoshimitsu et al. (2021) Dipeptidyl peptidase-4 inhibitors, glucagon-like peptide 1 receptor</a>                                                                                                                                                                                                                      | - Population not relevant to this review protocol                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                       |
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| <a href="#">agonists and sodium-glucose co-transporter-2 inhibitors for people with cardiovascular disease: a network meta-analysis</a> . The Cochrane database of systematic reviews 10: cd013650                                                                                                                                                                               |                                                                                              |
| <a href="#">Kann, P H, Wascher, T, Zackova, V et al. (2006) Starting insulin therapy in type 2 diabetes: twice-daily biphasic insulin Aspart 30 plus metformin versus once-daily insulin glargine plus glimepiride</a> . Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association 114(9): 527-32 | - Comparator in study does not match that specified in this review protocol                  |
| <a href="#">Kanna, Balavenkatesh and Abreu-Pacheco, Heidi (2007) An open, randomized, parallel-group study to compare the efficacy and safety profile of inhaled human insulin (Exubera) with glibenclamide as adjunctive therapy in patients with type 2 diabetes poorly controlled on metformin: response to Barnett et al</a> . Diabetes care 30(2): 445-446                  | - Not a peer-reviewed publication<br><i>This a letter response to a study (Barnett 2006)</i> |
| <a href="#">Kanozawa, Koichi, Noguchi, Yuichi, Sugahara, Souichi et al. (2018) The renoprotective effect and safety of a DPP-4 inhibitor, sitagliptin, at a small dose in type 2 diabetic patients with a renal dysfunction when changed from other DPP-4 inhibitors: REAL trial</a> . Clinical and experimental nephrology 22(4): 825-834                                       | - Study design not relevant to this review protocol<br><i>Single arm study</i>               |
| <a href="#">Karagianni, P., Polyzos, S.A., Kartali, N. et al. (2013) Comparative efficacy of exenatide versus insulin glargine on glycemic control in type 2 diabetes mellitus patients inadequately treated with metformin monotherapy</a> . Advances in Medical Sciences 58(1): 38-43                                                                                          | - Study design not relevant to this review protocol<br><i>Non-randomised trial</i>           |
| <a href="#">Karagiannis, T., Avgerinos, I., Tsapas, A. et al. (2022) Effect of tirzepatide on fasting lipids in patients with type 2 diabetes: Meta-analysis of randomised controlled trials</a> . Diabetologia 65(supplement1): 77                                                                                                                                              | - Conference abstract                                                                        |
| <a href="#">Karagiannis, T.; Tsapas, A.; Bekiari, E. (2022) Meta-analysis of sodium glucose cotransporter 2 inhibitors in older people with cardiorenal comorbidities</a> . European Geriatric Medicine 13(supplement1): 112-s113                                                                                                                                                | - Conference abstract                                                                        |
| <a href="#">Karagiannis, Thomas, Avgerinos, Ioannis, Liakos, Aris et al. (2022) Management of type 2</a>                                                                                                                                                                                                                                                                         | - Systematic review used as source of primary studies                                        |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                              |
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| <a href="#">diabetes with the dual GIP/GLP-1 receptor agonist tirzepatide: a systematic review and meta-analysis</a> . <i>Diabetologia</i> 65(8): 1251-1261                                                                                                                                                                                                                                                                 |                                                                                                     |
| <a href="#">Karagiannis, Thomas, Tsapas, Apostolos, Athanasiadou, Eleni et al. (2021) GLP-1 receptor agonists and SGLT2 inhibitors for older people with type 2 diabetes: A systematic review and meta-analysis</a> . <i>Diabetes research and clinical practice</i> 174: 108737                                                                                                                                            | - Study design not relevant to this review protocol<br><i>Minimum trial duration not specified.</i> |
| <a href="#">Kario, Kazuomi, Okada, Kenta, Kato, Mitsutoshi et al. (2018) 24-Hour Blood Pressure-Lowering Effect of an SGLT-2 Inhibitor in Patients with Diabetes and Uncontrolled Nocturnal Hypertension: Results from the Randomized, Placebo-Controlled SACRA Study</a> . <i>Circulation</i>                                                                                                                              | - Trial that has a treatment and follow up period of less than 24 weeks                             |
| <a href="#">Kashiwagi, A., Akiyama, N., Shiga, T. et al. (2015) Efficacy and safety of ipragliflozin as an add-on to a sulfonylurea in Japanese patients with inadequately controlled type 2 diabetes: results of the randomized, placebo-controlled, double-blind, phase III EMIT study</a> . <i>Diabetol Int</i> 6(2): 125-138                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK       |
| <a href="#">Kashiwagi, A., Kazuta, K., Goto, K. et al. (2015) Ipragliflozin in combination with metformin for the treatment of Japanese patients with type 2 diabetes: ILLUMINATE, a randomized, double-blind, placebo-controlled study</a> . <i>Diabetes Obes Metab</i> 17(3): 304-308                                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK       |
| <a href="#">Kashiwagi, A., Shiga, T., Akiyama, N. et al. (2015) Efficacy and safety of ipragliflozin as an add-on to pioglitazone in Japanese patients with inadequately controlled type 2 diabetes: a randomized, double-blind, placebo-controlled study (the SPOTLIGHT study)</a> . <i>Diabetol Int</i> 6(2): 104-116                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK       |
| <a href="#">Kashiwagi, A., Takahashi, H., Ishikawa, H. et al. (2015) A randomized, double-blind, placebo-controlled study on long-term efficacy and safety of ipragliflozin treatment in patients with type 2 diabetes mellitus and renal impairment: Results of the Long-Term ASP1941 Safety Evaluation in Patients with Type 2 Diabetes with Renal Impairment (LANTERN) study</a> . <i>Diab Obes Metab</i> 17(2): 152-160 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK       |
| <a href="#">Katakami, N., Mita, T., Yoshii, H. et al. (2020) Tofogliflozin does not delay progression of</a>                                                                                                                                                                                                                                                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK       |

| Study                                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                                                                                                                                                                              |
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| <a href="#">carotid atherosclerosis in patients with type 2 diabetes: a prospective, randomized, open-label, parallel-group comparative study.</a><br>Cardiovascular Diabetology 19(1): 110                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                     |
| <a href="#">Katakami, Naoto, Mita, Tomoya, Yoshii, Hidenori et al. (2013) Rationale, design, and baseline characteristics of a trial for the prevention of diabetic atherosclerosis using a DPP-4 inhibitor: the Study of Preventive Effects of Alogliptin on Diabetic Atherosclerosis (SPEAD-A).</a> Journal of atherosclerosis and thrombosis 20(12): 893-902 | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                                                         |
| <a href="#">Kato Eri, T, Silverman Michael, G, Mosenzon, Ofri et al. (2019) Effect of Dapagliflozin on Heart Failure and Mortality in Type 2 Diabetes Mellitus.</a> Circulation 139(22): 2528-2536                                                                                                                                                              | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                              |
| <a href="#">Kato, H., Nagai, Y., Ohta, A. et al. (2015) Effect of sitagliptin on intrahepatic lipid content and body fat in patients with type 2 diabetes.</a><br>Diabetes Res Clin Pract 109(1): 199-205                                                                                                                                                       | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naïve and therefore the study cannot be classified into review 1.1 or 1.2<br><br><i>Around 50% of people received metformin, 50% of people were treatment naïve. Excluded as cannot classify into either review.</i> |
| <a href="#">Kato, Y., Iwata, A., Zhang, B. et al. (2017) Effects of dipeptidyl peptidase-4 inhibitor sitagliptin on coronary atherosclerosis as assessed by intravascular ultrasound in type 2 diabetes mellitus with coronary artery disease.</a><br>IJC Metab Endocr 16: 1-9                                                                                  | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                              |
| <a href="#">Katsiadas, Nikolaos, Xanthopoulos, Andrew, Giamouzis, Grigorios et al. (2022) The effect of SGLT-2i administration on red blood cell distribution width in patients with heart failure and type 2 diabetes mellitus: A randomized study.</a> Frontiers in cardiovascular medicine 9: 984092                                                         | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                              |
| <a href="#">Katsuno, Tomoyuki, Shiraiwa, Toshihiko, Iwasaki, Shingo et al. (2021) Benefit of Early Add-on of Linagliptin to Insulin in Japanese Patients With Type 2 Diabetes Mellitus: Randomized-Controlled Open-Label Trial (TRUST2).</a> Advances in therapy 38(3): 1514-1535                                                                               | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                              |
| <a href="#">Kawai, Yuki, Uneda, Kazushi, Yamada, Takayuki et al. (2022) Comparison of effects of</a>                                                                                                                                                                                                                                                            | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                               |

| Study                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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| <a href="#">SGLT-2 inhibitors and GLP-1 receptor agonists on cardiovascular and renal outcomes in type 2 diabetes mellitus patients with/without albuminuria: A systematic review and network meta-analysis.</a> Diabetes research and clinical practice 183: 109146                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <a href="#">Kawazu, S., Kanazawa, Y., Iwamoto, Y. et al. (2017) Effect of antihyperglycemic drug monotherapy to prevent the progression of mild hyperglycemia in early type 2 diabetic patients: the Japan Early Diabetes Intervention Study (JEDIS).</a> Diabetol Int 8(4): 350-365 | <p>- Study design not relevant to this review protocol</p> <p><i>While this is a randomised trial, this combines data from two trials. Only the gliclazide and metformin arms are relevant to this protocol. However, data from two trials inform the metformin arm, while only one trial informs the gliclazide arm. Given this, the metformin arm data is effectively not randomised against the gliclazide arm by the time it is reconstituted for the analysis, making this an inappropriate comparison. Therefore, this data was excluded.</i></p> |
| <a href="#">Kayano, H., Koba, S., Hirano, T. et al. (2020) Dapagliflozin Influences Ventricular Hemodynamics and Exercise-Induced Pulmonary Hypertension in Type 2 Diabetes Patients - A Randomized Controlled Trial.</a> Circulation Journal 84(10): 1807-1817                      | <p>- Comparator in study does not match that specified in this review protocol</p> <p><i>Usual care comparator which is not specified in the protocol</i></p>                                                                                                                                                                                                                                                                                                                                                                                           |
| <a href="#">Kaze, Arnaud D, Zhuo, Min, Kim, Seoyoung C et al. (2022) Association of SGLT2 inhibitors with cardiovascular, kidney, and safety outcomes among patients with diabetic kidney disease: a meta-analysis.</a> Cardiovascular diabetology 21(1): 47                         | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <a href="#">Keidai, Yamato, Yoshiji, Satoshi, Hasebe, Masashi et al. (2023) Stabilization of kidney function and reduction in heart failure events with sodium-glucose co-transporter 2 inhibitors: A meta-analysis and meta-regression analysis.</a> Diabetes, obesity & metabolism | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <a href="#">Kelly, A. S., Thelen, A. M., Kaiser, D. R. et al. (2007) Rosiglitazone improves endothelial function and inflammation but not asymmetric dimethylarginine or oxidative stress in patients with type 2 diabetes mellitus.</a> Vasc Med 12(4): 311-8                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <a href="#">Kelly, Michael, Lewis, Jelena, Rao, Hindu et al. (2022) Effects of GLP-1 receptor agonists on cardiovascular outcomes in patients with type 2 diabetes and chronic kidney disease: A</a>                                                                                 | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

| Study                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                 |
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| <a href="#">systematic review and meta-analysis.</a><br>Pharmacotherapy 42(12): 921-928                                                                                                                                                                                                                                          |                                                                                                        |
| <a href="#">Khamnueva, LY and Andreeva, LS (2023) [Efficacy of treatment with glucagon-like peptide receptor agonists-1 in Asian patients with type 2 diabetes mellitus]. Problemy endokrinologii</a> 69(2): 38-46                                                                                                               | - Study not reported in English                                                                        |
| <a href="#">Khan, M, Murray, F T, Karunaratne, M et al. (2006) Pioglitazone and reductions in post-challenge glucose levels in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 8(1): 31-8                                                                                                                      | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Khan, Muhammad Shahzeb, Butler, Javed, Anker, Stefan D et al. (2023) Impact of Empagliflozin in Heart Failure With Reduced Ejection Fraction in Patients With Ischemic Versus Nonischemic Cause.</a> Journal of the American Heart Association 12(1): e027652                                                        | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                         |
| <a href="#">Khan, Muhammad Shahzeb, Segar, Matthew W, Usman, Muhammad Shariq et al. (2023) Effect of Canagliflozin on Heart Failure Hospitalization in Diabetes According to Baseline Heart Failure Risk.</a> JACC. Heart failure                                                                                                | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Khan, P, Venkatesh, S, Parveen, R et al. (2023) Longitudinal efficacy of Ertugliflozin in type 2 diabetes: a meta-analysis of randomized controlled trials.</a> Expert opinion on pharmacotherapy                                                                                                                    | - Systematic review used as source of primary studies                                                  |
| <a href="#">Khan, Z, Naeem, MO, Khan, SK et al. (2023) Comparing Efficacy and Safety of Different Doses of Tirzepatide for the Treatment of Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials.</a> Cureus 15(8): e44314                                                                                  | - Systematic review used as source of primary studies                                                  |
| <a href="#">Khanolkar, M. P., Morris, R. H., Thomas, A. W. et al. (2008) Rosiglitazone produces a greater reduction in circulating platelet activity compared with gliclazide in patients with type 2 diabetes mellitus--an effect probably mediated by direct platelet PPARgamma activation.</a> Atherosclerosis 197(2): 718-24 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kheniser, Karim and Kashyap, Sangeeta R (2017) Canagliflozin versus placebo for post-bariatric surgery patients with persistent type II</a>                                                                                                                                                                          | - Commentary only                                                                                      |



| Study                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                                                                                                                                                                                                                     |
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| <a href="#">diabetes: A randomized controlled trial (CARAT)</a> . Diabetes, obesity & metabolism 19(4): 609-610                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                            |
| <a href="#">Khorlampenko, AA, Karetnikova, VN, Kochergina, AM et al. (2020) Effect of empagliflozin on renal filtration in patients with coronary heart disease undergoing percutaneous coronary intervention</a> . Kardiologiia 60(6): 825                                                                                                                            | - Study not reported in English                                                                                                                                                                                                                                                                                                            |
| <a href="#">Kim, H. J., Jeong, I. K., Hur, K. Y. et al. (2022) Comparison of Efficacy of Glimepiride, Alogliptin, and Alogliptin-Pioglitazone as the Initial Periods of Therapy in Patients with Poorly Controlled Type 2 Diabetes Mellitus: an Open-Label, Multicenter, Randomized, Controlled Study</a> . Diabetes & metabolism journal                              | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naïve and therefore the study cannot be classified into review 1.1 or 1.2<br><br><i>Around 70% of people were taking another antidiabetic medication, around 30% were drug naïve. Excluded as difficult to classify into either review.</i> |
| <a href="#">Kim, Hye-Soon, Kim, Doo-Man, Cha, Bong-Soo et al. (2014) Efficacy of glimepiride/metformin fixed-dose combination vs metformin uptitration in type 2 diabetic patients inadequately controlled on low-dose metformin monotherapy: A randomized, open label, parallel group, multicenter study in Korea</a> . Journal of diabetes investigation 5(6): 701-8 | - Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>Treatment period ranged from 12 to 24 weeks</i>                                                                                                                                                                                                          |
| <a href="#">Kim, Ji Soo, Lee, Gyeongsil, Park, Kyung-Il et al. (2024) Comparative Effect of Glucose-Lowering Drugs for Type 2 Diabetes Mellitus on Stroke Prevention: A Systematic Review and Network Meta-Analysis</a> . Diabetes & metabolism journal                                                                                                                | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                      |
| <a href="#">Kim, N., Kim, J., Moon, J. et al. (2023) Efficacy of initial triple combination therapy with metformin, dapagliflozin and saxagliptin in drug-naïve patients with type 2 diabetes: a randomised controlled trial</a> . Diabetologia 66(supplement1): 151                                                                                                   | - Conference abstract                                                                                                                                                                                                                                                                                                                      |
| <a href="#">Kim, S. G., Kim, D. M., Woo, J. T. et al. (2014) Efficacy and safety of lomeglitazone monotherapy in patients with type 2 diabetes mellitus over 24-weeks: a multicenter, randomized, double-blind, parallel-group, placebo controlled trial</a> . PLoS ONE 9(4): e92843                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                              |
| <a href="#">Kim, S. G., Kim, K. J., Yoon, K. H. et al. (2020) Efficacy and safety of lomeglitazone versus</a>                                                                                                                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                 |
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| <a href="#">sitagliptin as an add-on to metformin in patients with type 2 diabetes with two or more components of metabolic syndrome over 24 weeks.</a> Diabetes Obes Metab                                                                                                                                                                     |                                                                                                        |
| <a href="#">Kim, Sun-Woo, Baik, Sei Hyun, Yoon, Kun Ho et al. (2010) Efficacy and safety of vildagliptin/pioglitazone combination therapy in Korean patients with diabetes.</a> World journal of diabetes 1(5): 153-60                                                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Kinduryte Schorling, Ona, Clark, Douglas, Zwiener, Isabella et al. (2020) Pooled Safety and Tolerability Analysis of Empagliflozin in Patients with Type 2 Diabetes Mellitus.</a> Advances in therapy 37(8): 3463-3484                                                                                                              | - Review article but not a systematic review                                                           |
| <a href="#">Kirkman, M. S., Shankar, R. R., Shankar, S. et al. (2006) Treating postprandial hyperglycemia does not appear to delay progression of early type 2 diabetes: the Early Diabetes Intervention Program.</a> Diabetes Care 29(9): 2095-101                                                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kis, S.G., Khunti, K., Maldonado, M. et al. (2016) Linagliptin (LINA) as add-on to empagliflozin (EMPA) and metformin in patients with type 2 diabetes (T2DM): Subgroup analysis by baseline demographics in two 24-week randomized, double-blind, parallel-group trials.</a> Diabetes 65(supplement1): a297-a298                   | - Conference abstract                                                                                  |
| <a href="#">Kitazawa, M., Katagiri, T., Suzuki, H. et al. (2021) A 52-week randomized controlled trial of ipragliflozin or sitagliptin in type 2 diabetes combined with metformin: The N-ISM study.</a> Diabetes, Obesity & Metabolism 23(3): 811-821                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kitazawa, T., Seino, H., Ohashi, H. et al. (2020) Comparison of tofogliflozin versus glimepiride as the third oral agent added to metformin plus a dipeptidyl peptidase-4 inhibitor in Japanese patients with type 2 diabetes: A randomized, 24-week, open-label, controlled trial (STOP-OB).</a> Diabetes Obes Metab 22: 1659-1663 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Kiyici, S., Ersoy, C., Kaderli, A. et al. (2009) Effect of rosiglitazone, metformin and medical nutrition treatment on arterial stiffness, serum MMP-9 and MCP-1 levels in drug naive type 2 diabetic patients.</a> Diabetes Res Clin Pract 86(1): 44-50                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                        |
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| <a href="#">Kiyosue, Arihiro, Seino, Yutaka, Nishijima, Keiji et al. (2018) Safety and efficacy of the combination of the glucagon-like peptide-1 receptor agonist liraglutide with an oral antidiabetic drug in Japanese patients with type 2 diabetes: Post-hoc analysis of a randomized, 52-week, open-label, parallel-group trial.</a> Journal of diabetes investigation 9(4): 831-839                              | - Comparator in study does not match that specified in this review protocol                   |
| <a href="#">Kjeldsen, S.A.S., Gluud, L.L., Werge, M. et al. (2023) Circulating Nephilysin Activity Is Increased In Type 2 Diabetes And Fatty Liver Disease, And Reduces Following Bariatric Surgery And Liraglutide Therapy.</a> Journal of the Endocrine Society 7(supplement1): a483-a484                                                                                                                             | - Conference abstract                                                                         |
| <a href="#">Klein, W (1991) Sulfonylurea-metformin-combination versus sulfonylurea-insulin-combination in secondary failures of sulfonylurea monotherapy. Results of a prospective randomized study in 50 patients.</a> Diabete & metabolisme 17(1pt2): 235-40                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Klonoff, David C, Buse, John B, Nielsen, Loretta L et al. (2008) Exenatide effects on diabetes, obesity, cardiovascular risk factors and hepatic biomarkers in patients with type 2 diabetes treated for at least 3 years.</a> Current medical research and opinion 24(1): 275-86                                                                                                                           | - Review article but not a systematic review<br><i>Pooled analysis</i>                        |
| <a href="#">Ko, G. T., Tsang, P. C., Wai, H. P. et al. (2006) Rosiglitazone versus bedtime insulin in the treatment of patients with conventional oral antidiabetic drug failure: a 1-year randomized clinical trial.</a> Adv Ther 23(5): 799-808                                                                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Kobo, O., Cavender, M.A., Jensen, T.J. et al. (2024) Once-weekly semaglutide reduces the risk of cardiovascular events in people with type 2 diabetes and polyvascular disease: A post hoc analysis.</a> Diabetes, Obesity and Metabolism 26(3): 1129-1132                                                                                                                                                  | - Post-hoc analysis of included study                                                         |
| <a href="#">Kodama, Satoru, Fujihara, Kazuya, Ishiguro, Hajime et al. (2023) Network meta-analysis of glucose-lowering drug treatment regimens with the potential risk of hypoglycemia in patients with type 2 diabetes mellitus in terms of glycemic control and severe hypoglycemia.</a> Journal of investigative medicine : the official publication of the American Federation for Clinical Research 71(4): 400-410 | - Trial that has a treatment and follow up period of less than 24 weeks                       |

| Study                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                         |
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| <a href="#">Kohan, Donald Elliott, Fioretto, Paola, Johnsson, Kristina et al. (2016) The effect of dapagliflozin on renal function in patients with type 2 diabetes. Journal of nephrology 29(3): 391-400</a>                                                                                                                                       | - Systematic review used as source of primary studies                                                                                                                                          |
| <a href="#">Kokic, Slaven, Bukovic, Damir, Radman, Maja et al. (2003) Lispro insulin and metformin versus other combination in the diabetes mellitus type 2 management after secondary oral antidiabetic drug failure. Collegium antropologicum 27(1): 181-7</a>                                                                                    | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                        |
| <a href="#">Kolkailah, A., Aharonovich, A., Lingvay, I. et al. (2022) Effects of once-weekly semaglutide on coronary outcomes in patients with type 2 diabetes mellitus with or at high risk for cardiovascular disease: insights from the SUSTAIN-6 trial. European Journal of Preventive Cardiology 29(suppl1): i59-i61</a>                       | - Conference abstract                                                                                                                                                                          |
| <a href="#">Kolkailah, Ahmed A, Lingvay, Ildiko, Dobrecky-Mery, Idit et al. (2023) Effects of once-weekly subcutaneous semaglutide on coronary artery disease outcomes in patients with type 2 diabetes with or at high risk for cardiovascular disease: Insights from the SUSTAIN-6 trial. Diabetes, obesity &amp; metabolism 25(4): 1117-1120</a> | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                                                                                                                 |
| <a href="#">Komiya, N (2011) PERISCOPE (Pioglitazone Effect on Regression of Intravascular Sonographic Coronary Obstruction Prospective Evaluation) trial. Nihon rinsho [Japanese journal of clinical medicine] 69suppl9: 331-335</a>                                                                                                               | - Study not reported in English                                                                                                                                                                |
| <a href="#">Komorizono, Yasuji, Hosoyamada, Kaori, Imamura, Naoko et al. (2021) Metformin dose increase versus added linagliptin in non-alcoholic fatty liver disease and type 2 diabetes: An analysis of the J-LINK study. Diabetes, obesity &amp; metabolism 23(3): 832-837</a>                                                                   | - Comparator in study does not match that specified in this review protocol<br><i>Linagliptin and metformin vs. higher dose of metformin in people who have previously received metformin.</i> |
| <a href="#">Kongmalai, Tanawan, Srinonprasert, Varalak, Anothaisintawee, Thunyarat et al. (2023) New anti-diabetic agents for the treatment of non-alcoholic fatty liver disease: a systematic review and network meta-analysis of randomized controlled trials. Frontiers in endocrinology 14: 1182037</a>                                         | - Population not relevant to this review protocol                                                                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                   |
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| <a href="#">Konig, Manige, Riddle, Matthew C, Colhoun, Helen M et al. (2021) Exploring potential mediators of the cardiovascular benefit of dulaglutide in type 2 diabetes patients in REWIND.</a> Cardiovascular diabetology 20(1): 194                                                                                                                                                             | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                                                                                           |
| <a href="#">Konwar, M., Bose, D., Jaiswal, S.K. et al. (2022) Efficacy and Safety of Liraglutide 3.0 mg in Patients with Overweight and Obese with or without Diabetes: A Systematic Review and Meta-Analysis.</a> International Journal of Clinical Practice 2022: 1201977                                                                                                                          | - Population not relevant to this review protocol<br><i>People with or without diabetes</i>                                                                              |
| <a href="#">Koshino, A., Neuen, B.L., Arnott, C.G. et al. (2023) Iron Biomarkers and Effects of Canagliflozin in Patients with Type 2 Diabetes and CKD: A Post Hoc Analysis of the CREDENCE Trial.</a> Journal of the American Society of Nephrology 34: 140                                                                                                                                         | - Conference abstract                                                                                                                                                    |
| <a href="#">Koshino, A., Schechter, M., Sen, T. et al. (2022) Interleukin-6 and cardiovascular outcome in patients with type 2 diabetes: New insights from CANVAS.</a> Diabetologia 65(supplement1): 282                                                                                                                                                                                             | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                                                                                           |
| <a href="#">Koshizaka, M., Ishikawa, K., Ishibashi, R. et al. (2019) Comparing the effects of ipragliflozin versus metformin on visceral fat reduction and metabolic dysfunction in Japanese patients with type 2 diabetes treated with sitagliptin: a prospective, multicentre, open-label, blinded-endpoint, randomized controlled study (PRIME-V study).</a> Diabetes Obes Metab 21(8): 1990-1995 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Koska, Juraj, Migrino, Raymond Q, Chan, Keith C et al. (2021) The Effect of Exenatide Once Weekly on Carotid Atherosclerosis in Individuals With Type 2 Diabetes: An 18-Month Randomized Placebo-Controlled Study.</a> Diabetes care 44(6): 1385-1392                                                                                                                                    | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Kovil, Rajiv, Chawla, Manoj, Shah, Tejas et al. (2022) Sodium-glucose Cotransporter-2 Inhibitors in Primary and Secondary Prevention of Cardiovascular and Renal Outcomes in Patients with Type 2 Diabetes Mellitus: A Meta-analysis.</a> The Journal of the Association of Physicians of India 70(8): 11-12                                                                             | - Study design not relevant to this review protocol<br><i>Trial duration for inclusion not specified.</i>                                                                |
| <a href="#">Kozlovski, Plamen, Foley, James, Shao, Qing et al. (2013) Vildagliptin-insulin combination</a>                                                                                                                                                                                                                                                                                           | - Post-hoc analysis of included study                                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                                   |
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| <a href="#">improves glycemic control in Asians with type 2 diabetes.</a> World journal of diabetes 4(4): 151-6                                                                                                                                                                                                                                 |                                                                                                                                                                          |
| <a href="#">Kragh, N., Nauck, M.A., Mann, J.F.E. et al. (2017) Health status assessed with EQ-5D in people with Type 2 diabetes participating in the LEADER trial.</a> Diabetic Medicine 34(supplement1): 80                                                                                                                                    | - Conference abstract                                                                                                                                                    |
| <a href="#">Kramer, C. K., Zinman, B., Choi, H. et al. (2015) The impact of chronic liraglutide therapy on glucagon secretion in type 2 diabetes: Insight from the LIBRA trial.</a> J Clin Endocrinol Metabol 100(10): 3702-9                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Kraus, Bettina J, Weir, Matthew R, Bakris, George L et al. (2021) Characterization and implications of the initial estimated glomerular filtration rate 'dip' upon sodium-glucose cotransporter-2 inhibition with empagliflozin in the EMPA-REG OUTCOME trial.</a> Kidney international 99(3): 750-762                              | - Study design not relevant to this review protocol<br><i>Posthoc analysis</i>                                                                                           |
| <a href="#">Krawczyk, A., Gajer, G., Grzeszczak, W. et al. (2005) The impact of metformin on metabolic control in obese type 2 diabetic patients treated with insulin. Preliminary observation. Polish.</a> Diabetologia Doswiadczalna i Kliniczna 5(1): 47-51                                                                                  | - Study not reported in English                                                                                                                                          |
| <a href="#">Kroonen, Marjolein Y A M, Koomen, Jeroen V, Petrykiv, Sergei I et al. (2020) Exposure-response relationships for the sodium-glucose co-transporter-2 inhibitor dapagliflozin with regard to renal risk markers.</a> Diabetes, obesity & metabolism 22(6): 916-921                                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Kubota, Yoshiaki, Yamamoto, Takeshi, Tara, Shuhei et al. (2018) Effect of Empagliflozin Versus Placebo on Cardiac Sympathetic Activity in Acute Myocardial Infarction Patients with Type 2 Diabetes Mellitus: Rationale.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 9(5): 2107-2116 | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Kuchay, M. S., Krishan, S., Mishra, S. K. et al. (2020) Effect of dulaglutide on liver fat in patients with type 2 diabetes and NAFLD: randomised controlled trial (D-LIFT trial).</a> Diabetologia 63(11): 2434-2445                                                                                                               | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                       |



| Study                                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                                                                                                                                                                      |
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| <a href="#">Kudo-Fujimaki, K., Hirose, T., Yoshihara, T. et al. (2014) Efficacy and safety of nateglinide plus vildagliptin combination therapy compared with switching to vildagliptin in type 2 diabetes patients inadequately controlled with nateglinide. J Diabetes Invest 5(4): 400-409</a>                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                               |
| <a href="#">Kunutsor, Setor K; Khunti, Kamlesh; Seidu, Samuel (2023) Racial, ethnic and regional differences in the effect of sodium-glucose co-transporter 2 inhibitors and glucagon-like peptide 1 receptor agonists on cardiovascular and renal outcomes: a systematic review and meta-analysis of cardiovascular outcome trials. Journal of the Royal Society of Medicine: 1410768231198442</a> | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                       |
| <a href="#">Kunutsor, Setor K, Zaccardi, Francesco, Balasubramanian, Victoria G et al. (2024) Glycaemic control and macrovascular and microvascular outcomes in type 2 diabetes: Systematic review and meta-analysis of cardiovascular outcome trials of novel glucose-lowering agents. Diabetes, obesity &amp; metabolism</a>                                                                      | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                       |
| <a href="#">Kuramitsu, S., Miyauchi, K., Yokoi, H. et al. (2017) Effect of sitagliptin on plaque changes in coronary artery following acute coronary syndrome in diabetic patients: the ESPECIAL-ACS study. Journal of cardiology 69(1): 369-376</a>                                                                                                                                                | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                                                          |
| <a href="#">Kuss, Oliver, Akbulut, Cihan, Schlesinger, Sabrina et al. (2022) Absolute treatment effects for the primary outcome and all-cause mortality in the cardiovascular outcome trials of new antidiabetic drugs: a meta-analysis of digitalized individual patient data. Acta diabetologica 59(10): 1349-1359</a>                                                                            | - Systematic review used as source of primary studies<br><i>Individual patient data meta analysis that combined studies that reported different population strata as categorised for the purposes of this review. Therefore, the analysis was not usable for this review. However, the studies were checked and included in the review.</i> |
| <a href="#">Kutoh, Eiji and Ukai, Yasuhiro (2012) Alogliptin as an initial therapy in patients with newly diagnosed, drug naive type 2 diabetes: a randomized, control trial. Endocrine 41(3): 435-41</a>                                                                                                                                                                                           | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                                                                                                     |
| <a href="#">Laakso, Markku, Rosenstock, Julio, Groop, Per-Henrik et al. (2015) Treatment with the dipeptidyl peptidase-4 inhibitor linagliptin or placebo followed by glimepiride in patients with</a>                                                                                                                                                                                              | - Conference abstract<br><i>Letter reporting data previously reported in conference posters.</i>                                                                                                                                                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                 |
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| <a href="#">type 2 diabetes with moderate to severe renal impairment: a 52-week, randomized, double-blind clinical trial.</a> Diabetes care 38(2): e15-7                                                                                                                                                                                          |                                                                                                        |
| <a href="#">Lam, K. S., Tiu, S. C., Tsang, M. W. et al. (1998) Acarbose in NIDDM patients with poor control on conventional oral agents. A 24-week placebo-controlled study.</a> Diabetes Care 21(7): 1154-8                                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Lambers Heerspink, H.J., Waijer, S.W., Vart, P. et al. (2021) Efficacy and safety of dapagliflozin on kidney and cardiovascular outcomes by baseline albuminuria: A secondary analysis of the DAPA-CKD trial.</a> Diabetologia 64(supplement1): 30                                                                                    | - Conference abstract                                                                                  |
| <a href="#">Lane, W, Weinrib, S, Rappaport, J et al. (2014) The effect of addition of liraglutide to high-dose intensive insulin therapy: a randomized prospective trial.</a> Diabetes, obesity & metabolism 16(9): 827-32                                                                                                                        | - Data not reported in an extractable format or a format that can be analysed                          |
| <a href="#">Langslet, G., Zinman, B., Wanner, C. et al. (2016) Cardiovascular (CV) outcomes according to LDL cholesterol (LDL-C) levels in empa-reg outcome.</a> Diabetes 65(supplement1): a111                                                                                                                                                   | - Conference abstract                                                                                  |
| <a href="#">Langslet, Gisle, Zinman, Bernard, Wanner, Christoph et al. (2020) Cardiovascular outcomes and LDL-cholesterol levels in EMPA-REG OUTCOME R.</a> Diabetes & vascular disease research 17(6): 1479164120975256                                                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Larkins, R G, Jerums, G, Taft, J L et al. (1988) Lack of effect of gliclazide on platelet aggregation in insulin-treated and non-insulin-treated diabetes: a two-year controlled study.</a> Diabetes research and clinical practice 4(2): 81-7                                                                                        | - No relevant outcomes reported                                                                        |
| <a href="#">Larsen, Emil List, Kjaer, Laura K, Lundby-Christensen, Louise et al. (2022) Effects of 18-months metformin versus placebo in combination with three insulin regimens on RNA and DNA oxidation in individuals with type 2 diabetes: A post-hoc analysis of a randomized clinical trial.</a> Free radical biology & medicine 178: 18-25 | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Lautsch, Dominik, Alsumali, Adnan, McLeod, Euan et al. (2021) Comparative Efficacy of Dual</a>                                                                                                                                                                                                                                        | - Comparator in study does not match that specified in this review protocol                            |

| Study                                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                                                                                                                                                                                                     |
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| <a href="#">and Single Initiation of Add-On Oral Antihyperglycemic Agents in Type 2 Diabetes Uncontrolled on Metformin Alone: A Systematic Literature Review and Network Meta-Analysis.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 12(1): 389-418                                                                                                | <i>Addition of dual or single drugs - not specified as a specific drug as stated in the protocol for this review</i>                                                                                                                                                                                                                       |
| <a href="#">Lavalle Cobo, Augusto, Masson, Walter, Lobo, Martin et al. (2023) Ethnic/Racial and Geographic Disparities on Major Cardiovascular Events in Glucagon Like Peptide-1 receptor Agonists Trials: A Meta-Analysis.</a> Current problems in cardiology 48(11): 101940                                                                                                                    | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                      |
| <a href="#">Lavalle-Cobo, Augusto, Masson, Walter, Lobo, Martin et al. (2021) Glucagon-like Peptide-1 Receptor Agonists and Cardioprotective Benefit in Patients with Type 2 Diabetes Without Baseline Metformin: A Systematic Review and Update Meta-analysis.</a> High blood pressure & cardiovascular prevention : the official journal of the Italian Society of Hypertension 28(6): 605-612 | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                      |
| <a href="#">Lavrynenko, O., Abdul-Ghani, M., Alatrach, M. et al. (2020) Triple Therapy with Exenatide/Pioglitazone/Metformin vs. Conventional Therapy: Changes in Liver Fibrosis Scores after 2 Years of Treatment in Patients with New-Onset Type 2 Diabetes Mellitus.</a> Metabolism: Clinical and Experimental 104(supplement): 154111                                                        | - Conference abstract                                                                                                                                                                                                                                                                                                                      |
| <a href="#">Lavrynenko, O, Abdul-Ghani, M, Alatrach, M et al. (2022) Combination Therapy with Pioglitazone/Exenatide Metformin Reduces the Prevalence of Hepatic Fibrosis and Steatosis: the Efficacy and Durability of Initial Combination Therapy for Type 2 Diabetes (EDICT) Trial.</a> Diabetes, obesity & metabolism                                                                        | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                                                                                |
| <a href="#">Lawrence, J. M., Reid, J., Taylor, G. J. et al. (2004) Favorable effects of pioglitazone and metformin compared with gliclazide on lipoprotein subfractions in overweight patients with early type 2 diabetes.</a> Diabetes Care 27(1): 41-6                                                                                                                                         | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naïve and therefore the study cannot be classified into review 1.1 or 1.2<br><br><i>Around 70% of people were taking another antidiabetic medication, around 30% were drug naïve. Excluded as difficult to classify into either review.</i> |
| <a href="#">Lebovitz, H. E., Dole, J. F., Patwardhan, R. et al. (2001) Rosiglitazone monotherapy is effective in</a>                                                                                                                                                                                                                                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                       |
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| <a href="#">patients with type 2 diabetes.</a> J Clin Endocrinol Metab 86(1): 280-8                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                              |
| <a href="#">Lee, Byung Wan, Min, KyungWan, Hong, Eun-Gyoung et al. (2023) Efficacy of Gemigliptin Add-on to Dapagliflozin and Metformin in Type 2 Diabetes Patients: A Randomized, Double-Blind, Placebo-Controlled Study (SOLUTION).</a> Endocrinology and metabolism (Seoul, Korea) 38(3): 328-337                                                                           | - Study does not contain an intervention relevant to this review protocol                                                                                                                    |
| <a href="#">Lee, C., Wiese, R., Allen, S. et al. (2023) IDF2022-0417 BMI category changes and percent meeting waist circumference goals with tirzepatide for type 2 diabetes from SURPASS 1-4.</a> Diabetes Research and Clinical Practice 197(supplement1): 110308                                                                                                            | - Post-hoc analysis of included study                                                                                                                                                        |
| <a href="#">Lee, Eun Young, Cho, Jae-Hyoung, Lee, Woo Je et al. (2023) Glucometabolic control of once-weekly dulaglutide switched from DPP4 inhibitor versus daily empagliflozin add-on in patients with type 2 diabetes inadequately controlled with metformin, sulfonylurea, and DPP4 inhibitor: A randomised trial.</a> Diabetes research and clinical practice 203: 110884 | - Study design not relevant to this review protocol<br><i>One of the arms was adding, and one of the arms was switching treatment. Therefore the concomitant treatment was not the same.</i> |
| <a href="#">Lee, Kai Wei, Devaraj, Navin Kumar, Ching, Siew Mooi et al. (2021) Effect of SGLT-2 Inhibitors on Non-alcoholic Fatty Liver Disease among Patients with Type 2 Diabetes Mellitus: Systematic Review with Meta-analysis and Trial Sequential Analysis of Randomized Clinical Trials.</a> Oman medical journal 36(3): e273                                           | - Comparator in study does not match that specified in this review protocol                                                                                                                  |
| <a href="#">Lee, M. M. Y., Brooksbank, K. J. M., Wetherall, K. et al. (2021) Effect of Empagliflozin on Left Ventricular Volumes in Patients With Type 2 Diabetes, or Prediabetes, and Heart Failure With Reduced Ejection Fraction (SUGAR-DM-HF).</a> Circulation 143(6): 516-525                                                                                             | - Population not relevant to this review protocol<br><i>&gt;20% had prediabetes</i>                                                                                                          |
| <a href="#">Lee, Matthew M Y, Ghouri, Nazim, McGuire, Darren K et al. (2021) Meta-analyses of Results From Randomized Outcome Trials Comparing Cardiovascular Effects of SGLT2is and GLP-1RAs in Asian Versus White Patients With and Without Type 2 Diabetes.</a> Diabetes care 44(5): 1236-1241                                                                              | - Population not relevant to this review protocol<br><i>With or without type 2 diabetes</i>                                                                                                  |
| <a href="#">Lee, Matthew M Y, Kristensen, Soren L, Gerstein, Hertz C et al. (2022) Cardiovascular and mortality outcomes with GLP-1 receptor</a>                                                                                                                                                                                                                               | - Systematic review used as source of primary studies                                                                                                                                        |

| Study                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                 |
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| <a href="#">agonists in patients with type 2 diabetes: A meta-analysis with the FREEDOM cardiovascular outcomes trial.</a> Diabetes & metabolic syndrome 16(1): 102382                                                                                                                                                        |                                                                                                        |
| <a href="#">Lee, S. H., Gantz, I., Round, E. et al. (2017) A randomized, placebo-controlled clinical trial evaluating the safety and efficacy of the once-weekly DPP-4 inhibitor omarigliptin in patients with type 2 diabetes mellitus inadequately controlled by glimepiride and metformin.</a> BMC Endocr Disord 17(1): 70 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Lee, Shaun Wen Huey, Chen, Won Sun, Sellappans, Renukha et al. (2023) Interventions for people with type 2 diabetes mellitus fasting during Ramadan.</a> The Cochrane database of systematic reviews 7: cd013178                                                                                                  | - Population not relevant to this review protocol                                                      |
| <a href="#">Lee, Yeong-Min, Lee, Soon-Hee, Kim, Tae-Hee et al. (2022) Cardiovascular outcomes with glucagon-like peptide 1 agonists and sodium-glucose cotransporter 2 inhibitors in patients with type 2 diabetes: A meta-analysis.</a> Cardiology journal 29(3): 499-508                                                    | - Systematic review used as source of primary studies                                                  |
| <a href="#">Leibowitz, G, Cahn, A, Bhatt D, L et al. (2015) Impact of treatment with saxagliptin on glycaemic stability and beta-cell function in the SAVOR-TIMI 53 study.</a> Diabetes, obesity & metabolism 17(5): 487-94                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Leiter Lawrence, A, Teoh, Hwee, Braunwald, Eugene et al. (2015) Efficacy and safety of saxagliptin in older participants in the SAVOR-TIMI 53 trial.</a> Diabetes care 38(6): 1145-53                                                                                                                             | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Leiter, L. A., Carr, M. C., Stewart, M. et al. (2014) Efficacy and safety of the once-weekly GLP-1 receptor agonist albiglutide versus sitagliptin in patients with type 2 diabetes and renal impairment: A randomized phase III study.</a> Diabetes Care 37(10): 2723-2730                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Leiter, L., Cefalu, W., DeBruin, T. et al. (2012) Dapagliflozin treatment for type 2 diabetes mellitus patients with a history of cardiovascular disease.</a> Diabetologia 55(suppl1): 310-s311                                                                                                                   | - Conference abstract                                                                                  |
| <a href="#">Leiter, Lawrence A, Langslet, Gisle, Vijapurkar, Ujjwala et al. (2016) Simultaneous Reduction in Both HbA1c and Body Weight with Canagliflozin</a>                                                                                                                                                                | - Study design not relevant to this review protocol                                                    |

| Study                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                             |
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| <a href="#">Versus Glimepiride in Patients with Type 2 Diabetes on Metformin.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 7(2): 269-78                                                                                                                                  | <i>Posthoc analysis</i>                                                                                                                            |
| <a href="#">Leonhardt, W., Hanefeld, M., Fischer, S. et al. (1991) Beneficial effects on serum lipids in noninsulin dependent diabetics by acarbose treatment.</a> Arzneimittel-Forschung 41(7): 735-8                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Lew, T., Ning, G., Ruiz, L.N. et al. (2016) Efficacy and safety of once-weekly dulaglutide versus insulin glargine in combination with metformin and/or a sulfonylurea in predominantly Asian patients with type 2 diabetes: Therapeutics of diabetes.</a> Journal of Diabetes Investigation 7(suppl2): 29 | - Conference abstract                                                                                                                              |
| <a href="#">Lewin, A., DeFronzo, R.A., Patel, S. et al. (2015) Combinations of empagliflozin/linagliptin for 24 weeks in drug-naïve subjects with Type 2 diabetes.</a> Diabetic Medicine 32(suppl1): 90                                                                                                                | - Conference abstract                                                                                                                              |
| <a href="#">Lewin, A., Lipetz, R., Wu, J. et al. (2007) Comparison of extended-release metformin in combination with a sulfonylurea (glyburide) to sulfonylurea monotherapy in adult patients with type 2 diabetes: a multicenter, double-blind, randomized, controlled, phase III study.</a> Clin Ther 29(5): 844-55  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Li, B., Luo, Y. R., Tian, F. et al. (2020) Sitagliptin attenuates the progression of coronary atherosclerosis in patients with coronary disease and type 2 diabetes.</a> Atherosclerosis 300: 10-18                                                                                                        | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Li, Chao, Zhou, Zien, Neuen, Brendon L et al. (2021) Sodium-glucose co-transporter-2 inhibition and ocular outcomes in patients with type 2 diabetes: A systematic review and meta-analysis.</a> Diabetes, obesity & metabolism 23(1): 252-257                                                             | - Trial that has a treatment and follow up period of less than 24 weeks                                                                            |
| <a href="#">Li, Chen, Luo, Jie, Jiang, Mingyan et al. (2022) The Efficacy and Safety of the Combination Therapy With GLP-1 Receptor Agonists and SGLT-2 Inhibitors in Type 2 Diabetes Mellitus: A Systematic Review and Meta-analysis.</a> Frontiers in pharmacology 13: 838277                                        | - Trial that has a treatment and follow up period of less than 24 weeks                                                                            |



| Study                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                                                                     |
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| <a href="#">Li, Chun Xing, Liu, Li Yan, Zhang, Chen Xiao et al. (2023) Comparative safety of different sodium-glucose transporter 2 inhibitors in patients with type 2 diabetes: a systematic review and network meta-analysis of randomized controlled trials. Frontiers in endocrinology 14: 1238399</a> | - Systematic review used as source of primary studies                                                                                                                                      |
| <a href="#">Li, Chun-Xing, Liang, Shuo, Gao, Lingyan et al. (2021) Cardiovascular outcomes associated with SGLT-2 inhibitors versus other glucose-lowering drugs in patients with type 2 diabetes: A real-world systematic review and meta-analysis. PloS one 16(2): e0244689</a>                          | - Study design not relevant to this review protocol<br><i>Systematic review of observational studies</i>                                                                                   |
| <a href="#">Li, D, Yang, J Yufeng, Wang, T et al. (2018) Risks of diabetic foot syndrome and amputation associated with sodium glucose co-transporter 2 inhibitors: A Meta-analysis of Randomized Controlled Trials. Diabetes &amp; metabolism 44(5): 410-414</a>                                          | - Systematic review used as source of primary studies                                                                                                                                      |
| <a href="#">Li, GuangZhi, Zhang, Dongmei, Ni, Jie et al. (2023) Clinical Efficacy of Different Doses of Canagliflozin Combined with Metformin in the Treatment of Type 2 Diabetes: Meta-Analysis. Alternative therapies in health and medicine 29(7): 328-334</a>                                          | - Systematic review used as source of primary studies                                                                                                                                      |
| <a href="#">Li, H., Xu, X., Wang, J. et al. (2019) A Randomized Study to Compare the Effects of Once-Weekly Dulaglutide Injection and Once-Daily Glimepiride on Glucose Fluctuation of Type 2 Diabetes Mellitus Patients: a 26-Week Follow-Up. Journal of diabetes research 2019: 6423987</a>              | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Subgroup analysis of Chinese participants, no relevant outcomes reported.</i> |
| <a href="#">Li, J. L., Feng, Z. P., Li, Q. F. et al. (2014) Insulin glargine effectively achieves glycemic control and improves insulin resistance in patients with early type 2 diabetes that exhibit a high risk for cardiovascular disease. Exp Ther Med 8(1): 147-152</a>                              | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                                         |
| <a href="#">Li, Jiaxi, Ji, Cheng, Zhang, Wen et al. (2023) Effect of new glucose-lowering drugs on stroke in patients with type 2 diabetes: A systematic review and Meta-analysis. Journal of diabetes and its complications 37(1): 108362</a>                                                             | - Study design not relevant to this review protocol<br><i>Minimum trial duration for inclusion not specified.</i>                                                                          |
| <a href="#">Li, Mengdi; Wang, Sining; Wang, Xiaoli (2023) Efficacy and Safety of Triple Therapy with</a>                                                                                                                                                                                                   | - Systematic review used as source of primary studies                                                                                                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                 |
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| <a href="#">SGLT-2 Inhibitor, DPP-4 Inhibitor, and Metformin in Type 2 Diabetes: A Meta-Analysis.</a><br>Alternative therapies in health and medicine                                                                                                                                                                                                               |                                                                                                                                        |
| <a href="#">Li, Mengnan, Zhang, Jian, Yang, Guimei et al. (2023) Effects of sodium-glucose cotransporter 2 inhibitors on renal risk factors in patients with abnormal glucose metabolism: a meta-analysis of randomized controlled trials.</a> European journal of clinical pharmacology 79(6): 859-871                                                             | - Population not relevant to this review protocol                                                                                      |
| <a href="#">Li, Tian, Providencia, Rui, Mu, Nan et al. (2021) Association of metformin monotherapy or combined therapy with cardiovascular risks in patients with type 2 diabetes mellitus.</a> Cardiovascular diabetology 20(1): 30                                                                                                                                | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Li, W, Chen, X, Xie, X et al. (2021) Comparison of sodium-glucose co-transporter 2 inhibitors and glucagon-like peptide receptor agonists for atrial fibrillation in type 2 diabetes mellitus: systematic review with network meta-analysis of randomised controlled trials.</a> Journal of cardiovascular pharmacology                                 | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Li, Wenjie, Chen, Xingqing, Xie, Xiangqi et al. (2022) Comparison of Sodium-Glucose Cotransporter 2 Inhibitors and Glucagon-like Peptide Receptor Agonists for Atrial Fibrillation in Type 2 Diabetes Mellitus: Systematic Review With Network Meta-analysis of Randomized Controlled Trials.</a> Journal of cardiovascular pharmacology 79(3): 281-288 | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Li, Xiang, Song, Yujie, Guo, Tao et al. (2022) Effect of glucagon-like peptide 1 receptor agonists on the renal protection in patients with type 2 diabetes: A systematic review and meta-analysis.</a> Diabetes & metabolism 48(5): 101366                                                                                                             | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Li, Xuexun, Zhang, Qian, Zhu, Lingming et al. (2021) Effects of SGLT2 inhibitors on cardiovascular, renal, and major safety outcomes in heart failure: A meta-analysis of randomized controlled trials.</a> International journal of cardiology 332: 119-126                                                                                            | - Review article but not a systematic review                                                                                           |
| <a href="#">Li, Yi Ming, Zhang, Li Hui, Li, Xue Jun et al. (2020) Efficacy and Safety of Dulaglutide Monotherapy Compared to Glimepiride in Oral Antihyperglycemic Medication-Naive Chinese patients with Type 2 Diabetes: A Post Hoc Analysis of AWARD-CHN1.</a> Diabetes therapy :                                                                                | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis</i> |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                           |
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| research, treatment and education of diabetes and related disorders 11(5): 1077-1090                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                  |
| <a href="#">Liang, Ying, Meng, Hua, Li, Ruiyu et al. (2021) A randomized controlled trial protocol of the cardiovascular safety and efficacy of liraglutide in the treatment of type 2 diabetes.</a> Medicine 100(3): e23948                                                                                                                                                                                                                                       | - Study design not relevant to this review protocol<br><i>Protocol only</i>                                                      |
| <a href="#">Liang, Ziwen, Wu, Qinan, Chen, Bing et al. (2013) Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: a randomized controlled trial.</a> Diabetes research and clinical practice 101(1): 50-6                                                                                                                                                                                                       | - Study does not contain an intervention relevant to this review protocol                                                        |
| <a href="#">Liao, Chao, Liang, Xinyin, Zhang, Xiao et al. (2023) The effects of GLP-1 receptor agonists on visceral fat and liver ectopic fat in an adult population with or without diabetes and nonalcoholic fatty liver disease: A systematic review and meta-analysis.</a> PloS one 18(8): e0289616                                                                                                                                                            | - Population not relevant to this review protocol                                                                                |
| <a href="#">Liao, Lin, Yang, Ming, Qiu, Lu-Lu et al. (2010) Appropriate insulin initiation dosage for insulin-naive type 2 diabetes outpatients receiving insulin monotherapy or in combination with metformin and/or pioglitazone.</a> Chinese medical journal 123(24): 3684-8                                                                                                                                                                                    | - Trial that has a treatment and follow up period of less than 24 weeks                                                          |
| <a href="#">Liao, Xiao-Xian, Li, Wen-Qiang, Peng, Zhi-Ke et al. (2022) Three new categories of hypoglycaemic agents and various cardiovascular diseases: A meta-analysis.</a> Journal of clinical pharmacy and therapeutics 47(5): 636-642                                                                                                                                                                                                                         | - Systematic review used as source of primary studies                                                                            |
| <a href="#">Ligthelm, Robert J, Gylvin, Titus, DeLuzio, Tony et al. (2011) A comparison of twice-daily biphasic insulin aspart 70/30 and once-daily insulin glargine in persons with type 2 diabetes mellitus inadequately controlled on basal insulin and oral therapy: a randomized, open-label study.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 17(1): 41-50 | - Comparator in study does not match that specified in this review protocol<br><i>Compares insulin to other types of insulin</i> |
| <a href="#">Lim, J.L., Bergero, G., Acharya, Y. et al. (2021) Efficacy and Safety of a Sodium-Glucose Co-Transporter-2 Inhibitor Versus Placebo as an Add-on Therapy for People With Type 2</a>                                                                                                                                                                                                                                                                    | - Conference abstract                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                      |
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| <a href="#">Diabetes Inadequately Treated With Metformin: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.</a> Journal of the Endocrine Society 5(supplement1): a469-a470                                                                                                                      |                                                                                                                             |
| <a href="#">Lim, S. and Cherney, D. (2019) Effect of dapagliflozin, a sodium-glucose cotransporter 2 inhibitor, on vascular function in patients with type 2 diabetes compared with gliclazide.</a> Diabetes 68(supplement1)                                                                                         | - Conference abstract                                                                                                       |
| <a href="#">Lim, S., Han, K. A., Yu, J. et al. (2017) Efficacy and safety of initial combination therapy with gemigliptin and metformin compared with monotherapy with either drug in patients with type 2 diabetes: A double-blind randomized controlled trial (INICOM study).</a> Diabetes Obes Metab 19(1): 87-97 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                               |
| <a href="#">Lim, S., Kim, K. M., Kim, S. G. et al. (2017) Effects of lobeglitazone, a novel thiazolidinedione, on bone mineral density in patients with type 2 diabetes mellitus over 52 weeks.</a> Diabetes Metab J 41(5): 377-385                                                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                               |
| <a href="#">Lin, B. J., Wu, H. P., Huang, H. S. et al. (2003) Efficacy and tolerability of acarbose in Asian patients with type 2 diabetes inadequately controlled with diet and sulfonylureas.</a> J Diabetes Complications 17(4): 179-85                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                               |
| <a href="#">Lin, Chu, Zhu, Xingyun, Cai, Xiaoling et al. (2021) SGLT2 inhibitors and lower limb complications: an updated meta-analysis.</a> Cardiovascular diabetology 20(1): 91                                                                                                                                    | - Population not relevant to this review protocol<br><i>Included people with type 1 or type 2 diabetes</i>                  |
| <a href="#">Lin, Donna Shu-Han; Lee, Jen-Kuang; Chen, Wen-Jone (2021) Clinical Adverse Events Associated with Sodium-Glucose Cotransporter 2 Inhibitors: A Meta-Analysis Involving 10 Randomized Clinical Trials and 71 553 Individuals.</a> The Journal of clinical endocrinology and metabolism 106(7): 2133-2145  | - Population not relevant to this review protocol<br><i>Included people with conditions other than just type 2 diabetes</i> |
| <a href="#">Lin, Donna Shu-Han, Lee, Jen-Kuang, Hung, Chi-Sheng et al. (2021) The efficacy and safety of novel classes of glucose-lowering drugs for cardiovascular outcomes: a network meta-analysis of randomised clinical trials.</a> Diabetologia 64(12): 2676-2686                                              | - Population not relevant to this review protocol                                                                           |

| Study                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                                                                                                                                                               |
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| <a href="#">Lin, Fei, Yu, Bin, Ling, Baodong et al. (2023) Weight loss efficiency and safety of tirzepatide: A Systematic review.</a> PloS one 18(5): e0285197                                                                                                                                                             | - Systematic review used as source of primary studies                                                                                                                                                                                                                                |
| <a href="#">Lin, Kaisang, Zhang, Wei, He, Fei et al. (2022) Evaluation of the Clinical Efficacy of the Treatment of Overweight and Obesity in Type 2 Diabetes Mellitus by the Telemedicine Management System Based on the Internet of Things Technology.</a> Computational intelligence and neuroscience 2022: 8149515     | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                                              |
| <a href="#">Lin, Z-W, Xu, H-W, You, H et al. (2019) Pioglitazone-metformin and basal insulin for type 2 diabetes mellitus patients with overweight or obesity and poor blood glucose control: a comparison of efficacy and metabolic effects.</a> Academic journal of second military medical university 40(10): 1089-1096 | - Study not reported in English                                                                                                                                                                                                                                                      |
| <a href="#">Lindley, R., Zhou, Z., Radholm, K. et al. (2018) Effects of canagliflozin on stroke in the canvas program.</a> European Stroke Journal 3(1supplement1): 38                                                                                                                                                     | - Conference abstract                                                                                                                                                                                                                                                                |
| <a href="#">Lindstrom, J.; Tuomilehto, J.; Spengler, M. (2000) Acarbose treatment does not change the habitual diet of patients with Type 2 diabetes mellitus.</a> Diabetic Med 17(1): 20-5                                                                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                        |
| <a href="#">Lindstrom, T, Nystrom, F H, Olsson, A G et al. (1999) The lipoprotein profile differs during insulin treatment alone and combination therapy with insulin and sulphonylureas in patients with Type 2 diabetes mellitus.</a> Diabetic medicine : a journal of the British Diabetic Association 16(10): 820-6    | - Study does not contain an intervention relevant to this review protocol                                                                                                                                                                                                            |
| <a href="#">Lingvay, I., Catariq, A., Frias, J.P. et al. (2019) Once-weekly semaglutide vs canagliflozin in type 2 diabetes: results of the SUSTAIN 8 trial.</a> Diabetologia 62(supplement1): 27-s28                                                                                                                      | - Conference abstract                                                                                                                                                                                                                                                                |
| <a href="#">Lingvay, I., Desouza, C. V., Lalic, K. S. et al. (2018) A 26-week randomized controlled trial of semaglutide once daily versus liraglutide and placebo in patients with type 2 diabetes suboptimally controlled on diet and exercise with or without metformin.</a> Diabetes Care 41(9): 1926-1937             | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2<br><br><i>States people may or may not have received metformin without stating the proportion of people</i> |

| Study                                                                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                             |
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| <a href="#">Lingvay, I., Greenberg, M.D., Gallo, S. et al. (2021) Efficacy and Safety of Ertugliflozin in Patients With Type 2 Diabetes Mellitus and Established Cardiovascular Disease Using Insulin. Journal of the Endocrine Society 5(supplement1): a331-a332</a>                                                                                                                              | - Conference abstract                                                                                                                              |
| <a href="#">Lingvay, Ildiko, Bauer, Robert, Baker-Knight, James et al. (2022) An Indirect Treatment Comparison of Semaglutide 2.0 mg vs Dulaglutide 3.0 mg and 4.5 mg Using Multilevel Network Meta-regression. The Journal of clinical endocrinology and metabolism 107(5): 1461-1469</a>                                                                                                         | - Systematic review used as source of primary studies<br><i>Identified in rerun search. No additional studies to add.</i>                          |
| <a href="#">Lingvay, Ildiko, Mosenzon, Ofri, Brown, Katelyn et al. (2023) Systolic blood pressure reduction with tirzepatide in patients with type 2 diabetes: insights from SURPASS clinical program. Cardiovascular diabetology 22(1): 66</a>                                                                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Linjawi, S., Sothiratham, R., Sari, R. et al. (2015) The study of once- and twice-daily biphasic insulin aspart 30 (BIAsp 30) with sitagliptin, and twice-daily BIAsp 30 without sitagliptin, in patients with type 2 diabetes uncontrolled on sitagliptin and metformin - The Sit2Mix trial. Primary Care Diabetes 9(5): 370-376</a>                                                  | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Linjawi, Sultan, Bode, Bruce W, Chaykin, Louis B et al. (2017) The Efficacy of IDegLira (Insulin Degludec/Liraglutide Combination) in Adults with Type 2 Diabetes Inadequately Controlled with a GLP-1 Receptor Agonist and Oral Therapy: DUAL III Randomized Clinical Trial. Diabetes therapy : research, treatment and education of diabetes and related disorders 8(1): 101-114</a> | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Linjawi, Sultan, Lee, Byung-Wan, Tabak, Omur et al. (2018) A 32-Week Randomized Comparison of Stepwise Insulin Intensification of Biphasic Insulin Aspart (BIAsp 30) Versus Basal-Bolus Therapy in Insulin-Naive Patients with Type 2 Diabetes. Diabetes therapy : research, treatment and education of diabetes and related disorders 9(1): 1-11</a>                                  | - Study does not contain an intervention relevant to this review protocol<br><i>Insulin being compared to other types of insulin</i>               |
| <a href="#">Lisco, Giuseppe, De Tullio, Anna, Disoteo, Olga et al. (2022) Basal insulin intensification with GLP-1RA and dual GIP and GLP-1RA in patients with uncontrolled type 2 diabetes</a>                                                                                                                                                                                                    | - Systematic review used as source of primary studies                                                                                              |



| Study                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                                                                                               |
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| <a href="#">mellitus: A rapid review of randomized controlled trials and meta-analysis</a> . Frontiers in endocrinology 13: 920541                                                                                                                                                                                                 | <i>Identified in rerun search. No additional studies to add.</i>                                                                                                                                                     |
| <a href="#">Liu, B.; Wang, J.; Wang, G. (2014) Beneficial effects of pioglitazone on retardation of persistent atrial fibrillation progression in diabetes mellitus patients</a> . Int Heart J 55(6): 499-505                                                                                                                      | - Population not relevant to this review protocol<br><br><i>Does not specify whether type 1 or type 2 despite clearly knowing difference (see references) so cannot elicit whether reaches T2 patient threshold.</i> |
| <a href="#">Liu, Geng, Zhong, Xueyu, Zheng, Juan et al. (2023) Comparative Efficacy of Novel Antidiabetic Drugs on Albuminuria Outcomes in Type 2 Diabetes: A Systematic Review</a> . Diabetes therapy : research, treatment and education of diabetes and related disorders                                                       | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                              |
| <a href="#">Liu, K, Ahemaiti, A, Tuernisaguli, K et al. (2023) Effect of metformin combined with DPP-4 inhibitor on alveolar bone density in patients with type 2 diabetes mellitus and chronic periodontitis</a> . Shanghai kou qiang yi xue [Shanghai journal of stomatology] 32(4): 410-416                                     | - Study not reported in English                                                                                                                                                                                      |
| <a href="#">Liu, L., Yan, H., Xia, M. et al. (2020) Efficacy of exenatide and insulin glargine on nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus</a> . Diabetes Metabol Res Rev                                                                                                                        | - Duplicate reference                                                                                                                                                                                                |
| <a href="#">Liu, Li, Shi, Fang-Hong, Xu, Hua et al. (2021) Efficacy and Safety of Ertugliflozin in Type 2 Diabetes: A Systematic Review and Meta-Analysis</a> . Frontiers in pharmacology 12: 752440                                                                                                                               | - Systematic review used as source of primary studies                                                                                                                                                                |
| <a href="#">Liu, Lin, Gao, Jian, Wang, Ruwen et al. (2023) Insulin Glargine is more suitable than Exenatide to prevent muscle loss in non-obese type 2 diabetic patients with NAFLD</a> . Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis providing no additional useful information</i>                                                                                       |
| <a href="#">Liu, Xindong, Chen, Ying, Liu, Tao et al. (2023) The effects of Sodium-glucose cotransporter 2 inhibitors on adipose tissue in patients with type 2 diabetes: A meta-analysis of randomized controlled trials</a> . Frontiers in endocrinology 14: 1115321                                                             | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                              |

| Study                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                               |
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| <a href="#">Liu, Yi, An, Chuan, Liu, Peilong et al. (2023) Comparative safety of sodium-glucose co-transporter 2 inhibitors in elderly patients with type 2 diabetes mellitus and diabetic kidney disease: a systematic review and meta-analysis. Renal failure 45(1): 2217287</a>           | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Liu, Zhijie, Bian, Ning, Wu, Shaorong et al. (2022) A meta-analysis evaluating indirectly GLP-1 receptor agonists and arrhythmias in patients with type 2 diabetes and myocardial infarction. Frontiers in cardiovascular medicine 9: 1019120</a>                                | - Trial that has a treatment and follow up period of less than 24 weeks                                                                              |
| <a href="#">Lofthouse, M. (2006) Exenatide and insulin glargine are equally effective in patients with suboptimally controlled type 2 diabetes. Nature Clinical Practice Endocrinology and Metabolism 2(1): 7</a>                                                                            | - Conference abstract                                                                                                                                |
| <a href="#">Loganathan, J., Cohen, A. C., Kaloupis, G. M. et al. (2022) A pilot clinical study to Evaluate Liraglutide-mediated Anti-platelet activity in patients with type-2 Diabetes (ELAID study). Journal of diabetes and its complications 36(5): 108188</a>                           | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Logstrup, P. (2023) Effects of semaglutide, empagliflozin or their combination on oxygenation, vascular autoregulation, and central thickness of the retina in persons with type 2 diabetes. Diabetologia 66(supplement1): 153</a>                                               | - Conference abstract                                                                                                                                |
| <a href="#">Long, Yang and Zhang, Yuxi (2023) Liraglutide combined with metformin treatment for obese people with type 2 diabetes mellitus: a systematic review and meta-analysis. Irish journal of medical science</a>                                                                      | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Lopez-Cano, Carolina, Santos, Maria Dolores, Sanchez, Enric et al. (2022) Dapagliflozin plus exenatide on patients with type 2 diabetes awaiting bariatric surgery in the DEXBASU study. Scientific reports 12(1): 3236</a>                                                      | - Comparator in study does not match that specified in this review protocol                                                                          |
| <a href="#">Lorenzo-Gonzalez, Cristina, Atienza-Sanchez, Elena, Reyes-Umpierrez, David et al. (2020) Safety And Efficacy Of Dpp-4 Inhibitors For The Management Of Hospitalized General Medicine And Surgery Patients with Type 2 Diabetes. Endocrine practice : official journal of the</a> | - Population not relevant to this review protocol                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                           |
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| American College of Endocrinology and the American Association of Clinical Endocrinologists 26(7): 722-728                                                                                                                                                                                                                                                   |                                                                                                                                  |
| <a href="#">Lou, N., Wu, X., Wang, Y. et al. (2020) Liraglutide improves postprandial blood glucose, blood glucose levels, insulin resistance and physical distribution of t2dm patients with ms. Int J Clin Experimental Med 13(2): 518-524</a>                                                                                                             | - Data not reported in an extractable format or a format that can be analysed<br><i>Outcomes reported in graphical form only</i> |
| <a href="#">Lu, C. H., Min, K. W., Chuang, L. M. et al. (2016) Efficacy, safety, and tolerability of ipragliflozin in Asian patients with type 2 diabetes mellitus and inadequate glycemic control with metformin: Results of a phase 3 randomized, placebo-controlled, double-blind, multicenter trial. J Diabetes Invest 7(3): 366-373</a>                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                    |
| <a href="#">Lu, J., Fu, L., Li, Y. et al. (2021) Henagliflozin monotherapy in patients with type 2 diabetes inadequately controlled on diet and exercise: A randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes, Obesity &amp; Metabolism 23(5): 1111-1120</a>                                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                    |
| <a href="#">Lu, Yang and Guo, Caiyun (2023) Risk of lower limb amputation in diabetic patients using SGLT2 inhibitors versus DPP4 inhibitors or GLP-1 agonists: a meta-analysis of 2 million patients. Therapeutic advances in drug safety 14: 20420986231178126</a>                                                                                         | - No relevant outcomes reported                                                                                                  |
| <a href="#">Lu, Zhengri; Ma, Genshan; Chen, Lijuan (2020) Sitagliptin on Carotid Intima-Media Thickness in Type 2 Diabetes Mellitus Patients and Anemia: A Subgroup Analysis of the PROLOGUE Study. Mediators of inflammation 2020: 8143835</a>                                                                                                              | - Comparator in study does not match that specified in this review protocol                                                      |
| <a href="#">Ludemann, Jorg; Dutting, Eva D; Dworak, Markus (2015) Patient preference and tolerability of a DPP-4 inhibitor versus a GLP-1 analog in patients with type 2 diabetes mellitus inadequately controlled with metformin: a 24-week, randomized, multicenter, crossover study. Therapeutic advances in endocrinology and metabolism 6(4): 141-8</a> | - Crossover trial with an inadequate washout period<br><i>12 weeks per crossover arm phase, no washout period</i>                |
| <a href="#">Ludvik, B., Giorgino, F., Jodar, E. et al. (2022) EFFICACY AND SAFETY OF TIRZEPATIDE, A DUAL GIP/GLP-1 RECEPTOR AGONIST, COMPARED TO INSULIN DEGLUDEC IN PATIENTS WITH TYPE 2 DIABETES</a>                                                                                                                                                       | - Conference abstract                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                               |
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| <a href="#">(SURPASS-3). Diabetologie und Stoffwechsel 17(supplement1): 30</a>                                                                                                                                                                                                                                              |                                                                                                                                                      |
| <a href="#">Luis Bautista, J, Bugos, Christine, Dirnberger, George et al. (2003) Efficacy and safety profile of glimepiride in Mexican American Patients with type 2 diabetes mellitus: a randomized, placebo-controlled study. Clinical therapeutics 25(1): 194-209</a>                                                    | - Trial that has a treatment and follow up period of less than 24 weeks                                                                              |
| <a href="#">Lukashevich, Valentina, Schweizer, Anja, Foley, James E et al. (2013) Efficacy of vildagliptin in combination with insulin in patients with type 2 diabetes and severe renal impairment. Vascular health and risk management 9: 21-8</a>                                                                        | - Study design not relevant to this review protocol<br><i>Post hoc analysis by degree of renal impairment</i>                                        |
| <a href="#">Lund, S. S., Tarnow, L., Frandsen, M. et al. (2009) Combining insulin with metformin or an insulin secretagogue in non-obese patients with type 2 diabetes: 12 month, randomised, double blind trial. BMJ 339: b4324</a>                                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |
| <a href="#">Luo, Cheng, He, Dongjuan, Yang, HongBin et al. (2022) The effect of liraglutide on renal function in type 2 diabetes: a meta-analysis of randomized controlled studies. African health sciences 22(3): 267-274</a>                                                                                              | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Lv, Xiaoyu, Wang, Hui, Chen, Chongyang et al. (2024) The Effect of Tirzepatide on Weight, Lipid Metabolism and Blood Pressure in Overweight/Obese Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Diabetes, metabolic syndrome and obesity : targets and therapy 17: 701-714</a> | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Ma, J, Liu, M, Wang, R et al. (2024) Efficacy and safety of tirzepatide in people with type 2 diabetes by baseline body mass index: an exploratory subgroup analysis of SURPASS-AP-Combo. Diabetes, obesity &amp; metabolism</a>                                                                                | - Data not reported in an extractable format or a format that can be analysed                                                                        |
| <a href="#">Ma, Jie, Fu, Jingzhi, Guo, Ningning et al. (2024) Clinical Efficacy and Safety of Liraglutide and Dapagliflozin on Glucose and Lipid Metabolism and Insulin Function in Patients with Type 2 Diabetes Mellitus. Alternative therapies in health and medicine</a>                                                | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Ma, Junhua, Lu, Jiancan, Shen, Peiling et al. (2023) Comparative efficacy and safety of sodium-glucose cotransporter 2 inhibitors for</a>                                                                                                                                                                       | - Systematic review used as source of primary studies                                                                                                |

| Study                                                                                                                                                                                                                                                                                                                            | Reason                                                                                        |
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| <a href="#">renal outcomes in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis.</a> Renal failure 45(2): 2222847                                                                                                                                                                            |                                                                                               |
| <a href="#">Ma, Yunke, Lin, Chu, Cai, Xiaoling et al. (2022) The association between the use of sodium glucose cotransporter 2 inhibitor and the risk of diabetic retinopathy and other eye disorders: a systematic review and meta-analysis.</a> Expert review of clinical pharmacology 15(7): 877-886                          | - Systematic review used as source of primary studies                                         |
| <a href="#">Madsbad, S., Kilhovd, B., Lager, I. et al. (2001) Comparison between repaglinide and glipizide in Type 2 diabetes mellitus: a 1-year multicentre study.</a> Diabetic Med 18(5): 395-401                                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Maffioli, P., Fogari, E., D'Angelo, A. et al. (2013) Ultrasonography modifications of visceral and subcutaneous adipose tissue after pioglitazone or glibenclamide therapy combined with rosuvastatin in type 2 diabetic patients not well controlled by metformin.</a> Eur J Gastroenterol Hepatol 25(9): 1113-1122 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Mahaffey, K.W., Li, J., Chang, T.I. et al. (2020) Independent predictors of heart failure in patients with type 2 diabetes and chronic kidney disease: Modeling from the CREDENCE trial.</a> European Heart Journal 41(suppl2): 1175                                                                                 | - Conference abstract                                                                         |
| <a href="#">Mahendra, A.I., Samsu, N., Gunawan, A. et al. (2023) SGLT-2 INHIBITORS DELAY KIDNEY FAILURE PROGRESSION AND REDUCE NEED OF DIALYSIS IN CHRONIC KIDNEY DISEASE PATIENTS: A META-ANALYSIS.</a> Nephrology Dialysis Transplantation 38(supplement1): i682                                                               | - Population not relevant to this review protocol                                             |
| <a href="#">Maiorino, Maria Ida, Longo, Miriam, Scappaticcio, Lorenzo et al. (2021) Improvement of glycemic control and reduction of major cardiovascular events in 18 cardiovascular outcome trials: an updated meta-regression.</a> Cardiovascular diabetology 20(1): 210                                                      | - Systematic review used as source of primary studies                                         |
| <a href="#">Mak, J.H.C., Fong, H.Y.C., Wong, Y. et al. (2023) Serum Thrombospondin-2 Level as a Novel Liver Fibrosis Biomarker That Changes with Liver Stiffness Improvement in Patients with Type 2 Diabetes.</a> Diabetes 72(supplement1)                                                                                      | - Conference abstract                                                                         |

| Study                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                     |
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| <a href="#">Mak, Jimmy Ho Cheung, Lui, David Tak-Wai, Fong, Carol Ho-Yi et al. (2024) Serum thrombospondin-2 level changes with liver stiffness improvement in patients with type 2 diabetes.</a> Clinical endocrinology 100(3): 230-237                                                                             | - Post-hoc analysis of included study                                                                                                                      |
| <a href="#">Makimattila, S; Nikkila, K; Yki-Jarvinen, H (1999) Causes of weight gain during insulin therapy with and without metformin in patients with Type II diabetes mellitus.</a> Diabetologia 42(4): 406-12                                                                                                    | - Comparator in study does not match that specified in this review protocol                                                                                |
| <a href="#">Mali, Niroj, Su, Feng, Ge, Jie et al. (2022) Efficacy of liraglutide in patients with diabetic nephropathy: a meta-analysis of randomized controlled trials.</a> BMC endocrine disorders 22(1): 93                                                                                                       | - Comparator in study does not match that specified in this review protocol<br><i>Compares to antihypertensives in most cases and usual care in others</i> |
| <a href="#">Malone, J K, Bai, S, Campaigne, B N et al. (2005) Twice-daily pre-mixed insulin rather than basal insulin therapy alone results in better overall glycaemic control in patients with Type 2 diabetes.</a> Diabetic medicine : a journal of the British Diabetic Association 22(4): 374-81                | - Comparator in study does not match that specified in this review protocol<br><i>Comparison of different types of insulin</i>                             |
| <a href="#">Mancia, Giuseppe, Cannon Christopher, P, Tikkanen, Ilkka et al. (2016) Impact of Empagliflozin on Blood Pressure in Patients With Type 2 Diabetes Mellitus and Hypertension by Background Antihypertensive Medication.</a> Hypertension (Dallas, Tex. : 1979) 68(6): 1355-1364                           | - Secondary publication of an included study that does not provide any additional relevant information                                                     |
| <a href="#">Mann, J.F., Fonseca, V.A., Mosenzon, O. et al. (2017) Safety of liraglutide versus placebo in patients with T2D and CKD in the leader trial.</a> Journal of the American Society of Nephrology 28: 575-576                                                                                               | - Conference abstract                                                                                                                                      |
| <a href="#">Mann, Johannes F E, Fonseca, Vivian A, Poulter, Neil R et al. (2020) Safety of Liraglutide in Type 2 Diabetes and Chronic Kidney Disease.</a> Clinical journal of the American Society of Nephrology : CJASN 15(4): 465-473                                                                              | - Study design not relevant to this review protocol<br><i>Post hoc analysis by the presence of macro or microalbuminuria and presence of CKD</i>           |
| <a href="#">Mannucci, Edoardo, Giaccari, Andrea, Gallo, Marco et al. (2022) Effects of pioglitazone on cardiovascular events and all-cause mortality in patients with type 2 diabetes: A meta-analysis of randomized controlled trials.</a> Nutrition, metabolism, and cardiovascular diseases : NMCD 32(3): 529-536 | - Systematic review used as source of primary studies                                                                                                      |



| Study                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                        |
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| <a href="#">Mannucci, Edoardo, Naletto, Lara, Vaccaro, Gabriele et al. (2021) Efficacy and safety of glucose-lowering agents in patients with type 2 diabetes: A network meta-analysis of randomized, active comparator-controlled trials. Nutrition, metabolism, and cardiovascular diseases : NMCD 31(4): 1027-1034</a> | - Systematic review used as source of primary studies                                                         |
| <a href="#">Mansouri, Mohammad Hadi, Mansouri, Pejman, Sadeghi, Masoumeh et al. (2023) Antianginal effects of empagliflozin in patients with type 2 diabetes and refractory angina: a randomized, double-blind placebo-controlled trial (EMPT-ANGINA Trial). Clinical cardiology</a>                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                       |
| <a href="#">Mantovani, A, Byrne, C D, Scorletti, E et al. (2020) Efficacy and safety of anti-hyperglycaemic drugs in patients with non-alcoholic fatty liver disease with or without diabetes: An updated systematic review of randomized controlled trials. Diabetes &amp; metabolism 46(6): 427-441</a>                 | - Population not relevant to this review protocol<br><i>Not all people included had type 2 diabetes</i>       |
| <a href="#">Marbury, T., Huang, W. C., Strange, P. et al. (1999) Repaglinide versus glyburide: a one-year comparison trial. Diabetes Res Clin Pract 43(3): 155-66</a>                                                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                 |
| <a href="#">Marilly, E., Cottin, J., Cabrera, N. et al. (2022) SGLT2 inhibitors in diabetes, a systematic review and meta-analysis of cardiovascular outcome trials balancing their benefits against their risks. European Journal of Clinical Pharmacology 78: 11-s12</a>                                                | - Conference abstract                                                                                         |
| <a href="#">Marilly, Elisa, Cottin, Judith, Cabrera, Natalia et al. (2022) SGLT2 inhibitors in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials balancing their risks and benefits. Diabetologia 65(12): 2000-2010</a>                                                             | - Systematic review used as source of primary studies                                                         |
| <a href="#">Maringwa, John, Sardu, Maria Luisa, Hang, Yaming et al. (2021) Characterizing Effects of Antidiabetic Drugs on Heart Rate, Systolic and Diastolic Blood Pressure. Clinical pharmacology and therapeutics 109(6): 1583-1592</a>                                                                                | - No relevant outcomes reported<br><i>Systematic review investigating outcomes not relevant to the review</i> |
| <a href="#">Marre, M., Gaal, L., Usadel, K. H. et al. (2002) Nateglinide improves glycaemic control when added to metformin monotherapy: results of a</a>                                                                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                 |

| Study                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                  |
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| <a href="#">randomized trial with type 2 diabetes patients.</a><br>Diabetes Obes Metab 4(3): 177-86                                                                                                                                                                            |                                                                                                                                                                         |
| <a href="#">Marso, Steven P, Nauck, Michael A, Monk Fries, Tea et al. (2018) Myocardial Infarction Subtypes in Patients With Type 2 Diabetes Mellitus and the Effect of Liraglutide Therapy (from the LEADER Trial).</a> The American journal of cardiology 121(12): 1467-1470 | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis</i>                                  |
| <a href="#">Martinez-Vizcaino, Vicente, Diez-Fernandez, Ana, Alvarez-Bueno, Celia et al. (2021) Safety and Efficacy of SGLT2 Inhibitors: A Multiple-Treatment Meta-Analysis of Clinical Decision Indicators.</a> Journal of clinical medicine 10(12)                           | - Systematic review used as source of primary studies<br><br><i>Identified in rerun search. No additional studies to add.</i>                                           |
| <a href="#">Maruhashi, Tatsuya, Higashi, Yukihiro, Kihara, Yasuki et al. (2016) Long-term effect of sitagliptin on endothelial function in type 2 diabetes: a sub-analysis of the PROLOGUE study.</a> Cardiovascular diabetology 15(1): 134                                    | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares to usual care which is not specified as a comparator in the protocol</i> |
| <a href="#">Marx, N. (2023) Impact of Empagliflozin on Insulin Use in Patients with Heart Failure with Preserved Ejection Fraction (HFpEF) and Type 2 Diabetes (T2DM): Sub-Analysis from EMPEROR-Preserved Trial.</a> Diabetologie und Stoffwechsel 18(supplement1): 43        | - Population not relevant to this review protocol                                                                                                                       |
| <a href="#">Maskery, M.P., Holscher, C., Jones, S.P. et al. (2021) Glucagon-like peptide-1 receptor agonists as neuroprotective agents for ischemic stroke: a systematic scoping review.</a> Journal of Cerebral Blood Flow and Metabolism 41(1): 14-30                        | - Study design not relevant to this review protocol<br><br><i>Includes preclinical studies and retrospective database studies that are not relevant to this review</i>  |
| <a href="#">Masson, Walter, Lavallo-Cobo, Augusto, Lobo, Martin et al. (2021) Novel antidiabetic drugs and risk of cardiovascular events in patients without baseline metformin use: a meta-analysis.</a> European journal of preventive cardiology 28(1): 69-75               | - Systematic review used as source of primary studies                                                                                                                   |
| <a href="#">Mather, K.J., Coskun, T., Pratt, E.J. et al. (2024) Improvements in post-challenge lipid response following tirzepatide treatment in patients with type 2 diabetes.</a> Diabetes, Obesity and Metabolism 26(2): 785-789                                            | - Additional outcomes relevant to living guideline work                                                                                                                 |
| <a href="#">Mather, K.J., Frias, J.P., Hsia, S. et al. (2023) Effect of orforglipron versus placebo and dulaglutide on glycaemic control and body</a>                                                                                                                          | - Conference abstract                                                                                                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                         |
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| <a href="#">weight in patients with type 2 diabetes.</a><br>Diabetologia 66(supplement1): 151-s152                                                                                                                                                                                                                                                      |                                                                                                                                                |
| <a href="#">Mathur, Winni, Kosta, Susmit, Reddy, Manoj et al. (2024) Effect of Swallow Balloon Therapy with the Combination of Semaglutide Oral Formulation: a Randomised Double-Blind Single-Centre Study.</a> Obesity surgery 34(1): 198-205                                                                                                          | - Population not relevant to this review protocol                                                                                              |
| <a href="#">Matthaei, S., Rohwedder, K., Grohl, A. et al. (2013) Dapagliflozin improves glycaemic control and reduces body weight as add-on therapy to metformin plus sulphonylurea.</a> Diabetologia 56(suppl1): 374-s375                                                                                                                              | - Conference abstract                                                                                                                          |
| <a href="#">Matthews David, R, Li, Qiang, Perkovic, Vlado et al. (2019) Effects of canagliflozin on amputation risk in type 2 diabetes: the CANVAS Program.</a> Diabetologia 62(6): 926-938                                                                                                                                                             | - Additional outcomes relevant to living guideline work                                                                                        |
| <a href="#">Matthews, D R, Paldanius, P M, Proot, P et al. (2019) Baseline characteristics in the VERIFY study: a randomized trial assessing the durability of glycaemic control with early vildagliptin-metformin combination in newly diagnosed Type 2 diabetes.</a> Diabetic medicine : a journal of the British Diabetic Association 36(4): 505-513 | - Comparator in study does not match that specified in this review protocol                                                                    |
| <a href="#">Matthews, D. R., Paldánus, P. M., Proot, P. et al. (2019) Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial.</a> Lancet 394(10208): 1519-1529                 | - Comparator in study does not match that specified in this review protocol                                                                    |
| <a href="#">Matthews, David R, Paldanius, Paivi M, Stumvoll, Michael et al. (2019) A pre-specified statistical analysis plan for the VERIFY study: Vildagliptin efficacy in combination with metformin for early treatment of T2DM.</a> Diabetes, obesity & metabolism 21(10): 2240-2247                                                                | - Comparator in study does not match that specified in this review protocol                                                                    |
| <a href="#">Matyjaszek-Matuszek, Beata, Lenart-Lipinska, Monika, Rogalska, Dorota et al. (2013) Exenatide twice daily versus insulin glargine for the treatment of type 2 diabetes in Poland - subgroup data from a randomised multinational</a>                                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Exploratory post hoc analysis</i> |

| Study                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                            |
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| <a href="#">trial GWAA</a> . Endokrynologia Polska 64(5): 375-82                                                                                                                                                                                                                                                                                           |                                                                                                                                                   |
| <a href="#">Mayer Gert, J, Wanner, Christoph, Weir Matthew, R et al. (2019) Analysis from the EMPA-REG OUTCOME R trial indicates empagliflozin may assist in preventing the progression of chronic kidney disease in patients with type 2 diabetes irrespective of medications that alter intrarenal hemodynamics.</a> Kidney international 96(2): 489-504 | - Secondary publication of an included study that does not provide any additional relevant information                                            |
| <a href="#">Mayhoub, H.; BouBou, A.; Kaddar, N. (2022) ASSESSMENT OF GENITAL AND URINARY TRACT INFECTIONS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS TREATED WITH DAPAGLIFLOZIN.</a> Bulletin of Pharmaceutical Sciences. Assiut 45(2): 953-965                                                                                                             | - Study design not relevant to this review protocol<br><br><i>Unclear if randomised trial (only states "patients were divided into 2 groups")</i> |
| <a href="#">Mayne, Kaitlin J, Staplin, Natalie, Keane, David F et al. (2024) Effects of Empagliflozin on Fluid Overload, Weight, and Blood Pressure in CKD.</a> Journal of the American Society of Nephrology : JASN 35(2): 202-215                                                                                                                        | - Population not relevant to this review protocol                                                                                                 |
| <a href="#">Mazer, D., Hare, G.M., Connelly, P.W. et al. (2019) Effect of empagliflozin on erythropoietin levels and red blood cell morphology in patients with type 2 diabetes and coronary artery disease.</a> Circulation 140(supplement1)                                                                                                              | - Study design not relevant to this review protocol<br><br><i>Letter only</i>                                                                     |
| <a href="#">Mazurek, M; Lip, GYH; Buse, JB (2016) 2016 - In patients with type 2 diabetes and high CV risk, liraglutide reduced a composite CV outcome at a median 3.8 y.</a> ACP journal club 165(8): 1-1                                                                                                                                                 | - Commentary only                                                                                                                                 |
| <a href="#">Mc Causland, Finnian R, Claggett, Brian L, Vaduganathan, Muthiah et al. (2024) Decline in Estimated Glomerular Filtration Rate After Dapagliflozin in Heart Failure With Mildly Reduced or Preserved Ejection Fraction: A Prespecified Secondary Analysis of the DELIVER Randomized Clinical Trial.</a> JAMA cardiology 9(2): 144-152          | - Subgroup analysis of a trial that was not relevant for inclusion                                                                                |
| <a href="#">McAlister F, A, Zheng, Y, Westerhout C, M et al. (2020) Association between glycated haemoglobin levels and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease: a secondary analysis of the TECOS randomized clinical trial.</a> European Journal of Heart Failure                                            | - Secondary publication of an included study that does not provide any additional relevant information                                            |

| Study                                                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                 |
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| <a href="#">Mcelroy, S.L., Guerdjikova, A.I., Blom, T.J. et al. (2024) Liraglutide in Obese or Overweight Individuals With Stable Bipolar Disorder. Journal of Clinical Psychopharmacology 44(2): 89-95</a>                                                                                                                                                                             | - Population not relevant to this review protocol                                                      |
| <a href="#">McEwan, P., McMurray, J.J.V., Jhund, P.S. et al. (2021) Evaluating the key predictors of health-related quality of life in patients with heart failure and reduced ejection fraction: results from the DAPA-HF trial. European Heart Journal 42(suppl1): 908</a>                                                                                                            | - Conference abstract                                                                                  |
| <a href="#">McGavin, Jane K; Perry, Caroline M; Goa, Karen L (2002) Gliclazide modified release. Drugs 62(9): 1357-6</a>                                                                                                                                                                                                                                                                | - Review article but not a systematic review                                                           |
| <a href="#">McGrath, Rachel T, Hocking, Samantha L, Priglinger, Miriam et al. (2016) Rationale and design of Short-Term EXenatide therapy in Acute ischaemic Stroke (STEXAS): a randomised, open-label, parallel-group study. BMJ open 6(2): e008203</a>                                                                                                                                | - Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>3 months</i>         |
| <a href="#">McGuire D, K, Zinman, B, Inzucchi S, E et al. (2020) Effects of empagliflozin on first and recurrent clinical events in patients with type 2 diabetes and atherosclerotic cardiovascular disease: a secondary analysis of the EMPA-REG OUTCOME trial. The Lancet Diabetes and Endocrinology 8(12): 949-959</a>                                                              | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">McGuire, D. K., Abdullah, S. M., See, R. et al. (2010) Randomized comparison of the effects of rosiglitazone vs. placebo on peak integrated cardiovascular performance, cardiac structure, and function. Eur Heart J 31(18): 2262-70</a>                                                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">McGuire, D.K., Zinman, B., Inzucchi, S.E. et al. (2018) Effect of empagliflozin on cardiovascular events including recurrent events in the EMPA-REG OUTCOME trial. European Heart Journal 39(supplement1): 1091</a>                                                                                                                                                         | - Conference abstract                                                                                  |
| <a href="#">McGuire, Darren K, Busui, Rodica P, Deanfield, John et al. (2023) Effects of oral semaglutide on cardiovascular outcomes in individuals with type 2 diabetes and established atherosclerotic cardiovascular disease and/or chronic kidney disease: Design and baseline characteristics of SOUL, a randomized trial. Diabetes, obesity &amp; metabolism 25(7): 1932-1941</a> | - Duplicate reference                                                                                  |

| Study                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                             |
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| <a href="#">McGuire, Darren K, Busui, Rodica P, Deanfield, John et al. (2023) Effects of oral semaglutide on cardiovascular outcomes in individuals with type 2 diabetes and established atherosclerotic cardiovascular disease and/or chronic kidney disease: SOUL, a randomized trial, design and baseline characteristics.</a> Diabetes, obesity & metabolism | - No relevant outcomes reported                                                                                                                    |
| <a href="#">McInnes, N., Hall, S., Lochnan, H.A. et al. (2021) Remission of type 2 diabetes following intensive treatment with insulin glargine, lixisenatide, metformin, and lifestyle approaches: Results of a multicenter randomized controlled trial.</a> Diabetes 70(suppl1)                                                                                | - Conference abstract                                                                                                                              |
| <a href="#">McInnes, Natalia, Hall, Stephanie, Hramiak, Irene et al. (2022) Remission of Type 2 Diabetes Following a Short-term Intensive Intervention With Insulin Glargine, Sitagliptin, and Metformin: Results of an Open-label Randomized Parallel-Design Trial.</a> Diabetes care 45(1): 178-185                                                            | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">McInnes, Natalia, Hall, Stephanie, Sultan, Farah et al. (2020) Remission of Type 2 Diabetes Following a Short-term Intervention With Insulin Glargine, Metformin, and Dapagliflozin.</a> The Journal of clinical endocrinology and metabolism 105(8)                                                                                                 | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">McIntyre, HD, Ma, A, Bird, DM et al. (1991) Metformin increases insulin sensitivity and basal glucose clearance in type 2 (non-insulin dependent) diabetes mellitus.</a> Australian and New Zealand journal of medicine 21(5): 714-719                                                                                                               | - Study design not relevant to this review protocol                                                                                                |
| <a href="#">McMurray, J.J.V., DeMets, D.L., Inzucchi, S.E. et al. (2019) The Dapagliflozin And Prevention of Adverse-outcomes in Heart Failure (DAPA-HF) trial: baseline characteristics.</a> European Journal of Heart Failure 21(11): 1402-1411                                                                                                                | - Population not relevant to this review protocol                                                                                                  |
| <a href="#">McMurray, John J V, Solomon, Scott D, Inzucchi, Silvio E et al. (2019) Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction.</a> The New England journal of medicine 381(21): 1995-2008                                                                                                                                        | - Population not relevant to this review protocol                                                                                                  |
| <a href="#">McMurray, John J V, Wheeler, David C, Stefansson, Bergur V et al. (2021) Effect of Dapagliflozin on Clinical Outcomes in Patients</a>                                                                                                                                                                                                                | - Population not relevant to this review protocol<br><i>&lt;20% of the population had type 2 diabetes</i>                                          |



| Study                                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                                 |
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| <a href="#">With Chronic Kidney Disease, With and Without Cardiovascular Disease.</a> Circulation 143(5): 438-448                                                                                                                                                                                                                                                          |                                                                                                                                                        |
| <a href="#">Mehta, Sanjana, Nain, Parminder, Agrawal, Bimal K et al. (2021) Effectiveness of Empagliflozin With Vitamin D Supplementation in Peripheral Neuropathy in Type 2 Diabetic Patients.</a> Cureus 13(12): e20208                                                                                                                                                  | - Comparator in study does not match that specified in this review protocol                                                                            |
| <a href="#">Meier, Juris J, Rosenstock, Julio, Hincelin-Mery, Agnes et al. (2015) Contrasting Effects of Lixisenatide and Liraglutide on Postprandial Glycemic Control, Gastric Emptying, and Safety Parameters in Patients With Type 2 Diabetes on Optimized Insulin Glargine With or Without Metformin: A Randomized, Open-Label Trial.</a> Diabetes care 38(7): 1263-73 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                |
| <a href="#">Mellbin, Linda G, Malmberg, Klas, Norhammar, Anna et al. (2008) The impact of glucose lowering treatment on long-term prognosis in patients with type 2 diabetes and myocardial infarction: a report from the DIGAMI 2 trial.</a> European heart journal 29(2): 166-76                                                                                         | - Study does not contain an intervention relevant to this review protocol<br><i>No specified drug therefore cannot be stratified for this analysis</i> |
| <a href="#">Memon, Rahat A, Akbariromani, Hanieh, Vohra, Rimsha R et al. (2022) Comparison of Cardiovascular Outcomes Between Dapagliflozin and Empagliflozin in Patients With Type 2 Diabetes: A Meta-Analysis.</a> Cureus 14(7): e27277                                                                                                                                  | - Study design not relevant to this review protocol<br><i>Retrospective studies included only</i>                                                      |
| <a href="#">Mende, Christian and Katz, Arie (2016) Cystatin C- and Creatinine-Based Estimates of Glomerular Filtration Rate in Dapagliflozin Phase 3 Clinical Trials.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 7(1): 139-51                                                                                              | - Study design not relevant to this review protocol<br><i>Post hoc analysis using pooled data from 9 trials.</i>                                       |
| <a href="#">Meneghini, L, Kesavadev, J, Demissie, M et al. (2013) Once-daily initiation of basal insulin as add-on to metformin: a 26-week, randomized, treat-to-target trial comparing insulin detemir with insulin glargine in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 15(8): 729-36                                                           | - Study does not contain an intervention relevant to this review protocol<br><i>compares detmir + metformin Vs. Glargine + Metformin</i>               |
| <a href="#">Meneilly, G. S., Ryan, E. A., Radziuk, J. et al. (2000) Effect of acarbose on insulin sensitivity in elderly patients with diabetes.</a> Diabetes Care 23(8): 1162-7                                                                                                                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |

| Study                                                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                                                   |
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| <a href="#">Merton, Katherine, Davies, Michael J, Vijapurkar, Ujjwala et al. (2018) Achieving the composite endpoint of HbA1c, body weight, and systolic blood pressure reduction with canagliflozin in patients with type 2 diabetes.</a> Current medical research and opinion 34(2): 313-318                                                                                                         | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis using pooled data form 4 trials.</i>                                                     |
| <a href="#">Merza, Nooraldin, Akram, Moeez, Mengal, Aqsa et al. (2023) The Safety and Efficacy of GLP-1 Receptor Agonists in Heart Failure Patients: A Systematic Review and Meta-Analysis.</a> Current problems in cardiology 48(5): 101602                                                                                                                                                           | - Population not relevant to this review protocol                                                                                                                        |
| <a href="#">Mesirabi, DM, Langade, DG, Kinagi, SB et al. (2005) Evaluation of efficacy and safety of fixed dose combination of glimepiride 2 mg plus pioglitazone 15 mg plus metformin SR 500 mg in the management of patients with type-2 diabetes mellitus.</a> Journal of the Indian Medical Association 103: 447-450                                                                               | - Study design not relevant to this review protocol                                                                                                                      |
| <a href="#">Middleton, Timothy L, Constantino, Maria I, McGill, Margaret et al. (2022) Improving beta-cell secretory function and glycaemia in young-onset type 2 diabetes: A pilot, 12-month, randomized trial of a novel, continuous glucose monitor-guided, rapid treatment intensification strategy incorporating empagliflozin and liraglutide.</a> Diabetes, obesity & metabolism 24(4): 747-751 | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Mikada, A., Narita, T., Yokoyama, H. et al. (2014) Effects of miglitol, sitagliptin, and initial combination therapy with both on plasma incretin responses to a mixed meal and visceral fat in over-weight Japanese patients with type 2 diabetes. "the MASTER randomized, controlled trial".</a> Diabetes Res Clin Pract 106(3): 538-47                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Miller, Sam, Krumins, Tania, Zhou, Haojin et al. (2018) Ertugliflozin and Sitagliptin Co-initiation in Patients with Type 2 Diabetes: The VERTIS SITA Randomized Study.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 9(1): 253-268                                                                                                           | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Mindadze, K. (2022) Effect of dapagliflozin on RV function in diabetic hypertensive women with HFpEF.</a> European Journal of Heart Failure 24(supplement2): 17                                                                                                                                                                                                                            | - Conference abstract                                                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                             |
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| <a href="#">Mishra, Rahul, Raj, Rishi, Elshimy, Ghada et al. (2023) Adverse Events Related to Tirzepatide. Journal of the Endocrine Society 7(4): bvad016</a>                                                                                                                                                                                   | - Systematic review used as source of primary studies                                                                                              |
| <a href="#">Mishriky, B M, Okunrintemi, V, Jain, S et al. (2021) Do GLP-1RAs and SGLT-2is reduce cardiovascular events in women with type 2 diabetes? A systematic review and meta-analysis. Diabetes &amp; metabolism 47(1): 101160</a>                                                                                                        | - Systematic review used as source of primary studies<br><i>Identified during the rerun search. No additional studies to add.</i>                  |
| <a href="#">Mita, T., Katakami, N., Shiraiwa, T. et al. (2016) Sitagliptin attenuates the progression of carotid intima-media thickening in insulin-treated patients with type 2 diabetes: The sitagliptin preventive study of intima-media thickness evaluation (SPIKE): A randomized controlled trial. Diabetes Care 39(3): 455-464</a>       | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Mita, T., Katakami, N., Yoshii, H. et al. (2016) Alogliptin, a Dipeptidyl Peptidase 4 Inhibitor, Prevents the Progression of Carotid Atherosclerosis in Patients with Type 2 Diabetes: The Study of Preventive Effects of Alogliptin on Diabetic Atherosclerosis (SPEAD-A). Diabetes Care 39(1): 139-148</a>                        | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Mita, T., Watada, H., Shimizu, T. et al. (2007) Nateglinide reduces carotid intima-media thickening in type 2 diabetic patients under good glycemic control. Arterioscler Thromb Vasc Biol 27(11): 2456-62</a>                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Mita, Tomoya, Hiyoshi, Toru, Yoshii, Hidenori et al. (2018) Study Protocol for the Initial Choice of DPP-4 Inhibitor in Japanese Patients with Type 2 diabetes Mellitus: Effect of Linagliptin on QOL (INTEL-QOL) Trial. Diabetes therapy : research, treatment and education of diabetes and related disorders 9(3): 1403-1412</a> | - No relevant outcomes reported                                                                                                                    |
| <a href="#">Mitrakou, A., Tountas, N., Raptis, A. E. et al. (1998) Long-term effectiveness of a new alpha-glucosidase inhibitor (BAY m1099-miglitol) in insulin-treated type 2 diabetes mellitus. Diabet Med 15(8): 657-60</a>                                                                                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Mohammedi, Kamel, Chalmers, John, Herrington, William et al. (2018) Associations between body mass index and the risk of renal events in patients with type 2 diabetes. Nutrition &amp; diabetes 8(1): 7</a>                                                                                                                        | - Comparator in study does not match that specified in this review protocol                                                                        |

| Study                                                                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                 |
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| <a href="#">Mohammedi, Kamel, Woodward, Mark, Hirakawa, Yoichiro et al. (2016) Microvascular and Macrovascular Disease and Risk for Major Peripheral Arterial Disease in Patients With Type 2 Diabetes.</a> Diabetes care 39(10): 1796-803                                                                                                                               | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Mohan, Viswanathan, Wangnoo, Subhash, Das, Sambit et al. (2022) Comparison of gliclazide vs linagliptin on hypoglycemia and cardiovascular events in type 2 diabetes mellitus: A systematic review.</a> World journal of diabetes 13(12): 1168-1183                                                                                                          | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Mohsen, Marwa, Elberry, Ahmed A, Rabea, Alaa Mohamed et al. (2022) A New Clinical Utility for Tubular Markers to Identify Kidney Responders to Saxagliptin Treatment in Adults With Diabetic Nephropathy.</a> Canadian journal of diabetes 46(2): 134-141e2                                                                                                  | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Mokta, J. K., Ramesh, null, Sahai, A. K. et al. (2018) Comparison of safety and efficacy of glimepiride-metformin and vildagliptin-metformin treatment in newly diagnosed type 2 diabetic patients.</a> J Assoc Physicians India 66(8): 30-35                                                                                                                | - Study design not relevant to this review protocol<br><i>Observational study (non-randomised)</i>     |
| <a href="#">Monteiro, Pedro, Bergenstal Richard, M, Toural, Elvira et al. (2019) Efficacy and safety of empagliflozin in older patients in the EMPA-REG OUTCOME R trial.</a> Age and ageing 48(6): 859-866                                                                                                                                                               | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Moon, Jun Sung, Park, Il Rae, Kim, Hae Jin et al. (2023) Efficacy and Safety of Evogliptin Add-on Therapy to Dapagliflozin/Metformin Combinations in Patients with Poorly Controlled Type 2 Diabetes Mellitus: A 24-Week Multicenter Randomized Placebo-Controlled Parallel-Design Phase-3 Trial with a 28-Week Extension.</a> Diabetes & metabolism journal | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Morales-Villegas, E.C., Aroda, V.R., Bardtrum, L. et al. (2021) Achievement of near-normal HbA1c with early initiation of oral semaglutide: An exploratory subgroup analysis of PIONEER 1.</a> Diabetologia 64(supplement1): 252-s253                                                                                                                        | - Conference abstract                                                                                  |
| <a href="#">Mori, Katsuhito, Emoto, Masanori, Araki, Takahiro et al. (2008) Effects of pioglitazone on serum fetuin-A levels in patients with type 2</a>                                                                                                                                                                                                                 | - Study design not relevant to this review protocol                                                    |

| Study                                                                                                                                                                                                                                                                                                      | Reason                                                                                                 |
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| <a href="#">diabetes mellitus</a> . Metabolism: clinical and experimental 57(9): 1248-52                                                                                                                                                                                                                   | <i>Non-randomised study</i>                                                                            |
| <a href="#">Morillas, H., Galcera, E., Alania, E. et al. (2022) Sodium-glucose Co-transporter 2 Inhibitors in Acute Heart Failure: A Review of the Available Evidence and Practical Guidance on Clinical Use</a> . Reviews in Cardiovascular Medicine 23(4): 139                                           | - Review article but not a systematic review                                                           |
| <a href="#">Morino, K., Inoue, H., Fuse, K. et al. (2018) Ipragliflozin, a SGLT2 inhibitor, reduced body weight and fat mass but not muscle mass in Japanese type 2 diabetic patients treated with insulin-a randomized clinical trial</a> . Diabetes 67: A322                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Morita, R., Tsukamoto, S., Obata, S. et al. (2023) THE EFFECT OF SODIUM-GLUCOSE COTRANSPORTER 2INHIBITORS, MINERALOCORTICOID RECEPTOR ANTAGONISTS, AND ITS COMBINATION ON ALBUMINURIA IN PATIENTS WITH DIABETIC NEPHROPATHY</a> . American Journal of Kidney Diseases 81(4supplement1): 81-s82 | - Conference abstract                                                                                  |
| <a href="#">Moriwaki, K., Takeuchi, T., Fujimoto, N. et al. (2018) Effect of sitagliptin on coronary flow reserve assessed by magnetic resonance imaging in type 2 diabetic patients with coronary artery disease</a> . Circ J 82(8): 2119-2127                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Moroney, Michael, Verma, Raj, Hibino, Makoto et al. (2023) Impact of diabetes duration on left ventricular mass regression with empagliflozin</a> . ESC heart failure 10(3): 2134-2140                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Mosenzon, O., Wiviott, S.D., Yanuv, I. et al. (2019) Risk of renal outcomes according to eGFR and categorical Urinary Albumin Creatinine Ratio (UACR) in the DECLARE-TIMI 58 trial</a> . Diabetologia 62(supplement1): 485-s486                                                                | - Conference abstract                                                                                  |
| <a href="#">Mosenzon, O, Bain S, C, Heerspink H, J.L et al. (2020) Cardiovascular and renal outcomes by baseline albuminuria status and renal function: Results from the LEADER randomized trial</a> . Diabetes, Obesity and Metabolism                                                                    | - Post-hoc analysis of included study                                                                  |

| Study                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                 |
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| <a href="#">Mosenzon, Ofri, Wiviott, Stephen D, Heerspink, Hidde J L et al. (2021) The Effect of Dapagliflozin on Albuminuria in DECLARE-TIMI 58. Diabetes care 44(8): 1805-1815</a>                                                                                                                                                                       | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Motoki, Hirohiko, Masuda, Izuru, Yasuno, Shinji et al. (2020) Rationale and design of the EMPYREAN study. ESC heart failure 7(5): 3134-3141</a>                                                                                                                                                                                                | - No relevant outcomes reported                                                                        |
| <a href="#">Mourad, J.-J., Voisin, O., Le Lorch, E. et al. (2021) Fragility index of various Gp1 agonists on cardiovascular outcomes in placebo controlled trials. Journal of Hypertension 39(suppl1): e210</a>                                                                                                                                            | - Conference abstract                                                                                  |
| <a href="#">Mozawa, Kosuke, Kubota, Yoshiaki, Hoshika, Yu et al. (2021) Empagliflozin confers reno-protection in acute myocardial infarction and type 2 diabetes mellitus. ESC heart failure 8(5): 4161-4173</a>                                                                                                                                           | - Subgroup analysis of a trial that was not relevant for inclusion                                     |
| <a href="#">Mu, Y., Bao, X., Eliaschewitz, F.G. et al. (2023) Efficacy and safety of once weekly semaglutide 2.4 mg for weight management in a predominantly Asian population with overweight or obesity in the STEP 7 randomised clinical trial. Obesity Facts 16(supplement1): 42-43</a>                                                                 | - Conference abstract                                                                                  |
| <a href="#">Mu, Yiming, Bao, Xiaolei, Eliaschewitz, Freddy G et al. (2024) Efficacy and safety of once weekly semaglutide 2.4 mg for weight management in a predominantly east Asian population with overweight or obesity (STEP 7): a double-blind, multicentre, randomised controlled trial. The lancet. Diabetes &amp; endocrinology 12(3): 184-195</a> | - Population not relevant to this review protocol                                                      |
| <a href="#">Mukhopadhyay, Pradip, Sanyal, Debmalya, Chatterjee, Purushottam et al. (2023) SGLT2 inhibitors: Effect on myocardial infarction and stroke in type 2 diabetes. The Journal of clinical endocrinology and metabolism</a>                                                                                                                        | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Munshi, M., Ritzel, R., Hramiak, I. et al. (2023) Advancing Type 2 Diabetes Therapy with iGlarLixi in Older People: Pooled Analysis of Four Randomized Controlled Trials. Metabolism: Clinical and Experimental 142(supplement): 155429</a>                                                                                                    | - Study design not relevant to this review protocol                                                    |



| Study                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                 |
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| <a href="#">Munteanu, M.A. and Diaconu, C.C. (2021) Heart failure and sodium-glucose co-transporters-2 (SGLT-2) inhibitors. Archives of the Balkan Medical Union 56(supplement1): 18</a>                                                                                                                                        | - Conference abstract                                                                                  |
| <a href="#">Murakami, T. and Ohsato, K. (2019) Long-term antidiabetic treatment by dapagliflozin provides multiple antiatherosclerotic effects independent of diabetic improvement for type-2 diabetics with coronary artery disease receiving statin or sartan. Circulation 140(supplement1)</a>                               | - Conference abstract                                                                                  |
| <a href="#">Murakami, T. and Ohsato, K. (2016) Dapagliflozin provides multiple ultrasonic-evaluated antiatherosclerotic effects independent of diabetic improvement for type-2 diabetics with coronary artery disease receiving statin or sartan. Circulation 134(supplement1)</a>                                              | - Conference abstract                                                                                  |
| <a href="#">Murakami, T. and Ohsato, K. (2016) Empagliflozin early reverses metabolic and cardiovascular overload in type-2 diabetics with chronic heart failure. Circulation 134(supplement1)</a>                                                                                                                              | - Conference abstract                                                                                  |
| <a href="#">Musch, A (2008) Diabetes mellitus type 2: combination with sitagliptin in moderately severe disease. Krankenhauspharmazie 29(10): 461-464</a>                                                                                                                                                                       | - Study not reported in English                                                                        |
| <a href="#">Muskiet, M H A, Bunck, M C, Heine, R J et al. (2019) Exenatide twice-daily does not affect renal function or albuminuria compared to titrated insulin glargine in patients with type 2 diabetes mellitus: A post-hoc analysis of a 52-week randomised trial. Diabetes research and clinical practice 153: 14-22</a> | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Muskiet, Marcel H A, Tonneijck, Lennart, Huang, Yao et al. (2018) Lixisenatide and renal outcomes in patients with type 2 diabetes and acute coronary syndrome: an exploratory analysis of the ELIXA randomised, placebo-controlled trial. The lancet. Diabetes &amp; endocrinology 6(11): 859-869</a>              | - Post-hoc analysis of included study                                                                  |
| <a href="#">Nabrdalik, Katarzyna, Skonieczna-Zydecka, Karolina, Irluk, Krzysztof et al. (2022) Gastrointestinal adverse events of metformin treatment in patients with type 2 diabetes mellitus: A systematic review, meta-analysis and</a>                                                                                     | - Trial that has a treatment and follow up period of less than 24 weeks                                |

| Study                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                                                                |
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| <a href="#">meta-regression of randomized controlled trials.</a><br>Frontiers in endocrinology 13: 975912                                                                                                                                                                                                                          |                                                                                                                                                                                       |
| <a href="#">Nagaike, Hiroe, Ohara, Makoto, Kohata, Yo et al. (2019) Effect of Dulaglutide Versus Liraglutide on Glucose Variability, Oxidative Stress, and Endothelial Function in Type 2 Diabetes: A Prospective Study.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 10(1): 215-228 | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparison (continuing treatment with liraglutide)</i>                               |
| <a href="#">Nagao, Mototsugu, Sasaki, Jun, Sugihara, Hitoshi et al. (2023) Efficacy and safety of sitagliptin treatment in older adults with moderately controlled type 2 diabetes: the STREAM study.</a> Scientific reports 13(1): 134                                                                                            | - Comparator in study does not match that specified in this review protocol                                                                                                           |
| <a href="#">Naing, Soe, Ramesh, Geeta, Garcha, Jasmine et al. (2021) Is the stepping-down approach a better option than multiple daily injections in obese patients with poorly controlled Type 2 diabetes on advanced insulin therapy?.</a><br>Endocrinology, diabetes & metabolism 4(2): e00204                                  | - Study does not contain an intervention relevant to this review protocol<br><br><i>Not stating the specific drug used so cannot be used in the analysis required for this review</i> |
| <a href="#">Nakaguchi, H.; Kondo, Y.; Terauchi, Y. (2019) Effects of liraglutide and empagliflozin add-on to insulin therapy in patients with type 2 diabetes: Ellena-it, a randomized controlled study.</a><br>Diabetes 68(supplement1)                                                                                           | - Conference abstract                                                                                                                                                                 |
| <a href="#">Nakaguchi, Hirotatsu, Kondo, Yoshinobu, Kyohara, Mayu et al. (2020) Effects of liraglutide and empagliflozin added to insulin therapy in patients with type 2 diabetes: A randomized controlled study.</a> Journal of diabetes investigation 11(6): 1542-1550                                                          | - Duplicate reference                                                                                                                                                                 |
| <a href="#">Nakamura, T., Matsuda, T., Kawagoe, Y. et al. (2004) Effect of pioglitazone on carotid intima-media thickness and arterial stiffness in type 2 diabetic nephropathy patients.</a> Metabolism 53(10): 1382-6                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                         |
| <a href="#">Nakamura, T., Sugaya, T., Kawagoe, Y. et al. (2006) Effect of pioglitazone on urinary liver-type fatty acid-binding protein concentrations in diabetes patients with microalbuminuria.</a><br>Diabetes Metab Res Rev 22(5): 385-9                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                         |
| <a href="#">Nakamura, T., Ushiyama, C., Osada, S. et al. (2001) Pioglitazone reduces urinary podocyte</a>                                                                                                                                                                                                                          | - Population not relevant to this review protocol                                                                                                                                     |

| Study                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                   |
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| <a href="#">excretion in type 2 diabetes patients with microalbuminuria.</a> Metabolism 50(10): 1193-6                                                                                                                                                                                                                                                        |                                                                                                                                                                          |
| <a href="#">Nakamura, T, Ushiyama, C, Osada, S et al. (2001) Effect of pioglitazone on dyslipidemia in hemodialysis patients with type 2 diabetes.</a> Renal failure 23(6): 863-4                                                                                                                                                                             | - Not a peer-reviewed publication                                                                                                                                        |
| <a href="#">Nakatani, Daisaku, Dohi, Tomoharu, Hikoso, Shungo et al. (2023) Relationship Between Canagliflozin, Sodium Glucose Cotransporter 2 Inhibitor, and Hematopoietic Effects in Patients With Diabetes and Mild Heart Failure: Results From the CANDLE Trial.</a> Journal of cardiovascular pharmacology 82(1): 61-68                                  | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Nakayama, Takashi, Komiyama, Nobuyuki, Yokoyama, Masaki et al. (2010) Pioglitazone induces regression of coronary atherosclerotic plaques in patients with type 2 diabetes mellitus or impaired glucose tolerance: a randomized prospective study using intravascular ultrasound.</a> International journal of cardiology 138(2): 157-65          | - Population not relevant to this review protocol                                                                                                                        |
| <a href="#">Nar, A. and Gedik, O. (2009) The effect of metformin on leptin in obese patients with type 2 diabetes mellitus and nonalcoholic fatty liver disease.</a> Acta Diabetol 46(2): 113-8                                                                                                                                                               | - Comparator in study does not match that specified in this review protocol<br><i>Lifestyle changes only which is not a comparator noted in the protocol</i>             |
| <a href="#">Nathan, D. M.; Roussell, A.; Godine, J. E. (1988) Glyburide or insulin for metabolic control in non-insulin-dependent diabetes mellitus. A randomized, double-blind study.</a> Ann Intern Med 108(3): 334-40                                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Nauck Michael, A, Muus, Ghorbani, Marie, Louise et al. (2019) Effects of Liraglutide Compared With Placebo on Events of Acute Gallbladder or Biliary Disease in Patients With Type 2 Diabetes at High Risk for Cardiovascular Events in the LEADER Randomized Trial.</a> Diabetes care 42(10): 1912-1920                                          | - Post-hoc analysis of included study                                                                                                                                    |
| <a href="#">Nauck, M. A., Stewart, M. W., Perkins, C. et al. (2016) Efficacy and safety of once-weekly GLP-1 receptor agonist albiglutide (HARMONY 2): 52 week primary endpoint results from a randomised, placebo-controlled trial in patients with type 2 diabetes mellitus inadequately controlled with diet and exercise.</a> Diabetologia 59(2): 266-274 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |

| Study                                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                                                                                                                                                                                           |
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| <a href="#">Nauck, M., Del Prato, S., Rohwedder, K. et al. (2010) Dapagliflozin vs glipizide in patients with type 2 diabetes mellitus inadequately controlled on metformin: 52-week results of a double-blind, randomised, controlled trial. Diabetologia 53(suppl1): 107</a>                                                           | - Conference abstract                                                                                                                                                                                                                                                                                            |
| <a href="#">Nauck, M.A., Pieper, K.S., Lokhnygina, Y. et al. (2017) No major impact seen with sitagliptin on rates of cardiovascular death or hospitalisation for heart failure following myocardial infarction during TECOS. Diabetologia 60(1supplement1): 356</a>                                                                     | - Conference abstract                                                                                                                                                                                                                                                                                            |
| <a href="#">Nauck, M, del Prato, S, Meier, JJ et al. (2013) Dapagliflozin versus glipizide as add-on therapy in patients with type 2 diabetes who have inadequate glycemic control with metformin. Deutsche medizinische Wochenschrift (1946) 138suppl1: S6-15</a>                                                                       | - Study not reported in English                                                                                                                                                                                                                                                                                  |
| <a href="#">Nauck, MA; Abd El Aziz, M; Quast, DR (2023) Meta-Analysis of Head-to-Head Clinical trials Comparing Incretin-Based Glucose-Lowering Medications and Basal Insulin - An Update Including Recently Developed GLP-1 Receptor Agonists and the GIP/GLP-1 Receptor Co-Agonist Tirzepatide. Diabetes, obesity &amp; metabolism</a> | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                            |
| <a href="#">Nauck, Michael A, Jensen, Thomas Jon, Rosenkilde, Carina et al. (2018) Neoplasms Reported With Liraglutide or Placebo in People With Type 2 Diabetes: Results From the LEADER Randomized Trial. Diabetes care 41(8): 1663-1671</a>                                                                                           | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis</i>                                                                                                                                                                           |
| <a href="#">Nauck, Michael A, Tornoe, Karen, Rasmussen, Soren et al. (2018) Cardiovascular outcomes in patients who experienced a myocardial infarction while treated with liraglutide versus placebo in the LEADER trial. Diabetes &amp; vascular disease research 15(5): 465-468</a>                                                   | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis using cox regression, with myocardial infarction as a time-dependent covariate, to analyse time to randomisation to the composite of cardiovascular death or hospitalisation for heart failure.</i><br><br>- Conference abstract |
| <a href="#">Nauck, Michael and Marre, Michel (2009) Adding liraglutide to oral antidiabetic drug</a>                                                                                                                                                                                                                                     | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                           |

| Study                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                            |
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| <a href="#">monotherapy: efficacy and weight benefits.</a><br>Postgraduate medicine 121(3): 5-15                                                                                                                                                                             |                                                                                                                                                                   |
| <a href="#">Neal, B., Perkovic, V., Mahaffey, K. W. et al. (2017) Canagliflozin and cardiovascular and renal events in type 2 diabetes.</a> N Engl J Med 377(7): 644-657                                                                                                     | - Duplicate reference                                                                                                                                             |
| <a href="#">Neal, Bruce, Perkovic, Vlado, de Zeeuw, Dick et al. (2015) Efficacy and safety of canagliflozin, an inhibitor of sodium-glucose cotransporter 2, when used in conjunction with insulin therapy in patients with type 2 diabetes.</a> Diabetes care 38(3): 403-11 | - Secondary publication of an included study that does not provide any additional relevant information                                                            |
| <a href="#">Neal, Bruce, Perkovic, Vlado, Mahaffey, Kenneth W et al. (2017) Optimizing the analysis strategy for the CANVAS Program: A prespecified plan for the integrated analyses of the CANVAS and CANVAS-R trials.</a> Diabetes, obesity & metabolism 19(7): 926-935    | - Study design not relevant to this review protocol<br><i>Protocol for the integration of CANVAS and CANVAS-R</i>                                                 |
| <a href="#">Neeland, Ian J, Eliasson, Bjorn, Kasai, Takatoshi et al. (2020) The Impact of Empagliflozin on Obstructive Sleep Apnea and Cardiovascular and Renal Outcomes: An Exploratory Analysis of the EMPA-REG OUTCOME Trial.</a> Diabetes care 43(12): 3007-3015         | - Study design not relevant to this review protocol<br><i>Post hoc analysis investigating prevalence of obstructive sleep apnea in the EMPA-REG OUTCOME trial</i> |
| <a href="#">Negro, R., Mangieri, T., Dazzi, D. et al. (2005) Rosiglitazone effects on blood pressure and metabolic parameters in nondipper diabetic patients.</a> Diabetes Res Clin Pract 70(1): 20-5                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                     |
| <a href="#">Nelson, Patric, Poon, Terri, Guan, Xuesong et al. (2007) The incretin mimetic exenatide as a monotherapy in patients with type 2 diabetes.</a> Diabetes technology & therapeutics 9(4): 317-26                                                                   | - Study design not relevant to this review protocol                                                                                                               |
| <a href="#">Neuen B, L, Ohkuma, T, Neal, B et al. (2020) Relative and Absolute Risk Reductions in Cardiovascular and Kidney Outcomes With Canagliflozin Across KDIGO Risk Categories: Findings From the CANVAS Program.</a> American Journal of Kidney Diseases              | - Post-hoc analysis of included study                                                                                                                             |
| <a href="#">Neuen Brendon, L, Ohkuma, Toshiaki, Neal, Bruce et al. (2018) Cardiovascular and Renal Outcomes With Canagliflozin According to Baseline Kidney Function.</a> Circulation 138(15): 1537-1550                                                                     | - Secondary publication of an included study that does not provide any additional relevant information                                                            |

| Study                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                 |
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| <a href="#">Neuen, B.L., Perkovic, V., Ohkuma, T. et al. (2019) Canagliflozin in patients with type 2 diabetes and macroalbuminuria: data from the CANVAS program. Diabetologia 62(supplement1): 341-s342</a>                                                                                       | - Conference abstract                                                                                                                  |
| <a href="#">Neuen, Brendon L, Arnott, Clare, Perkovic, Vlado et al. (2021) Sodium-glucose co-transporter-2 inhibitors with and without metformin: A meta-analysis of cardiovascular, kidney and mortality outcomes. Diabetes, obesity &amp; metabolism 23(2): 382-390</a>                           | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Neuen, Brendon L, Ohkuma, Toshiaki, Neal, Bruce et al. (2019) Effect of Canagliflozin on Renal and Cardiovascular Outcomes across Different Levels of Albuminuria: Data from the CANVAS Program. Journal of the American Society of Nephrology : JASN 30(11): 2229-2242</a>             | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis by the presence of albuminuria in the CANVAS trial</i> |
| <a href="#">Neuen, Brendon L, Oshima, Megumi, Agarwal, Rajiv et al. (2022) Sodium-Glucose Cotransporter 2 Inhibitors and Risk of Hyperkalemia in People With Type 2 Diabetes: A Meta-Analysis of Individual Participant Data From Randomized, Controlled Trials. Circulation 145(19): 1460-1470</a> | - Systematic review used as source of primary studies<br><br><i>IPD but no outcomes relevant to the review reported</i>                |
| <a href="#">Neuen, Brendon L, Oshima, Megumi, Perkovic, Vlado et al. (2021) Effects of canagliflozin on serum potassium in people with diabetes and chronic kidney disease: the CREDENCE trial. European heart journal 42(48): 4891-4901</a>                                                        | - Secondary publication of an included study that does not provide any additional relevant information                                 |
| <a href="#">Newman, J., McGill, J.B., Patel, S. et al. (2011) Long-term efficacy and safety of linagliptin in patients with type 2 diabetes and severe renal impairment. Diabetologia 54(suppl1): 333</a>                                                                                           | - Conference abstract                                                                                                                  |
| <a href="#">Ng, Nicholas Beng Hui, Low, Yue Wey, Rajgor, Dimple Dayaram et al. (2022) The effects of glucagon-like peptide (GLP)-1 receptor agonists on weight and glycaemic control in Prader-Willi syndrome: A systematic review. Clinical endocrinology 96(2): 144-154</a>                       | - Population not relevant to this review protocol<br><br><i>Prader-Willi Syndrome</i>                                                  |
| <a href="#">Nguyen, Bao-Ngoc, Nguyen, Le, Mital, Shweta et al. (2023) Comparative efficacy of sodium-glucose co-transporter-2 inhibitors, glucagon-like peptide-1 receptor agonists and non-steroidal mineralocorticoid receptor antagonists</a>                                                    | - Review article but not a systematic review                                                                                           |



| Study                                                                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                                                   |
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| <a href="#">in chronic kidney disease and type 2 diabetes: A systematic review and network meta-analysis.</a><br>Diabetes, obesity & metabolism                                                                                                                                                                                                                          |                                                                                                                                                                          |
| <a href="#">Nguyen, Tu N, Harris, Katie, Woodward, Mark et al. (2021) The Impact of Frailty on the Effectiveness and Safety of Intensive Glucose Control and Blood Pressure-Lowering Therapy for People With Type 2 Diabetes: Results From the ADVANCE Trial.</a> Diabetes care 44(7): 1622-1629                                                                         | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Nielsen, Roni, Jorsal, Anders, Iversen, Peter et al. (2019) Effect of liraglutide on myocardial glucose uptake and blood flow in stable chronic heart failure patients: A double-blind, randomized, placebo-controlled LIVE sub-study.</a> Journal of nuclear cardiology : official publication of the American Society of Nuclear Cardiology 26(2): 585-597 | - Population not relevant to this review protocol<br><i>People without type 2 diabetes</i>                                                                               |
| <a href="#">Nino, A., Okuda, I., Wilson, T. H. et al. (2017) Weekly glucagon-like peptide-1 receptor agonist albiglutide as monotherapy improves glycemic parameters in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled study.</a> J Diabetes Invest 9(3): 558-566                                                       | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Nishimura, A., Usui, S., Kumashiro, N. et al. (2016) Efficacy and safety of repaglinide added to sitagliptin in Japanese patients with type 2 diabetes: A randomized 24-week open-label clinical trial.</a> Endocrine J 63(12): 1087-1098                                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Nishio, K., Sakurai, M., Kusuyama, T. et al. (2006) A randomized comparison of pioglitazone to inhibit restenosis after coronary stenting in patients with type 2 diabetes.</a> Diabetes Care 29(1): 101-6                                                                                                                                                   | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                       |
| <a href="#">Niskanen, L., Cefalu, W.T., Leiter, L.A. et al. (2012) Efficacy and safety of canagliflozin, a sodium glucose co-transporter 2 inhibitor, compared with glimepiride in patients with type 2 diabetes on background metformin.</a> Diabetologia 55(suppl1): 314                                                                                               | - Conference abstract                                                                                                                                                    |
| <a href="#">Niu, J., Zhao, L., Wang, J. et al. (2020) Clinical effect of using a sodium-glucose cotransporter 2 inhibitor in type 2 diabetes mellitus.</a> International Journal of Clinical and Experimental Medicine 13(12): 9864-9870                                                                                                                                 | - Comparator in study does not match that specified in this review protocol                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                                                                |
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| <a href="#">Nomoto, Hiroshi, Oba-Yamamoto, Chiho, Takahashi, Yuka et al. (2021) Effects of Switching from Liraglutide or Dulaglutide to Subcutaneous Semaglutide on Glucose Metabolism and Treatment Satisfaction in Patients with Type 2 Diabetes: Protocol for a Multicenter, Prospective, Randomized, Open-Label, Blinded-Endpoint, Parallel-Group Comparison Study (The SWITCH-SEMA 1 Study).</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 12(3): 955-964 | - Study design not relevant to this review protocol<br><i>Protocol only</i>                                                                                                                                                                                           |
| <a href="#">Nomoto, Hiroshi, Takahashi, Yuka, Takano, Yoshinari et al. (2023) Effect of Switching to Once-Weekly Semaglutide on Non-Alcoholic Fatty Liver Disease: The SWITCH-SEMA 1 Subanalysis.</a> Pharmaceutics 15(8)                                                                                                                                                                                                                                                                                   | - Study design not relevant to this review protocol<br><i>Secondary analysis of another population that inappropriately excludes a lot of the randomised population (for example: people with hepatitis infections, autoimmune hepatitis, habitual drinking etc.)</i> |
| <a href="#">Nordklint, A K, Almdal, T P, Vestergaard, P et al. (2021) Effect of metformin and insulin vs. placebo and insulin on whole body composition in overweight patients with type 2 diabetes: a randomized placebo-controlled trial.</a> Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 32(9): 1837-1848                                                           | - No relevant outcomes reported                                                                                                                                                                                                                                       |
| <a href="#">Nozue, Tsuyoshi, Fukui, Kazuki, Koyama, Yutaka et al. (2016) Effects of sitagliptin on coronary atherosclerosis in patients with type 2 diabetes-A serial integrated backscatter-intravascular ultrasound study.</a> American journal of cardiovascular disease 6(4): 153-162                                                                                                                                                                                                                   | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                           |
| <a href="#">Nozue, Tsuyoshi, Fukui, Kazuki, Takamura, Takeshi et al. (2017) Effects of alogliptin on fractional flow reserve evaluated by coronary computed tomography angiography in patients with type 2 diabetes: Rationale and design of the TRACT study.</a> Journal of cardiology 69(3): 518-522                                                                                                                                                                                                      | - Study design not relevant to this review protocol<br><i>Protocol for a non-randomised study</i>                                                                                                                                                                     |
| <a href="#">Nyback-Nakell, A, Adamson, U, Lins, P E et al. (2014) Adding glimepiride to insulin+metformin in type 2 diabetes of more than 10 years' duration--a randomised, double-blind, placebo-controlled, cross-over study.</a> Diabetes research and clinical practice 103(2): 286-91                                                                                                                                                                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                               |

| Study                                                                                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                                |
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| <a href="#">Nybo, Mads, Preil, Simone Rordam, Juhl, Henning Friis et al. (2011) Rosiglitazone decreases plasma levels of osteoprotegerin in a randomized clinical trial with type 2 diabetes patients.</a> Basic & clinical pharmacology & toxicology 109(6): 481-5                                                                                                                                             | - No relevant outcomes reported                                                                                                                                       |
| <a href="#">Nystrom, Thomas, Santos-Pardo, Irene, Fang, Xin et al. (2019) Heart rate variability in type 2 diabetic subjects randomized to liraglutide or glimepiride treatment, both in combination with metformin: A randomized, open, parallel-group study.</a> Endocrinology, diabetes & metabolism 2(2): e00058                                                                                            | - Study design not relevant to this review protocol<br><i>Post hoc analysis of heart rate variability in people randomised to liraglutide compared to glimepiride</i> |
| <a href="#">Nystrom, Thomas, Santos-Pardo, Irene, Hedberg, Fredric et al. (2018) Corrigendum: Effects on Subclinical Heart Failure in Type 2 Diabetic Subjects on Liraglutide Treatment vs. Glimepiride Both in Combination with Metformin: A Randomized Open Parallel-Group Study.</a> Frontiers in endocrinology 9: 50                                                                                        | - Study design not relevant to this review protocol<br><i>Correction only</i>                                                                                         |
| <a href="#">O'Donoghue, Michelle L, Kato, Eri T, Mosenzon, Ofri et al. (2021) The efficacy and safety of dapagliflozin in women and men with type 2 diabetes mellitus.</a> Diabetologia 64(6): 1226-1234                                                                                                                                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information                                                                |
| <a href="#">O'Neil, Patrick M, Garvey, W Timothy, Gonzalez-Campoy, J Michael et al. (2016) EFFECTS OF LIRAGLUTIDE 3.0 MG ON WEIGHT AND RISK FACTORS IN HISPANIC VERSUS NON-HISPANIC POPULATIONS: SUBGROUP ANALYSIS FROM SCALE RANDOMIZED TRIALS.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 22(11): 1277-1287 | - Study design not relevant to this review protocol<br><i>Post hoc analysis where SCALE trial analysis were compared in Hispanic and non-Hispanic subgroups</i>       |
| <a href="#">Odutayo, Ayodele, da Costa, Bruno R, Pereira, Tiago V et al. (2021) Sodium-Glucose Cotransporter 2 Inhibitors, All-Cause Mortality, and Cardiovascular Outcomes in Adults with Type 2 Diabetes: A Bayesian Meta-Analysis and Meta-Regression.</a> Journal of the American Heart Association 10(18): e019918                                                                                         | - Systematic review used as source of primary studies                                                                                                                 |
| <a href="#">Oe, Hiroki, Nakamura, Kazufumi, Kihara, Hajime et al. (2015) Comparison of effects of sitagliptin and voglibose on left ventricular diastolic dysfunction in patients with type 2 diabetes:</a>                                                                                                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                         |

| Study                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                                         |
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| <a href="#">results of the 3D trial</a> . Cardiovascular Diabetology 14(1): 83                                                                                                                                                                                                                                                  |                                                                                                                                                                |
| <a href="#">Ogasawara, D., Shite, J., Shinke, T. et al. (2009) Pioglitazone reduces the necrotic-core component in coronary plaque in association with enhanced plasma adiponectin in patients with type 2 diabetes mellitus.</a> Circ J 73(2): 343-51                                                                          | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>         |
| <a href="#">Oh, SuA, Purja, Sujata, Shin, Hocheol et al. (2022) Hypoglycemic agents and glycemic variability in individuals with type 2 diabetes: A systematic review and network meta-analysis.</a> Diabetes & vascular disease research 19(3): 14791641221106866                                                              | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                        |
| <a href="#">Oh, Tae Jung, Yu, Jae Myung, Min, Kyung Wan et al. (2019) Efficacy and Safety of Voglibose Plus Metformin in Patients with Type 2 Diabetes Mellitus: A Randomized Controlled Trial.</a> Diabetes & metabolism journal 43(3): 276-286                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                  |
| <a href="#">Ohkuma, Toshiaki, Van Gaal, Luc, Shaw, Wayne et al. (2020) Clinical outcomes with canagliflozin according to baseline body mass index: results from post hoc analyses of the CANVAS Program.</a> Diabetes, obesity & metabolism 22(4): 530-539                                                                      | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis where CANVAS trial outcomes were compared according to BMI characteristics</i> |
| <a href="#">Oikonomaki, Dora, Dounousi, Evangelia, Duni, Anila et al. (2021) Incretin based therapies and SGLT-2 inhibitors in kidney transplant recipients with diabetes: A systematic review and meta-analysis.</a> Diabetes research and clinical practice 172: 108604                                                       | - Systematic review used as source of primary studies                                                                                                          |
| <a href="#">Olansky, L, Reasner, C, Seck, T L et al. (2011) A treatment strategy implementing combination therapy with sitagliptin and metformin results in superior glycaemic control versus metformin monotherapy due to a low rate of addition of antihyperglycaemic agents.</a> Diabetes, obesity & metabolism 13(9): 841-9 | - Comparator in study does not match that specified in this review protocol                                                                                    |
| <a href="#">Olsson, P O and Lindstrom, T (2002) Combination-therapy with bedtime nph insulin and sulphonylureas gives similar glycaemic control but lower weight gain than insulin twice daily in patients with type 2 diabetes.</a> Diabetes & metabolism 28(4pt1): 272-7                                                      | - Comparator in study does not match that specified in this review protocol                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                                                 | Reason                                                                                                                                                                   |
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| <a href="#">Onishi, Yukiko, Ishii, Hitoshi, Oura, Tomonori et al. (2020) Efficacy and Safety of Once-Weekly Dulaglutide in Type 2 Diabetes Patients Using Insulin: Exploratory Subgroup Analysis by Insulin Regimen.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 11(3): 735-745                                        | - Subgroup analysis of a trial that was not relevant for inclusion                                                                                                       |
| <a href="#">Onishi, Yukiko, Koshiyama, Hiroyuki, Imaoka, Takeshi et al. (2013) Safety of exenatide once weekly for 52 weeks in Japanese patients with type 2 diabetes mellitus.</a> Journal of diabetes investigation 4(2): 182-9                                                                                                                                     | - Comparator in study does not match that specified in this review protocol<br><i>Compares different dose regimes of the same medication</i>                             |
| <a href="#">Onishi, Yukiko, Niemoeller, Elisabeth, Ikeda, Yukio et al. (2015) Efficacy and safety of lixisenatide in Japanese patients with type 2 diabetes mellitus inadequately controlled by sulfonylurea with or without metformin: Subanalysis of GetGoal-S.</a> Journal of diabetes investigation 6(2): 201-9                                                   | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Only a subset of the population rather than all of them</i> |
| <a href="#">Onishi, Yukiko; Oura, Tomonori; Takeuchi, Masakazu (2024) Metabolic Abnormalities Following Tirzepatide Monotherapy in Japanese Patients with Type 2 Diabetes: A Phase 3 SURPASS J-mono Post Hoc Analysis.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 15(3): 649-661                                      | - Post-hoc analysis of included study                                                                                                                                    |
| <a href="#">Ono, Koh, Wada, Hiromichi, Satoh-Asahara, Noriko et al. (2020) Effects of Metformin on Left Ventricular Size and Function in Hypertensive Patients with Type 2 Diabetes Mellitus: Results of a Randomized, Controlled, Multicenter, Phase IV Trial.</a> American journal of cardiovascular drugs : drugs, devices, and other interventions 20(3): 283-293 | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Onoue, T., Goto, M., Wada, E. et al. (2020) Dipeptidyl peptidase-4 inhibitor anagliptin reduces fasting apolipoprotein B-48 levels in patients with type 2 diabetes: A randomized controlled trial.</a> PLoS ONE 15(1): e0228004                                                                                                                          | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                       |
| <a href="#">Onuchin, S. G., Elsukova, O. S., Solov'ev, O. V. et al. (2010) Capabilities of hypoglycemic therapy in women with decompensated type 2 diabetes mellitus.</a> Terapevticheski Arkhiv 82(8): 34-41                                                                                                                                                         | - Study not reported in English                                                                                                                                          |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                               |
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| <a href="#">Osei, Elizabeth, Zandbergen, Adrienne, Brouwers, Paul J A M et al. (2021) Safety, feasibility and efficacy of metformin and sitagliptin in patients with a TIA or minor ischaemic stroke and impaired glucose tolerance. BMJ open 11(9): e046113</a>                                                                                                                                                                           | - Population not relevant to this review protocol<br><i>Impaired glucose tolerance</i>                                               |
| <a href="#">Osei, Kwame, Rhinesmith, Scott, Gaillard, Trudy et al. (2003) Metabolic effects of chronic glipizide gastrointestinal therapeutic system on serum glucose, insulin secretion, insulin sensitivity, and hepatic insulin extraction in glucose-tolerant, first-degree relatives of African American patients with type 2 diabetes: new insights on mechanisms of action. Metabolism: clinical and experimental 52(5): 565-72</a> | - No relevant outcomes reported                                                                                                      |
| <a href="#">Oshima, Megumi, Jardine, Meg J, Agarwal, Rajiv et al. (2021) Insights from CREDENCE trial indicate an acute drop in estimated glomerular filtration rate during treatment with canagliflozin with implications for clinical practice. Kidney international 99(4): 999-1009</a>                                                                                                                                                 | - Study design not relevant to this review protocol<br><i>Posthoc analysis investigating drops in eGFR during the CREDENCE trial</i> |
| <a href="#">Oshima, Megumi, Neal, Bruce, Toyama, Tadashi et al. (2020) Different eGFR Decline Thresholds and Renal Effects of Canagliflozin: Data from the CANVAS Program. Journal of the American Society of Nephrology : JASN 31(10): 2446-2456</a>                                                                                                                                                                                      | - Secondary publication of an included study that does not provide any additional relevant information                               |
| <a href="#">Oshima, Megumi, Neuen, Brendon L, Li, JingWei et al. (2020) Early Change in Albuminuria with Canagliflozin Predicts Kidney and Cardiovascular Outcomes: A PostHoc Analysis from the CREDENCE Trial. Journal of the American Society of Nephrology : JASN 31(12): 2925-2936</a>                                                                                                                                                 | - Secondary publication of an included study that does not provide any additional relevant information                               |
| <a href="#">Osman, A., Otero, J., Brizolara, A. et al. (2004) Effect of rosiglitazone on restenosis after coronary stenting in patients with type 2 diabetes. Am Heart J 147(5): e23</a>                                                                                                                                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                        |
| <a href="#">Oulhaj, Abderrahim, Aziz, Faisal, Suliman, Abubaker et al. (2023) Joint longitudinal and time-to-event modelling compared with standard Cox modelling in patients with type 2 diabetes with and without established cardiovascular disease: An analysis of the EXSCel trial. Diabetes, obesity &amp; metabolism</a>                                                                                                            | - Secondary publication of an included study that does not provide any additional relevant information                               |



| Study                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                 |
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| <a href="#">Out, Mattijs, Kooy, Adriaan, Lehert, Philippe et al. (2018) Long-term treatment with metformin in type 2 diabetes and methylmalonic acid: Post hoc analysis of a randomized controlled 4.3year trial. Journal of diabetes and its complications 32(2): 171-178</a>                                                   | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis of Kooy 2009</i>    |
| <a href="#">Ovalle, F. and Bell, D. S. (2004) Effect of rosiglitazone versus insulin on the pancreatic beta-cell function of subjects with type 2 diabetes. Diabetes Care 27(11): 2585-9</a>                                                                                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |
| <a href="#">Ovchinnikov, AG, Borisov, AA, Zhrebchikova, KYu et al. (2021) Effects of empagliflozin on exercise tolerance and left ventricular diastolic function in patients with heart failure with preserved ejection fraction and type 2 diabetes: a prospective single-center study. Russian journal of cardiology 26(1)</a> | - Study not reported in English                                                                                                                        |
| <a href="#">Oyama, J., Murohara, T., Kitakaze, M. et al. (2016) The effect of sitagliptin on carotid artery atherosclerosis in type 2 diabetes: The PROLOGUE Randomized Controlled Trial. PLoS Med 13(6): e1002051</a>                                                                                                           | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Oyama, Jun-Ichi, Ishizu, Tomoko, Sato, Yasunori et al. (2014) Rationale and design of a study to evaluate the effects of sitagliptin on atherosclerosis in patients with diabetes mellitus: PROLOGUE study. International journal of cardiology 174(2): 383-4</a>                                                    | - Comparator in study does not match that specified in this review protocol                                                                            |
| <a href="#">Oyama, Kazuma, Raz, Itamar, Cahn, Avivit et al. (2022) Obesity and effects of dapagliflozin on cardiovascular and renal outcomes in patients with type 2 diabetes mellitus in the DECLARE-TIMI 58 trial. European heart journal 43(31): 2958-2967</a>                                                                | - Secondary publication of an included study that does not provide any additional relevant information                                                 |
| <a href="#">Oyama, T., Saiki, A., Endoh, K. et al. (2008) Effect of acarbose, an alpha-glucosidase inhibitor, on serum lipoprotein lipase mass levels and common carotid artery intima-media thickness in type 2 diabetes mellitus treated by sulfonylurea. J Atheroscler Thromb 15(3): 154-9</a>                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |
| <a href="#">Packer, Milton, Anker, Stefan D, Butler, Javed et al. (2021) Empagliflozin in Patients With Heart Failure, Reduced Ejection Fraction, and Volume Overload: EMPEROR-Reduced Trial. Journal of</a>                                                                                                                     | - Population not relevant to this review protocol                                                                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                 |
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| the American College of Cardiology 77(11): 1381-1392                                                                                                                                                                                                                                                                                                                                |                                                                                                        |
| <a href="#">Packer, Milton, Anker, Stefan D, Butler, Javed et al. (2020) Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. The New England journal of medicine 383(15): 1413-1424</a>                                                                                                                                                                          | - Population not relevant to this review protocol                                                      |
| <a href="#">Pagano, G., Marena, S., Corgiat-Mansin, L. et al. (1995) Comparison of miglitol and glibenclamide in diet-treated type 2 diabetic patients. Diabete Metab 21(3): 162-7</a>                                                                                                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Pagidipati, N., Zheng, Y., Green, J.B. et al. (2017) The association between obesity, diabetes control, and cardiovascular outcomes: Insights from the TECOS trial. European Heart Journal 38(supplement1): 608</a>                                                                                                                                                     | - Conference abstract                                                                                  |
| <a href="#">Pagidipati, Neha J, Navar, Ann Marie, Pieper, Karen S et al. (2017) Secondary Prevention of Cardiovascular Disease in Patients With Type 2 Diabetes Mellitus: International Insights From the TECOS Trial (Trial Evaluating Cardiovascular Outcomes With Sitagliptin). Circulation 136(13): 1193-1203</a>                                                               | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Paiman, Elisabeth H M, van Eyk, Huub J, van Aalst, Minke M A et al. (2020) Effect of Liraglutide on Cardiovascular Function and Myocardial Tissue Characteristics in Type 2 Diabetes Patients of South Asian Descent Living in the Netherlands: A Double-Blind, Randomized, Placebo-Controlled Trial. Journal of magnetic resonance imaging : JMRI 51(6): 1679-1688</a> | - Additional outcomes relevant to living guideline work                                                |
| <a href="#">Palmer, Suetonia C, Tendal, Britta, Mustafa, Reem A et al. (2021) Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. BMJ (Clinical research ed.) 372: m4573</a>                                         | - Systematic review used as source of primary studies                                                  |
| <a href="#">Pan, C., Yang, W., Barona, J. P. et al. (2008) Comparison of vildagliptin and acarbose monotherapy in patients with Type 2 diabetes: a 24-week, double-blind, randomized trial. Diabetic Med 25(4): 435-41</a>                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                                                             |
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| <a href="#">Pan, Changyu, Gross, Jorge L, Yang, Wenying et al. (2016) A Multinational, Randomized, Open-label, Treat-to-Target Trial Comparing Insulin Degludec and Insulin Glargine in Insulin-Naive Patients with Type 2 Diabetes Mellitus. Drugs in R&amp;D 16(2): 239-49</a>                                               | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i>                                                                                          |
| <a href="#">Pan, Runzhou, Zhang, Yan, Wang, Rongrong et al. (2022) Effect of SGLT-2 inhibitors on body composition in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. PloS one 17(12): e0279889</a>                                                                                   | - Systematic review used as source of primary studies<br><i>Identified at rerun. Additional studies identified for checking.</i>                                                                                   |
| <a href="#">Pandey, A., Kolkailah, A.A., McGuire, D.K. et al. (2023) HEART FAILURE OUTCOMES CAPTURED BY ADVERSE EVENT REPORTING IN PARTICIPANTS WITH TYPE 2 DIABETES AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE: OBSERVATIONS FROM THE VERTIS CV TRIAL. Journal of the American College of Cardiology 81(8supplement): 445</a> | - Conference abstract                                                                                                                                                                                              |
| <a href="#">Pandey, Arjun K, Dhingra, Nitish K, Hibino, Makoto et al. (2022) Sodium-glucose cotransporter 2 inhibitors in heart failure with reduced or preserved ejection fraction: a meta-analysis. ESC heart failure 9(2): 942-946</a>                                                                                      | - Population not relevant to this review protocol<br><i>Mixture of people with and without heart failure</i>                                                                                                       |
| <a href="#">Papa, G, Fedele, V, Chiavetta, A et al. (2008) Therapeutic options for elderly diabetic subjects: open label, randomized clinical trial of insulin glargine added to oral antidiabetic drugs versus increased dosage of oral antidiabetic drugs. Acta diabetologica 45(1): 53-9</a>                                | - Comparator in study does not match that specified in this review protocol<br><i>Compares adding insulin glargine to increasing dosages of oral drugs, which is not specified as a comparison in the protocol</i> |
| <a href="#">Paridari, Parsa, Jabermoradi, Sajjad, Gholamzadeh, Raheleh et al. (2023) Can metformin use reduce the risk of stroke in diabetic patients? A systematic review and meta-analysis. Diabetes &amp; metabolic syndrome 17(2): 102721</a>                                                                              | - Systematic review used as source of primary studies                                                                                                                                                              |
| <a href="#">Park, J., Park, S. W., Yoon, K. H. et al. (2017) Efficacy and safety of evogliptin monotherapy in patients with type 2 diabetes and moderately elevated glycated haemoglobin levels after diet and exercise. Diabetes Obes Metab 19(12): 1681-1687</a>                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                      |
| <a href="#">Parker, Victoria E R, Robertson, Darren, Erazo-Tapia, Edmundo et al. (2023) Cotadutide</a>                                                                                                                                                                                                                         | - Comparator in study does not match that specified in this review protocol                                                                                                                                        |

| Study                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                             |
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| <a href="#">promotes glycogenolysis in people with overweight or obesity diagnosed with type 2 diabetes.</a> Nature metabolism 5(12): 2086-2093                                                                                                                                                                                   |                                                                                                                                                    |
| <a href="#">Parmar Vinendra, M. and Goswami Sunita, S. (2019) Efficacy and safety of teneligliptin as add-on therapy to conventional therapy in Indian patients with type 2 diabetes mellitus.</a> Asian J Pharm Clin Res 12(12): 116-120                                                                                         | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Parthan, G., Bhansali, S., Kurpad, A. V. et al. (2018) Effect of Linagliptin and Voglibose on metabolic profile in patients with Type 2 Diabetes: a randomized, double-blind, placebo-controlled trial.</a> BMC Pharmacol Toxicol 19: 38                                                                              | - Data not reported in an extractable format or a format that can be analysed<br><i>Pilot study, all data reported as medians and IQR</i>          |
| <a href="#">Pasquel, F.J., Urrutia, M.A., Cardona, S. et al. (2020) A randomized controlled trial comparing liraglutide vs. glargine insulin for the management of patients with type 2 diabetes after hospital discharge.</a> Diabetes 69(supplement1)                                                                           | - Conference abstract                                                                                                                              |
| <a href="#">Pasquel, F.J., Urrutia, M.A., Cardona, S. et al. (2021) Liraglutide Hospital Discharge Trial: A Randomized Controlled Trial Comparing the Safety and Efficacy of Liraglutide versus Glargine Insulin for the Management of Patients with Type 2 Diabetes After Hospital Discharge.</a> Diabetes, obesity & metabolism | - Duplicate reference                                                                                                                              |
| <a href="#">Patel, Anushka, MacMahon, Stephen, Chalmers, John et al. (2008) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes.</a> The New England journal of medicine 358(24): 2560-72                                                                                                      | - Comparator in study does not match that specified in this review protocol                                                                        |
| <a href="#">Patel, T and Wanner, C (2016) 2016 - In patients with type 2 diabetes and CVD, empagliflozin reduced incident or worsening nephropathy at 3.1 y.</a> ACP journal club 165(8): 1-1                                                                                                                                     | - Commentary only                                                                                                                                  |
| <a href="#">Patel, Tirath, Nageeta, Fnu, Sohail, Rohab et al. (2023) Comparative efficacy and safety profile of once-weekly Semaglutide versus once-daily Sitagliptin as an add-on to metformin in patients with type 2 diabetes: a systematic review and meta-analysis.</a> Annals of medicine 55(2): 2239830                    | - Systematic review used as source of primary studies                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                 |
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| <a href="#">Patorno, Elisabetta, Pawar, Ajinkya, Bessette, Lily G et al. (2021) Comparative Effectiveness and Safety of Sodium-Glucose Cotransporter 2 Inhibitors Versus Glucagon-Like Peptide 1 Receptor Agonists in Older Adults.</a> Diabetes care 44(3): 826-835                                                                                                                              | - Study design not relevant to this review protocol<br><i>Non-randomised prospective database data</i> |
| <a href="#">Patoulas, D., Papadopoulos, C., Kassimis, G. et al. (2021) Updated Meta-Analysis of Cardiovascular Outcome Trials Evaluating Cardiovascular Efficacy of Glucagon-Like Peptide-1 Receptor Agonists.</a> American Journal of Cardiology 159: 143-146                                                                                                                                    | - Commentary only                                                                                      |
| <a href="#">Patoulas, D; Doumas, M; Papadopoulos, C (2022) Meta-Analysis Assessing the Effect of Tirzepatide on the Risk for Atrial Fibrillation in Patients With Type 2 Diabetes Mellitus.</a> The American journal of cardiology                                                                                                                                                                | - Conference abstract                                                                                  |
| <a href="#">Patoulas, Dimitrios Ioannis, Boulmpou, Aristi, Teperikidis, Eleftherios et al. (2021) Cardiovascular efficacy and safety of dipeptidyl peptidase-4 inhibitors: A meta-analysis of cardiovascular outcome trials.</a> World journal of cardiology 13(10): 585-592                                                                                                                      | - Systematic review used as source of primary studies                                                  |
| <a href="#">Patoulas, Dimitrios, Michailidis, Theodoros, Papadopoulos, Christodoulos et al. (2022) Meta-Analysis of Randomized Controlled Trials Evaluating the Effect of Dual Glucose-Dependent Insulinotropic Polypeptide and Glucagon-Like Peptide-1 Receptor Agonists on Blood Pressure Levels in Patients With Type 2 Diabetes Mellitus.</a> The American journal of cardiology 166: 144-145 | - Commentary only                                                                                      |
| <a href="#">Patoulas, Dimitrios, Papadopoulos, Christodoulos, Katsimardou, Alexandra et al. (2021) Meta-Analysis Assessing the Cardiovascular Efficacy of Sodium-Glucose Co-Transporter-2 Inhibitors According to Baseline Treatment of Interest.</a> The American journal of cardiology 139: 134-136                                                                                             | - Commentary only                                                                                      |
| <a href="#">Patoulas, Dimitrios, Papadopoulos, Christodoulos, Siskos, Fotios et al. (2021) The effect of glucagon-like peptide-1 receptor agonists on 24-hour ambulatory blood pressure: a confirmatory meta-analysis.</a> Blood pressure monitoring 26(4): 284-287                                                                                                                               | - Trial that has a treatment and follow up period of less than 24 weeks                                |

| Study                                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                               |
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| <a href="#">Patoulas, Dimitrios, Popovic, Djordje S, Stoian, Anca Pantea et al. (2023) Effect of semaglutide versus other glucagon-like peptide-1 receptor agonists on cardio-metabolic risk factors in patients with type 2 diabetes: A systematic review and meta-analysis of head-to-head, phase 3, randomized controlled trials. Journal of diabetes and its complications 37(8): 108529</a> | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Pavithra, D., Praveen, D., Chowdary, P. R. et al. (2019) A prospective randomized control study on effect of liraglutide on cardiovascular outcomes in type II diabetes mellitus. Drug Invention Today 12(11): 2549-2552</a>                                                                                                                                                         | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Pavlicek, V (2011) Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin. Diabetologie 7(1): 37-38</a>                                                                                                                                                                                                                       | - Study not reported in English                                                                                                                      |
| <a href="#">Pedersen, S.D., Davies, M., Faerch, L. et al. (2021) Effect of semaglutide 2.4 mg on glucose metabolism and body weight in adults with overweight or obesity and type 2 diabetes in the STEP 2 trial. Diabetologia 64(supplement1): 13</a>                                                                                                                                           | - Conference abstract                                                                                                                                |
| <a href="#">Peikert, A., Martinez, F.A., Vaduganathan, M. et al. (2022) Efficacy and Safety of Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction According to Age: The DELIVER Trial. Circulation: Heart Failure 15(10): e010080</a>                                                                                                                             | - Population not relevant to this review protocol<br><i>People with or without diabetes</i>                                                          |
| <a href="#">Pellicori, Pierpaolo, Fitchett, David, Kosiborod, Mikhail N et al. (2021) Use of diuretics and outcomes in patients with type 2 diabetes: findings from the EMPA-REG OUTCOME trial. European journal of heart failure 23(7): 1085-1093</a>                                                                                                                                           | - Secondary publication of an included study that does not provide any additional relevant information                                               |
| <a href="#">Pellicori, Pierpaolo, Ofstad, Anne Pernille, Fitchett, David et al. (2020) Early benefits of empagliflozin in patients with or without heart failure: findings from EMPA-REG OUTCOME. ESC heart failure 7(6): 3401-3407</a>                                                                                                                                                          | - Study design not relevant to this review protocol<br><i>Post hoc analysis by history of heart failure for people in the EMPA-REG OUTCOME trial</i> |
| <a href="#">Peng, H., Ishida, M., Hudgi, A. et al. (2021) EFFECTIVENESS OF GLUCAGON LIKE PEPTIDE-1 RECEPTOR AGONIST IN NON-ALCOHOLIC FATTY LIVER DISEASE WITH COEXISTING TYPE 2 DIABETES MELLITUS: A SYSTEMATIC REVIEW AND META-</a>                                                                                                                                                             | - Conference abstract                                                                                                                                |



| Study                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                                 |
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| <a href="#">ANALYSIS. Gastroenterology 160(6supplement): 842</a>                                                                                                                                                                                                                                                                                   |                                                                                                                                                        |
| <a href="#">Perez-Monteverde, A, Seck, T, Xu, L et al. (2011) Efficacy and safety of sitagliptin and the fixed-dose combination of sitagliptin and metformin vs. pioglitazone in drug-naïve patients with type 2 diabetes. International journal of clinical practice 65(9): 930-8</a>                                                             | - Study does not contain an intervention relevant to this review protocol<br><br><i>Phase A is too short, and the intervention changes in phase B.</i> |
| <a href="#">Perkovic, V., De Zeeuw, D., Mahaffey, K.W. et al. (2017) Canagliflozin and renal outcomes in type 2 diabetes: Data from the canvas program. Journal of the American Society of Nephrology 28: b4</a>                                                                                                                                   | - Conference abstract                                                                                                                                  |
| <a href="#">Perkovic, V., Koitka-Weber, A., Cooper, M.E. et al. (2021) Choice of endpoint in kidney outcome trials: Considerations from the EMPA-REG OUTCOMEVR trial. Nephrology Dialysis Transplantation 35(12): 2103-2111</a>                                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information                                                 |
| <a href="#">Perkovic, V., Levin, A., Wheeler, D. et al. (2017) Effects of empagliflozin on cardiovascular outcomes across KDIGO risk categories: Results from the EMPA-REG OUTCOME trial. Diabetes, Stoffwechsel und Herz 26(6): 355-356</a>                                                                                                       | - Conference abstract                                                                                                                                  |
| <a href="#">Perkovic, Vlado, de Zeeuw, Dick, Mahaffey Kenneth, W et al. (2018) Canagliflozin and renal outcomes in type 2 diabetes: results from the CANVAS Program randomised clinical trials. The lancet. Diabetes &amp; endocrinology 6(9): 691-704</a>                                                                                         | - Additional outcomes relevant to living guideline work                                                                                                |
| <a href="#">Perkovic, Vlado, Koitka-Weber, Audrey, Cooper, Mark E et al. (2020) Choice of endpoint in kidney outcome trials: considerations from the EMPA-REG OUTCOME R trial. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 35(12): 2103-2111</a> | - Secondary publication of an included study that does not provide any additional relevant information                                                 |
| <a href="#">Perl, Shira, Cook, William, Wei, Cheryl et al. (2016) Effects of Glimepiride versus Saxagliptin on beta-Cell Function and Hypoglycemia: A Post Hoc Analysis in Older Patients with Type 2 Diabetes Inadequately Controlled with Metformin. Clinical therapeutics 38(12): 2578-2588</a>                                                 | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis</i>                                                                    |

| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                               |
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| <a href="#">Permana, Hikmat; Yanto, Theo Audi; Hariyanto, Timotius Ivan (2022) Efficacy and safety of tirzepatide as novel treatment for type 2 diabetes: A systematic review and meta-analysis of randomized clinical trials.</a> Diabetes & metabolic syndrome 16(11): 102640                                              | - Systematic review used as source of primary studies                                                                                                |
| <a href="#">Perna, Simone, Mainardi, Manuela, Astrone, Paolo et al. (2018) 12-month effects of incretins versus SGLT2-Inhibitors on cognitive performance and metabolic profile. A randomized clinical trial in the elderly with Type-2 diabetes mellitus.</a> Clinical pharmacology : advances and applications 10: 141-151 | - Study does not contain an intervention relevant to this review protocol                                                                            |
| <a href="#">Perreault, L., Davies, M.J., Faerch, L. et al. (2021) Effect of semaglutide 2.4 mg on glucose metabolism and body weight in adults with overweight/obesity and type 2 diabetes in the step 2 trial.</a> Diabetes 70(suppl1)                                                                                      | - Conference abstract                                                                                                                                |
| <a href="#">Perriello, G., Pampanelli, S., Pietro, C. et al. (2006) Comparison of glycaemic control over 1 year with pioglitazone or gliclazide in patients with Type 2 diabetes.</a> Diabetic Med 23(3): 246-52                                                                                                             | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Persson, F., Sivalingam, S., Wasehuus, V. et al. (2023) Renal Effects of Empagliflozin Alone or in Combination with Semaglutide in Albuminuric Type 2 Diabetes: A Randomized, Placebo-Controlled Trial.</a> Journal of the American Society of Nephrology 34: 16                                                 | - Conference abstract                                                                                                                                |
| <a href="#">Persson, Frederik, Bain, Stephen C, Mosenzon, Ofri et al. (2021) Changes in Albuminuria Predict Cardiovascular and Renal Outcomes in Type 2 Diabetes: A Post Hoc Analysis of the LEADER Trial.</a> Diabetes care 44(4): 1020-1026                                                                                | - Study design not relevant to this review protocol<br><i>Post hoc analysis by albuminuria presence in the LEADER trial</i>                          |
| <a href="#">Petri, Kristin C C, Ingwersen, Steen H, Flint, Anne et al. (2018) Exposure-response analysis for evaluation of semaglutide dose levels in type 2 diabetes.</a> Diabetes, obesity & metabolism 20(9): 2238-2245                                                                                                   | - Study design not relevant to this review protocol<br><i>Pooled analysis of four trials</i>                                                         |
| <a href="#">Petrica, L., Petrica, M., Vlad, A. et al. (2009) Nephro- and neuroprotective effects of rosiglitazone versus glimepiride in normoalbuminuric patients with type 2 diabetes mellitus: a randomized controlled trial.</a> Wiener Klinische Wochenschrift 121(2324): 765-75                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                        |

| Study                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                                           |
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| <a href="#">Petrie, Mark C, Verma, Subodh, Docherty, Kieran F et al. (2020) Effect of Dapagliflozin on Worsening Heart Failure and Cardiovascular Death in Patients With Heart Failure With and Without Diabetes. JAMA 323(14): 1353-1368</a>                                                                                                           | - Population not relevant to this review protocol                                                                                                                                |
| <a href="#">Philis-Tsimikas, A., Asong, M., Franek, E. et al. (2023) Switching to once-weekly insulin icodec versus once-daily insulin degludec in individuals with basal insulin-treated type 2 diabetes (ONWARDS 2): a phase 3a, randomised, open label, multicentre, treat-to-target trial. The Lancet Diabetes and Endocrinology 11(6): 414-425</a> | - Study does not contain an intervention relevant to this review protocol                                                                                                        |
| <a href="#">Phillips, L. S., Grunberger, G., Miller, E. et al. (2001) Once- and twice-daily dosing with rosiglitazone improves glycemic control in patients with type 2 diabetes. Diabetes Care 24(2): 308-15</a>                                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                    |
| <a href="#">Phillips, P., Karrasch, J., Scott, R. et al. (2003) Acarbose improves glycemic control in overweight type 2 diabetic patients insufficiently treated with metformin. Diabetes Care 26(2): 269-73</a>                                                                                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                    |
| <a href="#">Phrueksotsai, Susrichit, Pinyopornpanish, Kanokwan, Euathrongchit, Juntima et al. (2021) The effects of dapagliflozin on hepatic and visceral fat in type 2 diabetes patients with non-alcoholic fatty liver disease. Journal of gastroenterology and hepatology 36(10): 2952-2959</a>                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                          |
| <a href="#">Piatti, P., Lahtela, J., Ahmann, A. et al. (2015) Efficacy and safety of liraglutide vs placebo when added to basal insulin analogues in subjects with type 2 diabetes: A randomised, placebo-controlled trial. Italian Journal of Medicine 9(suppl2): 80</a>                                                                               | - Conference abstract                                                                                                                                                            |
| <a href="#">Piera-Mardemootoo, Carole; Lambert, Philippe; Faillie, Jean-Luc (2021) Efficacy of metformin on glycemic control and weight in drug-naive type 2 diabetes mellitus patients: A systematic review and meta-analysis of placebo-controlled randomized trials. Therapie 76(6): 647-656</a>                                                     | - Systematic review used as source of primary studies<br><br><i>Identified in rerun search. No additional studies to add (or studies were too short a follow up to be added)</i> |
| <a href="#">Pirro, V., Lin, Y., Willency, J.A. et al. (2023) Tirzepatide improves amino acid profile in people with longstanding diabetes and</a>                                                                                                                                                                                                       | - Conference abstract                                                                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                                               |
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| <a href="#">increased cardiovascular risk in the SURPASS-4 trial</a> . Diabetologia 66(supplement1): 313-s314                                                                                                                                                                                                      |                                                                                                                                                                      |
| <a href="#">Pirro, Valentina, Roth, Kenneth D, Lin, Yanzhu et al. (2022) Effects of Tirzepatide, a Dual GIP and GLP-1 RA, on Lipid and Metabolite Profiles in Subjects With Type 2 Diabetes</a> . The Journal of clinical endocrinology and metabolism 107(2): 363-378                                             | - Secondary publication of an included study that does not provide any additional relevant information                                                               |
| <a href="#">Pistrosch, F., Passauer, J., Herbrig, K. et al. (2012) Effect of thiazolidinedione treatment on proteinuria and renal hemodynamic in type 2 diabetic patients with overt nephropathy</a> . Horm Metab Res 44(12): 914-8                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                        |
| <a href="#">Pitt, B., Filippatos, G., Agarwal, R. et al. (2021) Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes</a> . New England journal of medicine 385(24): 2252-2263                                                                                                               | - Study does not contain an intervention relevant to this review protocol                                                                                            |
| <a href="#">Pollack, Rena, Raz, Itamar, Wiviott, Stephen D et al. (2023) Efficacy and Safety of Dapagliflozin by Baseline Insulin Regimen and Dose: Post Hoc Analyses From DECLARE-TIMI 58</a> . Diabetes care 46(1): 156-164                                                                                      | - Study design not relevant to this review protocol<br><i>Post hoc analysis of results by baseline insulin regimen and dose for people in the DECLARE-TIMI trial</i> |
| <a href="#">Pollock, C., Wheeler, D.C., Rossing, P. et al. (2019) SAT-300 EFFECTS OF DAPAGLIFLOZIN AND DAPAGLIFLOZIN PLUS SAXAGLIPTIN ON HbA1c AND ALBUMINURIA IN PATIENTS WITH TYPE 2 DIABETES AND CHRONIC KIDNEY DISEASE: PHASE II/III DELIGHT STUDY</a> . Kidney International Reports 4(7supplement): 133-s134 | - Conference abstract                                                                                                                                                |
| <a href="#">Ponirakis, Georgios, Abdul-Ghani, Muhammad A, Jayyousi, Amin et al. (2021) Painful diabetic neuropathy is associated with increased nerve regeneration in patients with type 2 diabetes undergoing intensive glycemic control</a> . Journal of diabetes investigation 12(9): 1642-1650                 | - Secondary publication of an included study that does not provide any additional relevant information                                                               |
| <a href="#">Ponssen, HH; Elte, JWF; Lehert, JP (1998) Combined metformin and insulin treatment of non-insulin dependent diabetes (NIDDM)</a> . Netherlands journal of medicine 52: a7                                                                                                                              | - Conference abstract                                                                                                                                                |
| <a href="#">Pop-Busui, R., Oral, E., Raffel, D. et al. (2009) Impact of rosiglitazone and glyburide on nitrosative stress and myocardial blood flow</a>                                                                                                                                                            | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                        |

| Study                                                                                                                                                                                                                                                                                                                                     | Reason                                                                      |
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| <a href="#">regulation in type 2 diabetes mellitus.</a><br>Metabolism 58(7): 989-94                                                                                                                                                                                                                                                       |                                                                             |
| <a href="#">Poulter, Neil R (2009) Blood pressure and glucose control in subjects with diabetes: new analyses from ADVANCE.</a> Journal of hypertension. Supplement : official journal of the International Society of Hypertension 27(1): 3-8                                                                                            | - Comparator in study does not match that specified in this review protocol |
| <a href="#">Pratley, R.E., Aroda, V.R., Gondolf, T. et al. (2019) Efficacy and safety of once-weekly semaglutide low dose 0.5 mg vs once-weekly dulaglutide high dose 1.5 mg in type 2 diabetes: a post hoc analysis of SUSTAIN 7.</a> Diabetologia 62(supplement1): 374                                                                  | - Conference abstract                                                       |
| <a href="#">Pratley, Richard E, Cannon, Christopher P, Cherney, David Z I et al. (2023) Cardiorenal outcomes, kidney function, and other safety outcomes with ertugliflozin in older adults with type 2 diabetes (VERTIS CV): secondary analyses from a randomised, double-blind trial.</a> The lancet. Healthy longevity 4(4): e143-e154 | - Post-hoc analysis of included study                                       |
| <a href="#">Pratley, Richard E, Nauck, Michael A, Bailey, Timothy et al. (2012) Efficacy and safety of switching from the DPP-4 inhibitor sitagliptin to the human GLP-1 analog liraglutide after 52 weeks in metformin-treated patients with type 2 diabetes: a randomized, open-label trial.</a> Diabetes care 35(10): 1986-93          | - Comparator in study does not match that specified in this review protocol |
| <a href="#">Provenzano, M., Jongs, N., Stefansson, B.V. et al. (2022) POS-202 DAPAGLIFLOZIN IN PATIENTS WITH CHRONIC KIDNEY DISEASE TREATED WITH MINERALOCORTICOID RECEPTOR ANTAGONISTS: PRE-SPECIFIED ANALYSIS OF THE DAPA-CKD TRIAL.</a> Kidney International Reports 7(2supplement): 86-s87                                            | - Conference abstract                                                       |
| <a href="#">Puar, P., Mistry, N., Connelly, K. et al. (2022) INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-7 AS A MARKER OF CARDIAC REVERSE REMODELING WITH EMPAGLIFLOZIN: A SECONDARY ANALYSIS OF THE EMPA-HEART CARDIOLINK-6 RANDOMIZED CONTROLLED TRIAL.</a> Canadian Journal of Cardiology 38(10supplement2): 122                        | - Conference abstract                                                       |
| <a href="#">Qian, Weiyun; Liu, Fei; Yang, Qichao (2021) Effect of glucagon-like peptide-1 receptor agonists in subjects with type 2 diabetes</a>                                                                                                                                                                                          | - Systematic review used as source of primary studies                       |

| Study                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                             |
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| <a href="#">mellitus: A meta-analysis.</a> Journal of clinical pharmacy and therapeutics 46(6): 1650-1658                                                                                                                                                                                                                                     |                                                                                                                                                    |
| <a href="#">Qin, Jing and Song, Li (2022) Glucagon-like peptide-1 (GLP-1) receptor agonists and cardiovascular events in patients with type 2 diabetes mellitus: a meta-analysis of double-blind, randomized, placebo-controlled clinical trials.</a> BMC endocrine disorders 22(1): 125                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                                                            |
| <a href="#">Qin, Yuejuan, Adams, John, Solis-Herrera, Carolina et al. (2020) Clinical Parameters, Fuel Oxidation, and Glucose Kinetics in Patients With Type 2 Diabetes Treated With Dapagliflozin Plus Saxagliptin.</a> Diabetes care 43(10): 2519-2527                                                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                                                            |
| <a href="#">Qiu, M, Wei, W, Wei, XB et al. (2022) Updated network meta-analysis assessing the relative efficacy of 13 GLP-1 RA and SGLT2 inhibitor interventions on cardiorenal and mortality outcomes in type 2 diabetes.</a> European journal of clinical pharmacology 78(4): 695-697                                                       | - Study design not relevant to this review protocol<br><i>Letter only</i>                                                                          |
| <a href="#">Qiu, Mei, Ding, Liang-Liang, Wei, Xu-Bin et al. (2021) Comparative Efficacy of Glucagon-like Peptide 1 Receptor Agonists and Sodium Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular Events in Type 2 Diabetes: A Network Meta-analysis.</a> Journal of cardiovascular pharmacology 77(1): 34-37 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                            |
| <a href="#">Qiu, Mei; Ding, Liang-Liang; Zhou, Hai-Rong (2021) Factors affecting the efficacy of SGLT2is on heart failure events: a meta-analysis based on cardiovascular outcome trials.</a> Cardiovascular diagnosis and therapy 11(3): 699-706                                                                                             | - Population not relevant to this review protocol<br><i>Mixture of people with and without type 2 diabetes</i>                                     |
| <a href="#">Qiu, Mei; Ding, Liangliang; Zhou, Hairong (2021) Effects of SGLT2 inhibitors on cardiovascular and renal outcomes in type 2 diabetes: A meta-analysis with trial sequential analysis.</a> Medicine 100(10): e25121                                                                                                                | - Systematic review used as source of primary studies                                                                                              |
| <a href="#">Quatraro, A., Consoli, G., Ceriello, A. et al. (1986) Combined insulin and sulfonylurea therapy in non-insulin-dependent diabetics with secondary failure to oral drugs: a one year follow-up.</a> Diabetes Metab 12(6): 315-8                                                                                                    | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |



| Study                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                 |
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| <a href="#">Raghuveer, B. and Netaji, N. (2020) Efficacy of teneligliptin with metformin in type 2 diabetes mellitus patients.</a> National Journal of Physiology, Pharmacy and Pharmacology 10(8): 663-666                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Rahman, Hammad, Khan, Safi U, Lone, Ahmad N et al. (2023) Sodium-Glucose Cotransporter-2 Inhibitors and Primary Prevention of Atherosclerotic Cardiovascular Disease: A Meta-Analysis of Randomized Trials and Systematic Review.</a> Journal of the American Heart Association 12(16): e030578               | - Systematic review used as source of primary studies                                                  |
| <a href="#">Rahman, I. U., Malik, S. A., Bashir, M. et al. (2011) Monotherapy with metformin or glimepiride and changes in serum sialic acid in type 2 diabetes mellitus.</a> Br J Diabetes Vasc Dis 11(3): 137-40                                                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Rahman, S., Ismail, Aa- S., Ismail, S. B. et al. (2010) Effect of rosiglitazone and ramipril on macrovasculopathy in patients with type 2 diabetes: Needs longer treatment and/or higher doses?.</a> Clin Pharmacol Adv App 2(1): 83-7                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Rai, Archana, Connelly, Kim A, Verma, Subodh et al. (2022) Empagliflozin does not affect left ventricular diastolic function in patients with type 2 diabetes mellitus and coronary artery disease: insight from the EMPA-HEART CardioLink-6 randomized clinical trial.</a> Acta diabetologica 59(4): 575-578 | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Rajagopalan, Sujit, Dutta, Pinaki, Hota, Debasish et al. (2015) Effect of low dose pioglitazone on glycemic control and insulin resistance in Type 2 diabetes: A randomized, double blind, clinical trial.</a> Diabetes research and clinical practice 109(3): e32-5                                          | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Ramesh, Sahai, A.K., Kaundal, P.K. et al. (2021) Comparison of Safety and Efficacy of Combination of Glimepiride-Metformin Versus Vildagliptin-Metformin in Type 2 Diabetic Patients with Hba1c Between 7.5 To 10.</a> Indian Journal of Pharmacology 53(7supplement1): 594                                   | - Conference abstract                                                                                  |
| <a href="#">Rasalam, Roy, Atherton, John J, Deed, Gary et al. (2021) Sodium-glucose cotransporter 2 inhibitor effects on heart failure hospitalization</a>                                                                                                                                                                | - Population not relevant to this review protocol<br><i>People with and without type 2 diabetes</i>    |

| Study                                                                                                                                                                                                                                                                                 | Reason                                                                                                                                                                   |
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| <a href="#">and cardiac function: systematic review.</a> ESC heart failure 8(5): 4093-4118                                                                                                                                                                                            |                                                                                                                                                                          |
| <a href="#">Raskin, P., Lewin, A., Reinhardt, R. et al. (2009) Twice-daily dosing of a repaglinide/metformin fixed-dose combination tablet provides glycaemic control comparable to rosiglitazone/metformin tablet.</a> Diabetes Obes Metab 11(9): 865-73                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Raskin, P., McGill, J., Saad, M. F. et al. (2004) Combination therapy for type 2 diabetes: repaglinide plus rosiglitazone.</a> Diabetic Med 21(4): 329-35                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Raskin, P., Rendell, M., Riddle, M. C. et al. (2001) A randomized trial of rosiglitazone therapy in patients with inadequately controlled insulin-treated type 2 diabetes.</a> Diabetes Care 24(7): 1226-32                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Rasmussen, Ida K B, Zobel, Emilie H, Ripa, Rasmus S et al. (2021) Liraglutide reduces cardiac adipose tissue in type 2 diabetes: A secondary analysis of the LIRAFLAME randomized placebo-controlled trial.</a> Diabetes, obesity & metabolism 23(12): 2651-2659          | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Ratzl, V., Bugianesi, E., Cusi, K. et al. (2022) The role of body weight loss as a mediator of histological efficacy of semaglutide in non-alcoholic steatohepatitis.</a> Hepatology International 16(supplement1): 263                                                   | - Conference abstract                                                                                                                                                    |
| <a href="#">Rau, Matthias, Thiele, Kirsten, Hartmann, Niels-Ulrik Korbinian et al. (2022) Effects of empagliflozin on markers of calcium and phosphate homeostasis in patients with type 2 diabetes - Data from a randomized, placebo-controlled study.</a> Bone reports 16: 101175   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Raubenheimer, Peter J, Cushman, William C, Avezum, Alvaro et al. (2022) Dulaglutide and incident atrial fibrillation or flutter in patients with type 2 diabetes: A post hoc analysis from the REWIND randomized trial.</a> Diabetes, obesity & metabolism 24(4): 704-712 | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Ray, R., Shih, M., Constantz, N. et al. (2014) Pioglitazone for the treatment of insulin resistance in heart transplant recipients: Assessment of efficacy and safety.</a> Journal of                                                                                     | - Conference abstract                                                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                     |
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| Heart and Lung Transplantation 33(4suppl1): 282-s283                                                                                                                                                                                                                                                                                          |                                                                                                                                                                            |
| <a href="#">Rayner, Christopher K, Wu, Tongzhi, Aroda, Vanita R et al. (2021) Gastrointestinal adverse events with insulin glargine/lixisenatide fixed-ratio combination versus glucagon-like peptide-1 receptor agonists in people with type 2 diabetes mellitus: A network meta-analysis.</a> Diabetes, obesity & metabolism 23(1): 136-146 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                    |
| <a href="#">Raz, I., Bonaca, M.P., Mosenzon, O. et al. (2017) DECLARE-TIMI 58: Design and baseline characteristics.</a> Diabetes 66(supplement1): a333                                                                                                                                                                                        | - Conference abstract                                                                                                                                                      |
| <a href="#">Raz, I, Hanefeld, M, Xu, L et al. (2006) Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy in patients with type 2 diabetes mellitus.</a> Diabetologia 49(11): 2564-71                                                                                                                       | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                    |
| <a href="#">Raz, Itamar, Bhatt, Deepak L, Hirshberg, Boaz et al. (2014) Incidence of pancreatitis and pancreatic cancer in a randomized controlled multicenter trial (SAVOR-TIMI 53) of the dipeptidyl peptidase-4 inhibitor saxagliptin.</a> Diabetes care 37(9): 2435-41                                                                    | - Additional outcomes relevant to living guideline work                                                                                                                    |
| <a href="#">Rea, R., Blonde, L., Belousova, L. et al. (2019) Liraglutide as add-on to SGLT2 inhibitors in patients with inadequately controlled type 2 diabetes: a 26-week, randomised, doubleblind, placebo-controlled trial.</a> Diabetologia 62(supplement1): 371                                                                          | - Conference abstract                                                                                                                                                      |
| <a href="#">Reasner, C, Olansky, L, Seck, T L et al. (2011) The effect of initial therapy with the fixed-dose combination of sitagliptin and metformin compared with metformin monotherapy in patients with type 2 diabetes mellitus.</a> Diabetes, obesity & metabolism 13(7): 644-52                                                        | - Trial that has a treatment and follow up period of less than 24 weeks<br><br><i>While the study follows up for 26 weeks, the outcomes are reported for 18 weeks only</i> |
| <a href="#">Reaven, GM, Johnston, P, Hollenbeck, CB et al. (1992) Combined metformin-sulfonylurea treatment of patients with noninsulin-dependent diabetes in fair to poor glycemic control.</a> Journal of clinical endocrinology and metabolism 74(5): 1020-1026                                                                            | - Study design not relevant to this review protocol                                                                                                                        |
| <a href="#">Reed, Shelby D, Li, Yanhong, Dakin, Helen A et al. (2020) Within-Trial Evaluation of Medical Resources, Costs, and Quality of Life Among</a>                                                                                                                                                                                      | - Study design not relevant to this review protocol                                                                                                                        |

| Study                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                                   |
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| <a href="#">Patients With Type 2 Diabetes Participating in the Exenatide Study of Cardiovascular Event Lowering (EXSCEL).</a> Diabetes care 43(2): 374-381                                                                                                                                                                | <i>Economic study with no clinical data that can be used</i>                                                                                                             |
| <a href="#">Rella, Steven, Onyiah, Joseph, Baker, Chelsea et al. (2023) Design and rationale for the SIB trial: a randomized parallel comparison of semaglutide versus placebo on intestinal barrier function in type 2 diabetes mellitus.</a> Therapeutic advances in endocrinology and metabolism 14: 20420188231207348 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Rendell, Marc and Chrysant, Steven G (2011) Review of the safety and efficacy of linagliptin as add-on therapy to metformin in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study.</a> Postgraduate medicine 123(4): 183-6                                                   | - Commentary only                                                                                                                                                        |
| <a href="#">Retnakaran, R., Emery, A., Ye, C. et al. (2021) Short-term intensive insulin as induction and maintenance therapy for the preservation of beta-cell function in early type 2 diabetes (RESET-IT Main): A 2-year randomized controlled trial.</a> Diabetes, Obesity & Metabolism 23(8): 1926-1935              | - Comparator in study does not match that specified in this review protocol<br><br><i>Comparing different insulin therapy regimens</i>                                   |
| <a href="#">Retnakaran, Ravi, Choi, Haysook, Ye, Chang et al. (2018) Two-year trial of intermittent insulin therapy vs metformin for the preservation of beta-cell function after initial short-term intensive insulin induction in early type 2 diabetes.</a> Diabetes, obesity & metabolism 20(6): 1399-1407            | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Retnakaran, Ravi, Kramer, Caroline K, Choi, Haysook et al. (2014) Liraglutide and the preservation of pancreatic beta-cell function in early type 2 diabetes: the LIBRA trial.</a> Diabetes care 37(12): 3270-8                                                                                               | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Retnakaran, Ravi, Ye, Chang, Emery, Alexandra et al. (2022) The metabolic effects of adding exenatide to basal insulin therapy when targeting remission in early type 2 diabetes in a randomized clinical trial.</a> Nature communications 13(1): 6109                                                        | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Reusch, J., Stewart, M. W., Perkins, C. M. et al. (2014) Efficacy and safety of once-weekly glucagon-like peptide 1 receptor agonist albiglutide (HARMONY 1 trial): 52-week primary</a>                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |

| Study                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                   |
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| <a href="#">endpoint results from a randomized, double-blind, placebo-controlled trial in patients with type 2 diabetes mellitus not controlled on pioglitazone, with or without metformin.</a> Diabetes Obes Metab 16(12): 1257-64                                                                                                                               |                                                                                                                                                                          |
| <a href="#">Rey Adam Cordovez, R.A.B., Denila, R.W., Rivera, K.A. et al. (2022) Efficacy of sodium glucose cotransporter-2 inhibitors for heart failure with preserved and with mildly reduced ejection fraction: a systematic review and meta-analysis.</a> European Journal of Heart Failure 24(supplement2): 114                                               | - Conference abstract                                                                                                                                                    |
| <a href="#">Reynolds, L. R., Kingsley, F. J., Karounos, D. G. et al. (2007) Differential effects of rosiglitazone and insulin glargine on inflammatory markers, glycemic control, and lipids in type 2 diabetes.</a> Diabetes Res Clin Pract 77(2): 180-7                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Reynolds, L. R., Konz, E. C., Frederich, R. C. et al. (2002) Rosiglitazone amplifies the benefits of lifestyle intervention measures in long-standing type 2 diabetes mellitus.</a> Diabetes Obes Metab 4(4): 270-5                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Riddle, M C, Rosenstock, J, Vlainic, A et al. (2014) Randomized, 1-year comparison of three ways to initiate and advance insulin for type 2 diabetes: twice-daily premixed insulin versus basal insulin with either basal-plus one prandial insulin or basal-bolus up to three prandial injections.</a> Diabetes, obesity & metabolism 16(5): 396-402 | - Comparator in study does not match that specified in this review protocol<br><i>Comparing different insulin therapy regimens</i>                                       |
| <a href="#">Riddle, Matthew C, Gerstein, Hertzal C, Xavier, Denis et al. (2021) Efficacy and Safety of Dulaglutide in Older Patients: A post hoc Analysis of the REWIND trial.</a> The Journal of clinical endocrinology and metabolism 106(5): 1345-1351                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Rigato, Mauro; Fadini, Gian Paolo; Avogaro, Angelo (2023) Safety of sodium-glucose cotransporter 2 inhibitors in elderly patients with type 2 diabetes: A meta-analysis of randomized controlled trials.</a> Diabetes, obesity & metabolism 25(10): 2963-2969                                                                                         | - Systematic review used as source of primary studies                                                                                                                    |
| <a href="#">Ripa, R. S., Zobel, E. H., von Scholten, B. J. et al. (2021) Effect of Liraglutide on Arterial Inflammation Assessed as [18F]FDG Uptake in Patients With Type 2 Diabetes: a Randomized,</a>                                                                                                                                                           | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                         |
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| <a href="#">Double-Blind, Placebo-Controlled Trial.</a> Circulation. Cardiovascular imaging 14(7): e012174                                                                                                                                                                                                                                                                                                             | <i>Around 40% of people received other medication</i>                                                                          |
| <a href="#">Ristic, S., Collober-Maugeais, C., Pecher, E. et al. (2006) Comparison of nateglinide and gliclazide in combination with metformin, for treatment of patients with Type 2 diabetes mellitus inadequately controlled on maximum doses of metformin alone.</a> Diabetic Med 23(7): 757-62                                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                  |
| <a href="#">Rizvi, R., Roy, A., Ravi, R. et al. (2024) A COMPARISON OF GLP-1 RECEPTOR AGONISTS AND DPP-4 INHIBITORS FOR THE TREATMENT OF DIABETES MELLITUS TYPE 2: A SYSTEMATIC REVIEW.</a> Journal of Population Therapeutics and Clinical Pharmacology 31(2): 2622-2635                                                                                                                                              | - Systematic review used as source of primary studies                                                                          |
| <a href="#">Rizzi, Alessandro. Kloecker, David E, Pitocco, Dario et al. (2023) Translating trial results into interpretable risk estimates: Systematic analysis of cardiorenal outcome trials of glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter-2 inhibitors.</a> Nutrition, metabolism, and cardiovascular diseases : NMCD                                                                | - Systematic review used as source of primary studies                                                                          |
| <a href="#">Rizzo, M., Nauck, M., Pirags, V. et al. (2016) Once-daily liraglutide vs lixisenatide as add-on to metformin in type 2 diabetes: A 26-week randomised controlled clinical trial.</a> Italian Journal of Medicine 10(supplement2): 99                                                                                                                                                                       | - Conference abstract                                                                                                          |
| <a href="#">Robbins, D. C., Beisswenger, P. J., Ceriello, A. et al. (2007) Mealtime 50/50 basal + prandial insulin analogue mixture with a basal insulin analogue, both plus metformin, in the achievement of target HbA1c and pre- and postprandial blood glucose levels in patients with type 2 diabetes: a multinational, 24-week, randomized, open-label, parallel-group comparison.</a> Clin Ther 29(11): 2349-64 | - Comparator in study does not match that specified in this review protocol<br><br><i>Comparing different types of insulin</i> |
| <a href="#">Rodbard, H W, Cariou, B, Zinman, B et al. (2013) Comparison of insulin degludec with insulin glargine in insulin-naive subjects with Type 2 diabetes: a 2-year randomized, treat-to-target trial.</a> Diabetic medicine : a journal of the British Diabetic Association 30(11): 1298-304                                                                                                                   | - Comparator in study does not match that specified in this review protocol<br><br><i>Comparing different types of insulin</i> |
| <a href="#">Roden, M., Weng, J., Eilbracht, J. et al. (2013) Empagliflozin monotherapy with sitagliptin as an</a>                                                                                                                                                                                                                                                                                                      | - Longer-term data reported in included study                                                                                  |



| Study                                                                                                                                                                                                                                                                                       | Reason                                                                                                   |
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| <a href="#">active comparator in patients with type 2 diabetes: A randomised, double-blind, placebo-controlled, phase 3 trial.</a> Lancet Diabetes Endocrinol 1(3): 208-219                                                                                                                 | <i>Roden 2015 reports longer-term data</i>                                                               |
| <a href="#">Roden, M, Mariz, S, Brazzale, A R et al. (2009) Free fatty acid kinetics during long-term treatment with pioglitazone added to sulfonylurea or metformin in Type 2 diabetes.</a> Journal of internal medicine 265(4): 476-87                                                    | - No relevant outcomes reported                                                                          |
| <a href="#">Rodger, N W, Chiasson, J L, Josse, R G et al. (1995) Clinical experience with acarbose: results of a Canadian multicentre study.</a> Clinical and investigative medicine. Medecine clinique et experimentale 18(4): 318-24                                                      | - Study does not contain an intervention relevant to this review protocol                                |
| <a href="#">Rodriguez, A., Cusi, K., Gastaldelli, A. et al. (2023) Changes in liver and abdominal fat in tirzepatide-treated patients achieving normoglycaemia in the SURPASS-3 MRI substudy.</a> Diabetologia 66(supplement1): 333                                                         | - Conference abstract                                                                                    |
| <a href="#">Rodriguez-Valadez, Jose M, Tahsin, Malak, Masharani, Umesh et al. (2024) Potential Mediators for Treatment Effects of Novel Diabetes Medications on Cardiovascular and Renal Outcomes: A Meta-Regression Analysis.</a> Journal of the American Heart Association 13(4): e032463 | - SR - does not match PICO<br><i>Included participants with type 1 diabetes and gestational diabetes</i> |
| <a href="#">Romero-Gomez, Manuel, Lawitz, Eric, Shankar, R Ravi et al. (2023) A phase IIa active-comparator-controlled study to evaluate the efficacy and safety of efinopegdutide in patients with non-alcoholic fatty liver disease.</a> Journal of hepatology 79(4): 888-897             | - Study does not contain an intervention relevant to this review protocol                                |
| <a href="#">Rosenberg, A. E., Sigmon, K. N., Somerville, M. C. et al. (2018) Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial.</a> Lancet 392(10157): 1519-1529  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK            |
| <a href="#">Rosenstock, J., Baron, M. A., Dejager, S. et al. (2007) Comparison of vildagliptin and rosiglitazone monotherapy in patients with type 2 diabetes: a 24-week, double-blind, randomized trial.</a> Diabetes Care 30(2): 217-23                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK            |

| Study                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                                                                                   |
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| <a href="#">Rosenstock, J., Brown, A., Fischer, J. et al. (1998) Efficacy and safety of acarbose in metformin-treated patients with type 2 diabetes. Diabetes Care 21(12): 2050-5</a>                                                                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Rosenstock, J., Fonseca, V. A., Gross, J. L. et al. (2014) Advancing basal insulin replacement in type 2 diabetes inadequately controlled with insulin glargine plus oral agents: A comparison of adding albiglutide, a weekly GLP-1 receptor agonist, versus thrice-daily prandial insulin lispro. Diabetes Care 37(8): 2317-2325</a> | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Rosenstock, J., Goldstein, B. J., Vinik, A. I. et al. (2006) Effect of early addition of rosiglitazone to sulphonylurea therapy in older type 2 diabetes patients (&gt;60 years): the Rosiglitazone Early vs. SULphonylurea Titration (RESULT) study. Diabetes Obes Metab 8(1): 49-57</a>                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Rosenstock, J., Kahn, S.E., Johansen, O.E. et al. (2019) Relationship between hypoglycaemia, cardiovascular (CV) outcomes and all-cause mortality (ACM) in type 2 diabetes (T2D) in the CARMELINA trial. Diabetologia 62(supplement1): 65</a>                                                                                          | - Conference abstract                                                                                                                                                    |
| <a href="#">Rosenstock, J., Nino, A., Soffer, J. et al. (2020) Impact of a Weekly Glucagon-Like Peptide 1 Receptor Agonist, Albiglutide, on Glycemic Control and on Reducing Prandial Insulin Use in Type 2 Diabetes Inadequately Controlled on Multiple Insulin Therapy: A Randomized Trial. Diabetes Care 43(10): 2509-2518</a>                  | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                       |
| <a href="#">Rosenstock, J., Rood, J., Cobitz, A. et al. (2006) Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes. Diabetes Obes Metab 8(6): 650-60</a>                                                  | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Rosenstock, J., Sugimoto, D., Strange, P. et al. (2006) Triple therapy in type 2 diabetes: insulin glargine or rosiglitazone added to combination therapy of sulphonylurea plus metformin in insulin-naïve patients. Diabetes Care 29(3): 554-9</a>                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Rosenstock, J.; Wilson, C.; Fleck, P. (2013) Alogliptin versus glipizide monotherapy in elderly type 2 diabetes mellitus patients with mild hyperglycaemia: A prospective, double-</a>                                                                                                                                                 | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naïve and therefore the study cannot be classified into review 1.1 or 1.2 |

| Study                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                                                   |
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| <a href="#">blind, randomized, 1-year study.</a> Diabetes Obes Metab 15(10): 906-914                                                                                                                                                                                                                                                   |                                                                                                                                                                          |
| <a href="#">Rosenstock, J., Wysham, C., Frias, J. P. et al. (2021) Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial.</a> Lancet (london, england) 398(10295): 143-155                                            | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Rosenstock, Julio, Bajaj, Harpreet S, Janez, Andrej et al. (2020) Once-Weekly Insulin for Type 2 Diabetes without Previous Insulin Treatment.</a> The New England journal of medicine 383(22): 2107-2116                                                                                                                   | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i>                                                |
| <a href="#">Rosenstock, Julio, Franco, Denise, Korpachev, Vadym et al. (2015) Inhaled Technosphere Insulin Versus Inhaled Technosphere Placebo in Insulin-Naive Subjects With Type 2 Diabetes Inadequately Controlled on Oral Antidiabetes Agents.</a> Diabetes care 38(12): 2274-81                                                   | - Study does not contain an intervention relevant to this review protocol<br><i>Inhaled insulin</i>                                                                      |
| <a href="#">Rosenstock, Julio, Frias, Juan, Jastreboff, Ania M et al. (2023) Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA.</a> Lancet (London, England) 402(10401): 529-544 | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Rosenstock, Julio, Mathieu, Chantal, Chen, Hungta et al. (2018) Dapagliflozin versus saxagliptin as add-on therapy in patients with type 2 diabetes inadequately controlled with metformin.</a> Archives of endocrinology and metabolism 62(4): 424-430                                                                    | - Study design not relevant to this review protocol<br><i>Post hoc analysis</i>                                                                                          |
| <a href="#">Ross, S A, Zinman, B, Campos, R V et al. (2001) A comparative study of insulin lispro and human regular insulin in patients with type 2 diabetes mellitus and secondary failure of oral hypoglycemic agents.</a> Clinical and investigative medicine. Medecine clinique et experimentale 24(6): 292-8                      | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i>                                                |
| <a href="#">Ross, Stuart A, Caballero, A Enrique, Del Prato, Stefano et al. (2016) Linagliptin plus metformin in patients with newly diagnosed type 2 diabetes and marked hyperglycemia.</a> Postgraduate medicine 128(8): 747-754                                                                                                     | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |

| Study                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                                                                           |
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| <a href="#">Rubin, M. R., Manavalan, J. S., Agarwal, S. et al. (2014) Effects of rosiglitazone vs metformin on circulating osteoclast and osteogenic precursor cells in postmenopausal women with type 2 diabetes mellitus. Journal of Clinical Endocrinology &amp; Metabolism 99(10): E1933-42</a>                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                    |
| <a href="#">Rubino, D., Faerch, L., Meincke, H.H. et al. (2021) Semaglutide 2.4 mg improves health-related quality of life in adults with overweight/obesity and type 2 diabetes in the step 2 trial. Diabetes 70(suppl1)</a>                                                                                            | - Duplicate reference                                                                                                                                                                            |
| <a href="#">Rubino, D.M., Faerch, L., Meincke, H.H. et al. (2021) Semaglutide 2.4 mg improves health-related quality of life in adults with overweight or obesity and type 2 diabetes in the STEP 2 trial. Diabetologia 64(supplement1): 248-s249</a>                                                                    | - Conference abstract                                                                                                                                                                            |
| <a href="#">Ruff, C. T., Baron, M., Im, K. et al. (2022) Subcutaneous infusion of exenatide and cardiovascular outcomes in type 2 diabetes: a non-inferiority randomized controlled trial. Nature medicine 28(1): 89-95</a>                                                                                              | - Study does not contain an intervention relevant to this review protocol                                                                                                                        |
| <a href="#">Ruggenenti, Piero, Kraus, Bettina J, Inzucchi, Silvio E et al. (2022) Nephrotic-range proteinuria in type 2 diabetes: Effects of empagliflozin on kidney disease progression and clinical outcomes. EClinicalMedicine 43: 101240</a>                                                                         | - Study design not relevant to this review protocol<br><i>Post hoc analysis comparing the effects of drugs on kidney disease progression and clinical outcomes in the EMPA-REG OUTCOME trial</i> |
| <a href="#">Ryysy, L and Yki-Jarvinen, H (2001) Improvement of glycemic control by 1 year of insulin therapy leads to a sustained decrease in sE-selectin concentrations in type 2 diabetes. Diabetes care 24(3): 549-54</a>                                                                                             | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                    |
| <a href="#">Sabina, Michael and Alsamman, M Mrhaf (2024) Pulse of Progress: A Systematic Review of Glucagon-Like Peptide-1 Receptor Agonists in Cardiovascular Health. Cardiology research 15(1): 1-11</a>                                                                                                               | - Review article but not a systematic review                                                                                                                                                     |
| <a href="#">Sahay, Rakesh, Hafidh, Khadijah, Djaballah, Khier et al. (2020) Safety of lixisenatide plus basal insulin treatment regimen in Indian people with type 2 diabetes mellitus during Ramadan fast: A post hoc analysis of the LixiRam randomized trial. Diabetes research and clinical practice 163: 108148</a> | - Comparator in study does not match that specified in this review protocol<br><i>Includes a range of sulphonylureas so could not be included in a specific group for the analysis</i>           |

| Study                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                             |
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| <a href="#">Sahin, Serdar, Haliloglu, Ozlem, Polat Korkmaz, Ozge et al. (2020) Does treatment with sodium-glucose co-transporter-2 inhibitors have an effect on sleep quality, quality of life, and anxiety levels in people with Type 2 diabetes mellitus?. Turkish journal of medical sciences 51(2): 735-742</a>      | - Comparator in study does not match that specified in this review protocol                                                                        |
| <a href="#">Saito, Daisuke, Kanazawa, Akio, Shigihara, Nayumi et al. (2017) Efficacy and Safety of Vildagliptin as an Add-On Therapy in Inadequately Controlled Type 2 Diabetes Patients Treated With Basal Insulin. Journal of clinical medicine research 9(3): 193-199</a>                                             | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Salah, H.M., Al'Aref, S.J., Khan, M.S. et al. (2021) Effect of sodium-glucose cotransporter 2 inhibitors on cardiovascular and kidney outcomes-Systematic review and meta-analysis of randomized placebo-controlled trials: SGLT2i-Cardiovascular and Kidney Outcomes. American Heart Journal 232: 10-22</a> | - Systematic review used as source of primary studies<br><i>Identified during the rerun sift. No additional studies.</i>                           |
| <a href="#">Saleem, K., Yasin, M. A., Asrar, A. et al. (2011) Comparison of repaglinide with glibenclamide in the reduction of HbA1C of type 2 diabetic patients. Pakistan J Med Health Sci 5(1): 23-6</a>                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Salman, S., Salman, F., Satman, I. et al. (2001) Comparison of acarbose and gliclazide as first-line agents in patients with type 2 diabetes. Curr Med Res Opin 16(4): 296-306</a>                                                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Saloranta, C., Hershon, K., Ball, M. et al. (2002) Efficacy and safety of nateglinide in type 2 diabetic patients with modest fasting hyperglycemia. J Clin Endocrinol Metab 87(9): 4171-6</a>                                                                                                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Salsali, A. and Pratley, R.E. (2007) Does addition of sitagliptin to metformin monotherapy improve glycemic control in patients with type 2 diabetes mellitus?. Nature Clinical Practice Endocrinology and Metabolism 3(6): 450-451</a>                                                                      | - Commentary only                                                                                                                                  |
| <a href="#">Sam, Susan, Haffner, Steven, Davidson, Michael H et al. (2012) Pioglitazone-mediated changes in lipoprotein particle composition are predicted by changes in adiponectin level in type 2 diabetes. The Journal of clinical endocrinology and metabolism 97(1): e110-4</a>                                    | - Data not reported in an extractable format or a format that can be analysed                                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                                         |
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| <a href="#">Sambevski, S., Fitchett, D., Inzucchi, S. et al. (2019) Empagliflozin reduces mortality and hospitalisation for heart failure in patients with or without a history of myocardial infarction or stroke at baseline. Diabetologie und Stoffwechsel 14(supplement1): 65-s66</a>                                                                     | - Conference abstract                                                                                                                                                                          |
| <a href="#">Samsky, Marc D, Mentz, Robert J, Stebbins, Amanda et al. (2021) Polyvascular disease and increased risk of cardiovascular events in patients with type 2 diabetes: Insights from the EXSCEL trial. Atherosclerosis 338: 1-6</a>                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                                                                         |
| <a href="#">Samson, S. L., Sathyanarayana, P., Jogi, M. et al. (2011) Exenatide decreases hepatic fibroblast growth factor 21 resistance in non-alcoholic fatty liver disease in a mouse model of obesity and in a randomised controlled trial. Diabetologia 54(12): 3093-100</a>                                                                             | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and therefore the study cannot be classified into review 1.1 or 1.2<br><i>Additionally no usable outcomes</i> |
| <a href="#">Sandsdal, R., Jensen, S., Sorensen, V. et al. (2023) Exercise combined with GLP-1 receptor agonist preserves bone mineral density during weight loss maintenance. Diabetologia 66(supplement1): 275-s276</a>                                                                                                                                      | - Conference abstract                                                                                                                                                                          |
| <a href="#">Santos-Pardo, I.; Witt, N.; Nystrom, T. (2023) Effects of reendothelialisation with exenatide treatment add on to insulin vs insulin alone, both in combination with metformin in subjects with type 2 diabetes: Rebuild study. Diabetologia 66(supplement1): 328-s329</a>                                                                        | - Conference abstract                                                                                                                                                                          |
| <a href="#">Sarak, Bradley, Verma, Subodh, David Mazer, C et al. (2021) Impact of empagliflozin on right ventricular parameters and function among patients with type 2 diabetes. Cardiovascular diabetology 20(1): 200</a>                                                                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                                                                         |
| <a href="#">Sargeant, J. A., King, J. A., Yates, T. et al. (2022) The effects of empagliflozin, dietary energy restriction, or both on appetite-regulatory gut peptides in individuals with type 2 diabetes and overweight or obesity: the SEESAW randomized, double-blind, placebo-controlled trial. Diabetes, obesity &amp; metabolism 24(8): 1509-1521</a> | - No relevant outcomes reported                                                                                                                                                                |
| <a href="#">Sass, Marie Reeberg, Danielsen, Andreas Aalkjaer, Kohler-Forsberg, Ole et al. (2023) Effect of the GLP-1 receptor agonist semaglutide on metabolic disturbances in</a>                                                                                                                                                                            | - Population not relevant to this review protocol                                                                                                                                              |



| Study                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                                                                                                                                                                  |
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| <a href="#">clozapine-treated or olanzapine-treated patients with a schizophrenia spectrum disorder: study protocol of a placebo-controlled, randomised clinical trial (SemaPsychiatry).</a> BMJ open 13(1): e068652                                                                                    |                                                                                                                                                                                                                                                                                                         |
| <a href="#">Satirapoj, Bancha; Watanakijthavonkul, Khanin; Supasyndh, Ouppatham (2018) Safety and efficacy of low dose pioglitazone compared with standard dose pioglitazone in type 2 diabetes with chronic kidney disease: A randomized controlled trial.</a> PLoS one 13(10): e0206722               | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares standard dose to low dose formulations of the same medication</i>                                                                                                                                        |
| <a href="#">Sato, Ai, Takei, Masahiro, Hiramatsu, Kunihide et al. (2019) Effects of sitagliptin on pancreatic beta-cells in type 2 diabetes with sulfonylurea treatment: A prospective randomized study.</a> J Clin Med Res 11(1): 15-20                                                                | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care arm that received a higher dose of glimepiride - the committee agreed to pool together all doses of drugs therefore this appeared to be a usual care comparator that is not relevant to the review</i> |
| <a href="#">Sato, S., Saisho, Y., Kou, K. et al. (2015) Efficacy and safety of sitagliptin added to insulin in Japanese patients with type 2 Diabetes: The EDIT randomized trial.</a> PLoS ONE 10(3)                                                                                                    | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                  |
| <a href="#">Sato, T., Aizawa, Y., Yauasa, S et al. (2018) The effect of dapagliflozin treatment on epicardial adipose tissue volume.</a> Cardiovascular diabetology 17(1): 6                                                                                                                            | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                  |
| <a href="#">Sattar, Naveed, Fitchett, David, Hantel, Stefan et al. (2018) Empagliflozin is associated with improvements in liver enzymes potentially consistent with reductions in liver fat: results from randomised trials including the EMPA-REG OUTCOME R trial.</a> Diabetologia 61(10): 2155-2163 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                  |
| <a href="#">Sattar, Naveed, McGuire, Darren K, Pavo, Imre et al. (2022) Tirzepatide cardiovascular event risk assessment: a pre-specified meta-analysis.</a> Nature medicine 28(3): 591-598                                                                                                             | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                   |
| <a href="#">Sayour, Alex Ali, Olah, Attila, Ruppert, Mihaly et al. (2024) Effect of pharmacological selectivity of SGLT2 inhibitors on cardiovascular outcomes in patients with type 2 diabetes: a meta-analysis.</a> Scientific reports 14(1): 2188                                                    | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                   |

| Study                                                                                                                                                                                                                                                           | Reason                                                                                                 |
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| <a href="#">Schamarek, I (2023) Dapagliflozin reduces the risk for hospitalization in patients with type 2 diabetes: new results from the DECLARE-TIMI 58 trial.</a> Diabetologie 19(5): 702-704                                                                | - Study not reported in English                                                                        |
| <a href="#">Schechter, M., Jongs, N., Chertow, G. et al. (2022) Dapagliflozin Effect on Hospital Admissions in Patients With CKD: A Post Hoc Analysis of the DAPA-CKD Trial.</a> Journal of the American Society of Nephrology 33: 25                           | - Conference abstract                                                                                  |
| <a href="#">Schechter, M., Wiviott, S.D., Raz, I. et al. (2022) The Effect of Dapagliflozin on Hospital Admissions in Patients With Type 2 Diabetes: Post Hoc Analysis of the DECLARE-TIMI 58 Trial.</a> Circulation 146(supplement1)                           | - Conference abstract                                                                                  |
| <a href="#">Schechter, Meir, Jongs, Niels, Chertow, Glenn M et al. (2023) Effects of Dapagliflozin on Hospitalizations in Patients With Chronic Kidney Disease : A Post Hoc Analysis of DAPA-CKD.</a> Annals of internal medicine 176(1): 59-66                 | - Population not relevant to this review protocol                                                      |
| <a href="#">Schechter, Meir, Wiviott, Stephen D, Raz, Itamar et al. (2023) Effects of dapagliflozin on hospitalisations in people with type 2 diabetes: post-hoc analyses of the DECLARE-TIMI 58 trial.</a> The lancet. Diabetes & endocrinology 11(4): 233-241 | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Scheen, AJ (2019) Focus on empagliflozin : post hoc analyses of the cardiovascular outcome trial EMPA-REG OUTCOME.</a> Revue medicale de Liege 74(4): 185-191                                                                                       | - Study not reported in English                                                                        |
| <a href="#">Scheen, AJ and Lefèbvre, PJ (2005) Proactive study: secondary cardiovascular prevention with pioglitazone in type 2 diabetic patients.</a> Revue medicale de Liege 60(11): 896-901                                                                  | - Study not reported in English                                                                        |
| <a href="#">Scheen, Andre J (2021) Could metformin modulate cardiovascular outcomes differently with DPP-4 inhibitors compared with SGLT2 inhibitors?.</a> Diabetes & metabolism 47(4): 101209                                                                  | - Review article but not a systematic review                                                           |
| <a href="#">Scherthaner, G., Rosas-Guzman, J., Dotta, F. et al. (2015) Treatment escalation options for patients with type 2 diabetes after failure of exenatide twice daily or glimepiride added to metformin: Results from the prospective</a>                | - Comparator in study does not match that specified in this review protocol                            |

| Study                                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                                                                                                                                                                                     |
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| <a href="#">European Exenatide (EUREXA) study</a> . Diabetes Obes Metab 17(7): 689-698                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                            |
| <a href="#">Scherthaner, Guntram (2006) Organ protection in the secondary prevention of type 2 diabetes</a> . Drugs of today (Barcelona, Spain : 1998) 42supplc: 17-23                                                                                                                                                                                                              | - Full text paper not available<br><i>British Library unable to supply the paper. Publisher no longer hosts the article and is not available elsewhere. The abstract suggests it is a narrative article rather than a trial.</i>                                                                                                                           |
| <a href="#">Schiavon, M., Visentin, R., Gobel, B. et al. (2021) Improved postprandial glucose metabolism in type 2 diabetes by the dual glucagon-like peptide-1/glucagon receptor agonist SAR425899 in comparison with liraglutide</a> . Diabetes, Obesity & Metabolism 23(8): 1795-1805                                                                                            | - Data not reported in an extractable format or a format that can be analysed<br><i>Outcomes reported as medians and interquartile ranges</i>                                                                                                                                                                                                              |
| <a href="#">Schiavon, M., Visentin, R., Gobel, B. et al. (2021) Improved Postprandial Glucose Metabolism in Type 2 Diabetes by Dual Glucagon-like Peptide-1 / Glucagon Receptor Agonist SAR425899 in Comparison to Liraglutide</a> . Diabetes, obesity & metabolism                                                                                                                 | - Study design<br><i>Methods state that 296 participants were randomised to the study. This report appears to be associated with a subset of 70 participants from this study who underwent MMT tests, and it is unclear how participants were chosen to be in this subset. Therefore it is unclear whether the participants were adequately randomised</i> |
| <a href="#">Schmidt, W E, Christiansen, J S, Hammer, M et al. (2011) Patient-reported outcomes are superior in patients with Type 2 diabetes treated with liraglutide as compared with exenatide, when added to metformin, sulphonylurea or both: results from a randomized, open-label study</a> . Diabetic medicine : a journal of the British Diabetic Association 28(6): 715-23 | - Additional outcomes relevant to living guideline work                                                                                                                                                                                                                                                                                                    |
| <a href="#">Scholte, Martijn, Timmers, Leo, Bernink, Flip Jp et al. (2011) Effect of additional treatment with EXenatide in patients with an Acute Myocardial Infarction (EXAMI): study protocol for a randomized controlled trial</a> . Trials 12: 240                                                                                                                             | - Population not relevant to this review protocol<br><i>Protocol only. Also people with acute myocardial infarction who have had a PCI - not necessarily people with type 2 diabetes</i>                                                                                                                                                                   |
| <a href="#">Schondorf, Thomas, Lubben, Georg, Hoopmann, Markus et al. (2007) Relaxin expression correlates significantly with serum fibrinogen variation in response to antidiabetic treatment in women with type 2 diabetes mellitus</a> . Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology 23(6): 356-60            | - No relevant outcomes reported                                                                                                                                                                                                                                                                                                                            |

| Study                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                         |
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| <a href="#">Schurfeld, R (2023) Effects of tirzepatide versus insulin glargine on kidney outcomes in type 2 diabetes: post hoc analysis of an open-label, randomised, phase 3 trial.</a> Diabetologie 19(2): 205-207                                                                                              | - Study not reported in English                                                                                                                                                |
| <a href="#">Schweizer, A. and Dejager, S. (2013) Clinical experience with vildagliptin in patients &gt;= 75 years with type 2 diabetes mellitus and moderate or severe renal impairment.</a> Diabetologia 56(suppl1): 370-s371                                                                                    | - Conference abstract                                                                                                                                                          |
| <a href="#">Scirica Benjamin, M., Mosenzon, Ofri, Bhatt Deepak, L et al. (2018) Cardiovascular Outcomes According to Urinary Albumin and Kidney Disease in Patients With Type 2 Diabetes at High Cardiovascular Risk: Observations From the SAVOR-TIMI 53 Trial.</a> JAMA cardiology 3(2): 155-163                | - Secondary publication of an included study that does not provide any additional relevant information                                                                         |
| <a href="#">Scirica, Benjamin M, Braunwald, Eugene, Raz, Itamar et al. (2014) Heart failure, saxagliptin, and diabetes mellitus: observations from the SAVOR-TIMI 53 randomized trial.</a> Circulation 130(18): 1579-88                                                                                           | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Post hoc analysis</i>                                             |
| <a href="#">Seck, Thomas L, Engel, Samuel S, Williams-Herman, Debora E et al. (2011) Sitagliptin more effectively achieves a composite endpoint for A1C reduction, lack of hypoglycemia and no body weight gain compared with glipizide.</a> Diabetes research and clinical practice 93(1): e15-7                 | - Secondary publication of an included study that does not provide any additional relevant information                                                                         |
| <a href="#">Seferovic, Jelena P, Bentley-Lewis, Rhonda, Claggett, Brian et al. (2018) Retinopathy, Neuropathy, and Subsequent Cardiovascular Events in Patients with Type 2 Diabetes and Acute Coronary Syndrome in the ELIXA: The Importance of Disease Duration.</a> Journal of diabetes research 2018: 1631263 | - Study design not relevant to this review protocol<br><i>Post hoc analysis examining the presence of retinopathy and neuropathy in people who had been in the ELIXA trial</i> |
| <a href="#">Segal, P., Eliahou, H. E., Petzinna, D. et al. (2005) Long-term efficacy and tolerability of acarbose treatment in patients with type 2 diabetes mellitus.</a> Clin Drug Invest 25(9): 589-95                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                  |
| <a href="#">Segal, P., Feig, P. U., Schernthaner, G. et al. (1997) The efficacy and safety of miglitol therapy compared with glibenclamide in patients with NIDDM inadequately controlled by diet alone.</a> Diabetes Care 20(5): 687-91                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                  |

| Study                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                   |
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| <a href="#">Seino, Y (2014) Efficacy and safety of saxagliptin in Japanese patients with type 2 diabetes - Two multi-centre, randomized, double-blind, placebo-controlled studies.</a> Japanese pharmacology and therapeutics 42(7): 503-518                                                                                        | - Study not reported in English                                                                                                                                          |
| <a href="#">Seino, Y., Inagaki, N., Haneda, M. et al. (2015) Efficacy and safety of luseogliflozin added to various oral antidiabetic drugs in Japanese patients with type 2 diabetes mellitus.</a> J Diabetes Invest 6(4): 443-453                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Seino, Y., Sasaki, T., Fukatsu, A. et al. (2014) Efficacy and safety of luseogliflozin as monotherapy in Japanese patients with type 2 diabetes mellitus: A randomized, double-blind, placebo-controlled, phase 3 study.</a> Current Medical Research and Opinion 30(7): 1245-1255                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Seino, Y., Terauchi, Y., Osonoi, T. et al. (2018) Safety and efficacy of semaglutide once weekly vs sitagliptin once daily, both as monotherapy in Japanese people with type 2 diabetes.</a> Diabetes Obes Metab 20(2): 378-388                                                                                         | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Seino, Yutaka, Hiroi, Shinzo, Hirayama, Masashi et al. (2012) Efficacy and safety of alogliptin added to sulfonylurea in Japanese patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial with an open-label, long-term extension study.</a> Journal of diabetes investigation 3(6): 517-25 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Selvarajah, V., Robertson, D., Hansen, L. et al. (2023) EFFICACY AND SAFETY OF COTADUTIDE, A DUAL GLP1-GLUCAGON RECEPTOR AGONIST, IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND T2DM.</a> Nephrology Dialysis Transplantation 38(supplement1): i87                                                                        | - Study does not contain an intervention relevant to this review protocol                                                                                                |
| <a href="#">Sen, Taha, Koshino, Akihiko, Neal, Bruce et al. (2022) Mechanisms of action of the sodium-glucose cotransporter-2 (SGLT2) inhibitor canagliflozin on tubular inflammation and damage: A post hoc mediation analysis of the CANVAS trial.</a> Diabetes, obesity & metabolism 24(10): 1950-1956                           | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                      |
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| <a href="#">Sen, Taha, Li, Jingwei, Neuen, Brendon L et al. (2021) Association Between Circulating GDF-15 and Cardio-Renal Outcomes and Effect of Canagliflozin: Results From the CANVAS Trial. Journal of the American Heart Association 10(23): e021661</a>                                                                                                                                                                                                                                 | - Secondary publication of an included study that does not provide any additional relevant information                      |
| <a href="#">Seshadri, K., Sesti, G., Bardtrum, L. et al. (2019) DUAL VIII: More patients met treatment targets with insulin degludec/liraglutide versus insulin glargine 100 U/mL by week 26 in a 104-week randomized trial mirroring clinical practice. Indian Journal of Endocrinology and Metabolism 23(7supplement): 17</a>                                                                                                                                                               | - Conference abstract                                                                                                       |
| <a href="#">Sesti, Giorgio, Bardtrum, Lars, Dagdelen, Selcuk et al. (2020) A greater proportion of participants with type 2 diabetes achieve treatment targets with insulin degludec/liraglutide versus insulin glargine 100 units/mL at 26 weeks: DUAL VIII, a randomized trial designed to resemble clinical practice. Diabetes, obesity &amp; metabolism 22(5): 873-878</a>                                                                                                                | - Duplicate reference                                                                                                       |
| <a href="#">Seufert, J (2014) Oral add-on therapy to metformin in type 2 diabetes mellitus: a direct comparison between canagliflozin and glimepiride. Deutsche medizinische Wochenschrift (1946) 139(suppl1): S65-S69</a>                                                                                                                                                                                                                                                                    | - Study not reported in English                                                                                             |
| <a href="#">Sezai, Akira, Tanaka, Atsushi, Imai, Takumi et al. (2022) Comparing the Effects of Canagliflozin vs. Glimepiride by Body Mass Index in Patients with Type 2 Diabetes and Chronic Heart Failure: A Subanalysis of the CANDLE Trial. Biomedicines 10(7)</a>                                                                                                                                                                                                                         | - Secondary publication of an included study that does not provide any additional relevant information                      |
| <a href="#">Sfairopoulos, Dimitrios, Zhang, Nan, Wang, Yueying et al. (2022) Association between sodium-glucose cotransporter-2 inhibitors and risk of sudden cardiac death or ventricular arrhythmias: a meta-analysis of randomized controlled trials. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology 24(1): 20-30</a> | - Population not relevant to this review protocol<br><i>A mixture of trials with people with or without type 2 diabetes</i> |
| <a href="#">Shah, Z. H., Saleem, K., Mahboob, F. et al. (2011) A comparative study of repaglinide and glibenclamide in type 2 diabetic patients.</a>                                                                                                                                                                                                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                               |



| Study                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                                                                                                                                               |
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| Pakistan Journal of Medical and Health Sciences 5(3): 476-9                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                      |
| <a href="#">Shaienko, Zlatoslava O and Bobyрева, Lyudmila Ye (2018) Combination of metformin and pioglitazone and its effect in treatment of comorbid pathology.</a> Wiadomosci lekarskie (Warsaw, Poland : 1960) 71(2pt2): 278-280                                                                                                         | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                                                                                                                          |
| <a href="#">Shaienko, Zlatoslava O, Vynnyk, Nataliia I, Bobyрева, Lyudmila Ye et al. (2018) Chronic systemic inflammation in the pathogenesis of comorbid pathology and it's correction.</a> Wiadomosci lekarskie (Warsaw, Poland : 1960) 71(8): 1463-1465                                                                                  | - No relevant outcomes reported<br><br><i>Study evaluates the change in inflammatory markers (TNF and IL-6) before and after 6 months in patients with T2DM and IHD. No additional outcomes/ baseline data is reported.</i>                                                                                                                          |
| <a href="#">Shank, M L; Del Prato, S; DeFronzo, R A (1995) Bedtime insulin/daytime glipizide. Effective therapy for sulfonylurea failures in NIDDM.</a> Diabetes 44(2): 165-72                                                                                                                                                              | - Comparator in study does not match that specified in this review protocol<br><br><i>All people run into the trial by receiving glipizide and then receive insulin and either glipizide or placebo, which isn't an appropriate comparison for the protocol we are using. The statement of the phases makes it difficult to examine the results.</i> |
| <a href="#">Shankar, R. R., Inzucchi, S. E., Scarabello, V. et al. (2017) A randomized clinical trial evaluating the efficacy and safety of the once-weekly dipeptidyl peptidase-4 inhibitor omarigliptin in patients with type 2 diabetes inadequately controlled on metformin monotherapy.</a> Curr Med Res Opin 33(10): 1853-1860        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                                                        |
| <a href="#">Sharma, Abhinav, Cannon Christopher, P, White William, B et al. (2018) Early and Chronic Dipeptidyl-Peptidase-IV Inhibition and Cardiovascular Events in Patients With Type 2 Diabetes Mellitus After an Acute Coronary Syndrome: A Landmark Analysis of the EXAMINE Trial.</a> Journal of the American Heart Association 7(11) | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                                                               |
| <a href="#">Sharma, Abhinav, Green, Jennifer B, Dunning, Allison et al. (2017) Causes of Death in a Contemporary Cohort of Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease: Insights From the TECOS Trial.</a> Diabetes care 40(12): 1763-1770                                                                     | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis examining the causes of death and associated risk factors for people in the TECOS study</i>                                                                                                                                                                          |
| <a href="#">Sharma, Abhinav, Inzucchi, Silvio E, Testani, Jeffrey M et al. (2023) Kidney and heart failure events are bidirectionally associated in patients</a>                                                                                                                                                                            | - Post-hoc analysis of included study                                                                                                                                                                                                                                                                                                                |

| Study                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                 |
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| <a href="#">with type 2 diabetes and cardiovascular disease.</a> ESC heart failure                                                                                                                                                                                                                                                   | <i>It does not appear that the subgroup analysis was prespecified</i>                                                                  |
| <a href="#">Shavadia, Jay S, Zheng, Yinggan, Green, Jennifer B et al. (2019) Associations between beta-blocker therapy and cardiovascular outcomes in patients with diabetes and established cardiovascular disease.</a> American heart journal 218: 92-99                                                                           | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis</i> |
| <a href="#">Sheikh, Ibrahimkhalil M, Hassan, Omar A, Adam, Siad Mohammed et al. (2023) Association of Pioglitazone With Major Adverse Cardiovascular Events, All-Cause Mortality, and Heart Failure Hospitalizations: A Systematic Review.</a> Cureus 15(10): e46911                                                                 | - Study design not relevant to this review protocol                                                                                    |
| <a href="#">Sheng, Lei, Deng, Meixian, Li, Xin et al. (2024) The effect of subcutaneous Lixisenatide on weight loss in patients with type 2 Diabetes Mellitus: Systematic review and Meta-Analysis of randomized controlled trials.</a> Diabetes research and clinical practice 210: 111617                                          | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Shestakova, M. V., Wilding, J. P. H., Wilpshaar, W. et al. (2018) A phase 3 randomized placebo-controlled trial to assess the efficacy and safety of ipragliflozin as an add-on therapy to metformin in Russian patients with inadequately controlled type 2 diabetes mellitus.</a> Diabetes Res Clin Pract 146: 240-250 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                          |
| <a href="#">Sheu, W.H.H., Chan, J.C., Yoon, K.H. et al. (2022) IDF21-0199 Early combination therapy improves glycaemic control in newly diagnosed T2DM: VERIFY sub-regional analysis (East Asia).</a> Diabetes Research and Clinical Practice 186(supplement1): 109493                                                               | - Conference abstract                                                                                                                  |
| <a href="#">Sheu, Wayne H-H, Park, Sung Woo, Gong, Yan et al. (2015) Linagliptin improves glycemic control after 1 year as add-on therapy to basal insulin in Asian patients with type 2 diabetes mellitus.</a> Current medical research and opinion 31(3): 503-12                                                                   | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Post hoc analysis</i> |
| <a href="#">Shi, Li Xin, Liu, Xiao Min, Shi, Yong Quan et al. (2020) Efficacy and safety of dulaglutide monotherapy compared with glimepiride in Chinese patients with type 2 diabetes: Post-hoc analyses of a randomized, double-blind, phase</a>                                                                                   | - Post-hoc analysis of included study<br><br><i>International trial, reports results for Chinese participants only</i>                 |

| Study                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                 |
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| <a href="#">III study</a> . Journal of diabetes investigation 11(1): 142-150                                                                                                                                                                                                                  |                                                                                                                                        |
| <a href="#">Shi, Mengran, Zhang, Hao, Wang, Wei et al. (2023) Effect of dapagliflozin on liver and pancreatic fat in patients with type 2 diabetes and non-alcoholic fatty liver disease</a> . Journal of diabetes and its complications 37(10): 108610                                       | - Comparator in study does not match that specified in this review protocol                                                            |
| <a href="#">Shi, Nanjing, Shi, Yetan, Xu, Jingsi et al. (2021) SGLT-2i and Risk of Malignancy in Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials</a> . Frontiers in public health 9: 668368                                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                                                                |
| <a href="#">Shi, Qingyang, Nong, Kailei, Vandvik, Per Olav et al. (2023) Benefits and harms of drug treatment for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials</a> . BMJ (Clinical research ed.) 381: e074068                                 | - Study does not contain an intervention relevant to this review protocol<br><br>- Systematic review used as source of primary studies |
| <a href="#">Shi, Xiulin, Shi, Yalin, Chen, Ning et al. (2017) Effect of exenatide after short-time intensive insulin therapy on glycaemic remission maintenance in type 2 diabetes patients: a randomized controlled trial</a> . Scientific reports 7(1): 2383                                | - Trial that has a treatment and follow up period of less than 24 weeks                                                                |
| <a href="#">Shibuki, Katsuya; Shimada, Shuji; Aoyama, Takao (2022) Meta-analysis of seven heterogeneous studies on liraglutide add-on therapy in patients with type 2 diabetes mellitus treated with insulin</a> . Diabetes & metabolic syndrome 16(4): 102474                                | - Systematic review used as source of primary studies                                                                                  |
| <a href="#">Shibuya, T., Fushimi, N., Kawai, M. et al. (2018) Luseogliflozin improves liver fat deposition compared to metformin in type 2 diabetes patients with non-alcoholic fatty liver disease: a prospective randomized controlled pilot study</a> . Diabetes Obes Metab 20(2): 438-442 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                          |
| <a href="#">Shigematsu, Erina, Yamakawa, Tadashi, Oba, Mari S et al. (2017) A Randomized Controlled Trial of Vildagliptin Versus Alogliptin: Effective Switch From Sitagliptin in Patients With Type 2 Diabetes</a> . Journal of clinical medicine research 9(7): 567-572                     | - Trial that has a treatment and follow up period of less than 24 weeks                                                                |
| <a href="#">Shigiyama, Fumika, Kumashiro, Naoki, Fuchigami, Ayako et al. (2018) Rationale and</a>                                                                                                                                                                                             | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are                                                   |

| Study                                                                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                                                   |
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| <a href="#">design of study of dapagliflozin versus sitagliptin treatment efficacy on prevention of cardiovascular risk factors in type 2 diabetes patients: the DIVERSITY-CVR study.</a> Cardiovascular diabetology 17(1): 86                                                                                                                                                         | treatment naive and therefore the study cannot be classified into review 1.1 or 1.2                                                                                      |
| <a href="#">Shiina, Kazuki, Tomiyama, Hirofumi, Tanaka, Atsushi et al. (2023) Canagliflozin independently reduced plasma volume from conventional diuretics in patients with type 2 diabetes and chronic heart failure: a subanalysis of the CANDLE trial.</a> Hypertension research : official journal of the Japanese Society of Hypertension 46(2): 495-506                         | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Shim, C. Y., Seo, J., Cho, I. et al. (2021) Randomized, Controlled Trial to Evaluate the Effect of Dapagliflozin on Left Ventricular Diastolic Function in Patients With Type 2 Diabetes Mellitus: The IDIA Trial.</a> Circulation 143(5): 510-512                                                                                                                         | - Study design not relevant to this review protocol<br><i>Letter only</i>                                                                                                |
| <a href="#">Shimada Yuichi, J, Cannon Christopher, P, Liu, Yuyin et al. (2016) Ischemic cardiac outcomes and hospitalizations according to prior macrovascular disease status in patients with type 2 diabetes and recent acute coronary syndrome from the Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care trial.</a> American heart journal 175: 18-27 | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Shimizu, W., Kubota, Y., Hoshika, Y. et al. (2020) Effects of empagliflozin versus placebo on cardiac sympathetic activity in acute myocardial infarction patients with type 2 diabetes mellitus: the EMBODY trial.</a> Cardiovascular Diabetology 19(1): 148                                                                                                              | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Shimoda, Seiya, Iwashita, Shinsuke, Sekigami, Taiji et al. (2014) Comparison of the efficacy of sitagliptin and glimepiride dose-up in Japanese patients with type 2 diabetes poorly controlled by sitagliptin and glimepiride in combination.</a> Journal of diabetes investigation 5(3): 320-6                                                                           | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>12 weeks</i>                                                                               |
| <a href="#">Shuai, Y., Yang, G., Zhang, Q. et al. (2021) Efficacy and safety of polyethylene glycol loxenate monotherapy in type 2 diabetes patients: A multicentre, randomized, double-blind, placebo-controlled phase 3a clinical trial.</a> Diabetes, Obesity & Metabolism 23(1): 116-124                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                     |
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| <a href="#">Silverii, Giovanni Antonio; Monami, Matteo; Mannucci, Edoardo (2021) Sodium-glucose co-transporter-2 inhibitors and all-cause mortality: A meta-analysis of randomized controlled trials.</a> Diabetes, obesity & metabolism 23(4): 1052-1056                                                                                                                                                                  | - Systematic review used as source of primary studies<br><i>Identified during the rerun search. No additional studies.</i> |
| <a href="#">Sim, Ruth, Chong, Chun Wie, Loganadan, Navin K et al. (2022) Comparative effectiveness of cardiovascular, renal and safety outcomes of second-line antidiabetic drugs use in people with type 2 diabetes: A systematic review and network meta-analysis of randomised controlled trials.</a> Diabetic medicine : a journal of the British Diabetic Association 39(3): e14780                                   | - More recent systematic review included that covers the same topic                                                        |
| <a href="#">Sinclair, Alan J, Bode, Bruce, Harris, Stewart et al. (2016) Efficacy and Safety of Canagliflozin in Individuals Aged 75 and Older with Type 2 Diabetes Mellitus: A Pooled Analysis.</a> Journal of the American Geriatrics Society 64(3): 543-52                                                                                                                                                              | - Study design not relevant to this review protocol<br><i>Pooled analysis</i>                                              |
| <a href="#">Singh, AK; Singh, A; Singh, R (2023) Cardiovascular and Renal Outcomes with SGLT-2 inhibitors and DPP-4 inhibitors Combination Therapy: A Meta-analysis of Randomized Cardiovascular Outcome Trials.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists                                                              | - Systematic review used as source of primary studies                                                                      |
| <a href="#">Singh, Awadhesh Kumar; Singh, Akriti; Singh, Ritu (2023) Cardiovascular and Renal Outcomes With Sodium-Glucose Cotransporter-2 Inhibitors and Dipeptidyl Peptidase-4 Inhibitors Combination Therapy: A Meta-Analysis of Randomized Cardiovascular Outcome Trials.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists | - Systematic review used as source of primary studies                                                                      |
| <a href="#">Singh, Awadhesh Kumar and Singh, Ritu (2021) Effect of background insulin therapy on cardiovascular outcomes with SGLT-2 inhibitors in type 2 diabetes: A meta-analysis of cardiovascular outcome trials.</a> Diabetes research and clinical practice 172: 108648                                                                                                                                              | - Population not relevant to this review protocol                                                                          |
| <a href="#">Singh, Awadhesh Kumar and Singh, Ritu (2021) Cardiovascular Outcomes with SGLT-2 inhibitors in patients with heart failure with or</a>                                                                                                                                                                                                                                                                         | - Systematic review used as source of primary studies                                                                      |

| Study                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| <a href="#">without type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials</a> . Diabetes & metabolic syndrome 15(1): 351-359                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <a href="#">Singh, Awadhesh Kumar; Singh, Ritu; Misra, Anoop (2022) Oral semaglutide in type 2 diabetes mellitus: Comprehensive review, critical appraisal and clinical consideration of its use in India</a> . Diabetes & metabolic syndrome 16(3): 102436                                                      | - Systematic review used as source of primary studies<br><br><i>Identified during the rerun search. No additional studies.</i>                                                                                                                                                                                                                                                                                                                                                                                   |
| <a href="#">Singh, J. S. S., Mordi, I. R., Vickneson, K. et al. (2020) Dapagliflozin versus placebo on left ventricular remodeling in patients with diabetes and heart failure: The REFORM Trial</a> . Diabetes Care 43(6): 1356-1359                                                                            | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2<br><br><i>Although study reports that, at baseline, 55.4% on metformin, 39.3% on other oral anti-hyperglycaemic drugs, and 28.6% on insulin, article does not make clear if participants are taking each of these on their own or if combined. Therefore unclear how many participants on blood glucose-lowering drugs at baseline.</i> |
| <a href="#">Singh, R., Mehta, S., Singh, P. et al. (2022) Comparison of Efficacy And Safety Of Vildagliptin And Dapagliflozin In Combination With Metformin In Patients With Type 2 Diabetes Mellitus: A Randomized Open Labeled Parallel Study In Tertiary Care Hospital</a> . NeuroQuantology 20(7): 2609-2617 | - Full text paper not available                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <a href="#">Singh, S., Singh, D.P., Singh, S.S. et al. (2019) Efficacy and safety of sitagliptin in patients of type 2 diabetes when added to insulin therapy alone or in combination with metformin</a> . International Journal of Diabetes in Developing Countries 39(1supplement): 41-s42                     | - Full text paper not available                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <a href="#">Sinha, Binayak; Datta, Debasis; Ghosal, Samit (2021) Meta-analysis of the effects of sodium glucose cotransporter 2 inhibitors in non-alcoholic fatty liver disease patients with type 2 diabetes</a> . JGH open : an open access journal of gastroenterology and hepatology 5(2): 219-227           | - Comparator in study does not match that specified in this review protocol<br><br><i>Either not relevant comparison, too short a follow up period, drug is not licensed for use in the United Kingdom or study was already included in the review</i>                                                                                                                                                                                                                                                           |
| <a href="#">Sinha, Binayak and Ghosal, Samit (2020) Is it Worth CANVASing for CREDENCE? A Benefit-risk Analysis</a> . Current diabetes reviews 16(5): 509-514                                                                                                                                                    | - Study design not relevant to this review protocol                                                                                                                                                                                                                                                                                                                                                                                                                                                              |



| Study                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                                                                                     |
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| <a href="#">Siskind, Dan J, Russell, Anthony W, Gamble, Clare et al. (2018) Treatment of clozapine-associated obesity and diabetes with exenatide in adults with schizophrenia: A randomized controlled trial (CODEX).</a> Diabetes, obesity & metabolism 20(4): 1050-1055                 | - Population not relevant to this review protocol                                                                                                                                                          |
| <a href="#">Sivalingam, S., Soendergaard Wasehuus, V., Rotbain Curovic, V. et al. (2023) Renal effects of empagliflozin alone or in combination with semaglutide in albuminuric type 2 diabetes: a randomised, placebocontrolled trial.</a> Diabetologia 66(supplement1): 125              | - Conference abstract                                                                                                                                                                                      |
| <a href="#">Siwy, Justyna, Klein, Thomas, Rosler, Marcel et al. (2019) Urinary Proteomics as a Tool to Identify Kidney Responders to Dipeptidyl Peptidase-4 Inhibition: A Hypothesis-Generating Analysis from the MARLINA-T2D Trial.</a> Proteomics. Clinical applications 13(2): e1800144 | - Study design not relevant to this review protocol                                                                                                                                                        |
| <a href="#">Skov, J, Pedersen, M, Holst, J J et al. (2016) Short-term effects of liraglutide on kidney function and vasoactive hormones in type 2 diabetes: a randomized clinical trial.</a> Diabetes, obesity & metabolism 18(6): 581-9                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                    |
| <a href="#">Smith, S. R., Jonge, L., Volaufova, J. et al. (2005) Effect of pioglitazone on body composition and energy expenditure: a randomized controlled trial.</a> Metabolism 54(1): 24-32                                                                                             | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2<br><br>~48% were on sulphonylurea |
| <a href="#">Smits, Mark M, Fluitman, Kristina S, Herrema, Hilde et al. (2021) Liraglutide and sitagliptin have no effect on intestinal microbiota composition: A 12-week randomized placebo-controlled trial in adults with type 2 diabetes.</a> Diabetes & metabolism 47(5): 101223       | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                    |
| <a href="#">Sohn, Minji; Frias, Juan P; Lim, Soo (2023) Cardiovascular efficacy and safety of antidiabetic agents: A network meta-analysis of randomized controlled trials.</a> Diabetes, obesity & metabolism 25(12): 3560-3577                                                           | - Systematic review used as source of primary studies                                                                                                                                                      |
| <a href="#">Sohn, T. S., Lee, J. I., Kim, I. J. et al. (2008) The effect of rosiglitazone and metformin therapy, as an initial therapy, in patients with type 2</a>                                                                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                              |

| Study                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                                   |
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| <a href="#">diabetes mellitus</a> . Korean Diabetes J 32(5): 445-52                                                                                                                                                                                                                        |                                                                                                                                                          |
| <a href="#">Sone, Hirohito, Kaneko, Tatsuroh, Shiki, Kosuke et al. (2020) Efficacy and safety of empagliflozin as add-on to insulin in Japanese patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial</a> . Diabetes, obesity & metabolism 22(3): 417-426    | - Duplicate reference                                                                                                                                    |
| <a href="#">Sourij, C., Aziz, F., Tripolt, N.J. et al. (2024) Effects of empagliflozin in women and men with acute myocardial infarction: An analysis from the EMMY trial</a> . Hellenic Journal of Cardiology 75: 3-8                                                                     | - No relevant outcomes reported                                                                                                                          |
| <a href="#">Sousa, Lucas Silva, Nascimento, Felipe de Araújo, Rocha, Juliano et al. (2022) Cardioprotective Effects of Sodium-glucose Cotransporter 2 Inhibitors Regardless of Type 2 Diabetes Mellitus: A Meta-analysis</a> . Int. j. cardiovasc. sci. (Impr.) 35(1): 95-106              | - Population not relevant to this review protocol<br><i>People with or without type 2 diabetes</i>                                                       |
| <a href="#">Spanheimer, Robert, Betteridge D, John, Tan Meng, H et al. (2009) Long-term lipid effects of pioglitazone by baseline anti-hyperglycemia medication therapy and statin use from the PROactive experience (PROactive 14)</a> . The American journal of cardiology 104(2): 234-9 | - Secondary publication of an included study that does not provide any additional relevant information                                                   |
| <a href="#">Spinar, J; Spinarova, L; Vitovec, J (2020) Emperor reduced – cardiac and renal targets with empagliflozin in patients with heart failure with reduced ejection fraction</a> . Kardiologicka revue 22(3): 118-122                                                               | - Study not reported in English                                                                                                                          |
| <a href="#">Sridhar, V., Cosentino, F., Dagogo-Jack, S. et al. (2023) Effects of Ertugliflozin by Uric Acid Quintile: Observations from VERTIS CV</a> . Journal of the American Society of Nephrology 34: 854-855                                                                          | - Conference abstract                                                                                                                                    |
| <a href="#">Sridhar, Vikas S, Neuen, Brendon L, Fletcher, Robert A et al. (2023) Kidney protection with canagliflozin: A combined analysis of the randomized CANVAS program and CREDENCE trials</a> . Diabetes, obesity & metabolism                                                       | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Pooled analysis of two included studies</i> |
| <a href="#">St. John Sutton, M., Rendell, M., Dandona, P. et al. (2002) A comparison of the effects of rosiglitazone and glyburide on cardiovascular</a>                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                            |

| Study                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                                |
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| <a href="#">function and glycemic control in patients with type 2 diabetes.</a> Diabetes Care 25(11): 2058-64                                                                                                                                                                                                                                       |                                                                                                                                                                                                       |
| <a href="#">Standl, E., Baumgartl, H. J., Füchtenbusch, M. et al. (1999) Effect of acarbose on additional insulin therapy in type 2 diabetic patients with late failure of sulphonylurea therapy.</a> Diabetes Obes Metab 1(4): 215-20                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                         |
| <a href="#">Standl, E., Schernthaner, G., Rybka, J. et al. (2001) Improved glycaemic control with miglitol in inadequately-controlled type 2 diabetics.</a> Diabetes Res Clin Pract 51(3): 205-13                                                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                         |
| <a href="#">Standl, Eberhard, Stevens, Susanna R, Armstrong, Paul W et al. (2018) Increased Risk of Severe Hypoglycemic Events Before and After Cardiovascular Outcomes in TECOS Suggests an At-Risk Type 2 Diabetes Frail Patient Phenotype.</a> Diabetes care 41(3): 596-603                                                                      | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis investigating the risk of severe hypoglycaemic events before and after cardiovascular outcomes in the TECOS study</i> |
| <a href="#">Standl, Eberhard, Stevens, Susanna R, Lokhnygina, Yuliya et al. (2020) Confirming the Bidirectional Nature of the Association Between Severe Hypoglycemic and Cardiovascular Events in Type 2 Diabetes: Insights From EXSCEL.</a> Diabetes care 43(3): 643-652                                                                          | - Post-hoc analysis of included study                                                                                                                                                                 |
| <a href="#">Stefanou, Maria-Ioanna, Theodorou, Aikaterini, Malhotra, Konark et al. (2024) Risk of major adverse cardiovascular events and stroke associated with treatment with GLP-1 or the dual GIP/GLP-1 receptor agonist tirzepatide for type 2 diabetes: A systematic review and meta-analysis.</a> European stroke journal: 23969873241234238 | - Systematic review used as source of primary studies                                                                                                                                                 |
| <a href="#">Stefansson, Bergur V, Heerspink, Hiddo J L, Wheeler, David C et al. (2021) Data from a pooled post hoc analysis of 14 placebo-controlled, dapagliflozin treatment studies in patients with type 2 diabetes with and without anemia at baseline.</a> Data in brief 37: 107237                                                            | - Study design not relevant to this review protocol<br><br><i>Pooled post hoc analysis of RCTs</i>                                                                                                    |
| <a href="#">Steinberg William, M, Buse John, B, Ghorbani Marie Louise, Muus et al. (2017) Amylase, Lipase, and Acute Pancreatitis in People With Type 2 Diabetes Treated With Liraglutide: Results From the LEADER Randomized Trial.</a> Diabetes care 40(7): 966-972                                                                               | - Additional outcomes relevant to living guideline work                                                                                                                                               |

| Study                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                 |
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| <a href="#">Stenlof, Kaj, Cefalu, William T, Kim, Kyoung-Ah et al. (2014) Long-term efficacy and safety of canagliflozin monotherapy in patients with type 2 diabetes inadequately controlled with diet and exercise: findings from the 52-week CANTATA-M study.</a> Current medical research and opinion 30(2): 163-75 | - Comparator in study does not match that specified in this review protocol                            |
| <a href="#">Sternhufvud, C., Rohwedder, K., Sugg, J. et al. (2014) Change in quality of life (EQ-5D) among type 2 diabetes mellitus patients inadequately controlled with metformin plus sulfonylurea and treated with dapagliflozin as triple therapy regimen for 24 weeks.</a> Value in Health 17(3): a257            | - Conference abstract                                                                                  |
| <a href="#">Stewart, M. W., Cirkel, D. T., Furuseth, K. et al. (2006) Effect of metformin plus rosiglitazone compared with metformin alone on glycaemic control in well-controlled Type 2 diabetes.</a> Diabet Med 23(10): 1069-78                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Stocker, D. J., Taylor, A. J., Langley, R. W. et al. (2007) A randomized trial of the effects of rosiglitazone and metformin on inflammation and subclinical atherosclerosis in patients with type 2 diabetes.</a> Am Heart J 153(3): 445.e1-6                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Stojanovic, J., Andjelic Jelic, M., Vuksanovic, M. et al. (2023) The effects of early short-term insulin treatment vs. glimepiride on beta cell function in newly diagnosed type 2 diabetes with HbA1c above 9%.</a> Turkish Journal of Medical Sciences 53(2): 552-562                                     | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Strain, W David, Frenkel, Ofir, James, Martin A et al. (2022) Effects of Semaglutide on Stroke Subtypes in Type 2 Diabetes: Post Hoc Analysis of the Randomized SUSTAIN 6 and PIONEER 6.</a> Stroke 53(9): 2749-2757                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Stretton, Brandon, Kovoov, Joshua, Bacchi, Stephen et al. (2023) Weight loss with subcutaneous semaglutide versus other glucagon-like peptide 1 receptor agonists in type 2 diabetes: a systematic review.</a> Internal medicine journal                                                                    | - Systematic review used as source of primary studies                                                  |
| <a href="#">Striepe, Kristina, Jumar, Agnes, Ott, Christian et al. (2017) Effects of the Selective Sodium-Glucose Cotransporter 2 Inhibitor Empagliflozin on Vascular Function and Central</a>                                                                                                                          | - Trial that has a treatment and follow up period of less than 24 weeks                                |

| Study                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                                   |
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| <a href="#">Hemodynamics in Patients With Type 2 Diabetes Mellitus</a> . Circulation 136(12): 1167-1169                                                                                                                                                                                                          |                                                                                                                                                                          |
| <a href="#">Strojek, K., Bebakar, W. M., Khutsoane, D. T. et al. (2009) Once-daily initiation with biphasic insulin aspart 30 versus insulin glargine in patients with type 2 diabetes inadequately controlled with oral drugs: an open-label, multinational RCT</a> . Curr Med Res Opin 25(12): 2887-94         | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i>                                                |
| <a href="#">Strom Halden, T. A., Kvitne, K. E., Midtvedt, K. et al. (2019) Efficacy and safety of empagliflozin in renal transplant recipients with posttransplant diabetes mellitus</a> . Diabetes Care 42(6): 1067-1074                                                                                        | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Stultiens, Johanna M G, Top, Wiebe M C, Kimenai, Dorien M et al. (2022) Metformin and high-sensitivity cardiac troponin I and T trajectories in type 2 diabetes patients: a post-hoc analysis of a randomized controlled trial</a> . Cardiovascular diabetology 21(1): 49                            | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Su, Y, Lu, L-F, Li, Q-Z et al. (2014) A randomized controlled clinical trials for the treatment of type 2 diabetes by vildagliptin and alpha-glucosidase inhibitor</a> . Chinese journal of new drugs 23(22): 2655-2658                                                                              | - Study not reported in English                                                                                                                                          |
| <a href="#">Succurro, E., Miceli, S., Ruffo, M. et al. (2014) Effect of both liraglutide and sitagliptin on left ventricular ejection fraction and functional status in diabetic patients with chronic heart failure</a> . High Blood Pressure and Cardiovascular Prevention 21(2): 169                          | - Conference abstract                                                                                                                                                    |
| <a href="#">Succurro, E, Vizza, P, Papa, A et al. (2022) Effects of 26-week treatment with empagliflozin versus glimepiride on myocardial glucose metabolic rate in patients with type 2 diabetes: the randomized, open-label, active-controlled crossover FIORE trial</a> . Diabetes, obesity & metabolism      | - Crossover trial with an inadequate washout period                                                                                                                      |
| <a href="#">Sugimoto, D.H., Dex, T., Stager, W. et al. (2018) Efficacy of iGlarLixi, a fixed-ratio combination of insulin glargine and lixisenatide, in patients with type 2 diabetes stratified as at high or low risk according to HEDIS measurements</a> . Diabetes, Obesity and Metabolism 20(11): 2680-2684 | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |

| Study                                                                                                                                                                                                                                                                                                                                                                                    | Reason                                                                                        |
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| <a href="#">Sun, W., Zeng, C., Liao, L. et al. (2016) Comparison of acarbose and metformin therapy in newly diagnosed type 2 diabetic patients with overweight and/or obesity.</a> Current Medical Research and Opinion 32(8): 1389-1396                                                                                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK |
| <a href="#">Sun, Z., Ren, X., Jin, H. et al. (2006) Effect of pioglitazone on serum advanced glycosylation end product peptide and monocyte chemoattractant protein-1 in type 2 diabetic patients.</a> Jiangsu Medical Journal 32(2): 101-3                                                                                                                                              | - Study not reported in English                                                               |
| <a href="#">Sundstrom, Johan, Kristofi, Robin, Ostlund, Ollie et al. (2021) A registry-based randomised trial comparing an SGLT2 inhibitor and metformin as standard treatment of early stage type 2 diabetes (SMARTTEST): Rationale, design and protocol.</a> Journal of diabetes and its complications 35(10): 107996                                                                  | - No relevant outcomes reported                                                               |
| <a href="#">Suzuki, K; Yoshioka, T; Wakui, Y (2013) Comparison between sitagliptin as add-on therapy to insulin and insulin dose-increase therapy in uncontrolled type 2 diabetes -CASA study-.</a> Therapeutic research 34(3): 371-378                                                                                                                                                  | - Study not reported in English                                                               |
| <a href="#">Suzuki, Luka, Kanazawa, Akio, Uzawa, Hirotsugu et al. (2017) Safety and efficacy of metformin up-titration in Japanese patients with type 2 diabetes mellitus treated with vildagliptin and low-dose metformin.</a> Expert opinion on pharmacotherapy 18(18): 1921-1928                                                                                                      | - Comparator in study does not match that specified in this review protocol                   |
| <a href="#">Swinnen, Sanne G H A, Snoek, Frank J, Dain, Marie-Paule et al. (2009) Rationale, design, and baseline data of the insulin glargine (Lantus) versus insulin detemir (Levemir) Treat-To-Target (L2T3) study: A multinational, randomized noninferiority trial of basal insulin initiation in type 2 diabetes.</a> Diabetes technology & therapeutics 11(11): 739-43            | - Study design not relevant to this review protocol<br><i>Protocol only</i>                   |
| <a href="#">Tabak, Adam G, Anderson, John, Aschner, Pablo et al. (2020) Efficacy and Safety of iGlarLixi, Fixed-Ratio Combination of Insulin Glargine and Lixisenatide, Compared with Basal-Bolus Regimen in Patients with Type 2 Diabetes: Propensity Score Matched Analysis.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 11(1): 305-318 | - Study design not relevant to this review protocol                                           |



| Study                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                             |
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| <a href="#">Tack, Cees J, Jacob, Stephan, Desouza, Cyrus et al. (2019) Long-term efficacy and safety of combined insulin and glucagon-like peptide-1 therapy: Evidence from the LEADER trial.</a> Diabetes, obesity & metabolism 21(11): 2450-2458                                                                                                               | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Tager, Tobias, Atar, Dan, Agewall, Stefan et al. (2021) Comparative efficacy of sodium-glucose cotransporter-2 inhibitors (SGLT2i) for cardiovascular outcomes in type 2 diabetes: a systematic review and network meta-analysis of randomised controlled trials.</a> Heart failure reviews 26(6): 1421-1435                                         | - Systematic review used as source of primary studies                                                                                              |
| <a href="#">Tager, Tobias, Frankenstein, Lutz, Atar, Dan et al. (2022) Influence of receptor selectivity on benefits from SGLT2 inhibitors in patients with heart failure: a systematic review and head-to-head comparative efficacy network meta-analysis.</a> Clinical research in cardiology : official journal of the German Cardiac Society 111(4): 428-439 | - Population not relevant to this review protocol<br><i>Mixture of people with and without type 2 diabetes</i>                                     |
| <a href="#">Taheri, H., Chiti, H., Reshadmanesh, T. et al. (2023) Empagliflozin improves high-sensitive cardiac troponin-I and high-density lipoprotein cholesterol in patients with type 2 diabetes mellitus and coronary artery disease: a post-hoc analysis of EMPA-CARD Trial.</a> Journal of Diabetes and Metabolic Disorders                               | - Additional outcomes relevant to living guideline work                                                                                            |
| <a href="#">Tajima, Naoko, Kadowaki, Takashi, Odawara, Masato et al. (2016) Safety and efficacy of addition of sitagliptin to rapid-acting insulin secretagogues for glycemic control, including post-prandial hyperglycemia, among Japanese with type 2 diabetes mellitus.</a> Diabetology international 7(2): 155-166                                          | - Trial that has a treatment and follow up period of less than 24 weeks                                                                            |
| <a href="#">Takagi, T., Okura, H., Kobayashi, Y. et al. (2009) A prospective, multicenter, randomized trial to assess efficacy of pioglitazone on in-stent neointimal suppression in type 2 diabetes: POPPS (Prevention of In-Stent Neointimal Proliferation by Pioglitazone Study).</a> JACC Cardiol Interv 2(6): 524-31                                        | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Takagi, T., Yamamuro, A., Tamita, K. et al. (2005) Thiazolidinedione treatment attenuates diffuse neointimal hyperplasia in restenotic lesions after coronary stent implantation in type</a>                                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |

| Study                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                 |
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| <a href="#">2 diabetic patients: An intravascular ultrasound study.</a> Journal of Cardiology 45(4): 139-147                                                                                                                                                                                              |                                                                                                                                                        |
| <a href="#">Takagi, T., Yamamuro, A., Tamita, K. et al. (2003) Pioglitazone reduces neointimal tissue proliferation after coronary stent implantation in patients with type 2 diabetes mellitus: an intravascular ultrasound scanning study.</a> Am Heart J 146(2): e5                                    | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Takahara, M., Shiraiwa, T., Matsuoka, T. A. et al. (2020) Investigation of the effect of canagliflozin on the disposition index, a marker of pancreatic beta cell function, in patients with type 2 diabetes.</a> Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 13: 4457-4468 | - Comparator in study does not match that specified in this review protocol                                                                            |
| <a href="#">Takahashi, H., Kessoku, T., Kawanaka, M. et al. (2022) Ipragliflozin Improves the Hepatic Outcomes of Patients With Diabetes with NAFLD.</a> Hepatology communications 6(1): 120-132                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |
| <a href="#">Takahashi, H., Sakai, K., Kawanishi, K. et al. (2015) Efficacy of switching from premix analog insulin twice daily injection to insulin glargine once daily injection with sitagliptin.</a> Diabetology International 6(1): 33-38                                                             | - Comparator in study does not match that specified in this review protocol                                                                            |
| <a href="#">Takase, H., Nakazawa, A., Yamashita, S. et al. (2007) Pioglitazone produces rapid and persistent reduction of vascular inflammation in patients with hypertension and type 2 diabetes mellitus who are receiving angiotensin II receptor blockers.</a> Metabolism 56(4): 559-64               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |
| <a href="#">Takashima, H., Yoshida, Y., Nagura, C. et al. (2018) Renoprotective effects of canagliflozin, a sodium glucose cotransporter 2 inhibitor, in type 2 diabetes patients with chronic kidney disease: a randomized open-label prospective trial.</a> Diabetes Vasc Dis Res 15(5): 469-472        | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Takeshita, Y., Honda, M., Harada, K. et al. (2022) Comparison of Tofogliflozin and Glimepiride Effects on Nonalcoholic Fatty Liver Disease in Participants With Type 2 Diabetes: a Randomized, 48-Week, Open-Label, Active-Controlled Trial.</a> Diabetes care: 2064-2075                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |

| Study                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                                                   |
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| <a href="#">Takeshita, Yumie, Kita, Yuki, Tanaka, Takeo et al. (2022) Insulin-glucagon-like peptide-1 receptor agonist relay and glucagon-like peptide-1 receptor agonist first regimens in individuals with type 2 diabetes: A randomized, open-label trial study. Journal of diabetes investigation 13(6): 965-974</a>               | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Takuma, K.; Fuchigami, A.; Hirose, T. (2023) Effects of sitagliptin versus dapagliflozin on time in range in Japanese patients with type 2 diabetes stratified by body mass index: a sub-analysis of the DIVERSITY-CVR study. Diabetologia 66(supplement1): 350-s351</a>                                                   | - Conference abstract                                                                                                                                                    |
| <a href="#">Takuma, Kota, Fuchigami, Ayako, Shigiyama, Fumika et al. (2023) Comparison of the effects of sitagliptin and dapagliflozin on time in range in Japanese patients with type 2 diabetes stratified by body mass index: A sub-analysis of the DIVERSITY-CVR study. Diabetes, obesity &amp; metabolism</a>                     | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Tamaki, Shunsuke, Yamada, Takahisa, Watanabe, Tetsuya et al. (2021) Effect of Empagliflozin as an Add-On Therapy on Decongestion and Renal Function in Patients With Diabetes Hospitalized for Acute Decompensated Heart Failure: A Prospective Randomized Controlled Study. Circulation. Heart failure 14(3): e007048</a> | - Comparator in study does not match that specified in this review protocol                                                                                              |
| <a href="#">Tamez-Pérez, HE (2015) Efficacy and safety of initial treatment with glimepiride versus sitagliptin in type 2 diabetes. Revista medica del Instituto Mexicano del Seguro Social 53(2): 142-148</a>                                                                                                                         | - Study not reported in English                                                                                                                                          |
| <a href="#">Tan, M. H., Johns, D., Strand, J. et al. (2004) Sustained effects of pioglitazone vs. glibenclamide on insulin sensitivity, glycaemic control, and lipid profiles in patients with Type 2 diabetes. Diabet Med 21(8): 859-66</a>                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Tanaka, A., Hisauchi, I., Taguchi, I. et al. (2019) Effects of canagliflozin in patients with type 2 diabetes and chronic heart failure: A randomized clinical trial (candle). Circulation 140(supplement1)</a>                                                                                                            | - Conference abstract                                                                                                                                                    |
| <a href="#">Tanaka, A., Hisauchi, I., Taguchi, I. et al. (2020) Effects of canagliflozin in patients with type 2</a>                                                                                                                                                                                                                   | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are                                                                                     |

| Study                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                                   |
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| <a href="#">diabetes and chronic heart failure: a randomized trial (CANDLE)</a> . ESC heart failure 7(4): 1585-1594                                                                                                                                                                                                                     | treatment naive and therefore the study cannot be classified into review 1.1 or 1.2                                                                                      |
| <a href="#">Tanaka, A., Komukai, S., Shibata, Y. et al. (2018) Effect of pioglitazone on cardiometabolic profiles and safety in patients with type 2 diabetes undergoing percutaneous coronary artery intervention: a prospective, multicenter, randomized trial</a> . Heart Vessel 33(9): 965-977                                      | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                   |
| <a href="#">Tanaka, A., Shimabukuro, M., Machii, N. et al. (2019) Short-term effect of empagliflozin on endothelial function in patients with type 2 diabetes and cardiovascular diseases: a placebocontrolled randomised trial (EMBLEM)</a> . Diabetologia 62(supplement1): 560-s561                                                   | - Conference abstract                                                                                                                                                    |
| <a href="#">Tanaka, Atsushi, Imai, Takumi, Shimabukuro, Michio et al. (2022) Effect of canagliflozin on white blood cell counts in patients with type 2 diabetes and heart failure: A subanalysis of the randomized CANDLE trial</a> . Journal of diabetes investigation 13(12): 1990-1999                                              | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Tanaka, Atsushi, Inoue, Teruo, Kitakaze, Masafumi et al. (2016) Rationale and design of a randomized trial to test the safety and non-inferiority of canagliflozin in patients with diabetes with chronic heart failure: the CANDLE trial</a> . Cardiovascular diabetology 15: 57                                           | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Tanaka, Atsushi, Shimabukuro, Michio, Teragawa, Hiroki et al. (2021) Comparison of the clinical effect of empagliflozin on glycemic and non-glycemic parameters in Japanese patients with type 2 diabetes and cardiovascular disease treated with or without baseline metformin</a> . Cardiovascular diabetology 20(1): 160 | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis of the EMBLEM trial comparing people treated with or without baseline metformin</i>      |
| <a href="#">Tanaka, Atsushi, Toyoda, Shigeru, Imai, Takumi et al. (2021) Effect of canagliflozin on N-terminal pro-brain natriuretic peptide in patients with type 2 diabetes and chronic heart failure according to baseline use of glucose-lowering agents</a> . Cardiovascular diabetology 20(1): 175                                | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Tanaka, K., Saisho, Y., Kawai, T. et al. (2015) Efficacy and safety of liraglutide monotherapy compared with metformin in Japanese overweight/obese patients with type 2 diabetes</a> . Endocrine J 62(5): 399-409                                                                                                          | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |

| Study                                                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                                                                      |
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| <a href="#">Tanaka, Kumiko, Saisho, Yoshifumi, Manesso, Erica et al. (2015) Effects of Liraglutide Monotherapy on Beta Cell Function and Pancreatic Enzymes Compared with Metformin in Japanese Overweight/Obese Patients with Type 2 Diabetes Mellitus: A Subpopulation Analysis of the KIND-LM Randomized Trial.</a> Clinical drug investigation 35(10): 675-84 | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2                    |
| <a href="#">Taneda, Shinji, Hyllested-Winge, Jacob, Gall, Mari-Anne et al. (2017) Insulin degludec/insulin aspart versus biphasic insulin aspart 30 twice daily in insulin-experienced Japanese subjects with uncontrolled type 2 diabetes: Subgroup analysis of a Pan-Asian, treat-to-target Phase 3 Trial.</a> Journal of diabetes 9(3): 243-247                | - Comparator in study does not match that specified in this review protocol<br><i>Compares insulin to other types of insulin</i><br><br>- Conference abstract                               |
| <a href="#">Tang, H., Kimmel, S.E., Smith, S.M. et al. (2022) Comparable Cardiorenal Benefits of SGLT2 Inhibitors and GLP-1RAs in Asian and White Populations: An Updated Meta-analysis of Results From Randomized Outcome Trials.</a> Diabetes Care 45(4): 1007-1012                                                                                             | - Population not relevant to this review protocol<br><i>People with and without type 2 diabetes</i>                                                                                         |
| <a href="#">Tang, Huilin, Chen, Weihan, Bian, Jiang et al. (2023) Ethnic Variations in Cardiovascular and Renal Outcomes From Newer Glucose-Lowering Drugs: A Meta-Analysis of Randomized Outcome Trials.</a> Journal of the American Heart Association 12(10): e026791                                                                                           | - Systematic review used as source of primary studies                                                                                                                                       |
| <a href="#">Tanimura-Inagaki, K., Nagao, M., Harada, T. et al. (2020) Sitagliptin improves plasma apolipoprotein profile in type 2 diabetes: A randomized clinical trial of sitagliptin effect on lipid and glucose metabolism (SLIM) study.</a> Diabetes Research & Clinical Practice 162: 108119                                                                | - Comparator in study does not match that specified in this review protocol<br><i>Comparator group is a non-sitagliptin group which is not a relevant comparator listed in the protocol</i> |
| <a href="#">Tanner, M (2013) 2012 - Metformin reduced CV events compared with glipizide in patients with type 2 diabetes and CAD.</a> ACP journal club 158(8): 1-1                                                                                                                                                                                                | - Commentary only                                                                                                                                                                           |
| <a href="#">Teo, Yao H, Chia, Alys Z Q, Teo, Yao N et al. (2022) The impact of sodium-glucose cotransporter inhibitors on blood pressure: a meta-analysis and metaregression of 111 randomized-controlled trials.</a> Journal of hypertension 40(12): 2353-2372                                                                                                   | - No relevant outcomes reported<br><i>Investigates systolic and diastolic blood pressure which are not outcomes of interest in the protocol.</i>                                            |

| Study                                                                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                                   |
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| <a href="#">Teramoto, T., Yamada, N., Shirai, K. et al. (2007) Effects of pioglitazone hydrochloride on Japanese patients with type 2 diabetes mellitus. J Atheroscler Thromb 14(2): 86-93</a>                                                                                                                                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Terauchi, Yasuo, Utsunomiya, Kazunori, Yasui, Atsutaka et al. (2019) Safety and Efficacy of Empagliflozin as Add-On Therapy to GLP-1 Receptor Agonist (Liraglutide) in Japanese Patients with Type 2 Diabetes Mellitus: A Randomised, Double-Blind, Parallel-Group Phase 4 Study. Diabetes therapy : research, treatment and education of diabetes and related disorders 10(3): 951-963</a> | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares different doses of the same medication</i>                                |
| <a href="#">Terawaki, Y., Iwaya, C., Nomiya, T. et al. (2020) Efficacy and safety of a combination of an insulin secretagogue and a dipeptidyl peptidase-4 inhibitor in Japanese patients with type 2 diabetes mellitus; the repaglinide glucose oscillation study in Fukuoka (REGO-F). Diabetol Int</a>                                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Terenzi, D., Verma, S., Trac, J. et al. (2019) A NOVEL ROLE OF SGLT2 INHIBITORS TO INCREASE CIRCULATING PROANGIOGENIC PROGENITOR CELLS IN PATIENTS WITH TYPE 2 DIABETES AND ESTABLISHED CARDIOVASCULAR DISEASE: A SUB-STUDY OF THE EMPA-HEART CARDIOLINK-6 TRIAL. Canadian Journal of Cardiology 35(10supplement): 77-s78</a>                                                               | - Conference abstract                                                                                                                                                    |
| <a href="#">Terra, S. G., Focht, K., Davies, M. et al. (2017) Phase III, efficacy and safety study of ertugliflozin monotherapy in people with type 2 diabetes mellitus inadequately controlled with diet and exercise alone. Diabetes Obes Metab 19(5): 721-728</a>                                                                                                                                    | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Testa, M.A., Hayes, J.F., Lind, M. et al. (2018) Durability of improved patient-reported outcomes in type 2 diabetes patients treated with dapagliflozin plus saxagliptin vs insulin glargine. Diabetologia 61(supplement1): 408</a>                                                                                                                                                        | - Conference abstract                                                                                                                                                    |
| <a href="#">Teupe, B. and Bergis, K. (1991) Prospective randomized two-years clinical study comparing additional metformin treatment with reducing diet in type 2 diabetes. Diabète Metab 17(1pt2): 213-7</a>                                                                                                                                                                                           | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i>                   |



| Study                                                                                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                                   |
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| <a href="#">Thethi T, K; Pratley, R; Meier J, J (2020) Efficacy, safety and cardiovascular outcomes of once-daily oral semaglutide in patients with type 2 diabetes: The PIONEER programme.</a> Diabetes, Obesity and Metabolism 22(8): 1263-1277                                                                                                                                                           | - Review article but not a systematic review                                                                                                                                                                                             |
| <a href="#">Thiagaraj, Suvedha, Shukla, Twisha S, Gutlapalli, Sai Dheeraj et al. (2023) The Efficacy of Sodium-Glucose Cotransporter-2 Inhibitors in Improving Morbidity and Mortality of Heart Failure: A Systematic Review.</a> Cureus 15(2): e34942                                                                                                                                                      | - Population not relevant to this review protocol                                                                                                                                                                                        |
| <a href="#">Thiele, Kirsten, Rau, Matthias, Hartmann, Niels-Ulrik K et al. (2021) Effects of empagliflozin on erythropoiesis in patients with type 2 diabetes: Data from a randomized, placebo-controlled study.</a> Diabetes, obesity & metabolism 23(12): 2814-2818                                                                                                                                       | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                  |
| <a href="#">Thomas, M.K., Nikooienejad, A., Bray, R. et al. (2019) Tirzepatide, a dual GIP and GLP-1 receptor agonist, improves markers of beta cell function and insulin sensitivity in type 2 diabetes patients.</a> Diabetologia 62(supplement1): 354                                                                                                                                                    | - Conference abstract                                                                                                                                                                                                                    |
| <a href="#">Thomas, Melissa K, Nikooienejad, Amir, Bray, Ross et al. (2021) Dual GIP and GLP-1 Receptor Agonist Tirzepatide Improves Beta-cell Function and Insulin Sensitivity in Type 2 Diabetes.</a> The Journal of clinical endocrinology and metabolism 106(2): 388-396                                                                                                                                | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                   |
| <a href="#">Tian, B, Deng, Y, Cai, Y et al. (2021) Efficacy and safety of Combination Therapy with Sodium-glucose Transporter 2 Inhibitors and Renin-Angiotensin System Blockers in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis.</a> Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares SGLT2 inhibitor treatment with ACE inhibitors/ARBs to treatment with ACE inhibitors/ARBs alone, which is not included in the protocol</i> |
| <a href="#">Tian, Lei, Cai, Yuzi, Zheng, Huijuan et al. (2021) Canagliflozin for Prevention of Cardiovascular and Renal Outcomes in type2 Diabetes: A Systematic Review and Meta-analysis of Randomized Controlled Trials.</a> Frontiers in pharmacology 12: 691878                                                                                                                                         | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                  |

| Study                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                   |
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| <a href="#">Tian, Qi, Guo, Keyu, Deng, Jiayi et al. (2022) Effects of SGLT2 inhibitors on haematocrit and haemoglobin levels and the associated cardiorenal benefits in T2DM patients: A meta-analysis. Journal of cellular and molecular medicine 26(2): 540-547</a>                                                         | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Toba-Oluboka, T.; Vochoskova, K.; Hajek, T. (2022) Are the antidepressant effects of insulin-sensitizing medications related to improvements in metabolic markers?. Translational Psychiatry 12(1): 469</a>                                                                                                       | - Population not relevant to this review protocol<br><i>People with or without type 2 diabetes (depression is the main area of interest)</i>                             |
| <a href="#">Tolba, M.K.A.; El Khashab, K.A.; Said, A.S.A. (2017) The effect of dipeptidyl peptidase-4 inhibitors on cardiovascular disease risk in type 2 diabetes mellitus. International Journal of Pharmacy and Pharmaceutical Sciences 9(1): 254-259</a>                                                                  | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2 |
| <a href="#">Tolman, K. G., Freston, J. W., Kupfer, S. et al. (2009) Liver safety in patients with type 2 diabetes treated with pioglitazone: results from a 3-year, randomized, comparator-controlled study in the US. Drug Safety 32(9): 787-800</a>                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Tommerdahl, Kalie L; Kendrick, Jessica; Bjornstad, Petter (2022) The Role of Glucagon-Like Peptide 1 (GLP-1) Receptor Agonists in the Prevention and Treatment of Diabetic Kidney Disease: Insights from the AMPLITUDE-O Trial. Clinical journal of the American Society of Nephrology : CJASN 17(6): 905-907</a> | - Commentary only                                                                                                                                                        |
| <a href="#">Tong, G., Lu, S., Kuang, H. et al. (2024) Effect of baseline characteristics on the efficacy of dulaglutide added to basal insulin in Chinese patients with type 2 diabetes: A subgroup analysis of AWARD-CHN3. Diabetes, Obesity and Metabolism 26(4): 1540-1543</a>                                             | - Secondary publication of an included study that does not provide any additional relevant information                                                                   |
| <a href="#">Tonneijck, Lennart, Smits, Mark M, Muskiet, Marcel H A et al. (2016) Acute renal effects of the GLP-1 receptor agonist exenatide in overweight type 2 diabetes patients: a randomised, double-blind, placebo-controlled trial. Diabetologia 59(7): 1412-1421</a>                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Torimoto, Keiichi, Okada, Yosuke, Goshima, Yukiko et al. (2019) Addition of canagliflozin to insulin improves glycaemic control and reduces insulin dose in patients with type 2 diabetes</a>                                                                                                                     | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |

| Study                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                                                   |
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| <a href="#">mellitus: A randomized controlled trial.</a> Diabetes, obesity & metabolism 21(9): 2174-2179                                                                                                                                                                                                                                       |                                                                                                                                                                          |
| <a href="#">Tornyos, Daniel, Meuer, Maximilian, Lukacs, Reka et al. (2022) Cardiovascular outcomes in patients treated with sodium-glucose transport protein 2 inhibitors, a network meta-analysis of randomized trials.</a> Frontiers in cardiovascular medicine 9: 1041200                                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                  |
| <a href="#">Toufiq, O., Gillani, S.W., Mohamed, F. et al. (2021) Efficacy and safety comparison between pioglitazone and linagliptin in combination with metformin among patients with Type 2 diabetes mellitus: A meta-analysis of randomized controlled trials.</a> Journal of Pharmacology and Pharmacotherapeutics 12(1): 1-9              | - Systematic review used as source of primary studies                                                                                                                    |
| <a href="#">Tougaard, Rasmus Stilling, Jorsal, Anders, Tarnow, Lise et al. (2020) Heart rate increases in liraglutide treated chronic heart failure patients: association with clinical parameters and adverse events.</a> Scandinavian cardiovascular journal : SCJ 54(5): 294-299                                                            | - Population not relevant to this review protocol<br><i>Sub-study of Jorsal 2019. includes population with and without diabetes. Results are not reported separately</i> |
| <a href="#">Trakarnvanich, T., Satirapoj, B., Suraamornkul, S. et al. (2021) Effect of Dipeptidyl Peptidase-4 (DPP-4) Inhibition on Biomarkers of Kidney Injury and Vascular Calcification in Diabetic Kidney Disease: A Randomized Controlled Trial.</a> Journal of Diabetes Research 2021: 7382620                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                            |
| <a href="#">Treewaree, S., Kulthamrongsri, N., Owattanapanich, W. et al. (2023) Is it time for class I recommendation for sodium-glucose cotransporter-2 inhibitors in heart failure with mildly reduced or preserved ejection fraction?: An updated systematic review and meta-analysis.</a> Frontiers in Cardiovascular Medicine 10: 1046194 | - Population not relevant to this review protocol<br><i>Mixture of people with or without type 2 diabetes</i>                                                            |
| <a href="#">Tripathy, Devjit, Schwenke, Dawn C, Banerji, MaryAnn et al. (2016) Diabetes Incidence and Glucose Tolerance after Termination of Pioglitazone Therapy: Results from ACT NOW.</a> The Journal of clinical endocrinology and metabolism 101(5): 2056-62                                                                              | - Population not relevant to this review protocol                                                                                                                        |
| <a href="#">Tripolt, Norbert J, Kolesnik, Ewald, Pferschy, Peter N et al. (2020) Impact of EMPagliflozin on cardiac function and biomarkers of heart failure in patients with acute MYocardial infarction-The EMMY trial.</a> American heart journal 221: 39-47                                                                                | - Study design not relevant to this review protocol<br><i>Protocol only</i>                                                                                              |

| Study                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                     |
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| <a href="#">Truitt, K. E., Goldberg, R. B., Rosenstock, J. et al. (2010) A 26-week, placebo- and pioglitazone-controlled, dose-ranging study of rivoglitazone, a novel thiazolidinedione for the treatment of type 2 diabetes. Curr Med Res Opin 26(6): 1321-31</a>                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                              |
| <a href="#">Trujillo, Jennifer M, Roberts, Michelle, Dex, Terry et al. (2018) Low incidence of gastrointestinal adverse events over time with a fixed-ratio combination of insulin glargine and lixisenatide versus lixisenatide alone. Diabetes, obesity &amp; metabolism 20(11): 2690-2694</a>         | - Secondary publication of an included study that does not provide any additional relevant information                                     |
| <a href="#">Tsai, Pei-Chien, Chuang, Wei-Jung, Ko, Albert Min-Shan et al. (2023) Neutral effects of SGLT2 inhibitors in acute coronary syndromes, peripheral arterial occlusive disease, or ischemic stroke: a meta-analysis of randomized controlled trials. Cardiovascular diabetology 22(1): 57</a>   | - Population not relevant to this review protocol<br><i>People with and without type 2 diabetes</i>                                        |
| <a href="#">Tsai, Wen-Hsuan, Chuang, Shih-Ming, Liu, Sung-Chen et al. (2021) Effects of SGLT2 inhibitors on stroke and its subtypes in patients with type 2 diabetes: a systematic review and meta-analysis. Scientific reports 11(1): 15364</a>                                                         | - Systematic review used as source of primary studies                                                                                      |
| <a href="#">Tsapas, Apostolos, Karagiannis, Thomas, Avgerinos, Ioannis et al. (2021) GLP-1 receptor agonists for cardiovascular outcomes with and without metformin. A systematic review and meta-analysis of cardiovascular outcomes trials. Diabetes research and clinical practice 177: 108921</a>    | - Systematic review used as source of primary studies                                                                                      |
| <a href="#">Tsumura, K (1995) Clinical evaluation of glimepiride (HOE490) in NIDDM, including a double blind comparative study versus gliclazide. Diabetes research and clinical practice 28suppl: 147-9</a>                                                                                             | - Study design not relevant to this review protocol<br><i>Methods in paper not sufficient and does not state whether it was randomised</i> |
| <a href="#">Turner, R C, Cull, C A, Frighi, V et al. (1999) Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. JAMA 281(21): 2005-12</a> | - Comparator in study does not match that specified in this review protocol                                                                |
| <a href="#">Tuttle, K., Bain, S.C., Cherney, D. et al. (2022) CHANGE IN KDIGO KIDNEY RISK</a>                                                                                                                                                                                                            | - Conference abstract                                                                                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                                                                                                                                                                  |
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| <a href="#">CATEGORY WITH SEMAGLUTIDE TREATMENT-A POST HOC ANALYSIS OF THE SUSTAIN 6 TRIAL</a> . Nephrology Dialysis Transplantation 37(suppl3): i331                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                         |
| <a href="#">Tuttle, K.R., Lakshmanan, M.C., Gross, J.L. et al. (2018) Comparable glycemic control, greater weight loss, and lower hypoglycemia with once weekly dulaglutide versus insulin glargine, both combined with lispro, in type 2 diabetes and moderate to severe chronic kidney disease (AWARD-7)</a> . Diabetology and Metabolic Syndrome 10(supplement1) | - Conference abstract                                                                                                                                                                                                                                                                                                   |
| <a href="#">Tuttle, Katherine R, Lakshmanan, Mark C, Rayner, Brian et al. (2019) Body weight and eGFR during dulaglutide treatment in type 2 diabetes and moderate-to-severe chronic kidney disease (AWARD-7)</a> . Diabetes, obesity & metabolism 21(6): 1493-1497                                                                                                 | - Study design not relevant to this review protocol<br><i>post hoc analysis</i>                                                                                                                                                                                                                                         |
| <a href="#">Tuttle, Katherine R, Levin, Adeera, Nangaku, Masaomi et al. (2022) Safety of Empagliflozin in Patients With Type 2 Diabetes and Chronic Kidney Disease: Pooled Analysis of Placebo-Controlled Clinical Trials</a> . Diabetes care 45(6): 1445-1452                                                                                                      | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Pooled analysis</i>                                                                                                                                                                                        |
| <a href="#">Tuttle, Katherine R, Rayner, Brian, Lakshmanan, Mark C et al. (2021) Clinical Outcomes by Albuminuria Status with Dulaglutide versus Insulin Glargine in Participants with Diabetes and CKD: AWARD-7 Exploratory Analysis</a> . Kidney360 2(2): 254-262                                                                                                 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                                  |
| <a href="#">Tuttolomondo, A., Cirrincione, A., Casuccio, A. et al. (2021) Efficacy of dulaglutide on vascular health indexes in subjects with type 2 diabetes: a randomized trial</a> . Cardiovascular Diabetology 20(1): 1                                                                                                                                         | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                                                                                                                                                                      |
| <a href="#">Tye, Sok Cin, de Vries, Sieta T, Wanner, Christoph et al. (2021) Prediction of the Effects of Empagliflozin on Cardiovascular and Kidney Outcomes Based on Short-Term Changes in Multiple Risk Markers</a> . Frontiers in pharmacology 12: 786706                                                                                                       | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Secondary analysis applying a prediction model to predict the effects of empagliflozin on cardiovascular and kidney outcomes based on short-term changes on risk markers in the EMPA-RED OUTCOME trial</i> |
| <a href="#">Türkmen Kemal, Y., Güvener Demirag, N., Yildirim, A. et al. (2007) Effects of rosiglitazone</a>                                                                                                                                                                                                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                                                           |

| Study                                                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
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| <a href="#">on plasma brain natriuretic peptide levels and myocardial performance index in patients with type 2 diabetes mellitus.</a> Acta Diabetologica 44(3): 149-56                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <a href="#">Udell, Jacob A, Bhatt, Deepak L, Braunwald, Eugene et al. (2015) Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes and moderate or severe renal impairment: observations from the SAVOR-TIMI 53 Trial.</a> Diabetes care 38(4): 696-705                                                                  | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                                                                                                                                                                                                                                                                   |
| <a href="#">Umayahara, Rieko, Yonemoto, Takako, Kyou, Chika et al. (2014) Low-dose glimepiride with sitagliptin improves glycemic control without dose-dependency in patients with type 2 diabetes inadequately controlled on high-dose glimepiride.</a> Endocrine journal 61(12): 1163-70                                                  | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares different doses of the same medication</i>                                                                                                                                                                                                                                                                                                                |
| <a href="#">Umpierrez, G. E., Cardona, S., Chachkhiani, D. et al. (2018) A randomized controlled study comparing a DPP4 inhibitor (Linagliptin) and basal insulin (Glargine) in patients with type 2 diabetes in long-term care and skilled nursing facilities: Linagliptin-LTC Trial.</a> J Am Med Dir Assoc 19(5): 399-404                | - Not categorisable as switching or adding trial<br><br><i>81% participants on background drug therapy; all oral drugs stopped except for those (~58%) on metformin. Participants randomised to linagliptin or basal insulin, both with concomitant insulin lispro. Therefore 58% of participants had linagliptin or basal insulin (both with lispro) added to their metformin, whilst 42% of participants switched to linagliptin or basal insulin.</i> |
| <a href="#">Uneda, Kazushi, Kawai, Yuki, Yamada, Takayuki et al. (2021) Systematic review and meta-analysis for prevention of cardiovascular complications using GLP-1 receptor agonists and SGLT-2 inhibitors in obese diabetic patients.</a> Scientific reports 11(1): 10166                                                              | - Systematic review used as source of primary studies                                                                                                                                                                                                                                                                                                                                                                                                    |
| <a href="#">Unger, J., Kaltoft, M., Kolhe, D. et al. (2020) LIRA-PRIME: A randomized trial in primary care settings of liraglutide vs. OAD for glycemic control in patients with type 2 diabetes not in control on metformin.</a> Diabetes 69(supplement1)                                                                                  | - Conference abstract                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <a href="#">Vaccaro, O., Masulli, M., Nicolucci, A. et al. (2017) Effects on the incidence of cardiovascular events of the addition of pioglitazone versus sulfonylureas in patients with type 2 diabetes inadequately controlled with metformin (TOSCA.IT): a randomised, multicentre trial.</a> Lancet Diabetes Endocrinol 5(11): 887-897 | - Comparator in study does not match that specified in this review protocol<br><br><i>Does not specify the sulfonylurea so cannot be stratified for the analysis as required</i>                                                                                                                                                                                                                                                                         |



| Study                                                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                            |
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| <a href="#">Vaccaro, O, Masulli, M, Bonora, E et al. (2012) Addition of either pioglitazone or a sulfonylurea in type 2 diabetic patients inadequately controlled with metformin alone: impact on cardiovascular events. A randomized controlled trial. Nutrition, metabolism, and cardiovascular diseases : NMCD 22(11): 997-1006</a>                                                       | - Comparator in study does not match that specified in this review protocol                                                       |
| <a href="#">Vaduganathan, M., Inzucchi, S.E., Claggett, B.L. et al. (2023) Effects of dapagliflozin in type 2 diabetes and heart failure with mildly reduced or preserved ejection fraction across the background of glucose-lowering therapy in DELIVER. Diabetologia 66(supplement1): 91-s92</a>                                                                                           | - Conference abstract                                                                                                             |
| <a href="#">Vaduganathan, Muthiah, Docherty, Kieran F, Claggett, Brian L et al. (2022) SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials. Lancet (London, England) 400(10354): 757-767</a>                                                                                                                                | - Population not relevant to this review protocol<br><i>People with heart failure who do not necessarily have type 2 diabetes</i> |
| <a href="#">Vaduganathan, Muthiah, Sattar, Naveed, Xu, Jialin et al. (2022) Stress Cardiac Biomarkers, Cardiovascular and Renal Outcomes, and Response to Canagliflozin. Journal of the American College of Cardiology 79(5): 432-444</a>                                                                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information                            |
| <a href="#">van Bommel, Erik J M, Muskiet, Marcel H A, van Baar, Michael J B et al. (2020) The renal hemodynamic effects of the SGLT2 inhibitor dapagliflozin are caused by post-glomerular vasodilatation rather than pre-glomerular vasoconstriction in metformin-treated patients with type 2 diabetes in the randomized, double-blind RED trial. Kidney international 97(1): 202-212</a> | - Trial that has a treatment and follow up period of less than 24 weeks<br><i>12 weeks</i>                                        |
| <a href="#">van der Aart-van der Beek, Annemarie B, Clegg, Lindsay E, Penland, Robert C et al. (2020) Effect of once-weekly exenatide on estimated glomerular filtration rate slope depends on baseline renal risk: A post hoc analysis of the EXSCEL trial. Diabetes, obesity &amp; metabolism 22(12): 2493-2498</a>                                                                        | - Secondary publication of an included study that does not provide any additional relevant information                            |
| <a href="#">van Ruiten, Charlotte C, Veltman, Dick J, Nieuwdorp, Max et al. (2022) Brain Activation in Response to Low-Calorie Food Pictures: An Explorative Analysis of a Randomized Trial With Dapagliflozin and Exenatide. Frontiers in endocrinology 13: 863592</a>                                                                                                                      | - Trial that has a treatment and follow up period of less than 24 weeks                                                           |

| Study                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                                                                                                                                               |
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| <a href="#">van Ruiten, Charlotte C, Veltman, Dick J, Schrantee, Anouk et al. (2022) Effects of Dapagliflozin and Combination Therapy With Exenatide on Food-Cue Induced Brain Activation in Patients With Type 2 Diabetes.</a> The Journal of clinical endocrinology and metabolism 107(6): e2590-e2599                         | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                                              |
| <a href="#">Vanderheiden, Anna, Harrison, Lindsay B, Warshauer, Jeremy T et al. (2016) Mechanisms of Action of Liraglutide in Patients With Type 2 Diabetes Treated With High-Dose Insulin.</a> The Journal of clinical endocrinology and metabolism 101(4): 1798-806                                                            | - No relevant outcomes reported                                                                                                                                                                                                                                                      |
| <a href="#">Vargas, Kris G, Rutten, Tobias, Siemes, Benedikt et al. (2024) Assessing the potential for precision medicine in body weight reduction with regard to type 2 diabetes mellitus therapies: A meta-regression analysis of 120 randomized controlled trials.</a> Diabetes, obesity & metabolism                         | - Data not reported in an extractable format or a format that can be analysed<br><i>SR - does not list included studies</i>                                                                                                                                                          |
| <a href="#">Varghese, A., Yee, M. S., Chan, C. F. et al. (2009) Effect of rosiglitazone on progression of atherosclerosis: insights using 3D carotid cardiovascular magnetic resonance.</a> J Cardiovasc Magn Reson 11: 24                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                                                                                                                                        |
| <a href="#">Vart, Priya, Butt, Jawad H, Jongs, Niels et al. (2023) Efficacy and Safety of Dapagliflozin in Patients with Chronic Kidney Disease across the Spectrum of Frailty.</a> The journals of gerontology. Series A, Biological sciences and medical sciences                                                              | - Population not relevant to this review protocol                                                                                                                                                                                                                                    |
| <a href="#">Veleba, J., Janovska, P., Kuda, O. et al. (2015) Combined intervention with pioglitazone and n-3 fatty acids in metformin-treated type 2 diabetic patients: Improvement of lipid metabolism.</a> Nutrition and Metabolism 12(1): 52                                                                                  | - Comparator in study does not match that specified in this review protocol<br><i>Placebo used in the comparison is described as a comparison to the omega-3 rather than to the pioglitazone. Therefore, there is no valid comparison that matches the protocol for this review.</i> |
| <a href="#">Vellanki, Priyathama, Rasouli, Neda, Baldwin, David et al. (2019) Glycaemic efficacy and safety of linagliptin compared to a basal-bolus insulin regimen in patients with type 2 diabetes undergoing non-cardiac surgery: A multicentre randomized clinical trial.</a> Diabetes, obesity & metabolism 21(4): 837-843 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                                                                                              |

| Study                                                                                                                                                                                                                                                                                 | Reason                                                                                                                                       |
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| <a href="#">Vellanki, Priyathama, Smiley, Dawn D, Stefanovski, Darko et al. (2016) Randomized Controlled Study of Metformin and Sitagliptin on Long-term Normoglycemia Remission in African American Patients With Hyperglycemic Crises. Diabetes care 39(11): 1948-1955</a>          | - Population not relevant to this review protocol                                                                                            |
| <a href="#">Vemulapalli, Hema Srikanth, Vajje, Jaahnavi, Rehman, Wajeeh et al. (2023) Safety and Efficacy of Liraglutide on Cardiovascular Outcomes in Patients With Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials. Cureus 15(9): e45421</a>                     | - Systematic review used as source of primary studies                                                                                        |
| <a href="#">Vencio, Sergio, Manosalva, Juan P, Mathieu, Chantal et al. (2021) Exploring early combination strategy in Latin American patients with newly diagnosed type 2 diabetes: a sub-analysis of the VERIFY study. Diabetology &amp; metabolic syndrome 13(1): 68</a>            | - Secondary publication of an included study that does not provide any additional relevant information                                       |
| <a href="#">Verma, R., Moroney, M., Hibino, M. et al. (2023) BASELINE NEUTROPHIL TO LYMPHOCYTE RATIO AND EFFICACY OF SGLT2 INHIBITION WITH EMPAGLIFLOZIN ON CARDIAC REMODELING. Journal of the American College of Cardiology 81(8supplement): 292</a>                                | - Conference abstract                                                                                                                        |
| <a href="#">Verma, S., Bain, S.C., Honore, J.B. et al. (2019) DURATION OF DIABETES AND CARDIORENAL EFFICACY OF LIRAGLUTIDE AND SEMAGLUTIDE: A POST HOC ANALYSIS OF THE LEADER AND SUSTAIN-6 CLINICAL TRIALS. Journal of the American College of Cardiology 73(9supplement1): 1704</a> | - Conference abstract                                                                                                                        |
| <a href="#">Verma, S., Ji, Q., Bhatt, D.L. et al. (2020) The Association Between Uric Acid Levels and Cardio-renal Outcomes and Death in Patients with Type 2 Diabetes: A Subanalysis of EMPA-REG OUTCOME. Diabetes, obesity &amp; metabolism</a>                                     | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis comparing uric acid levels in the EMPA-REG OUTCOME trial</i> |
| <a href="#">Verma, S, Mazer, CD, Al-Omran, M et al. (2018) Cardiovascular outcomes and safety of empagliflozin in patients with type 2 diabetes mellitus and peripheral artery disease: a subanalysis of EMPA-REG OUTCOME. 137: 405-407</a>                                           | - Secondary publication of an included study that does not provide any additional relevant information                                       |

| Study                                                                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                                                                 |
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| <a href="#">Verma, Subodh, Bain, Stephen C, Honore, Julie Broe et al. (2020) Impact of microvascular disease on cardiovascular outcomes in type 2 diabetes: Results from the LEADER and SUSTAIN 6 clinical trials.</a> Diabetes, obesity & metabolism 22(11): 2193-2198                                                                                             | - Secondary publication of an included study that does not provide any additional relevant information                                                                 |
| <a href="#">Verma, Subodh, Mazer, C David, Inzucchi, Silvio E et al. (2021) Impact of polyvascular disease with and without co-existent kidney dysfunction on cardiovascular outcomes in diabetes: A post hoc analysis of EMPA-REG OUTCOME.</a> Diabetes, obesity & metabolism 23(5): 1173-1181                                                                     | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis comparing people with co-existing kidney dysfunction in the EMPA-REG OUTCOME trial</i> |
| <a href="#">Verma, Subodh, Mazer, C David, Yan, Andrew T et al. (2019) Effect of Empagliflozin on Left Ventricular Mass in Patients With Type 2 Diabetes Mellitus and Coronary Artery Disease: The EMPA-HEART CardioLink-6 Randomized Clinical Trial.</a> Circulation 140(21): 1693-1702                                                                            | - Duplicate reference                                                                                                                                                  |
| <a href="#">Verma, Subodh, Poulter Neil, R, Bhatt Deepak, L et al. (2018) Effects of Liraglutide on Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus With or Without History of Myocardial Infarction or Stroke.</a> Circulation 138(25): 2884-2894                                                                                                | - Post-hoc analysis of included study                                                                                                                                  |
| <a href="#">Verma, Subodh, Sharma, Abhinav, Zinman, Bernard et al. (2020) Empagliflozin reduces the risk of mortality and hospitalization for heart failure across Thrombolysis In Myocardial Infarction Risk Score for Heart Failure in Diabetes categories: Post hoc analysis of the EMPA-REG OUTCOME trial.</a> Diabetes, obesity & metabolism 22(7): 1141-1150  | - Secondary publication of an included study that does not provide any additional relevant information                                                                 |
| <a href="#">Vernstrom, Liv, Gullaksen, Soren, Sorensen, Steffen S et al. (2024) Separate and combined effects of empagliflozin and semaglutide on vascular function: A 32-week randomized trial.</a> Diabetes, obesity & metabolism                                                                                                                                 | - Additional outcomes relevant to living guideline work                                                                                                                |
| <a href="#">Viljoen, Adie, Pantalone, Kevin M, Galindo, Rodolfo J et al. (2023) Time to Reach Glycaemic and Body Weight Loss Thresholds with Tirzepatide in Patients with Type 2 Diabetes: A Pre-planned Exploratory Analysis of SURPASS-2 and SURPASS-3.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders 14(5): 925-936 | - Secondary publication of an included study that does not provide any additional relevant information                                                                 |

| Study                                                                                                                                                                                                                                                                                                                                              | Reason                                                                                                 |
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| <a href="#">VilSBoll, T., Ekholm, E., Johnsson, E. et al. (2020) Efficacy and safety of dapagliflozin plus saxagliptin versus insulin glargine over 52weeks as add-on to metformin with or without sulfonylurea in patients with type 2 diabetes: A randomized, parallel-design, open-label, phase 3 trial. Diabetes, obesity &amp; metabolism</a> | - Duplicate reference                                                                                  |
| <a href="#">VilSBoll, T, Zdravkovic, M, Le-thi, TD et al. (2008) Liraglutide significantly improves blood sugar adjustment and reduces body weight, without causing hypoglycaemias, in patients with type-2 diabetes. Medizinische Klinik 103(3): 45</a>                                                                                           | - Conference abstract                                                                                  |
| <a href="#">VilSBoll, Tina, Bain Stephen, C, Leiter Lawrence, A et al. (2018) Semaglutide, reduction in glycated haemoglobin and the risk of diabetic retinopathy. Diabetes, obesity &amp; metabolism 20(4): 889-897</a>                                                                                                                           | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Visolyi, Gergely A, Domjan, Beatrix A, Svebis, Mark M et al. (2023) Comparison of the efficacy and safety of commercially available fixed ratio combinations of insulin degludec/liraglutide (IDegLira) and insulin glargine/lixisenatide (iGlarLixi) - a network meta-analysis. Canadian journal of diabetes</a>                      | - Systematic review used as source of primary studies                                                  |
| <a href="#">Visolyi, Gergely A, Domjan, Beatrix A, Svebis, Mark M et al. (2023) Comparison of Efficacy and Safety of Commercially Available Fixed-Ratio Combinations of Insulin Degludec/Liraglutide and Insulin Glargine/Lixisenatide: A Network Meta-analysis. Canadian journal of diabetes 47(4): 368-377</a>                                   | - Systematic review used as source of primary studies                                                  |
| <a href="#">Volpe, Massimo and Patrono, Carlo (2020) Do VERTIS-CV trial results question a class-effect of cardiovascular protection with sodium-glucose cotransporter 2 inhibitors?. European heart journal 41(44): 4232-4233</a>                                                                                                                 | - Commentary only                                                                                      |
| <a href="#">Vongthavaravat, V., Wajchenberg, B. L., Waitman, J. N. et al. (2002) An international study of the effects of rosiglitazone plus sulphonylurea in patients with type 2 diabetes. Curr Med Res Opin 18(8): 456-61</a>                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Vora, J, Cohen, N, Evans, M et al. (2015) Intensifying insulin regimen after basal insulin optimization in adults with type 2 diabetes: a 24-</a>                                                                                                                                                                                      | - Comparator in study does not match that specified in this review protocol                            |

| Study                                                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                     |
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| <a href="#">week, randomized, open-label trial comparing insulin glargine plus insulin glulisine with biphasic insulin aspart (LanScape).</a> Diabetes, obesity & metabolism 17(12): 1133-41                                                                                                                                                                 |                                                                                                                            |
| <a href="#">Wada, T., Mori-Anai, K., Takahashi, A. et al. (2022) Effect of canagliflozin on the decline of estimated glomerular filtration rate in chronic kidney disease patients with type 2 diabetes mellitus: a multicenter, randomized, double-blind, placebo-controlled, parallel-group, phase 3 study in Japan.</a> Journal of diabetes investigation | - Duplicate reference                                                                                                      |
| <a href="#">Waijer, Simke W, Xie, Di, Inzucchi, Silvio E et al. (2020) Short-Term Changes in Albuminuria and Risk of Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus: A Post Hoc Analysis of the EMPA-REG OUTCOME Trial.</a> Journal of the American Heart Association 9(18): e016976                                                          | - Post-hoc analysis of included study                                                                                      |
| <a href="#">Wajsborg, E., Sriwijitkamol, A., Musi, N. et al. (2007) Relationship between vascular reactivity and lipids in Mexican-Americans with type 2 diabetes treated with pioglitazone.</a> J Clin Endocrinol Metab 92(4): 1256-62                                                                                                                      | - Population not relevant to this review protocol                                                                          |
| <a href="#">Wang, Feiyu, Mao, Yinjun, Wang, Hang et al. (2022) Semaglutide and Diabetic Retinopathy Risk in Patients with Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials.</a> Clinical drug investigation 42(1): 17-28                                                                                                            | - Systematic review used as source of primary studies<br><i>Identified during the rerun search. No additional studies.</i> |
| <a href="#">Wang, G., Wei, J., Guan, Y. et al. (2005) Peroxisome proliferator-activated receptor-gamma agonist rosiglitazone reduces clinical inflammatory responses in type 2 diabetes with coronary artery disease after coronary angioplasty.</a> Metabolism 54(5): 590-7                                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                              |
| <a href="#">Wang, Jie, Li, Hui-Qin, Xu, Xiao-Hua et al. (2019) The Effects of Once-Weekly Dulaglutide and Insulin Glargine on Glucose Fluctuation in Poorly Oral-Antidiabetic Controlled Patients with Type 2 Diabetes Mellitus.</a> BioMed research international 2019: 2682657                                                                             | - Secondary publication of an included study that does not provide any additional relevant information                     |
| <a href="#">Wang, L, Xin, Q, Wang, Y et al. (2021) Efficacy and safety of liraglutide in type 2 diabetes mellitus patients complicated with coronary artery diseases: a systematic review and meta-analysis of randomized controlled trials.</a> Pharmacological research: 105765                                                                            | - Systematic review used as source of primary studies                                                                      |



| Study                                                                                                                                                                                                                                                                                                            | Reason                                                                                                 |
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|                                                                                                                                                                                                                                                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Wang, Lidan, Xin, Qiqi, Wang, Ya et al. (2021) Efficacy and safety of liraglutide in type 2 diabetes mellitus patients complicated with coronary artery disease: A systematic review and meta-analysis of randomized controlled trials.</a> Pharmacological research 171: 105765                     | - Conference abstract                                                                                  |
| <a href="#">Wang, M. M., Lin, S., Chen, Y. M. et al. (2015) Saxagliptin is similar in glycaemic variability more effective in metabolic control than acarbose in aged type 2 diabetes inadequately controlled with metformin.</a> Diabetes Res Clin Pract 108(3): e67-e70                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Wang, Meng-Jun, Liu, Jun-Liang, Wang, Ning et al. (2022) The effectiveness and safety of linagliptin within elderly type 2 diabetes mellitus: a meta-analysis and systematic review.</a> Minerva endocrinology                                                                                       | - Systematic review used as source of primary studies                                                  |
| <a href="#">Wang, Miaomiao, Zhang, Yao, Wang, Zhiyong et al. (2022) The effectiveness of SGLT2 inhibitor in the incidence of atrial fibrillation/atrial flutter in patients with type 2 diabetes mellitus/heart failure: a systematic review and meta-analysis.</a> Journal of thoracic disease 14(5): 1620-1637 | - Population not relevant to this review protocol<br><i>People with and without type 2 diabetes</i>    |
| <a href="#">Wang, Q., Tian, L., Sun, R. et al. (2022) EFFECTS OF SGLT-2 INHIBITORS ON 24H AMBULATORY BLOOD PRESSURE IN PATIENTS WITH TYPE 2 DIABETIC AND HYPERTENSION: A SYSTEMATIC REVIEW AND META-ANALYSIS.</a> Journal of Hypertension 40(supplement1): e184-e185                                             | - Conference abstract                                                                                  |
| <a href="#">Wang, Rui, Luo, Shuoming, Xiao, Zilin et al. (2024) Efficacy and safety of fixed-ratio combination insulin degludec/liraglutide in type 2 diabetes: A systematic review and meta-analysis of randomised controlled trials.</a> Diabetes/metabolism research and reviews 40(3): e3752                 | - Systematic review used as source of primary studies                                                  |
| <a href="#">Wang, X., Zhang, Q., Guan, M. et al. (2020) Exenatide and renal outcomes in patients with type 2 diabetes and diabetic kidney disease: A</a>                                                                                                                                                         | - Conference abstract                                                                                  |

| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                                                                                   |
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| <a href="#">multicenter, randomized, parallel study.</a><br>Diabetes 69(supplement1)                                                                                                                                                                                                                                         |                                                                                                                                                          |
| <a href="#">Wang, Xianghong, Wu, Niujian, Sun, Chuanchuan et al. (2023) Effects of SGLT-2 inhibitors on adipose tissue distribution in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials.</a> Diabetology & metabolic syndrome 15(1): 113                        | - No relevant outcomes reported                                                                                                                          |
| <a href="#">Wang, Xiaonan, Fu, Ran, Liu, Hongtao et al. (2021) The effects of sodium glucose co-transporter (SGLT) 2 inhibitors on hematocrit levels: a systematic review and meta-analysis of randomized controlled trials.</a> Annals of palliative medicine 10(6): 6467-6481                                              | - Systematic review used as source of primary studies<br><i>Identified in rerun search. No additional studies to add.</i>                                |
| <a href="#">Wang, Xingyue, Wang, You, Hou, Junjie et al. (2024) Plasma proteome profiling reveals the therapeutic effects of the PPAR pan-agonist chiglitazar on insulin sensitivity, lipid metabolism, and inflammation in type 2 diabetes.</a> Scientific reports 14(1): 638                                               | - Post-hoc analysis of included study                                                                                                                    |
| <a href="#">Wang, Yang and Xia, Ning (2022) Influence of Sodium-Glucose Cotransporter-2 Inhibitors on Plasma Adiponectin in Patients with Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials.</a> Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme 54(12): 833-844 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                            |
| <a href="#">Wang, Yao; Shao, Xian; Liu, Zewen (2022) Efficacy and safety of sodium-glucose co-transporter 2 inhibitors in the elderly versus non-elderly patients with type 2 diabetes mellitus: a meta-analysis.</a> Endocrine journal 69(6): 669-679                                                                       | - Comparator in study does not match that specified in this review protocol<br><i>Compares in younger and older people, not relevant to our protocol</i> |
| <a href="#">Wanner, C., Naderali, E., Maldonado, M. et al. (2016) Empagliflozin as add-on to linagliptin and metformin in patients with type 2 diabetes (T2DM): Subgroup analysis by region in a 24-week randomized trial.</a> Diabetes 65(supplement1): a288-a289                                                           | - Conference abstract                                                                                                                                    |
| <a href="#">Wanner, C, Inzucchi S, E, Zinman, B et al. (2020) Consistent effects of empagliflozin on cardiovascular and kidney outcomes irrespective of diabetic kidney disease categories: Insights from the EMPA-REG OUTCOME trial.</a> Diabetes, Obesity and Metabolism 22(12): 2335-2347                                 | - Post-hoc analysis of included study                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                             | Reason                                                                                                                                             |
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| <a href="#">Wanner, Christoph, Cooper, Mark E, Johansen, Odd Erik et al. (2021) Effect of linagliptin versus placebo on cardiovascular and kidney outcomes in nephrotic-range proteinuria and type 2 diabetes: the CARMELINA randomized controlled trial. Clinical kidney journal 14(1): 226-236</a>                              | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Wanner, Christoph, Cooper, Mark E, Johansen, Odd Erik et al. (2021) Erratum to: Effect of linagliptin versus placebo on cardiovascular and kidney outcomes in nephrotic-range proteinuria and type 2 diabetes (t2d): the carmelina randomised controlled trial. Clinical kidney journal 14(9): 2136</a>               | - Commentary only                                                                                                                                  |
| <a href="#">Wanner, Christoph, Heerspink Hiddo J, L, Zinman, Bernard et al. (2018) Empagliflozin and Kidney Function Decline in Patients with Type 2 Diabetes: A Slope Analysis from the EMPA-REG OUTCOME Trial. Journal of the American Society of Nephrology : JASN 29(11): 2755-2769</a>                                       | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Wanner, Christoph, Inzucchi Silvio, E, Lachin John, M et al. (2016) Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes. The New England journal of medicine 375(4): 323-34</a>                                                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Wanner, Christoph, Nangaku, Masaomi, Kraus, Bettina J et al. (2024) How do SGLT2 inhibitors protect the kidney? A mediation analysis of the EMPA-REG OUTCOME trial. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association</a> | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Watanabe, I., Tani, S., Anazawa, T. et al. (2005) Effect of pioglitazone on arteriosclerosis in comparison with that of glibenclamide. Diabetes Res Clin Pract 68(2): 104-10</a>                                                                                                                                      | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                      |
| <a href="#">Watts, Nelson B, Bilezikian, John P, Usiskin, Keith et al. (2016) Effects of Canagliflozin on Fracture Risk in Patients With Type 2 Diabetes Mellitus. The Journal of clinical endocrinology and metabolism 101(1): 157-66</a>                                                                                        | - Review article but not a systematic review<br><i>Pooled analysis of multiple RCTs investigating a outcome that is not relevant to the review</i> |
| <a href="#">Webb, D.R., Htike, Z.Z., Swarbrick, D.J. et al. (2020) A randomised, open label, active comparator trial assessing the effects of</a>                                                                                                                                                                                 | - Duplicate reference                                                                                                                              |

| Study                                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                   |
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| <a href="#">26weeks of liraglutide or sitagliptin on cardiovascular function in young obese adults with type 2 diabetes.</a> Diabetes, obesity & metabolism                                                                                                                                                                                          |                                                                                                                          |
| <a href="#">Weber, Michael A, Mansfield, Traci A, Cain, Valerie A et al. (2016) Blood pressure and glycaemic effects of dapagliflozin versus placebo in patients with type 2 diabetes on combination antihypertensive therapy: a randomised, double-blind, placebo-controlled, phase 3 study.</a> The lancet. Diabetes & endocrinology 4(3): 211-220 | - Trial that has a treatment and follow up period of less than 24 weeks                                                  |
| <a href="#">Wei, Jinjing, Wang, Ruxin, Ye, Haowen et al. (2022) Effects of GLP-1 receptor agonists on arrhythmias and its subtypes in patients with type 2 diabetes: A systematic review and meta-analysis.</a> Frontiers in endocrinology 13: 910256                                                                                                | - Systematic review used as source of primary studies                                                                    |
| <a href="#">Wei, Jinjing, Yang, Bing, Wang, Ruxin et al. (2022) Risk of stroke and retinopathy during GLP-1 receptor agonist cardiovascular outcome trials: An eight RCTs meta-analysis.</a> Frontiers in endocrinology 13: 1007980                                                                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                                                  |
| <a href="#">Wei, Qiong, Xu, Xinyue, Guo, Li et al. (2021) Effect of SGLT2 Inhibitors on Type 2 Diabetes Mellitus With Non-Alcoholic Fatty Liver Disease: A Meta-Analysis of Randomized Controlled Trials.</a> Frontiers in endocrinology 12: 635556                                                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                                                  |
| <a href="#">Wei, Ran, Wang, Weihao, Pan, Qi et al. (2022) Effects of SGLT-2 Inhibitors on Vascular Endothelial Function and Arterial Stiffness in Subjects With Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.</a> Frontiers in endocrinology 13: 826604                                                    | - Study design not relevant to this review protocol<br><br><i>Systematic review that includes non-randomised studies</i> |
| <a href="#">Wei, Xu-Bin, Wei, Wei, Ding, Liang-Liang et al. (2021) Comparison of the effects of 10 GLP-1 RA and SGLT2 inhibitor interventions on cardiovascular, mortality, and kidney outcomes in type 2 diabetes: A network meta-analysis of large randomized trials.</a> Primary care diabetes 15(2): 208-211                                     | - Trial that has a treatment and follow up period of less than 24 weeks                                                  |
| <a href="#">Weingold, R., Zinman, B., Mattheus, M. et al. (2023) Shifts in KDIGO CKD risk groups with empagliflozin: Kidney-protection from SGLT2 inhibition across the spectrum of risk.</a> Journal of Diabetes and its Complications 37(11): 108628                                                                                               | - No relevant outcomes reported                                                                                          |

| Study                                                                                                                                                                                                                                                                                                                          | Reason                                                                                                                                       |
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| <a href="#">Weir, Matthew R, Gogate, Jagadish, Damaraju, C V et al. (2022) Effects of canagliflozin on major adverse cardiovascular events by baseline estimated glomerular filtration rate: Pooled Hispanic subgroup analyses from the CANVAS Program and CREDENCE trial. Diabetes, obesity &amp; metabolism 24(1): 12-20</a> | - Secondary publication of an included study that does not provide any additional relevant information                                       |
| <a href="#">Weissman, P. N., Carr, M. C., Ye, J. et al. (2014) HARMONY 4: randomised clinical trial comparing once-weekly albiglutide and insulin glargine in patients with type 2 diabetes inadequately controlled with metformin with or without sulfonylurea. Diabetologia 57(12): 2475-84</a>                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                |
| <a href="#">Weng, J., Li, Y., Xu, W. et al. (2008) Effect of intensive insulin therapy on beta-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial. The Lancet 371(9626): 1753-1760</a>                                                        | - Study does not contain an intervention relevant to this review protocol                                                                    |
| <a href="#">Weng, J., Zeng, L., Zhang, Y. et al. (2021) Henagliflozin as add-on therapy to metformin in patients with type 2 diabetes inadequately controlled with metformin: A multicentre, randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes, Obesity &amp; Metabolism 23(8): 1754-1764</a>              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                |
| <a href="#">Wexler, Deborah J, de Boer, Ian H, Ghosh, Alokanda et al. (2023) Comparative Effects of Glucose-Lowering Medications on Kidney Outcomes in Type 2 Diabetes: The GRADE Randomized Clinical Trial. JAMA internal medicine</a>                                                                                        | - Comparator in study does not match that specified in this review protocol                                                                  |
| <a href="#">Wharton, S., Meincke, H.H., Kushner, R.F. et al. (2021) Semaglutide 2.4 mg improves patient reported outcome measures of physical functioning in adults with overweight/obesity and type 2 diabetes in the step 2 trial. Diabetes 70(suppl1)</a>                                                                   | - Conference abstract                                                                                                                        |
| <a href="#">Wharton, Sean, Calanna, Salvatore, Davies, Melanie et al. (2022) Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss. Diabetes, obesity &amp; metabolism 24(1): 94-105</a>          | - Study design not relevant to this review protocol<br><br><i>Pooled analysis of three trials which are already included in the analysis</i> |

| Study                                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                 |
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| <a href="#">Wheeler, D.C., Dekkers, C., Sjostrom, D. et al. (2017) Effect of the SGLT2 inhibitor dapagliflozin in patients with type 2 diabetes and stages 3b-4 CKD. Journal of the American Society of Nephrology 28: 61</a>                                                                                                          | - Conference abstract                                                                                  |
| <a href="#">Wheeler, D.C., Toto, R.D., Stefansson, B.V. et al. (2021) A pre-specified analysis of the DAPA-CKD trial indicates effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. Kidney international</a>                                                                                      | - Population not relevant to this review protocol                                                      |
| <a href="#">Wheeler, David C, Stefansson, Bergur V, Jongs, Niels et al. (2021) Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. The lancet. Diabetes &amp; endocrinology 9(1): 22-31</a> | - Population not relevant to this review protocol                                                      |
| <a href="#">White William, B, Heller Simon, R, Cannon Christopher, P et al. (2018) Alogliptin in Patients with Type 2 Diabetes Receiving Metformin and Sulfonylurea Therapies in the EXAMINE Trial. The American journal of medicine 131(7): 813-819e5</a>                                                                             | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">White William, B, Jalil, Fatima, Cushman William, C et al. (2018) Average Clinician-Measured Blood Pressures and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Ischemic Heart Disease in the EXAMINE Trial. Journal of the American Heart Association 7(20): e009114</a>                           | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">White William, B, Kupfer, Stuart, Zannad, Faiez et al. (2016) Cardiovascular Mortality in Patients With Type 2 Diabetes and Recent Acute Coronary Syndromes From the EXAMINE Trial. Diabetes care 39(7): 1267-73</a>                                                                                                       | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">White, W.B., Wilson, C., Bakris, G. et al. (2015) Ace inhibitor use and major cardiovascular outcomes in type 2 diabetes treated with the DPP-4 inhibitor alogliptin. Journal of the American College of Cardiology 65(10suppl1): a1411</a>                                                                                | - Conference abstract                                                                                  |
| <a href="#">White, William B, Bakris, George L, Bergenstal, Richard M et al. (2011) EXamination of cArdiovascular outcoMes with alogliptIN versus standard of carE in patients with type 2 diabetes</a>                                                                                                                                | - Study design                                                                                         |



| Study                                                                                                                                                                                                                                                                                                      | Reason                                                                                                                                                                                                             |
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| <a href="#">mellitus and acute coronary syndrome (EXAMINE): a cardiovascular safety study of the dipeptidyl peptidase 4 inhibitor alogliptin in patients with type 2 diabetes with acute coronary syndrome.</a> American heart journal 162(4): 620-626e1                                                   |                                                                                                                                                                                                                    |
| <a href="#">White, William B, Wilson, Craig A, Bakris, George L et al. (2016) Angiotensin-Converting Enzyme Inhibitor Use and Major Cardiovascular Outcomes in Type 2 Diabetes Mellitus Treated With the Dipeptidyl Peptidase 4 Inhibitor Alogliptin.</a> Hypertension (Dallas, Tex. : 1979) 68(3): 606-13 | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Secondary analysis of the EXAMINE trial results by whether people were using an ACE inhibitor</i> |
| <a href="#">Widiarti, Wynne, Sukmajaya, Alverina Cynthia, Nugraha, David et al. (2021) Cardioprotective properties of glucagon-like peptide-1 receptor agonists in type 2 diabetes mellitus patients: A systematic review.</a> Diabetes & metabolic syndrome 15(3): 837-843                                | - Study design not relevant to this review protocol<br><br><i>Systematic review that includes non-randomised studies</i>                                                                                           |
| <a href="#">Wilcox, Robert, Bousser, Marie-Germaine, Betteridge D, John et al. (2007) Effects of pioglitazone in patients with type 2 diabetes with or without previous stroke: results from PROactive (PROspective pioglitAzone Clinical Trial In macroVascular Events 04).</a> Stroke 38(3): 865-73      | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                             |
| <a href="#">Wilding, J., Mathieu, C., Deng, L. et al. (2012) Canagliflozin, a sodium glucose co-transporter 2 inhibitor, improves glycaemia in subjects with type 2 diabetes inadequately controlled with metformin plus sulphonylurea.</a> Diabetologia 55(suppl1): 315-s316                              | - Conference abstract                                                                                                                                                                                              |
| <a href="#">Wilding, J.P.H., Batterham, R.L., Calanna, S. et al. (2021) Efficacy and Safety of Once-Weekly Subcutaneous Semaglutide 2.4 MG in Adults With Overweight or Obesity (STEP 1).</a> Journal of the Endocrine Society 5(supplement1): a10                                                         | - Conference abstract                                                                                                                                                                                              |
| <a href="#">Wilding, John P H, Blonde, Lawrence, Leiter, Lawrence A et al. (2015) Efficacy and safety of canagliflozin by baseline HbA1c and known duration of type 2 diabetes mellitus.</a> Journal of diabetes and its complications 29(3): 438-44                                                       | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                             |
| <a href="#">Wilding, JP, Woo, V, Soler, NG et al. (2013) Long-term efficacy of dapagliflozin in patients with type 2 diabetes mellitus receiving high</a>                                                                                                                                                  | - Study not reported in English                                                                                                                                                                                    |

| Study                                                                                                                                                                                                                                                                                                                  | Reason                                                                                                                                                                                                                                        |
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| <a href="#">doses of insulin</a> . Deutsche medizinische Wochenschrift (1946) 138suppl1: S27-38                                                                                                                                                                                                                        |                                                                                                                                                                                                                                               |
| <a href="#">Williams-Herman, D, Johnson, J, Teng, R et al. (2010) Efficacy and safety of sitagliptin and metformin as initial combination therapy and as monotherapy over 2 years in patients with type 2 diabetes</a> . Diabetes, obesity & metabolism 12(5): 442-51                                                  | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Extension study without all comparisons as placebo arm switched at 24 weeks. 24 week outcomes taken from Goldstein 2007.</i> |
| <a href="#">Williams-Herman, Debora, Johnson, Jeremy, Teng, Rujun et al. (2009) Efficacy and safety of initial combination therapy with sitagliptin and metformin in patients with type 2 diabetes: a 54-week study</a> . Current medical research and opinion 25(3): 569-83                                           | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Extension study without all comparisons as placebo arm switched at 24 weeks. 24 week outcomes taken from Goldstein 2007.</i> |
| <a href="#">Wilson, C. and Fleck, P. (2012) Effect of alogliptin in combination with pioglitazone on glycaemic control by baseline HbA1c</a> . Diabetologia 55(suppl1): 348                                                                                                                                            | - Conference abstract                                                                                                                                                                                                                         |
| <a href="#">Wilson, J., Nikooienejad, A., Lin, Y. et al. (2021) The dual gip and GLP-1 receptor agonist tirzepatide improves biomarkers associated with cardiovascular risk in patients with type 2 diabetes (T2D)</a> . Diabetes Technology and Therapeutics 23(suppl2): a164-a165                                    | - Conference abstract                                                                                                                                                                                                                         |
| <a href="#">Wilson, J.M., Lin, Y., Considine, G. et al. (2020) The Dual GIP/GLP-1 Receptor Agonist Tirzepatide Improves Cardiovascular Risk Protein Biomarkers in Patients with Type 2 Diabetes</a> . Circulation 142(suppl3)                                                                                          | - Conference abstract                                                                                                                                                                                                                         |
| <a href="#">Wilson, J.M., Nikooienejad, A., Bowsman, L.M. et al. (2019) The dual GIP/GLP-1 receptor agonist tirzepatide improves lipoprotein biomarkers associated with insulin resistance and cardiovascular risk in patients with type 2 diabetes</a> . Diabetologia 62(supplement1): 558-s559                       | - Conference abstract                                                                                                                                                                                                                         |
| <a href="#">Wilson, Jonathan M, Nikooienejad, Amir, Robins, Deborah A et al. (2020) The dual glucose-dependent insulintropic peptide and glucagon-like peptide-1 receptor agonist, tirzepatide, improves lipoprotein biomarkers associated with insulin resistance and cardiovascular risk in patients with type 2</a> | - Post-hoc analysis of included study                                                                                                                                                                                                         |

| Study                                                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                 |
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| <a href="#">diabetes</a> . Diabetes, obesity & metabolism 22(12): 2451-2459                                                                                                                                                                                                                                                                             |                                                                                                        |
| <a href="#">Wojeck, Brian S, Inzucchi, Silvio E, Neeland, Ian J et al. (2022) Ertugliflozin and incident obstructive sleep apnea: an analysis from the VERTIS CV trial</a> . Sleep & breathing = Schlaf & Atmung                                                                                                                                        | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Wolffenbittel, B. H., Gomis, R., Squatrito, S. et al. (2000) Addition of low-dose rosiglitazone to sulphonylurea therapy improves glycaemic control in Type 2 diabetic patients</a> . Diabetic Med 17(1): 40-7                                                                                                                              | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Wolffenbittel, B. H. and Landgraf, R. (1999) A 1-year multicenter randomized double-blind comparison of repaglinide and glyburide for the treatment of type 2 diabetes. Dutch and German Repaglinide Study Group</a> . Diabetes Care 22(3): 463-7                                                                                           | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Wollenhaupt, Dominik, Wolters, Jannik, Abd El Aziz, Mirna et al. (2023) Impact of concomitant oral glucose-lowering medications on the success of basal insulin titration in insulin-naïve patients with type 2 diabetes: a systematic analysis</a> . BMJ open diabetes research & care 11(4)                                               | - Systematic review used as source of primary studies                                                  |
| <a href="#">Wong, E., Cope, R., Dima, L. et al. (2023) Erratum: Tirzepatide: A Dual Glucose-Dependent Insulinotropic Polypeptide and Glucagon-Like Peptide-1 Agonist for the Management of Type 2 Diabetes Mellitus (Am J Ther. (2023) 30 (e26-e35) DOI: 10.1097/MJT.0000000000001588)</a> . American Journal of Therapeutics 30(3): e311               | - Commentary only                                                                                      |
| <a href="#">Wong, John; Chan, Kwan Yi; Lo, Kenneth (2021) Sodium-glucose co-transporter 2 inhibitors on weight change and cardiometabolic profiles in individuals with overweight or obesity and without diabetes: A meta-analysis</a> . Obesity reviews : an official journal of the International Association for the Study of Obesity 22(12): e13336 | - Population not relevant to this review protocol<br><i>People without diabetes</i>                    |
| <a href="#">Wong, T. Y., Szeto, C. C., Chow, K. M. et al. (2005) Rosiglitazone reduces insulin requirement and C-reactive protein levels in type 2 diabetic patients receiving peritoneal dialysis</a> . Am J Kidney Dis 46(4): 713-9                                                                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |

| Study                                                                                                                                                                                                                                                                                                                                                | Reason                                                                                                                                                                    |
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| <a href="#">Woodhams, Louise M, Chalmers, Leanne, Sim, Tin Fei et al. (2023) Efficacy and safety of sodium glucose cotransporter 2 inhibitors plus standard care in diabetic kidney disease: A systematic review and meta-analysis.</a> Journal of diabetes and its complications 37(6): 108456                                                      | - Comparator in study does not match that specified in this review protocol                                                                                               |
| <a href="#">Wu, Li-Da, Zhou, Nan, Sun, Jin-Yu et al. (2022) Effects of sitagliptin on serum lipid levels in patients with type 2 diabetes: a systematic review and meta-analysis.</a> Journal of cardiovascular medicine (Hagerstown, Md.) 23(5): 308-317                                                                                            | - Systematic review used as source of primary studies                                                                                                                     |
| <a href="#">Wu, Qian-Long, Zheng, Ting, Li, Sheng-Zhen et al. (2022) Effects of dapagliflozin in the progression of atherosclerosis in patients with type 2 diabetes: a meta-analysis of randomized controlled trials.</a> Diabetology & metabolic syndrome 14(1): 41                                                                                | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                   |
| <a href="#">Wu, Sijin, Lu, Wenzhao, Chen, Zhongli et al. (2022) Association of glucagon-like peptide-1 receptor agonists with cardiac arrhythmias in patients with type 2 diabetes or obesity: a systematic review and meta-analysis of randomized controlled trials.</a> Diabetology & metabolic syndrome 14(1): 195                                | - Systematic review used as source of primary studies<br><br><i>Includes trials of medication that is no longer used in the UK. Otherwise studies already identified.</i> |
| <a href="#">Wu, Tingting, Wong, Carlos K H, Lui, David T W et al. (2023) Bariatric surgery, novel glucose-lowering agents, and insulin for type 2 diabetes and obesity: Bayesian network meta-analysis of randomized controlled trials.</a> BJS open 7(4)                                                                                            | - Study does not contain an intervention relevant to this review protocol                                                                                                 |
| <a href="#">Wysham, Carol H, Rosenstock, Julio, Vetter, Marion L et al. (2018) Efficacy and tolerability of the new autoinjected suspension of exenatide once weekly versus exenatide twice daily in patients with type 2 diabetes.</a> Diabetes, obesity & metabolism 20(1): 165-172                                                                | - Comparator in study does not match that specified in this review protocol<br><br><i>Compares two different formulations of the same medication</i>                      |
| <a href="#">Wysham, Carol H, Rosenstock, Julio, Vetter, Marion L et al. (2020) Further improvement in glycemic control after switching from exenatide two times per day to exenatide once-weekly autoinjected suspension in patients with type 2 diabetes: 52-week results from the DURATION-NEO-1 study.</a> BMJ open diabetes research & care 8(1) | - Study design not relevant to this review protocol                                                                                                                       |

| Study                                                                                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                 |
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| <a href="#">Wysham, Carol, Blevins, Thomas, Arakaki, Richard et al. (2015) Erratum. Efficacy and Safety of Dulaglutide Added Onto Pioglitazone and Metformin Versus Exenatide in Type 2 Diabetes in a Randomized Controlled Trial (AWARD-1). Diabetes Care 2014;37:2159-2167. Diabetes care 38(7): 1393-4</a>                                                                                              | - Commentary only                                                                                      |
| <a href="#">Wysham, Carol, Bonadonna, Riccardo C, Aroda, Vanita R et al. (2017) Consistent findings in glycaemic control, body weight and hypoglycaemia with iGlarLixi (insulin glargine/lixisenatide titratable fixed-ratio combination) vs insulin glargine across baseline HbA1c, BMI and diabetes duration categories in the LixiLan-L trial. Diabetes, obesity &amp; metabolism 19(10): 1408-1415</a> | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Xia, Lin, Shen, Tiantian, Dong, Wenliang et al. (2021) Comparative efficacy and safety of 8 GLP-1RAs in patients with type 2 diabetes: A network meta-analysis. Diabetes research and clinical practice 177: 108904</a>                                                                                                                                                                        | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK          |
| <a href="#">Xiao, X., Wang, C., Lai, X. et al. (2019) Achieving composite endpoint of glycated haemoglobin &lt;7.0% without weight gain or hypoglycemia with once-weekly dulaglutide in Chinese patients with type 2 diabetes: A post-hoc analysis. Journal of diabetes investigation</a>                                                                                                                  | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Xie, Zeyu, Hu, Jia, Gu, Hangye et al. (2023) Comparison of the efficacy and safety of 10 glucagon-like peptide-1 receptor agonists as add-on to metformin in patients with type 2 diabetes: a systematic review. Frontiers in endocrinology 14: 1244432</a>                                                                                                                                    | - Systematic review used as source of primary studies                                                  |
| <a href="#">Xu, Bo; Kang, Bo; Zhou, Jiecan (2024) Sodium glucose cotransporter 2 inhibitors with cardiac arrhythmias in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized placebo-controlled trials. Clinical research in cardiology : official journal of the German Cardiac Society</a>                                                                        | - Systematic review used as source of primary studies                                                  |
| <a href="#">Xu, Chunmei, He, Liping, Zhang, Jing et al. (2022) The Cardiovascular Benefits and Infections Risk of SGLT2i versus Metformin in Type 2 Diabetes: A Systemic Review and Meta-Analysis. Metabolites 12(10)</a>                                                                                                                                                                                  | - Systematic review used as source of primary studies                                                  |

| Study                                                                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                 |
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| <a href="#">Xu, J., Ling, H., Geng, J. et al. (2022) Efficacy and safety of DBPR108 (prusogliptin) as an add-on to metformin therapy in patients with type 2 diabetes: A 24-week, multi-centre, randomized, double-blind, placebo-controlled, superiority, phase III clinical trial.</a> Diabetes, Obesity and Metabolism 24(11): 2232-2240                               | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                          |
| <a href="#">Xu, Xuezhong, Xu, Wen, Zhuo, Qingqing et al. (2022) The efficacy and safety of dapagliflozin combined with oral hypoglycemic agents in patients with type 2 diabetes: a systematic review and meta-analysis.</a> Annals of palliative medicine 11(3): 1028-1037                                                                                               | - Systematic review used as source of primary studies<br><br><i>Identified in rerun search. No additional studies to add.</i>                          |
| <a href="#">Yabe, Daisuke, Eto, Takashi, Shiramoto, Masanari et al. (2017) Effects of DPP-4 inhibitor linagliptin and GLP-1 receptor agonist liraglutide on physiological response to hypoglycaemia in Japanese subjects with type 2 diabetes: A randomized, open-label, 2-arm parallel comparative, exploratory trial.</a> Diabetes, obesity & metabolism 19(3): 442-447 | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                |
| <a href="#">Yabe, Daisuke, Kawamori, Dan, Seino, Yusuke et al. (2023) Change in pharmacodynamic variables following once-weekly tirzepatide treatment versus dulaglutide in Japanese patients with type 2 diabetes (SURPASS J-mono substudy).</a> Diabetes, obesity & metabolism 25(2): 398-406                                                                           | - Secondary publication of an included study that does not provide any additional relevant information                                                 |
| <a href="#">Yadav, P.; Joshi, B.; Geetha Bhavani, A. (2022) CLINICAL DIAGNOSIS and SAFETY of VILDAGLIPTIN VERSUS GLIMEPIRIDE with METFORMIN over PATIENTS of TYPE-2 DIABETES MELLITUS.</a> International Journal of Pharmaceutical Sciences and Research 13(1): 384-391                                                                                                   | - Study design not relevant to this review protocol                                                                                                    |
| <a href="#">Yaggi, H.K., Eliasson, B., Kasai, T. et al. (2020) Obstructive sleep apnoe and cardiovascular, heart failure and mortality outcomes with empagliflozin versus placebo in the EMPA-REG OUTCOME trial.</a> European Heart Journal 41(suppl2): 2883                                                                                                              | - Conference abstract                                                                                                                                  |
| <a href="#">Yagoglu, A. I., Dizdar, O. S., Erdem, S. et al. (2020) The effect of linagliptin on renal progression in type-2 diabetes mellitus patients with chronic kidney disease: A prospective randomized controlled study.</a> Nefrologia 40(6): 664-671                                                                                                              | - Comparator in study does not match that specified in this review protocol<br><br><i>Usual care comparator which is not specified in the protocol</i> |



| Study                                                                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                                                                             |
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| <a href="#">Yale, Jean-Francois, Xie, John, Sherman Stephen, E et al. (2017) Canagliflozin in Conjunction With Sulfonylurea Maintains Glycemic Control and Weight Loss Over 52 Weeks: A Randomized, Controlled Trial in Patients With Type 2 Diabetes Mellitus. Clinical therapeutics 39(11): 2230-2242e2</a>                                                                                   | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Yale, JF, Bakris, G, Cariou, B et al. (2015) Efficacy and safety of canagliflozin (CANA) in subjects with type 2 diabetes mellitus T2DM) and chronic kidney disease (CKD) over 52 weeks. Canadian journal of diabetes 37(suppl4): 27</a>                                                                                                                                            | - Conference abstract                                                                                                                              |
| <a href="#">Yamada, Hirotugu, Tanaka, Atsushi, Kusunose, Kenya et al. (2017) Effect of sitagliptin on the echocardiographic parameters of left ventricular diastolic function in patients with type 2 diabetes: a subgroup analysis of the PROLOGUE study. Cardiovascular diabetology 16(1): 63</a>                                                                                             | - Comparator in study does not match that specified in this review protocol                                                                        |
| <a href="#">Yamada, Takayuki, Wakabayashi, Mako, Bhalla, Abhinav et al. (2021) Cardiovascular and renal outcomes with SGLT-2 inhibitors versus GLP-1 receptor agonists in patients with type 2 diabetes mellitus and chronic kidney disease: a systematic review and network meta-analysis. Cardiovascular diabetology 20(1): 14</a>                                                            | - Systematic review used as source of primary studies<br><i>Identified in rerun search. No additional studies to add.</i>                          |
| <a href="#">Yamaguchi, S, Shimabukuro, M, Tanaka, A et al. (2022) Canagliflozin reduces proteinuria by targeting hyperinsulinemia in diabetic patients with heart failure: a post-hoc analysis of the CANDLE trial. Diabetes, obesity &amp; metabolism</a>                                                                                                                                      | - Study design not relevant to this review protocol<br><i>post hoc analysis</i>                                                                    |
| <a href="#">Yamakage, H., Tanaka, M., Inoue, T. et al. (2020) Effects of dapagliflozin on the serum levels of fibroblast growth factor 21 and myokines and muscle mass in Japanese patients with type 2 diabetes: A randomized, controlled trial. Journal of Diabetes Investigation 11(3): 653-661</a>                                                                                          | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Yamamoto, S., Hayashi, T., Ohara, M. et al. (2018) Comparison of liraglutide plus basal insulin and basal-bolus insulin therapy (BBIT) for glycemic control, body weight stability, and treatment satisfaction in patients treated using BBIT for type 2 diabetes without severe insulin deficiency: A randomized prospective pilot study. Diabetes Res Clin Pract 140: 339-346</a> | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i>                          |

| Study                                                                                                                                                                                                                                                                                                                                           | Reason                                                                                             |
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| <a href="#">Yamasaki, Y., Katakami, N., Hayaishi-Okano, R. et al. (2005) alpha-Glucosidase inhibitor reduces the progression of carotid intima-media thickness. Diabetes Res Clin Pract 67(3): 204-10</a>                                                                                                                                       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK      |
| <a href="#">Yanai, Hidekatsu, Adachi, Hiroki, Hakoshima, Mariko et al. (2023) Glucagon-Like Peptide 1 Receptor Agonists Versus Sodium-Glucose Cotransporter 2 Inhibitors for Atherosclerotic Cardiovascular Disease in Patients With Type 2 Diabetes. Cardiology research 14(1): 12-21</a>                                                      | - Review article but not a systematic review                                                       |
| <a href="#">Yang, H. K., Min, K. W., Park, S. W. et al. (2015) A randomized, placebo-controlled, double-blind, phase 3 trial to evaluate the efficacy and safety of anagliptin in drug-naïve patients with type 2 diabetes. Endocr J 62(5): 449-62</a>                                                                                          | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK      |
| <a href="#">Yang, Qing, Lang, Yanlin, Yang, Wenjie et al. (2023) Efficacy and safety of drugs for people with type 2 diabetes mellitus and chronic kidney disease on kidney and cardiovascular outcomes: A systematic review and network meta-analysis of randomized controlled trials. Diabetes research and clinical practice 198: 110592</a> | - Comparator in study does not match that specified in this review protocol                        |
| <a href="#">Yang, S. J., Min, K. W., Gupta, S. K. et al. (2013) A multicentre, multinational, randomized, placebo-controlled, double-blind, phase 3 trial to evaluate the efficacy and safety of gemigliptin (LC15-0444) in patients with type 2 diabetes. Diabetes Obes Metab 15(5): 410-6</a>                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK      |
| <a href="#">Yang, S, Shen, W, Zhang, HZ et al. (2023) Efficacy and Safety of Finerenone for Prevention of Cardiovascular Events in Type 2 Diabetes Mellitus with Chronic Kidney Disease: A Meta-analysis of Randomized Controlled Trials. Journal of cardiovascular pharmacology 81(1): 55-62</a>                                               | - Study does not contain an intervention relevant to this review protocol<br><br><i>Finerenone</i> |
| <a href="#">Yang, Shiwen, Liu, Ying, Zhang, Shengzhao et al. (2023) Risk of diabetic ketoacidosis of SGLT2 inhibitors in patients with type 2 diabetes: a systematic review and network meta-analysis of randomized controlled trials. Frontiers in pharmacology 14: 1145587</a>                                                                | - Systematic review used as source of primary studies                                              |
| <a href="#">Yang, Shuo, Zhao, Lu, Mi, Yaochuan et al. (2022) Effects of sodium-glucose cotransporter-</a>                                                                                                                                                                                                                                       | - Systematic review used as source of primary studies                                              |

| Study                                                                                                                                                                                                                                                                                                                    | Reason                                                                                                                                                    |
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| <a href="#">2 inhibitors and aldosterone antagonists, in addition to renin-angiotensin system antagonists, on major adverse kidney outcomes in patients with type 2 diabetes and chronic kidney disease: A systematic review and network meta-analysis.</a> Diabetes, obesity & metabolism 24(11): 2159-2168             | <i>Identified after the rerun search. No additional studies (otherwise includes studies discussing finerenone which is not relevant to the protocol).</i> |
| <a href="#">Yang, W. S., Jeng, C. Y., Wu, T. J. et al. (2002) Synthetic peroxisome proliferator-activated receptor-gamma agonist, rosiglitazone, increases plasma levels of adiponectin in type 2 diabetic patients.</a> Diabetes Care 25(2): 376-80                                                                     | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                             |
| <a href="#">Yang, W., Shan, Z., Tian, H. et al. (2014) Acarbose compared with metformin as initial therapy in patients with newly diagnosed type 2 diabetes: An open-label, non-inferiority randomised trial.</a> Lancet Diabetes Endocrinol 2(1): 46-55                                                                 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                             |
| <a href="#">Yang, Wenying, Ma, Jianhua, Hong, Tianpei et al. (2019) Efficacy and safety of insulin degludec/insulin aspart versus biphasic insulin aspart 30 in Chinese adults with type 2 diabetes: A phase III, open-label, 2:1 randomized, treat-to-target trial.</a> Diabetes, obesity & metabolism 21(7): 1652-1660 | - Comparator in study does not match that specified in this review protocol<br><i>Compares different types of insulin</i>                                 |
| <a href="#">Yang, Wenying, Xu, Xiangjin, Liu, Xiaomin et al. (2013) Treat-to-target comparison between once daily biphasic insulin aspart 30 and insulin glargine in Chinese and Japanese insulin-naïve subjects with type 2 diabetes.</a> Current medical research and opinion 29(12): 1599-608                         | - Study does not contain an intervention relevant to this review protocol                                                                                 |
| <a href="#">Yang, X-Y, Yin, S, Yu, Y-F et al. (2023) Is tirzepatide 15 mg the preferred treatment strategy for type 2 diabetes? A meta-analysis and trial-sequence-analysis.</a> European review for medical and pharmacological sciences 27(15): 7164-7179                                                              | - Systematic review used as source of primary studies                                                                                                     |
| <a href="#">Yao, Jun, Zhang, Minlu, Zhang, Xia et al. (2023) Impact of Type 2 Diabetes Duration on the Efficacy and Safety of Add-on Lixisenatide in Asian Individuals Receiving Basal Insulin: A Pooled Analysis.</a> Diabetes therapy : research, treatment and education of diabetes and related disorders            | - Secondary publication of an included study that does not provide any additional relevant information                                                    |
| <a href="#">Yasunari, E., Takeno, K., Funayama, H. et al. (2011) Efficacy of pioglitazone on glycemic</a>                                                                                                                                                                                                                | - Comparator in study does not match that specified in this review protocol                                                                               |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Reason                                                                                                                                                                    |
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| <a href="#">control and carotid intima-media thickness in type 2 diabetes patients with inadequate insulin therapy.</a> J Diabetes Invest 2(1): 56-62                                                                                                                                                                                                                                                                                                                                     | <i>Usual care comparator which is not specified in the protocol</i>                                                                                                       |
| <a href="#">Ye, Nan, Jardine, Meg J, Oshima, Megumi et al. (2021) Blood Pressure Effects of Canagliflozin and Clinical Outcomes in Type 2 Diabetes and Chronic Kidney Disease: Insights From the CREDENCE Trial.</a> Circulation 143(18): 1735-1749                                                                                                                                                                                                                                       | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis examining the effects on the CREDENCE trial result based on blood pressure background</i> |
| <a href="#">Yee, M. S., Pavitt, D. V., Dhanjil, S. et al. (2010) The effects of rosiglitazone on atherosclerotic progression in patients with Type 2 diabetes at high cardiovascular risk.</a> Diabet Med 27(12): 1392-400                                                                                                                                                                                                                                                                | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                             |
| <a href="#">Yilmaz, Hamiyet, Gursoy, Alptekin, Sahin, Mustafa et al. (2007) Comparison of insulin monotherapy and combination therapy with insulin and metformin or insulin and rosiglitazone or insulin and acarbose in type 2 diabetes.</a> Acta diabetologica 44(4): 187-92                                                                                                                                                                                                            | - Comparator in study does not match that specified in this review protocol                                                                                               |
| <a href="#">Yin, Dao-Gen, Ding, Liang-Liang, Zhou, Hai-Rong et al. (2021) Comprehensive analysis of the safety of semaglutide in type 2 diabetes: a meta-analysis of the SUSTAIN and PIONEER trials.</a> Endocrine journal 68(6): 739-742                                                                                                                                                                                                                                                 | - Systematic review used as source of primary studies<br><br><i>Identified in rerun search. No additional studies to add.</i>                                             |
| <a href="#">Yin, Ziwei; Zheng, Huizhen; Guo, Zhihua (2022) Effect of Sodium-Glucose Co-transporter Protein 2 Inhibitors on Arrhythmia in Heart Failure Patients With or Without Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials.</a> Frontiers in cardiovascular medicine 9: 902923                                                                                                                                                                                      | - Population not relevant to this review protocol<br><br><i>Mixture of trials for people with or without type 2 diabetes</i>                                              |
| <a href="#">Yki-Järvinen, H., Ryysy, L., Nikkilä, K. et al. (1999) Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus. A randomized, controlled trial.</a> Ann Intern Med 130(5): 389-96                                                                                                                                                                                                                                                                    | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                             |
| <a href="#">Yokoh, H., Kobayashi, K., Sato, Y. et al. (2015) Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin compared with alpha-glucosidase inhibitor in Japanese patients with type 2 diabetes inadequately controlled on metformin or pioglitazone alone (Study for an Ultimate Combination Therapy to Control Diabetes with Sitagliptin-1): A multicenter, randomized, open-label, non-inferiority trial.</a> Journal of Diabetes Investigation 6(2): 182-191 | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                                             |

| Study                                                                                                                                                                                                                                                                                                                   | Reason                                                                                                                                                    |
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| <a href="#">Yoneda, M., Honda, Y., Ogawa, Y. et al. (2021) Comparing the effects of tofogliflozin and pioglitazone in non-alcoholic fatty liver disease patients with type 2 diabetes mellitus (ToPiND study): a randomized prospective open-label controlled trial. BMJ Open Diabetes Research &amp; Care 9(1): 02</a> | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                                                             |
| <a href="#">Yoo, Soon-Jib, Chang, Sang-Ah, Sohn, Tae Seo et al. (2021) Long-Term Glycaemic Durability of Early Combination Therapy Strategy versus Metformin Monotherapy in Korean Patients with Newly Diagnosed Type 2 Diabetes Mellitus. Diabetes &amp; metabolism journal 45(6): 954-959</a>                         | - Comparator in study does not match that specified in this review protocol                                                                               |
| <a href="#">Yoon, K. H., Shockey, G. R., Teng, R. et al. (2011) Effect of initial combination therapy with sitagliptin, a dipeptidyl peptidase-4 inhibitor, and pioglitazone on glycemic control and measures of <math>\beta</math>-cell function in patients with type 2 diabetes. Int J Clin Pract 65(2): 154-64</a>  | - Longer-term data reported in included study<br><i>See Yoon 2012 for 54 week results</i>                                                                 |
| <a href="#">Yoshida, Yilin, Joshi, Preeti, Barri, Saba et al. (2022) Progression of retinopathy with glucagon-like peptide-1 receptor agonists with cardiovascular benefits in type 2 diabetes - A systematic review and meta-analysis. Journal of diabetes and its complications 36(8): 108255</a>                     | - Systematic review used as source of primary studies<br><i>Identified during the rerun search. No additional studies.</i>                                |
| <a href="#">Yoshii, Hidenori, Onuma, Tomio, Yamazaki, Tsutomu et al. (2014) Effects of pioglitazone on macrovascular events in patients with type 2 diabetes mellitus at high risk of stroke: the PROFIT-J study. Journal of atherosclerosis and thrombosis 21(6): 563-73</a>                                           | - Comparator in study does not match that specified in this review protocol<br><i>Compares pioglitazone arm with non-pioglitazone (various drugs) arm</i> |
| <a href="#">Yoshiji, Satoshi, Minamino, Hiroto, Tanaka, Daisuke et al. (2022) Effects of glucagon-like peptide-1 receptor agonists on cardiovascular and renal outcomes: A meta-analysis and meta-regression analysis. Diabetes, obesity &amp; metabolism 24(6): 1029-1037</a>                                          | - Systematic review used as source of primary studies<br><i>Identified during rerun search. No additional studies.</i>                                    |
| <a href="#">Yoshikawa, Fukumi, Uchino, Hiroshi, Nagashima, Tomoko et al. (2022) Dipeptidyl peptidase-4 inhibitor improves glycemic variability in multiple daily insulin-treated type 2 diabetes: a prospective randomized-controlled trial. Diabetology international 13(1): 124-131</a>                               | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                   |
| <a href="#">Younes, Ahmed M, Salem, Mahmoud, Maraey, Ahmed et al. (2022) Safety outcomes of SGLT2i</a>                                                                                                                                                                                                                  | - Systematic review used as source of primary studies                                                                                                     |

| Study                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                                                                                     |
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| <a href="#">in the heart failure trials: A systematic review and Meta-analysis</a> . International journal of cardiology 366: 51-56                                                                                                                                                                                                           |                                                                                                                                                                                                            |
| <a href="#">Young, Tamara K, Li, Jing-Wei, Kang, Amy et al. (2021) Effects of canagliflozin compared with placebo on major adverse cardiovascular and kidney events in patient groups with different baseline levels of HbA1c, disease duration and treatment intensity: results from the CANVAS Program</a> . Diabetologia 64(11): 2402-2414 | - Study design not relevant to this review protocol<br><br><i>Post hoc analysis of the CANVAS study that investigates outcomes based on baseline HbA1c level, disease duration and treatment intensity</i> |
| <a href="#">Yousuf, M.K., Fatima, M., Haris, S. et al. (2021) Comparative analysis of metformin and its combination with dapagliflozin in type 2 diabetes: Randomized control trial</a> . Medical Forum Monthly 32(7): 82-87                                                                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                    |
| <a href="#">Yu, Jie, Arnott, Clare, Neuen, Brendon L et al. (2021) Cardiovascular and renal outcomes with canagliflozin according to baseline diuretic use: a post hoc analysis from the CANVAS Program</a> . ESC heart failure 8(2): 1482-1493                                                                                               | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                     |
| <a href="#">Yu, M., Boye, K., Huh, R. et al. (2021) Patient-reported outcomes in patients with type 2 diabetes treated with tirzepatide or placebo as an add-on to basal insulin (SURPASS-5)</a> . Diabetologia 64(supplement1): 244-s245                                                                                                     | - Conference abstract<br><br>- Duplicate reference                                                                                                                                                         |
| <a href="#">Yu, M., Bray, R., Brown, K. et al. (2022) IDF21-0036 Patient-Reported Outcomes in Patients with Type 2 Diabetes Treated with Tirzepatide or Insulin Degludec (SURPASS-3)</a> . Diabetes Research and Clinical Practice 186(supplement1): 109700                                                                                   | - Conference abstract                                                                                                                                                                                      |
| <a href="#">Yu, M, Van Brunt, K, Varnado, O J et al. (2016) Patient-reported outcome results in patients with type 2 diabetes treated with once-weekly dulaglutide: data from the AWARD phase III clinical trial programme</a> . Diabetes, obesity & metabolism 18(4): 419-24                                                                 | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                     |
| <a href="#">Yu, Yi-Wen, Zhao, Xue-Mei, Wang, Yun-Hong et al. (2021) Effect of sodium-glucose cotransporter 2 inhibitors on cardiac structure and function in type 2 diabetes mellitus patients with or without chronic heart failure: a meta-analysis</a> . Cardiovascular diabetology 20(1): 25                                              | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                    |



| Study                                                                                                                                                                                                                                                                                                                                      | Reason                                                                                                 |
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| <a href="#">Yuan, Xia, Gao, Zhe, Yang, Caixuan et al. (2023) Comparing the effectiveness of long-term use of daily and weekly glucagon-like peptide-1 receptor agonists treatments in patients with nonalcoholic fatty liver disease and type 2 diabetes mellitus: a network meta-analysis. Frontiers in endocrinology 14: 1170881</a>     | - Systematic review used as source of primary studies                                                  |
| <a href="#">Zaazouee, Mohamed Sayed, Hamdallah, Aboalmagd, Helmy, Sara Kamel et al. (2022) Semaglutide for the treatment of type 2 Diabetes Mellitus: A systematic review and network meta-analysis of safety and efficacy outcomes. Diabetes &amp; metabolic syndrome 16(6): 102511</a>                                                   | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Zaghlol, Louay Y, Beirat, Amir F, Amarin, Justin Z et al. (2021) Effect of Dosage Reduction of Hypoglycemic Multidrug Regimens on the Incidences of Acute Glycemic Complications in People With Type 2 Diabetes Who Fast During Ramadan: A Randomized Controlled Trial. Frontiers in endocrinology 12: 613826</a>              | - Trial that has a treatment and follow up period of less than 24 weeks                                |
| <a href="#">Zaki, Hany A, Iftikhar, Haris, Shallik, Nabil A et al. (2023) A Systematic Review and Meta-Analysis of Randomized Controlled Trials Comparing the Effects of Biguanides (Metformin) and Thiazolidinediones on Glucose Tolerance and Insulin Sensitivity in Patients With Type II Diabetes Mellitus. Cureus 15(5): e39445</a>   | - Systematic review used as source of primary studies                                                  |
| <a href="#">Zein, Ahmad Fariz Malvi Zamzam and Raffaello, Wilson Matthew (2022) Dipeptidyl peptidase-4 (DPP-IV) inhibitor was associated with mortality reduction in COVID-19 - A systematic review and meta-analysis. Primary care diabetes 16(1): 162-167</a>                                                                            | - Population not relevant to this review protocol<br>COVID-19                                          |
| <a href="#">Zelniker, Thomas A, Morrow, David A, Mosenzon, Ofri et al. (2021) Relationship between baseline cardiac biomarkers and cardiovascular death or hospitalization for heart failure with and without sodium-glucose co-transporter 2 inhibitor therapy in DECLARE-TIMI 58. European journal of heart failure 23(6): 1026-1036</a> | - Secondary publication of an included study that does not provide any additional relevant information |
| <a href="#">Zeng, YH, Liu, SC, Lee, CC et al. (2022) Effect of empagliflozin versus linagliptin on body composition in Asian patients with type 2</a>                                                                                                                                                                                      | - No relevant outcomes reported                                                                        |

| Study                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Reason                                                                                                                                                                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">diabetes treated with premixed insulin</a> . Scientific reports 12(1): 17065                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                           |
| <a href="#">Zeng, Zhengpei, Yang, Jin-Kui, Tong, Nanwei et al. (2013) Efficacy and safety of linagliptin added to metformin and sulphonylurea in Chinese patients with type 2 diabetes: a sub-analysis of data from a randomised clinical trial</a> . Current medical research and opinion 29(8): 921-9                                                                                                                                                          | - Secondary publication of an included study that does not provide any additional relevant information<br><br><i>Chinese subgroup of participants that is not specified as a subgroup in the protocol</i> |
| <a href="#">Zhang, F.; Wang, W.; Hou, X. (2021) Effectiveness and safety of ertugliflozin for type 2 diabetes: a meta-analysis data from randomized controlled trials</a> . Journal of diabetes investigation                                                                                                                                                                                                                                                    | - Trial that has a treatment and follow up period of less than 24 weeks                                                                                                                                   |
| <a href="#">Zhang, Fang, Tang, Lizhi, Li, Jing et al. (2021) Comparison Between Pioglitazone/Metformin Combination Therapy and Sitagliptin/Metformin Combination Therapy on the Efficacy in Chinese Type 2 Diabetic Adults Insufficiently Controlled with Metformin: Study Protocol of an Open-Label, Multicenter, Non-Inferiority Parallel-Group Randomized Controlled Trial</a> . Diabetes, metabolic syndrome and obesity : targets and therapy 14: 1243-1252 | - No relevant outcomes reported                                                                                                                                                                           |
| <a href="#">Zhang, Fudan; Wang, Wenting; Hou, Xu (2022) Effectiveness and safety of ertugliflozin for type 2 diabetes: A meta-analysis of data from randomized controlled trials</a> . Journal of diabetes investigation 13(3): 478-488                                                                                                                                                                                                                          | - Systematic review used as source of primary studies                                                                                                                                                     |
| <a href="#">Zhang, Jie, Xian, Tong-Zhang, Wu, Ming-Xiao et al. (2022) Comparing the effects of twice-daily exenatide and insulin on renal function in patients with type 2 diabetes mellitus: secondary analysis of a randomized controlled trial</a> . Journal of investigative medicine : the official publication of the American Federation for Clinical Research 70(7): 1529-1535                                                                           | - Secondary publication of an included study that does not provide any additional relevant information                                                                                                    |
| <a href="#">Zhang, Jingyi, Van Spall, Harriette Gc, Li, Likang et al. (2023) Effects of glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter-2 inhibitors on cardiovascular and kidney outcomes in Asian versus White patients with type 2 diabetes mellitus</a> . Diabetes & metabolic syndrome 17(7): 102804                                                                                                                             | - Systematic review used as source of primary studies                                                                                                                                                     |
| <a href="#">Zhang, Li, Wang, Tongdan, Kong, Yan et al. (2023) Sodium-dependent glucose transporter 2</a>                                                                                                                                                                                                                                                                                                                                                         | - Unclear how many people are receiving concomitant antihyperglycaemic treatment and                                                                                                                      |

| Study                                                                                                                                                                                                                                                                                                                                                          | Reason                                                                                           |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| <a href="#">inhibitor alleviates renal lipid deposition and improves renal oxygenation levels in newly diagnosed type 2 diabetes mellitus patients: a randomized controlled trial.</a> Diabetology & metabolic syndrome 15(1): 256                                                                                                                             | therefore the study cannot be classified into review 1.1 or 1.2                                  |
| <a href="#">Zhang, Nan, Wang, Yueying, Tse, Gary et al. (2022) Effect of sodium-glucose cotransporter-2 inhibitors on cardiac remodelling: a systematic review and meta-analysis.</a> European journal of preventive cardiology 28(17): 1961-1973                                                                                                              | - Population not relevant to this review protocol<br><i>People with or without heart failure</i> |
| <a href="#">Zhang, Qian, Zhang, Qingqing, Yang, Liu et al. (2023) Renal, cardiovascular, and safety outcomes of adding sodium-glucose cotransporter-2 inhibitors to insulin therapy in patients with type-2 diabetes: a meta-analysis.</a> International urology and nephrology                                                                                | - Systematic review used as source of primary studies                                            |
| <a href="#">Zhang, Qin; Zhou, Siyuan; Liu, Lijun (2023) Efficacy and safety evaluation of SGLT2i on blood pressure control in patients with type 2 diabetes and hypertension: a new meta-analysis.</a> Diabetology & metabolic syndrome 15(1): 118                                                                                                             | - Systematic review used as source of primary studies                                            |
| <a href="#">Zhang, Rong, Cheng, Keran, Xu, Shizan et al. (2017) Metformin and Diammonium Glycyrrhizinate Enteric-Coated Capsule versus Metformin Alone versus Diammonium Glycyrrhizinate Enteric-Coated Capsule Alone in Patients with Nonalcoholic Fatty Liver Disease and Type 2 Diabetes Mellitus.</a> Gastroenterology research and practice 2017: 8491742 | - Comparator in study does not match that specified in this review protocol                      |
| <a href="#">Zhang, Sha, Qi, Zhan, Wang, Yidong et al. (2023) Effect of sodium-glucose transporter 2 inhibitors on sarcopenia in patients with type 2 diabetes mellitus: a systematic review and meta-analysis.</a> Frontiers in endocrinology 14: 1203666                                                                                                      | - Systematic review used as source of primary studies                                            |
| <a href="#">Zhang, X, Wang, M, Wang, X et al. (2021) Comparison of New Glucose-Lowering Drugs on Risk of Pancreatitis in Type 2 Diabetes: A Network Meta-Analysis.</a> Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists                                                | - Systematic review used as source of primary studies                                            |
| <a href="#">Zhang, Yaofu, Wang, Junheng, Jiang, Li et al. (2022) Network meta-analysis on the efficacy and safety of finerenone versus SGLT2</a>                                                                                                                                                                                                               | - Study does not contain an intervention relevant to this review protocol                        |

| Study                                                                                                                                                                                                                                                                                                               | Reason                                                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| <a href="#">inhibitors on reducing new-onset of atrial fibrillation in patients with type 2 diabetes mellitus and chronic kidney disease.</a> Diabetology & metabolic syndrome 14(1): 156                                                                                                                           | <i>Finerenone is not relevant to the protocol</i>                                                                           |
| <a href="#">Zhao, Huilei, Liu, Yang, Liu, Menglu et al. (2023) Clinical Outcomes with GLP-1 Receptor Agonists in Patients with Heart Failure: A Systematic Review and Meta-analysis of Randomized Controlled Trials.</a> Drugs 83(14): 1293-1307                                                                    | - Systematic review used as source of primary studies                                                                       |
| <a href="#">Zhao, Li-Min, Huang, Jia-Nan, Qiu, Mei et al. (2021) Gliflozins for the prevention of stroke in diabetes and cardiorenal diseases: A meta-analysis of cardiovascular outcome trials.</a> Medicine 100(39): e27362                                                                                       | - Population not relevant to this review protocol                                                                           |
| <a href="#">Zhao, Lingyue, Guo, Wenqin, Huang, Weichao et al. (2022) Benefit of sodium-glucose cotransporter-2 inhibitors on survival outcome is related to the type of heart failure: A meta-analysis.</a> Diabetes research and clinical practice 187: 109871                                                     | - Population not relevant to this review protocol<br><i>People with heart failure, not necessarily with type 2 diabetes</i> |
| <a href="#">Zhao, S.-D., Zhou, L., Tao, Y.-Y. et al. (2022) Renal outcomes in Asian patients with type 2 diabetes mellitus treated with SGLT2 inhibitors: a systematic review and meta-analysis of randomized controlled trials.</a> International Journal of Diabetes in Developing Countries 42(2): 178-190       | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                               |
| <a href="#">Zhao, Yan, Zhao, Wenli, Bu, Huaian et al. (2023) Liraglutide on type 2 diabetes mellitus with nonalcoholic fatty liver disease: A systematic review and meta-analysis of 16 RCTs.</a> Medicine 102(6): e32892                                                                                           | - Systematic review used as source of primary studies                                                                       |
| <a href="#">Zhao, Ying; Zhang, Rui; Wang, Su (2022) Effect of Dapagliflozin Combined with Cognitive Behavior Training on Quality of Life and Cognitive Function in Elderly Patients with Type 2 Diabetes Mellitus Complicated with Mild Cognitive Impairment.</a> Iranian journal of public health 51(6): 1251-1258 | - Comparator in study does not match that specified in this review protocol                                                 |
| <a href="#">Zhao, Yunjuan, Yang, Lin, Xiang, Yufei et al. (2014) Dipeptidyl peptidase 4 inhibitor sitagliptin maintains beta-cell function in patients with recent-onset latent autoimmune diabetes in adults: one year prospective study.</a> The Journal                                                          | - Population not relevant to this review protocol                                                                           |

| Study                                                                                                                                                                                                                                                                                                                        | Reason                                                                                             |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| of clinical endocrinology and metabolism 99(5): e876-80                                                                                                                                                                                                                                                                      |                                                                                                    |
| <a href="#">Zhao, Z., Jin, P., Zhang, Y. et al. (2022) SGLT2 Inhibitors in Diabetic Patients With Cardiovascular Disease or at High Cardiovascular Risk: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Frontiers in Cardiovascular Medicine 9: 826684</a>                                           | - Systematic review used as source of primary studies                                              |
| <a href="#">Zheng, Ru-Jie, Wang, Yue, Tang, Jun-Nan et al. (2022) Association of SGLT2 Inhibitors With Risk of Atrial Fibrillation and Stroke in Patients With and Without Type 2 Diabetes: A Systemic Review and Meta-Analysis of Randomized Controlled Trials. Journal of cardiovascular pharmacology 79(2): e145-e152</a> | - Population not relevant to this review protocol<br><i>People with or without type 2 diabetes</i> |
| <a href="#">Zheng, Zhigui, He, Dongyuan, Chen, Jianguo et al. (2023) Risk of Urinary Tract Infection in Patients with Type 2 Diabetes Mellitus Treated with Dapagliflozin: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Clinical drug investigation 43(4): 209-225</a>                             | - Trial that has a treatment and follow up period of less than 24 weeks                            |
| <a href="#">Zhong, Ping, Zeng, Hai, Huang, Miaochun et al. (2021) Efficacy and Safety of Subcutaneous and Oral Semaglutide Administration in Patients With Type 2 Diabetes: A Meta-Analysis. Frontiers in pharmacology 12: 695182</a>                                                                                        | - Systematic review used as source of primary studies                                              |
| <a href="#">Zhou, Bin, Shi, Yetan, Fu, Rongrong et al. (2022) Relationship Between SGLT-2i and Ocular Diseases in Patients With Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials. Frontiers in endocrinology 13: 907340</a>                                                                         | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK      |
| <a href="#">Zhou, Pei, Tang, Xiangyu, Deng, Yunxia et al. (2024) The Effect of Empagliflozin on Janus Kinase 2/Signal Transducer and Activator of Transcription 3 Pathway in Patients with Type 2 Cardiorenal Syndrome. Anatolian journal of cardiology</a>                                                                  | - Trial that has a treatment and follow up period of less than 24 weeks                            |
| <a href="#">Zhou, Qian, Lei, Xingxing, Fu, Shunlian et al. (2023) Efficacy and safety of tirzepatide, dual GLP-1/GIP receptor agonists, in the management of type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Diabetology &amp; metabolic syndrome 15(1): 222</a>                     | - Systematic review used as source of primary studies                                              |

| Study                                                                                                                                                                                                                                                                                                       | Reason                                                                                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| <a href="#">Zhou, Xianling, Shi, Heng, Zhu, Shiping et al. (2022) Dipeptidyl peptidase-4 inhibitor and insulin combination treatment in type 2 diabetes and chronic kidney disease: A meta-analysis. Journal of diabetes investigation 13(3): 468-477</a>                                                   | - Systematic review used as source of primary studies<br><i>Identified in rerun search. No additional studies to add.</i> |
| <a href="#">Zhou, Yi, Wang, Feng-Rong, Wen, Fei-Fei et al. (2023) The association between sodium/glucose cotransporter-2 inhibitors and adverse clinical events in patients with chronic kidney disease: a systematic review and meta-analysis of randomised controlled trials. Acta cardiologica: 1-10</a> | - Population not relevant to this review protocol                                                                         |
| <a href="#">Zhou, Zien, Jardine, Meg J, Li, Qiang et al. (2021) Effect of SGLT2 Inhibitors on Stroke and Atrial Fibrillation in Diabetic Kidney Disease: Results From the CREDENCE Trial and Meta-Analysis. Stroke 52(5): 1545-1556</a>                                                                     | - Post-hoc analysis of included study                                                                                     |
| <a href="#">Zhou, Zien, Jardine, Meg, Perkovic, Vlado et al. (2019) Canagliflozin and fracture risk in individuals with type 2 diabetes: results from the CANVAS Program. Diabetologia 62(10): 1854-1867</a>                                                                                                | - Secondary publication of an included study that does not provide any additional relevant information                    |
| <a href="#">Zhou, Zien, Lindley, Richard I, Radholm, Karin et al. (2019) Canagliflozin and Stroke in Type 2 Diabetes Mellitus. Stroke 50(2): 396-404</a>                                                                                                                                                    | - Duplicate reference                                                                                                     |
| <a href="#">Zhou, Zijing, Zheng, Min, Zuo, Zhihong et al. (2024) Comparison of cardiovascular outcomes of new antihyperglycemic agents in Type 2 Diabetes Mellitus: a meta-analysis. ESC heart failure</a>                                                                                                  | - SR - does not match PICO<br><i>Studies with participants who either had HF or diabetes</i>                              |
| <a href="#">Zhu, H; Wei, Y; Ke, Z (2022) Effect of metformin on diabetic retinopathy and its possible mechanism. Recent advances in ophthalmology 42(8): 608-611</a>                                                                                                                                        | - Study not reported in English                                                                                           |
| <a href="#">Zhu, X. X., Pan, C. Y., Li, G. W. et al. (2003) Addition of rosiglitazone to existing sulfonylurea treatment in chinese patients with type 2 diabetes and exposure to hepatitis B or C. Diabetes Technol Ther 5(1): 33-42</a>                                                                   | - Trial of a treatment which is not available, rarely used, or no longer available, in the UK                             |
| <a href="#">Zhuang, Yan, Song, Jin, Ying, Miaofa et al. (2020) Efficacy and safety of dapagliflozin plus saxagliptin vs monotherapy as added to</a>                                                                                                                                                         | - Systematic review used as source of primary studies                                                                     |



| Study                                                                                                                                                                                                                                                                                                                                                                         | Reason                                                                                                                                             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">metformin in patients with type 2 diabetes: A meta-analysis.</a> Medicine 99(30): e21409                                                                                                                                                                                                                                                                          |                                                                                                                                                    |
| <a href="#">Zhuo, Chuanjun, Lin, Chongguang, Zhou, Chunhua et al. (2021) Comparative Cardio-Renal Outcomes of Type 2 Diabetes Patients Administered Glucagon-Like Peptide-1 Receptor Agonists: A Network Meta-Analysis.</a> Frontiers in pharmacology 12: 759262                                                                                                              | - Systematic review used as source of primary studies                                                                                              |
| <a href="#">Zib, I., Jacob, A. N., Lingvay, I. et al. (2007) Effect of pioglitazone therapy on myocardial and hepatic steatosis in insulin-treated patients with type 2 diabetes.</a> J Investig Med 55(5): 230-6                                                                                                                                                             | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i> |
| <a href="#">Zinman, B., Rosenstock, J., Johansen, O.E. et al. (2020) Incident and recurrent hypoglycemia with linagliptin and glimepiride in the carolina trial.</a> Diabetes 69(supplement1)                                                                                                                                                                                 | - Conference abstract                                                                                                                              |
| <a href="#">Zinman, Bernard, DeVries, J Hans, Bode, Bruce et al. (2013) Efficacy and safety of insulin degludec three times a week versus insulin glargine once a day in insulin-naïve patients with type 2 diabetes: results of two phase 3, 26 week, randomised, open-label, treat-to-target, non-inferiority trials.</a> The lancet. Diabetes & endocrinology 1(2): 123-31 | - Conference abstract                                                                                                                              |
| <a href="#">Zinman, Bernard, Inzucchi, Silvio E, Lachin, John M et al. (2017) Empagliflozin and Cerebrovascular Events in Patients With Type 2 Diabetes Mellitus at High Cardiovascular Risk.</a> Stroke 48(5): 1218-1225                                                                                                                                                     | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Zinman, Bernard, Marso, Steven P, Christiansen, Erik et al. (2018) Hypoglycemia, Cardiovascular Outcomes, and Death: The LEADER Experience.</a> Diabetes care 41(8): 1783-1791                                                                                                                                                                                    | - Secondary publication of an included study that does not provide any additional relevant information                                             |
| <a href="#">Zinman, Bernard, Philis-Tsimikas, Athena, Cariou, Bertrand et al. (2012) Insulin degludec versus insulin glargine in insulin-naïve patients with type 2 diabetes: a 1-year, randomized, treat-to-target trial (BEGIN Once Long).</a> Diabetes care 35(12): 2464-71                                                                                                | - Comparator in study does not match that specified in this review protocol<br><i>Compares insulin to other types of insulin</i>                   |
| <a href="#">Zisman, Ariel, Dex, Terry, Roberts, Michelle et al. (2018) Bedtime-to-Morning Glucose Difference and iGlarLixi in Type 2 Diabetes:</a>                                                                                                                                                                                                                            | - Secondary publication of an included study that does not provide any additional relevant information                                             |

| Study                                                                                                                                                                                                                                                                       | Reason                                                                                                                                                                                                                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <a href="#">Post Hoc Analysis of LixiLan-L</a> . Diabetes therapy : research, treatment and education of diabetes and related disorders 9(5): 2155-2162                                                                                                                     |                                                                                                                                                                                                                                            |
| <a href="#">Zobel, Emilie H, von Scholten, Bernt J, Goldman, Bryan et al. (2019) Pleiotropic effects of liraglutide in patients with type 2 diabetes and moderate renal impairment: Individual effects of treatment</a> . Diabetes, obesity & metabolism 21(5): 1261-1265   | - Secondary publication of an included study that does not provide any additional relevant information<br><i>Investigating responder effects against risk factors in the LIRA-RENAL trial</i>                                              |
| <a href="#">Zobel, Emilie H, Wretling, Asger, Ripa, Rasmus S et al. (2021) Ceramides and phospholipids are downregulated with liraglutide treatment: results from the LiraFlame randomized controlled trial</a> . BMJ open diabetes research & care 9(1)                    | - <75% of people are receiving concomitant antihyperglycaemic treatment and <75% are treatment naive and therefore the study cannot be classified into review 1.1 or 1.2<br><i>Around 50% received another glucose lowering medication</i> |
| <a href="#">Zoghbi, M., Kalsoft, M.S., Kolhe, D. et al. (2020) LIRA-PRIME: A randomised trial in primary care settings of liraglutide versus OAD for glycaemic control in patients with type 2 diabetes not in control on metformin</a> . Diabetologia 63(suppl1): 285-s286 | - Comparator in study does not match that specified in this review protocol<br><i>Usual care comparator which is not specified in the protocol</i>                                                                                         |
| <a href="#">Zografou, I., Sampanis, C., Papageorgiou, A. et al. (2013) The effect of vildagliptin on arterial stiffness in drug naive patients with type 2 diabetes mellitus</a> . Diabetes 62(suppl1): a596                                                                | - Conference abstract                                                                                                                                                                                                                      |
| <a href="#">Zografou, I., Sampanis, C., Papageorgiou, A. et al. (2012) The combination therapy with metformin and vildagliptin decreases lymphocytes count in patients with type 2 diabetes mellitus</a> . Diabetes 61(suppl1): a600                                        | - Conference abstract                                                                                                                                                                                                                      |
| <a href="#">Zou, Hai-Tao, Yang, Guo-Huan, Cai, Yu-Jun et al. (2022) Are High- or Low-dose SGLT2 Inhibitors Associated With Cardiovascular and Respiratory Adverse Events? A Meta-analysis</a> . Journal of cardiovascular pharmacology 79(5): 655-662                       | - Comparator in study does not match that specified in this review protocol<br><i>Comparison is not an area of interest for this review. Mixture of people with or without type 2 diabetes.</i>                                            |
| <a href="#">Zou, Xinyu, Shi, Qingyang, Vandvik, Per Olav et al. (2022) Sodium-Glucose Cotransporter-2 Inhibitors in Patients With Heart Failure : A Systematic Review and Meta-analysis</a> . Annals of internal medicine 175(6): 851-861                                   | - Commentary only                                                                                                                                                                                                                          |
| <a href="#">Zoungas, Sophia, de Galan, Bastiaan E, Ninomiya, Toshiharu et al. (2009) Combined</a>                                                                                                                                                                           | - Comparator in study does not match that specified in this review protocol                                                                                                                                                                |

| Study                                                                                                                                                                                                                                       | Reason |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| <a href="#">effects of routine blood pressure lowering and intensive glucose control on macrovascular and microvascular outcomes in patients with type 2 diabetes: New results from the ADVANCE trial.</a><br>Diabetes care 32(11): 2068-74 |        |

## J.2 Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2008 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

**Table 4: Studies excluded from the health economic review**

| Reference                                                                                                                                                                                                                      | Reason for exclusion                                                                                                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ihana-Sugiyama 2020. Comparison of effectiveness and drug cost between dipeptidyl peptidase-4 inhibitor and biguanide as the first-line anti-hyperglycaemic medication among Japanese working generation with type 2 diabetes. | Selectively excluded as NG28 2015 and 2022 were more applicable to review question. NG28 were based on a UK NHS perspective whereas this study was not. |

## Appendix K Risk of bias and directness table

**Table 5: Risk of bias and directness information for studies included in the review for initial therapy, model 5 (people at high cardiovascular risk)**

| Study name            | Comparison details                                  | Outcome                                      | Risk of bias  | Bias comments  | Directness           | Directness comments                                                                                                                                            |
|-----------------------|-----------------------------------------------------|----------------------------------------------|---------------|----------------|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Aggarwal 2018         | Metformin slow release v Metformin standard release | All-cause mortality                          | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |
| Aggarwal 2018         | Metformin slow release v Metformin standard release | HbA1c change                                 | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |
| Aggarwal 2018         | Metformin slow release v Metformin standard release | Hypoglycaemia episodes                       | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |
| Aggarwal 2018         | Metformin slow release v Metformin standard release | Weight change                                | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |
| Aggarwal 2018         | Metformin slow release v Metformin standard release | Persistent signs of worsening kidney disease | Some concerns | None specified | Partially applicable | Outcome reported as an adverse event leading to study discontinuation. Possible this outcome occurred in other participants but didn't lead to discontinuation |
| Arjona Ferreira 2013A | Glipizide v Sitagliptin                             | All-cause mortality                          | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |
| Arjona Ferreira 2013A | Glipizide v Sitagliptin                             | HbA1c change                                 | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |
| Arjona Ferreira 2013A | Glipizide v Sitagliptin                             | Hospitalisation for heart failure            | Some concerns | None specified | Directly applicable  | None specified                                                                                                                                                 |

| Study name            | Comparison details      | Outcome                                 | Risk of bias  | Bias comments  | Directness          | Directness comments |
|-----------------------|-------------------------|-----------------------------------------|---------------|----------------|---------------------|---------------------|
| Arjona Ferreira 2013A | Glipizide v Sitagliptin | Severe hypoglycaemic episodes           | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013A | Glipizide v Sitagliptin | Weight change                           | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | All-cause mortality                     | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Cardiovascular mortality                | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Development of end stage kidney disease | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Diabetic ketoacidosis                   | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | HbA1c change                            | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Hospitalisation for heart failure       | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Non-fatal stroke                        | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Severe hypoglycaemic episodes           | Some concerns | None specified | Directly applicable | None specified      |
| Arjona Ferreira 2013B | Glipizide v Sitagliptin | Weight change                           | Some concerns | None specified | Directly applicable | None specified      |
| Aroda 2019B           | Semaglutide v Placebo   | Acute kidney injury                     | Low           | None specified | Directly applicable | None specified      |
| Aroda 2019B           | Semaglutide v Placebo   | All-cause mortality                     | Low           | None specified | Directly applicable | None specified      |
| Aroda 2019B           | Semaglutide v Placebo   | BMI change                              | Low           | None specified | Directly applicable | None specified      |

| Study name   | Comparison details     | Outcome                           | Risk of bias | Bias comments  | Directness           | Directness comments                                                                                                                                                    |
|--------------|------------------------|-----------------------------------|--------------|----------------|----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Aroda 2019B  | Semaglutide v Placebo  | Cardiovascular mortality          | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | HbA1c change                      | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | Hospitalisation for heart failure | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | Hypoglycaemia episodes            | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | Non-fatal stroke                  | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | Severe hypoglycaemic episodes     | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | Weight change                     | Low          | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aroda 2019B  | Semaglutide v Placebo  | Non-fatal myocardial infarction   | Low          | None specified | Partially applicable | Reports acute coronary syndrome which may include other types of acute coronary syndrome rather than just myocardial infarction. Included here to capture the outcome. |
| Aronoff 2000 | Pioglitazone v Placebo | HbA1c change                      | High         | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aronoff 2000 | Pioglitazone v Placebo | Hypoglycaemia episodes            | High         | None specified | Directly applicable  | None specified                                                                                                                                                         |
| Aronoff 2000 | Pioglitazone v Placebo | Weight change                     | High         | None specified | Directly applicable  | None specified                                                                                                                                                         |



| Study name                      | Comparison details      | Outcome                         | Risk of bias  | Bias comments  | Directness          | Directness comments                         |
|---------------------------------|-------------------------|---------------------------------|---------------|----------------|---------------------|---------------------------------------------|
| Aronoff 2000 drug naïve         | Pioglitazone v Placebo  | HbA1c change                    | High          | None specified | Directly applicable | None specified                              |
| Aronoff 2000 previous treatment | Pioglitazone v Placebo  | HbA1c change                    | High          | None specified | Directly applicable | None specified                              |
| Aschner 2006                    | Sitagliptin v Placebo   | HbA1c change                    | High          | None specified | Directly applicable | None specified                              |
| Aschner 2006                    | Sitagliptin v Placebo   | Weight change                   | High          | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | All-cause mortality             | Some concerns | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | Cardiac arrhythmia              | Some concerns | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | HbA1c change                    | Some concerns | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | Hypoglycaemia episodes          | Some concerns | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | Non-fatal myocardial infarction | Some concerns | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | Severe hypoglycaemic episodes   | Some concerns | None specified | Directly applicable | None specified                              |
| Aschner 2010                    | Sitagliptin v Metformin | Weight change                   | Some concerns | None specified | Directly applicable | None specified                              |
| Bailey 2012                     | Dapagliflozin v Placebo | All-cause mortality             | Low           | None specified | Directly applicable | Multisite study but does not include the UK |
| Bailey 2012                     | Dapagliflozin v Placebo | HbA1c change                    | Low           | None specified | Directly applicable | Multisite study but does not include the UK |
| Bailey 2012                     | Dapagliflozin v Placebo | Hypoglycaemia episodes          | Low           | None specified | Directly applicable | Multisite study but does not include the UK |

| Study name    | Comparison details      | Outcome                       | Risk of bias  | Bias comments                                                                                              | Directness          | Directness comments                         |
|---------------|-------------------------|-------------------------------|---------------|------------------------------------------------------------------------------------------------------------|---------------------|---------------------------------------------|
| Bailey 2012   | Dapagliflozin v Placebo | Weight change                 | Low           | None specified                                                                                             | Directly applicable | Multisite study but does not include the UK |
| Banerji 1995  | Glipizide v Placebo     | BMI change                    | Some concerns | Allocation concealment                                                                                     | Directly applicable | None specified                              |
| Banerji 1995  | Glipizide v Placebo     | Severe hypoglycaemic episodes | Some concerns | Allocation concealment                                                                                     | Directly applicable | None specified                              |
| Banerji 1995  | Glipizide v Placebo     | HbA1c change                  | High          | Allocation concealment, missing outcome data                                                               | Directly applicable | None specified                              |
| Barzilai 2011 | Sitagliptin v Placebo   | HbA1c change                  | High          | >10% attrition rate between study arms with 13 participants withdrawn from placebo group due to high HbA1c | Directly applicable | None specified                              |
| Barzilai 2011 | Sitagliptin v Placebo   | Hypoglycaemia episodes        | High          | >10% attrition rate between study arms with 13 participants withdrawn from placebo group due to high HbA1c | Directly applicable | None specified                              |
| Barzilai 2011 | Sitagliptin v Placebo   | Weight change                 | High          | >10% attrition rate between study arms with 13 participants withdrawn from placebo group due to high HbA1c | Directly applicable | None specified                              |
| Bi 2013       | Glipizide v Metformin   | HbA1c change                  | High          | None specified                                                                                             | Directly applicable | None specified                              |

| Study name     | Comparison details                      | Outcome                         | Risk of bias  | Bias comments  | Directness          | Directness comments |
|----------------|-----------------------------------------|---------------------------------|---------------|----------------|---------------------|---------------------|
| Bi 2013        | Glipizide v Metformin                   | Weight change                   | High          | None specified | Directly applicable | None specified      |
| Birkeland 1994 | Glipizide v Placebo                     | Hypoglycaemia episodes          | High          | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Metformin    | All-cause mortality             | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Vildagliptin | All-cause mortality             | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin v Metformin                | All-cause mortality             | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Metformin    | HbA1c change                    | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Vildagliptin | HbA1c change                    | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin v Metformin                | HbA1c change                    | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Metformin    | Non-fatal myocardial infarction | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Vildagliptin | Non-fatal myocardial infarction | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin v Metformin                | Non-fatal myocardial infarction | Some concerns | None specified | Directly applicable | None specified      |
| Bosi 2009      | Vildagliptin + Metformin v Metformin    | Severe hypoglycaemic episodes   | Some concerns | None specified | Directly applicable | None specified      |

| Study name            | Comparison details                      | Outcome                       | Risk of bias  | Bias comments                                                             | Directness          | Directness comments |
|-----------------------|-----------------------------------------|-------------------------------|---------------|---------------------------------------------------------------------------|---------------------|---------------------|
| Bosi 2009             | Vildagliptin + Metformin v Vildagliptin | Severe hypoglycaemic episodes | Some concerns | None specified                                                            | Directly applicable | None specified      |
| Bosi 2009             | Vildagliptin v Metformin                | Severe hypoglycaemic episodes | Some concerns | None specified                                                            | Directly applicable | None specified      |
| Bosi 2009             | Vildagliptin + Metformin v Metformin    | Weight change                 | Some concerns | None specified                                                            | Directly applicable | None specified      |
| Bosi 2009             | Vildagliptin + Metformin v Vildagliptin | Weight change                 | Some concerns | None specified                                                            | Directly applicable | None specified      |
| Bosi 2009             | Vildagliptin v Metformin                | Weight change                 | Some concerns | None specified                                                            | Directly applicable | None specified      |
| Camerini-Davalos 1988 | Glipizide v Placebo                     | HbA1c change                  | Some concerns | None specified                                                            | Directly applicable | None specified      |
| Campbell 1994         | Glipizide v Metformin                   | HbA1c change                  | High          | None specified                                                            | Directly applicable | None specified      |
| Campbell 1994         | Glipizide v Metformin                   | Hypoglycaemia episodes        | High          | None specified                                                            | Directly applicable | None specified      |
| Campbell 1994         | Glipizide v Metformin                   | Severe hypoglycaemic episodes | High          | None specified                                                            | Directly applicable | None specified      |
| Campbell 1994         | Glipizide v Metformin                   | Weight change                 | High          | None specified                                                            | Directly applicable | None specified      |
| Chakraborty 2011      | Metformin v Placebo                     | BMI change                    | High          | None specified                                                            | Directly applicable | None specified      |
| Chakraborty 2011      | Metformin v Placebo                     | HbA1c change                  | High          | None specified                                                            | Directly applicable | None specified      |
| Charbonnel 2005       | Pioglitazone v Gliclazide               | HbA1c change                  | High          | Allocation concealment unclear, baseline characteristics unclear, unclear | Directly applicable | None specified      |

| Study name      | Comparison details        | Outcome                         | Risk of bias  | Bias comments                                                                                                                                                             | Directness          | Directness comments |
|-----------------|---------------------------|---------------------------------|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|                 |                           |                                 |               | reporting of methods used, unclear attrition, selective reporting of HbA1c confidence intervals                                                                           |                     |                     |
| Charbonnel 2005 | Pioglitazone v Gliclazide | Hypoglycaemia episodes          | High          | Allocation concealment unclear, baseline characteristics unclear, unclear reporting of methods used, unclear attrition, selective reporting of HbA1c confidence intervals | Directly applicable | None specified      |
| Chen 2015       | Linagliptin v Placebo     | HbA1c change                    | Some concerns | Self-administered intervention and no adherence monitoring included. Intention to treat analysis fails to account for non-adherence.                                      | Directly applicable | None specified      |
| Chen 2015       | Linagliptin v Placebo     | Non-fatal myocardial infarction | Some concerns | Self-administered intervention and no adherence monitoring included. Intention to treat analysis fails to account for non-adherence.                                      | Directly applicable | None specified      |

| Study name | Comparison details        | Outcome                       | Risk of bias  | Bias comments                                                                                                                        | Directness          | Directness comments |
|------------|---------------------------|-------------------------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Chen 2015  | Linagliptin v Placebo     | Severe hypoglycaemic episodes | Some concerns | Self-administered intervention and no adherence monitoring included. Intention to treat analysis fails to account for non-adherence. | Directly applicable | None specified      |
| Chen 2015  | Linagliptin v Placebo     | Weight change                 | Some concerns | Self-administered intervention and no adherence monitoring included. Intention to treat analysis fails to account for non-adherence. | Directly applicable | None specified      |
| Chen 2018B | Glimepiride v Dulaglutide | HbA1c change                  | High          | Double-blind, double-dummy trial. Significant difference in baseline tobacco use.                                                    | Directly applicable | None specified      |
| Chen 2018B | Glimepiride v Dulaglutide | Weight change                 | High          | Double-blind, double-dummy trial. Significant difference in baseline tobacco use.                                                    | Directly applicable | None specified      |
| Chen 2018B | Glimepiride v Dulaglutide | All-cause mortality           | High          | Double-blind, double-dummy trial. Significant difference in baseline tobacco use; 'As-treated'                                       | Directly applicable | None specified      |



| Study name | Comparison details        | Outcome                         | Risk of bias | Bias comments                                                                                                                          | Directness          | Directness comments |
|------------|---------------------------|---------------------------------|--------------|----------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                           |                                 |              | analysis conducted for safety outcomes.                                                                                                |                     |                     |
| Chen 2018B | Glimepiride v Dulaglutide | At night hypoglycaemic episodes | High         | Double-blind, double-dummy trial. Significant difference in baseline tobacco use; 'As-treated' analysis conducted for safety outcomes. | Directly applicable | None specified      |
| Chen 2018B | Glimepiride v Dulaglutide | Cardiovascular mortality        | High         | Double-blind, double-dummy trial. Significant difference in baseline tobacco use; 'As-treated' analysis conducted for safety outcomes. | Directly applicable | None specified      |
| Chen 2018B | Glimepiride v Dulaglutide | Hypoglycaemia episodes          | High         | Double-blind, double-dummy trial. Significant difference in baseline tobacco use; 'As-treated' analysis conducted for safety outcomes. | Directly applicable | None specified      |
| Chen 2018B | Glimepiride v Dulaglutide | Non-fatal stroke                | High         | Double-blind, double-dummy trial. Significant difference in baseline tobacco use; 'As-treated' analysis conducted for safety outcomes. | Directly applicable | None specified      |

| Study name    | Comparison details                                 | Outcome                       | Risk of bias  | Bias comments                                                                                                                          | Directness          | Directness comments |
|---------------|----------------------------------------------------|-------------------------------|---------------|----------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Chen 2018B    | Glimepiride v Dulaglutide                          | Severe hypoglycaemic episodes | High          | Double-blind, double-dummy trial. Significant difference in baseline tobacco use; 'As-treated' analysis conducted for safety outcomes. | Directly applicable | None specified      |
| Chen 2022     | Gliclazide + Saxagliptin v Saxagliptin + Metformin | Hypoglycaemia episodes        | Some concerns | Concerns in outcome assessment                                                                                                         | Directly applicable | None specified      |
| Chen 2022     | Gliclazide + Saxagliptin v Saxagliptin + Metformin | All-cause mortality           | Low           | None specified                                                                                                                         | Directly applicable | None specified      |
| Chen 2022     | Gliclazide + Saxagliptin v Saxagliptin + Metformin | BMI change                    | Low           | None specified                                                                                                                         | Directly applicable | None specified      |
| Chen 2022     | Gliclazide + Saxagliptin v Saxagliptin + Metformin | Cardiovascular mortality      | Low           | None specified                                                                                                                         | Directly applicable | None specified      |
| Chen 2022     | Gliclazide + Saxagliptin v Saxagliptin + Metformin | HbA1c change                  | Low           | None specified                                                                                                                         | Directly applicable | None specified      |
| Chiasson 2001 | Metformin v Placebo                                | HbA1c change                  | High          | None specified                                                                                                                         | Directly applicable | None specified      |
| Chiasson 2001 | Metformin v Placebo                                | Hypoglycaemia episodes        | High          | None specified                                                                                                                         | Directly applicable | None specified      |
| Chiasson 2001 | Metformin v Placebo                                | Weight change                 | High          | None specified                                                                                                                         | Directly applicable | None specified      |

| Study name | Comparison details     | Outcome                  | Risk of bias  | Bias comments                                                                                                                                                                                                         | Directness          | Directness comments |
|------------|------------------------|--------------------------|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Chou 2012  | Pioglitazone v Placebo | All-cause mortality      | Some concerns | Large amount of missing outcome data who's missingness could be related to true value, as patients may leave study by request due to lack of tx effect, however, as this was balanced across arms this seems unlikely | Directly applicable | None specified      |
| Chou 2012  | Pioglitazone v Placebo | Cardiovascular mortality | Some concerns | Large amount of missing outcome data who's missingness could be related to true value, as patients may leave study by request due to lack of tx effect, however, as this was balanced across arms this seems unlikely | Directly applicable | None specified      |
| Chou 2012  | Pioglitazone v Placebo | HbA1c change             | Some concerns | Large amount of missing outcome data who's missingness could be related to true value, as patients may leave study by request due to lack of tx effect, however,                                                      | Directly applicable | None specified      |

| Study name | Comparison details     | Outcome                           | Risk of bias  | Bias comments                                                                                                                                                                                                         | Directness          | Directness comments |
|------------|------------------------|-----------------------------------|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                        |                                   |               | as this was balanced across arms this seems unlikely                                                                                                                                                                  |                     |                     |
| Chou 2012  | Pioglitazone v Placebo | Hospitalisation for heart failure | Some concerns | Large amount of missing outcome data who's missingness could be related to true value, as patients may leave study by request due to lack of tx effect, however, as this was balanced across arms this seems unlikely | Directly applicable | None specified      |
| Chou 2012  | Pioglitazone v Placebo | Hypoglycaemia episodes            | Some concerns | Large amount of missing outcome data who's missingness could be related to true value, as patients may leave study by request due to lack of tx effect, however, as this was balanced across arms this seems unlikely | Directly applicable | None specified      |
| Chou 2012  | Pioglitazone v Placebo | Non-fatal myocardial infarction   | Some concerns | Large amount of missing outcome data who's missingness could be related to true                                                                                                                                       | Directly applicable | None specified      |

| Study name    | Comparison details     | Outcome                  | Risk of bias  | Bias comments                                                                                                                                                                                                         | Directness          | Directness comments |
|---------------|------------------------|--------------------------|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|               |                        |                          |               | value, as patients may leave syudy by request due to lack of tx effect, however, as this was balanced across arms this seems unlikely                                                                                 |                     |                     |
| Chou 2012     | Pioglitazone v Placebo | Non-fatal stroke         | Some concerns | Large amount of missing outcome data who's missingness could be related to true value, as patients may leave syudy by request due to lack of tx effect, however, as this was balanced across arms this seems unlikely | Directly applicable | None specified      |
| de Boer 2017  | Linagliptin v Placebo  | HbA1c change             | Low           | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| de Boer 2017  | Linagliptin v Placebo  | Weight change            | Low           | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| DeFronzo 1995 | Metformin v Placebo    | All-cause mortality      | High          | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| DeFronzo 1995 | Metformin v Placebo    | Cardiovascular mortality | High          | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| DeFronzo 1995 | Metformin v Placebo    | HbA1c change             | High          | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| DeFronzo 1995 | Metformin v Placebo    | Hypoglycaemia episodes   | High          | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| DeFronzo 1995 | Metformin v Placebo    | Weight change            | High          | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |
| DeFronzo 2008 | Alogliptin v Placebo   | All-cause mortality      | High          | None specified                                                                                                                                                                                                        | Directly applicable | None specified      |

| Study name     | Comparison details                  | Outcome                       | Risk of bias | Bias comments  | Directness          | Directness comments |
|----------------|-------------------------------------|-------------------------------|--------------|----------------|---------------------|---------------------|
| DeFronzo 2008  | Alogliptin v Placebo                | Cardiovascular mortality      | High         | None specified | Directly applicable | None specified      |
| DeFronzo 2008  | Alogliptin v Placebo                | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| DeFronzo 2008  | Alogliptin v Placebo                | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| DeFronzo 2008  | Alogliptin v Placebo                | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Dejager 2007   | Vildagliptin v Placebo              | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Dejager 2007   | Vildagliptin v Placebo              | Weight change                 | High         | None specified | Directly applicable | None specified      |
| del Prato 2003 | Metformin v Placebo                 | BMI change                    | High         | None specified | Directly applicable | None specified      |
| del Prato 2003 | Metformin v Placebo                 | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| del Prato 2003 | Metformin v Placebo                 | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Del Prato 2011 | Linagliptin v Placebo               | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Del Prato 2011 | Linagliptin v Placebo               | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Derosa 2004    | Glimepiride v Metformin             | BMI change                    | High         | None specified | Directly applicable | None specified      |
| Derosa 2004    | Glimepiride v Metformin             | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Derosa 2004    | Glimepiride v Metformin             | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Derosa 2004    | Glimepiride v Metformin             | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| Derosa 2009    | Glimepiride + Metformin v Metformin | BMI change                    | Low          | None specified | Directly applicable | None specified      |



| Study name  | Comparison details                                 | Outcome      | Risk of bias | Bias comments  | Directness          | Directness comments |
|-------------|----------------------------------------------------|--------------|--------------|----------------|---------------------|---------------------|
| Derosa 2009 | Glimepiride + Metformin v Pioglitazone             | BMI change   | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Glimepiride + Metformin | BMI change   | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Metformin               | BMI change   | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Pioglitazone            | BMI change   | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone v Metformin                           | BMI change   | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Glimepiride + Metformin v Metformin                | HbA1c change | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Glimepiride + Metformin v Pioglitazone             | HbA1c change | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Glimepiride + Metformin | HbA1c change | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Metformin               | HbA1c change | Low          | None specified | Directly applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Pioglitazone            | HbA1c change | Low          | None specified | Directly applicable | None specified      |

| Study name  | Comparison details                                 | Outcome                | Risk of bias | Bias comments                                                                                          | Directness           | Directness comments |
|-------------|----------------------------------------------------|------------------------|--------------|--------------------------------------------------------------------------------------------------------|----------------------|---------------------|
| Derosa 2009 | Pioglitazone v Metformin                           | HbA1c change           | Low          | None specified                                                                                         | Directly applicable  | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Glimepiride + Metformin | Hypoglycaemia episodes | Low          | None specified                                                                                         | Partially applicable | None specified      |
| Derosa 2009 | Glimepiride + Metformin v Metformin                | Hypoglycaemia episodes | Low          | Outcome indirectness - withdrawal from study due to hypoglycaemia rather than all hypoglycaemia events | Partially applicable | None specified      |
| Derosa 2009 | Glimepiride + Metformin v Pioglitazone             | Hypoglycaemia episodes | Low          | Outcome indirectness - withdrawal from study due to hypoglycaemia rather than all hypoglycaemia events | Partially applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Metformin               | Hypoglycaemia episodes | Low          | Outcome indirectness - withdrawal from study due to hypoglycaemia rather than all hypoglycaemia events | Partially applicable | None specified      |
| Derosa 2009 | Pioglitazone + Metformin v Pioglitazone            | Hypoglycaemia episodes | Low          | Outcome indirectness - withdrawal from study due to                                                    | Partially applicable | None specified      |

| Study name  | Comparison details                    | Outcome                | Risk of bias | Bias comments                                                                                          | Directness           | Directness comments |
|-------------|---------------------------------------|------------------------|--------------|--------------------------------------------------------------------------------------------------------|----------------------|---------------------|
|             |                                       |                        |              | hypoglycaemia rather than all hypoglycaemia events                                                     |                      |                     |
| Derosa 2009 | Pioglitazone v Metformin              | Hypoglycaemia episodes | Low          | Outcome indirectness - withdrawal from study due to hypoglycaemia rather than all hypoglycaemia events | Partially applicable | None specified      |
| Dou 2018    | Saxagliptin + Metformin v Metformin   | All-cause mortality    | High         | None specified                                                                                         | Directly applicable  | None specified      |
| Dou 2018    | Saxagliptin + Metformin v Saxagliptin | All-cause mortality    | High         | None specified                                                                                         | Directly applicable  | None specified      |
| Dou 2018    | Saxagliptin v Metformin               | All-cause mortality    | High         | None specified                                                                                         | Directly applicable  | None specified      |
| Dou 2018    | Saxagliptin + Metformin v Metformin   | BMI change             | High         | None specified                                                                                         | Directly applicable  | None specified      |
| Dou 2018    | Saxagliptin + Metformin v Saxagliptin | BMI change             | High         | None specified                                                                                         | Directly applicable  | None specified      |
| Dou 2018    | Saxagliptin v Metformin               | BMI change             | High         | None specified                                                                                         | Directly applicable  | None specified      |
| Dou 2018    | Saxagliptin + Metformin v Metformin   | HbA1c change           | High         | None specified                                                                                         | Directly applicable  | None specified      |

| Study name | Comparison details                    | Outcome                         | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|---------------------------------|--------------|----------------|---------------------|---------------------|
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Metformin   | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Metformin   | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Metformin   | Non-fatal stroke                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | Non-fatal stroke                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | Non-fatal stroke                | High         | None specified | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                                      | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|----------------------------------------------|--------------|----------------|---------------------|---------------------|
| Dou 2018   | Saxagliptin + Metformin v Metformin   | Persistent signs of worsening kidney disease | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | Persistent signs of worsening kidney disease | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | Persistent signs of worsening kidney disease | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Metformin   | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Metformin   | Weight change                                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin + Metformin v Saxagliptin | Weight change                                | High         | None specified | Directly applicable | None specified      |
| Dou 2018   | Saxagliptin v Metformin               | Weight change                                | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Gliclazide v Metformin                | All-cause mortality                          | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Gliclazide             | All-cause mortality                          | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Metformin              | All-cause mortality                          | High         | None specified | Directly applicable | None specified      |

| Study name | Comparison details        | Outcome                           | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------|-----------------------------------|--------------|----------------|---------------------|---------------------|
| Erem 2014  | Gliclazide v Metformin    | BMI change                        | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Gliclazide | BMI change                        | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Metformin  | BMI change                        | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Gliclazide v Metformin    | Cardiovascular mortality          | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Gliclazide | Cardiovascular mortality          | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Metformin  | Cardiovascular mortality          | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Gliclazide v Metformin    | HbA1c change                      | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Gliclazide | HbA1c change                      | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Metformin  | HbA1c change                      | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Gliclazide v Metformin    | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Gliclazide | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Metformin  | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Gliclazide v Metformin    | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Gliclazide | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Erem 2014  | Pioglitazone v Metformin  | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |



| Study name    | Comparison details        | Outcome                         | Risk of bias | Bias comments  | Directness          | Directness comments |
|---------------|---------------------------|---------------------------------|--------------|----------------|---------------------|---------------------|
| Erem 2014     | Gliclazide v Metformin    | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Pioglitazone v Gliclazide | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Pioglitazone v Metformin  | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Gliclazide v Metformin    | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Pioglitazone v Gliclazide | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Pioglitazone v Metformin  | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Gliclazide v Metformin    | Weight change                   | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Pioglitazone v Gliclazide | Weight change                   | High         | None specified | Directly applicable | None specified      |
| Erem 2014     | Pioglitazone v Metformin  | Weight change                   | High         | None specified | Directly applicable | None specified      |
| Esposito 2011 | Pioglitazone v Metformin  | All-cause mortality             | Low          | None specified | Directly applicable | None specified      |
| Esposito 2011 | Pioglitazone v Metformin  | BMI change                      | Low          | None specified | Directly applicable | None specified      |
| Esposito 2011 | Pioglitazone v Metformin  | Cardiovascular mortality        | Low          | None specified | Directly applicable | None specified      |
| Esposito 2011 | Pioglitazone v Metformin  | HbA1c change                    | Low          | None specified | Directly applicable | None specified      |

| Study name      | Comparison details       | Outcome                           | Risk of bias  | Bias comments                                                | Directness          | Directness comments |
|-----------------|--------------------------|-----------------------------------|---------------|--------------------------------------------------------------|---------------------|---------------------|
| Esposito 2011   | Pioglitazone v Metformin | Hospitalisation for heart failure | Low           | None specified                                               | Directly applicable | None specified      |
| Esposito 2011   | Pioglitazone v Metformin | Weight change                     | Low           | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Liraglutide | BMI change                        | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Metformin   | BMI change                        | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Liraglutide v Metformin  | BMI change                        | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Liraglutide | HbA1c change                      | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Metformin   | HbA1c change                      | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Liraglutide v Metformin  | HbA1c change                      | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Liraglutide | Hypoglycaemia episodes            | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Metformin   | Hypoglycaemia episodes            | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Liraglutide v Metformin  | Hypoglycaemia episodes            | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Liraglutide | Weight change                     | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Gliclazide v Metformin   | Weight change                     | High          | None specified                                               | Directly applicable | None specified      |
| Feng 2017       | Liraglutide v Metformin  | Weight change                     | High          | None specified                                               | Directly applicable | None specified      |
| Ferrannini 2010 | Dapagliflozin v Placebo  | All-cause mortality               | Some concerns | 1) Higher attrition, lack of information on outcome analysis | Directly applicable | None specified      |

| Study name      | Comparison details      | Outcome                | Risk of bias  | Bias comments                                                                                                                                                                                                    | Directness          | Directness comments |
|-----------------|-------------------------|------------------------|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|                 |                         |                        |               | plan but presentation of results suggests that they used ITT<br>2) observed number of events is not greater than the number that withdrew                                                                        |                     |                     |
| Ferrannini 2010 | Dapagliflozin v Placebo | Hypoglycaemia episodes | Some concerns | 1) Higher attrition, lack of information on outcome analysis plan but presentation of results suggests that they used ITT<br>2) observed number of events is not that much greater than the number that withdrew | Directly applicable | None specified      |
| Ferrannini 2010 | Dapagliflozin v Placebo | HbA1c change           | Some concerns | Higher attrition, lack of information on outcome analysis plan but presentation of results suggests that they used ITT                                                                                           | Directly applicable | None specified      |
| Ferrannini 2010 | Dapagliflozin v Placebo | Weight change          | Some concerns | Higher attrition, lack of information on outcome analysis plan but presentation of results suggests that they used ITT                                                                                           | Directly applicable | None specified      |

| Study name     | Comparison details        | Outcome                  | Risk of bias  | Bias comments                                                       | Directness          | Directness comments |
|----------------|---------------------------|--------------------------|---------------|---------------------------------------------------------------------|---------------------|---------------------|
| Foley 2009     | Gliclazide v Vildagliptin | All-cause mortality      | High          | None specified                                                      | Directly applicable | None specified      |
| Foley 2009     | Gliclazide v Vildagliptin | HbA1c change             | High          | None specified                                                      | Directly applicable | None specified      |
| Foley 2009     | Gliclazide v Vildagliptin | Weight change            | High          | None specified                                                      | Directly applicable | None specified      |
| Foley 2011     | Vildagliptin v Placebo    | HbA1c change             | High          | None specified                                                      | Directly applicable | None specified      |
| Frederich 2012 | Saxagliptin v Placebo     | All-cause mortality      | High          | Concerns regarding allocation concealment, adherence and attrition. | Directly applicable | None specified      |
| Frederich 2012 | Saxagliptin v Placebo     | Cardiovascular mortality | High          | Concerns regarding allocation concealment, adherence and attrition. | Directly applicable | None specified      |
| Frederich 2012 | Saxagliptin v Placebo     | HbA1c change             | High          | Concerns regarding allocation concealment, adherence and attrition. | Directly applicable | None specified      |
| Frederich 2012 | Saxagliptin v Placebo     | Weight change            | High          | Concerns regarding allocation concealment, adherence and attrition. | Directly applicable | None specified      |
| Gantz 2017D    | Sitagliptin v Placebo     | Hypoglycaemia episodes   | High          | None specified                                                      | Directly applicable | None specified      |
| Gantz 2017D    | Sitagliptin v Placebo     | All-cause mortality      | Some concerns | None specified                                                      | Directly applicable | None specified      |

| Study name      | Comparison details        | Outcome                       | Risk of bias  | Bias comments                                                                          | Directness          | Directness comments |
|-----------------|---------------------------|-------------------------------|---------------|----------------------------------------------------------------------------------------|---------------------|---------------------|
| Gantz 2017D     | Sitagliptin v Placebo     | Cardiovascular mortality      | Some concerns | None specified                                                                         | Directly applicable | None specified      |
| Gantz 2017D     | Sitagliptin v Placebo     | HbA1c change                  | Some concerns | None specified                                                                         | Directly applicable | None specified      |
| Gantz 2017D     | Sitagliptin v Placebo     | Severe hypoglycaemic episodes | Some concerns | None specified                                                                         | Directly applicable | None specified      |
| Gantz 2017D     | Sitagliptin v Placebo     | Weight change                 | Some concerns | None specified                                                                         | Directly applicable | None specified      |
| Garber 2009 1.1 | Glimepiride v Liraglutide | HbA1c change                  | High          | None specified                                                                         | Directly applicable | None specified      |
| Goldner 1971    | Tolbutamide v Insulin     | All-cause mortality           | High          | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971    | Tolbutamide v Placebo     | All-cause mortality           | High          | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971    | Tolbutamide v Insulin     | Cardiac arrhythmia            | High          | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971    | Tolbutamide v Placebo     | Cardiac arrhythmia            | High          | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971    | Tolbutamide v Insulin     | Cardiovascular mortality      | High          | Missing baseline characteristics data, missing information                             | Directly applicable | None specified      |

| Study name     | Comparison details                  | Outcome                                      | Risk of bias | Bias comments                                                                          | Directness          | Directness comments |
|----------------|-------------------------------------|----------------------------------------------|--------------|----------------------------------------------------------------------------------------|---------------------|---------------------|
|                |                                     |                                              |              | about outcome analysis plan                                                            |                     |                     |
| Goldner 1971   | Tolbutamide v Placebo               | Cardiovascular mortality                     | High         | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971   | Tolbutamide v Insulin               | Persistent signs of worsening kidney disease | High         | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971   | Tolbutamide v Placebo               | Persistent signs of worsening kidney disease | High         | Missing baseline characteristics data, missing information about outcome analysis plan | Directly applicable | None specified      |
| Goldner 1971   | Insulin v Placebo                   | All-cause mortality                          | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldner 1971   | Insulin v Placebo                   | Cardiac arrhythmia                           | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldner 1971   | Insulin v Placebo                   | Cardiovascular mortality                     | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldner 1971   | Insulin v Placebo                   | Persistent signs of worsening kidney disease | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldstein 2007 | Metformin v Placebo                 | All-cause mortality                          | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Metformin | All-cause mortality                          | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Placebo   | All-cause mortality                          | High         | None specified                                                                         | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Placebo               | All-cause mortality                          | High         | None specified                                                                         | Directly applicable | None specified      |



| Study name     | Comparison details                  | Outcome                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|----------------|-------------------------------------|--------------------------|--------------|----------------|---------------------|---------------------|
| Goldstein 2007 | Metformin v Placebo                 | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Metformin | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Placebo   | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Metformin             | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Placebo               | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Metformin v Placebo                 | Diabetic ketoacidosis    | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Metformin | Diabetic ketoacidosis    | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Placebo   | Diabetic ketoacidosis    | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Placebo               | Diabetic ketoacidosis    | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Metformin v Placebo                 | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Metformin | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Placebo   | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Placebo               | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Metformin v Placebo                 | Hypoglycaemia episodes   | High         | None specified | Directly applicable | None specified      |

| Study name     | Comparison details                    | Outcome                  | Risk of bias  | Bias comments  | Directness          | Directness comments |
|----------------|---------------------------------------|--------------------------|---------------|----------------|---------------------|---------------------|
| Goldstein 2007 | Sitagliptin + Metformin v Metformin   | Hypoglycaemia episodes   | High          | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Placebo     | Hypoglycaemia episodes   | High          | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Placebo                 | Hypoglycaemia episodes   | High          | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Sitagliptin | All-cause mortality      | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Metformin               | All-cause mortality      | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Sitagliptin | Cardiovascular mortality | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Sitagliptin | Diabetic ketoacidosis    | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Metformin               | Diabetic ketoacidosis    | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Sitagliptin | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Metformin               | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin + Metformin v Sitagliptin | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Goldstein 2007 | Sitagliptin v Metformin               | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Grant 1996     | Metformin v Placebo                   | HbA1c change             | High          | None specified | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|--------------------------|--------------|----------------|---------------------|---------------------|
| Guo 2014   | Metformin v Placebo                   | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Linagliptin | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Metformin   | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Placebo     | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Metformin               | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Placebo                 | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Metformin v Placebo                   | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Linagliptin | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Metformin   | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Placebo     | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Metformin               | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Placebo                 | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Metformin v Placebo                   | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Linagliptin | HbA1c change             | High         | None specified | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                       | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|-------------------------------|--------------|----------------|---------------------|---------------------|
| Haak 2012  | Linagliptin + Metformin v Metformin   | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Placebo     | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Metformin               | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Placebo                 | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Metformin v Placebo                   | HbA1c change                  | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Linagliptin | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Metformin   | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Placebo     | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Metformin               | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin v Placebo                 | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Metformin v Placebo                   | Hypoglycaemia episodes        | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Linagliptin | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| Haak 2012  | Linagliptin + Metformin v Metformin   | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |

| Study name   | Comparison details                        | Outcome                       | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------|-------------------------------------------|-------------------------------|--------------|----------------|---------------------|---------------------|
| Haak 2012    | Linagliptin + Metformin v Placebo         | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin v Metformin                   | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin v Placebo                     | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Metformin v Placebo                       | Severe hypoglycaemic episodes | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin + Metformin v Linagliptin     | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin + Metformin v Metformin       | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin + Metformin v Placebo         | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin v Metformin                   | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Linagliptin v Placebo                     | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Haak 2012    | Metformin v Placebo                       | Weight change                 | High         | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Empagliflozin | All-cause mortality           | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Metformin     | All-cause mortality           | Low          | None specified | Directly applicable | None specified      |

| Study name   | Comparison details                        | Outcome                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------|-------------------------------------------|--------------------------|--------------|----------------|---------------------|---------------------|
| Hadjadj 2016 | Empagliflozin v Metformin                 | All-cause mortality      | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Empagliflozin | Cardiovascular mortality | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Metformin     | Cardiovascular mortality | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin v Metformin                 | Cardiovascular mortality | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Empagliflozin | HbA1c change             | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Metformin     | HbA1c change             | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin v Metformin                 | HbA1c change             | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Empagliflozin | Hypoglycaemia episodes   | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin + Metformin v Metformin     | Hypoglycaemia episodes   | Low          | None specified | Directly applicable | None specified      |
| Hadjadj 2016 | Empagliflozin v Metformin                 | Hypoglycaemia episodes   | Low          | None specified | Directly applicable | None specified      |
| Hartley 2015 | Glimepiride v Sitagliptin                 | All-cause mortality      | Low          | No concerns    | Directly applicable | None specified      |
| Hartley 2015 | Glimepiride v Sitagliptin                 | Cardiovascular mortality | Low          | No concerns    | Directly applicable | None specified      |
| Hartley 2015 | Glimepiride v Sitagliptin                 | Hypoglycaemia episodes   | Low          | No concerns    | Directly applicable | None specified      |

| Study name   | Comparison details                        | Outcome                       | Risk of bias | Bias comments                                                                                          | Directness          | Directness comments |
|--------------|-------------------------------------------|-------------------------------|--------------|--------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Hartley 2015 | Glimepiride v Sitagliptin                 | Severe hypoglycaemic episodes | Low          | No concerns                                                                                            | Directly applicable | None specified      |
| Hartley 2015 | Glimepiride v Sitagliptin                 | Weight change                 | Low          | No concerns                                                                                            | Directly applicable | None specified      |
| Hartley 2015 | Glimepiride v Sitagliptin                 | HbA1c change                  | High         | Results were not adequately reported for the full-analysis set, despite this being a secondary outcome | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin + Metformin v Dapagliflozin | All-cause mortality           | Low          | None specified                                                                                         | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin + Metformin v Metformin     | All-cause mortality           | Low          | None specified                                                                                         | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin v Metformin                 | All-cause mortality           | Low          | None specified                                                                                         | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin + Metformin v Dapagliflozin | Cardiovascular mortality      | Low          | None specified                                                                                         | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin + Metformin v Metformin     | Cardiovascular mortality      | Low          | None specified                                                                                         | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin v Metformin                 | Cardiovascular mortality      | Low          | None specified                                                                                         | Directly applicable | None specified      |
| Henry 2012A  | Dapagliflozin + Metformin v Dapagliflozin | HbA1c change                  | Low          | None specified                                                                                         | Directly applicable | None specified      |



| Study name  | Comparison details                        | Outcome                       | Risk of bias | Bias comments  | Directness          | Directness comments |
|-------------|-------------------------------------------|-------------------------------|--------------|----------------|---------------------|---------------------|
| Henry 2012A | Dapagliflozin + Metformin v Metformin     | HbA1c change                  | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin v Metformin                 | HbA1c change                  | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin + Metformin v Dapagliflozin | Hypoglycaemia episodes        | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin + Metformin v Metformin     | Hypoglycaemia episodes        | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin v Metformin                 | Hypoglycaemia episodes        | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin + Metformin v Dapagliflozin | Severe hypoglycaemic episodes | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin + Metformin v Metformin     | Severe hypoglycaemic episodes | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin v Metformin                 | Severe hypoglycaemic episodes | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin + Metformin v Dapagliflozin | Weight change                 | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin + Metformin v Metformin     | Weight change                 | Low          | None specified | Directly applicable | None specified      |
| Henry 2012A | Dapagliflozin v Metformin                 | Weight change                 | Low          | None specified | Directly applicable | None specified      |

| Study name  | Comparison details                        | Outcome                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|-------------|-------------------------------------------|--------------------------|--------------|----------------|---------------------|---------------------|
| Henry 2012B | Dapagliflozin + Metformin v Dapagliflozin | All-cause mortality      | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Metformin     | All-cause mortality      | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin v Metformin                 | All-cause mortality      | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Dapagliflozin | Cardiovascular mortality | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Metformin     | Cardiovascular mortality | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin v Metformin                 | Cardiovascular mortality | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Dapagliflozin | HbA1c change             | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Metformin     | HbA1c change             | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin v Metformin                 | HbA1c change             | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Dapagliflozin | Hypoglycaemia episodes   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Metformin     | Hypoglycaemia episodes   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin v Metformin                 | Hypoglycaemia episodes   | Low          | None specified | Directly applicable | None specified      |

| Study name  | Comparison details                        | Outcome                         | Risk of bias | Bias comments  | Directness          | Directness comments |
|-------------|-------------------------------------------|---------------------------------|--------------|----------------|---------------------|---------------------|
| Henry 2012B | Dapagliflozin + Metformin v Dapagliflozin | Severe hypoglycaemic episodes   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Metformin     | Severe hypoglycaemic episodes   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin v Metformin                 | Severe hypoglycaemic episodes   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Dapagliflozin | Weight change                   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin + Metformin v Metformin     | Weight change                   | Low          | None specified | Directly applicable | None specified      |
| Henry 2012B | Dapagliflozin v Metformin                 | Weight change                   | Low          | None specified | Directly applicable | None specified      |
| Henry 2014  | Pioglitazone v Sitagliptin                | All-cause mortality             | High         | None specified | Directly applicable | None specified      |
| Henry 2014  | Pioglitazone v Sitagliptin                | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Henry 2014  | Pioglitazone v Sitagliptin                | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Henry 2014  | Pioglitazone v Sitagliptin                | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Henry 2014  | Pioglitazone v Sitagliptin                | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Henry 2014  | Pioglitazone v Sitagliptin                | Non-fatal stroke                | High         | None specified | Directly applicable | None specified      |

| Study name   | Comparison details         | Outcome                       | Risk of bias | Bias comments                                                                                                                                                                                                                                                                                                                                                                                    | Directness          | Directness comments                                                                                                                                            |
|--------------|----------------------------|-------------------------------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Henry 2014   | Pioglitazone v Sitagliptin | Severe hypoglycaemic episodes | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                   | Directly applicable | None specified                                                                                                                                                 |
| Henry 2014   | Pioglitazone v Sitagliptin | Weight change                 | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                   | Directly applicable | None specified                                                                                                                                                 |
| Horton 2000  | Metformin v Placebo        | All-cause mortality           | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                   | Directly applicable | None specified                                                                                                                                                 |
| Horton 2000  | Metformin v Placebo        | Cardiovascular mortality      | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                   | Directly applicable | None specified                                                                                                                                                 |
| Horton 2000  | Metformin v Placebo        | Severe hypoglycaemic episodes | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                   | Directly applicable | None specified                                                                                                                                                 |
| Inagaki 2014 | Canagliflozin v Placebo    | HbA1c change                  | High         | 1) Differences in baseline characteristics for two of the characteristics (gender and EGFR baseline) 2) Last observation carried forward used to account for missing values - should not be assumed that this has corrected for bias due to missing outcome data. 3) 11% attrition in total; attrition is not balanced across arms, PCB group has a higher % attrition ( 20% ) compared with the | Directly applicable | The population of adults with T2DM is applicable however the participants are recruited from Japan which may make the results less applicable to a UK setting. |

| Study name   | Comparison details      | Outcome                       | Risk of bias | Bias comments                                                                                                                                                                                                                                  | Directness          | Directness comments                                                                                                                                            |
|--------------|-------------------------|-------------------------------|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              |                         |                               |              | canagliflozin arm (7% )                                                                                                                                                                                                                        |                     |                                                                                                                                                                |
| Inagaki 2014 | Canagliflozin v Placebo | Hypoglycaemia episodes        | High         | 1) Differences in baseline characteristics for two of the characteristics (gender and EGFR baseline) 2) the observed number of events is not much greater than the number of participants with missing outcome data, so potential risk of bias | Directly applicable | The population of adults with T2DM is applicable however the participants are recruited from Japan which may make the results less applicable to a UK setting. |
| Inagaki 2014 | Canagliflozin v Placebo | Severe hypoglycaemic episodes | High         | 1) Differences in baseline characteristics for two of the characteristics (gender and EGFR baseline) 2) the observed number of events is not much greater than the number of participants with missing outcome data, so potential risk of bias | Directly applicable | The population of adults with T2DM is applicable however the participants are recruited from Japan which may make the results less applicable to a UK setting. |
| Inagaki 2014 | Canagliflozin v Placebo | Weight change                 | High         | 1) Differences in baseline characteristics for                                                                                                                                                                                                 | Directly applicable | The population of adults with T2DM is applicable however                                                                                                       |

| Study name   | Comparison details        | Outcome                | Risk of bias  | Bias comments                                                                                                                                                                                                                                                                                                                                                                         | Directness          | Directness comments                                                                                   |
|--------------|---------------------------|------------------------|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------------------------------------------------|
|              |                           |                        |               | two of the characteristics (gender and EGFR baseline) <sup>2</sup> ) Last observation carried forward used to account for missing values - should not be assumed that this has corrected for bias due to missing outcome data. 3) 11% attrition in total; attrition is not balanced across arms, PCB group has a higher % attrition ( 20% ) compared with the canagliflozin arm (7% ) |                     | the participants are recruited from Japan which may make the results less applicable to a UK setting. |
| Inagaki 2015 | Alogliptin v Placebo      | HbA1c change           | Low           | None specified                                                                                                                                                                                                                                                                                                                                                                        | Directly applicable | None specified                                                                                        |
| Inagaki 2015 | Alogliptin v Placebo      | Hypoglycaemia episodes | Low           | None specified                                                                                                                                                                                                                                                                                                                                                                        | Directly applicable | None specified                                                                                        |
| Inagaki 2022 | Tirzepatide v Dulaglutide | 3-point MACE           | Some concerns | Double-blind trial. mITT analysis conducted for this outcome.                                                                                                                                                                                                                                                                                                                         | Directly applicable | None specified                                                                                        |
| Inagaki 2022 | Tirzepatide v Dulaglutide | All-cause mortality    | Some concerns | Double-blind trial. mITT analysis conducted for this outcome.                                                                                                                                                                                                                                                                                                                         | Directly applicable | None specified                                                                                        |

| Study name   | Comparison details        | Outcome                         | Risk of bias  | Bias comments                                                 | Directness          | Directness comments |
|--------------|---------------------------|---------------------------------|---------------|---------------------------------------------------------------|---------------------|---------------------|
| Inagaki 2022 | Tirzepatide v Dulaglutide | Cardiac arrhythmia              | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | Cardiovascular mortality        | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | HbA1c change                    | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | Hypoglycaemia episodes          | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | Non-fatal myocardial infarction | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | Severe hypoglycaemic episodes   | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | Unstable angina                 | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |
| Inagaki 2022 | Tirzepatide v Dulaglutide | Weight change                   | Some concerns | Double-blind trial. mITT analysis conducted for this outcome. | Directly applicable | None specified      |



| Study name | Comparison details      | Outcome                                      | Risk of bias  | Bias comments                                                                                              | Directness          | Directness comments |
|------------|-------------------------|----------------------------------------------|---------------|------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Ji 2014    | Dapagliflozin v Placebo | All-cause mortality                          | Some concerns | Multisite trial but some concerns around attrition and doesn't seem to have been accounted for in analysis | Directly applicable | None specified      |
| Ji 2014    | Dapagliflozin v Placebo | Cardiovascular mortality                     | Some concerns | Multisite trial but some concerns around attrition and doesn't seem to have been accounted for in analysis | Directly applicable | None specified      |
| Ji 2014    | Dapagliflozin v Placebo | HbA1c change                                 | Some concerns | Multisite trial but some concerns around attrition and doesn't seem to have been accounted for in analysis | Directly applicable | None specified      |
| Ji 2014    | Dapagliflozin v Placebo | Hypoglycaemia episodes                       | Some concerns | Multisite trial but some concerns around attrition and doesn't seem to have been accounted for in analysis | Directly applicable | None specified      |
| Ji 2014    | Dapagliflozin v Placebo | Persistent signs of worsening kidney disease | Some concerns | Multisite trial but some concerns around attrition and doesn't seem to have been                           | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                  | Risk of bias  | Bias comments                                                                                              | Directness          | Directness comments |
|------------|---------------------------------------|--------------------------|---------------|------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                                       |                          |               | accounted for in analysis                                                                                  |                     |                     |
| Ji 2014    | Dapagliflozin v Placebo               | Weight change            | Some concerns | Multisite trial but some concerns around attrition and doesn't seem to have been accounted for in analysis | Directly applicable | None specified      |
| Ji 2016A   | Metformin v Placebo                   | All-cause mortality      | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Metformin   | All-cause mortality      | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Placebo     | All-cause mortality      | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Sitagliptin | All-cause mortality      | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Metformin               | All-cause mortality      | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Placebo                 | All-cause mortality      | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Metformin v Placebo                   | Cardiovascular mortality | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Metformin   | Cardiovascular mortality | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Placebo     | Cardiovascular mortality | Some concerns | None specified                                                                                             | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Sitagliptin | Cardiovascular mortality | Some concerns | None specified                                                                                             | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                  | Risk of bias  | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|--------------------------|---------------|----------------|---------------------|---------------------|
| Ji 2016A   | Sitagliptin v Metformin               | Cardiovascular mortality | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Placebo                 | Cardiovascular mortality | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Metformin v Placebo                   | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Metformin   | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Placebo     | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Sitagliptin | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Metformin               | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Placebo                 | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Metformin v Placebo                   | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Metformin   | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Placebo     | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Sitagliptin | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Metformin               | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Placebo                 | Hypoglycaemia episodes   | Some concerns | None specified | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                       | Risk of bias  | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|-------------------------------|---------------|----------------|---------------------|---------------------|
| Ji 2016A   | Metformin v Placebo                   | Severe hypoglycaemic episodes | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Metformin   | Severe hypoglycaemic episodes | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Placebo     | Severe hypoglycaemic episodes | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Sitagliptin | Severe hypoglycaemic episodes | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Metformin               | Severe hypoglycaemic episodes | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Placebo                 | Severe hypoglycaemic episodes | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Metformin v Placebo                   | Weight change                 | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Metformin   | Weight change                 | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Placebo     | Weight change                 | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin + Metformin v Sitagliptin | Weight change                 | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Metformin               | Weight change                 | Some concerns | None specified | Directly applicable | None specified      |
| Ji 2016A   | Sitagliptin v Placebo                 | Weight change                 | Some concerns | None specified | Directly applicable | None specified      |

| Study name | Comparison details                  | Outcome                | Risk of bias  | Bias comments                | Directness          | Directness comments |
|------------|-------------------------------------|------------------------|---------------|------------------------------|---------------------|---------------------|
| Ji 2017    | Alogliptin + Metformin v Alogliptin | HbA1c change           | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin + Metformin v Metformin  | HbA1c change           | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin + Metformin v Placebo    | HbA1c change           | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin v Metformin              | HbA1c change           | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin v Placebo                | HbA1c change           | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Metformin v Placebo                 | HbA1c change           | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin + Metformin v Alogliptin | Hypoglycaemia episodes | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin + Metformin v Metformin  | Hypoglycaemia episodes | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin + Metformin v Placebo    | Hypoglycaemia episodes | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin v Metformin              | Hypoglycaemia episodes | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Alogliptin v Placebo                | Hypoglycaemia episodes | High          | None specified               | Directly applicable | None specified      |
| Ji 2017    | Metformin v Placebo                 | Hypoglycaemia episodes | High          | None specified               | Directly applicable | None specified      |
| Kahl 2019  | Empagliflozin v Placebo             | HbA1c change           | Some concerns | Concerns regarding attrition | Directly applicable | None specified      |
| Kahl 2019  | Empagliflozin v Placebo             | Weight change          | Some concerns | Concerns regarding attrition | Directly applicable | None specified      |

| Study name | Comparison details                          | Outcome                                      | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------------|----------------------------------------------|--------------|----------------|---------------------|---------------------|
| Kaku 2014  | Dapagliflozin v Placebo                     | HbA1c change                                 | Low          | None specified | Directly applicable | None specified      |
| Kaku 2014  | Dapagliflozin v Placebo                     | Persistent signs of worsening kidney disease | Low          | None specified | Directly applicable | None specified      |
| Kaku 2014  | Dapagliflozin v Placebo                     | Weight change                                | Low          | None specified | Directly applicable | None specified      |
| Kaku 2018A | Empagliflozin + Linagliptin v Empagliflozin | All-cause mortality                          | High         | None specified | Directly applicable | None specified      |
| Kaku 2018A | Empagliflozin + Linagliptin v Empagliflozin | Cardiovascular mortality                     | High         | None specified | Directly applicable | None specified      |
| Kaku 2018A | Empagliflozin + Linagliptin v Empagliflozin | HbA1c change                                 | High         | None specified | Directly applicable | None specified      |
| Kaku 2018A | Empagliflozin + Linagliptin v Empagliflozin | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Kaku 2018B | Empagliflozin + Linagliptin v Empagliflozin | All-cause mortality                          | High         | None specified | Directly applicable | None specified      |
| Kaku 2018B | Empagliflozin + Linagliptin v Empagliflozin | Cardiovascular mortality                     | High         | None specified | Directly applicable | None specified      |
| Kaku 2018B | Empagliflozin + Linagliptin v Empagliflozin | HbA1c change                                 | High         | None specified | Directly applicable | None specified      |
| Kaku 2018B | Empagliflozin + Linagliptin v Empagliflozin | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |

| Study name   | Comparison details                    | Outcome                         | Risk of bias | Bias comments                                                                                                   | Directness          | Directness comments |
|--------------|---------------------------------------|---------------------------------|--------------|-----------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Kashyap 2020 | Canagliflozin v Placebo               | BMI change                      | High         | None specified                                                                                                  | Directly applicable | None specified      |
| Kashyap 2020 | Canagliflozin v Placebo               | HbA1c change                    | High         | None specified                                                                                                  | Directly applicable | None specified      |
| Kashyap 2020 | Canagliflozin v Placebo               | Hypoglycaemia episodes          | High         | None specified                                                                                                  | Directly applicable | None specified      |
| Kashyap 2020 | Canagliflozin v Placebo               | Weight change                   | High         | None specified                                                                                                  | Directly applicable | None specified      |
| Kikuchi 2012 | Pioglitazone v Placebo                | HbA1c change                    | High         | Missing data due to Aes in int arm couldve biased results and not appropriately controlled for in LOCF analysis | Directly applicable | None specified      |
| Kikuchi 2012 | Pioglitazone v Placebo                | Weight change                   | High         | Missing data due to Aes in int arm couldve biased results and not appropriately controlled for in LOCF analysis | Directly applicable | None specified      |
| Kikuchi 2012 | Pioglitazone v Placebo                | Non-fatal myocardial infarction | Low          | None specified                                                                                                  | Directly applicable | None specified      |
| Kim 2017     | Sitagliptin + Metformin v Glimepiride | All-cause mortality             | High         | None specified                                                                                                  | Directly applicable | None specified      |
| Kim 2017     | Sitagliptin + Metformin v Glimepiride | Cardiovascular mortality        | High         | None specified                                                                                                  | Directly applicable | None specified      |



| Study name | Comparison details                    | Outcome                                      | Risk of bias  | Bias comments                               | Directness          | Directness comments |
|------------|---------------------------------------|----------------------------------------------|---------------|---------------------------------------------|---------------------|---------------------|
| Kim 2017   | Sitagliptin + Metformin v Glimepiride | HbA1c change                                 | High          | None specified                              | Directly applicable | None specified      |
| Kim 2017   | Sitagliptin + Metformin v Glimepiride | Hypoglycaemia episodes                       | High          | None specified                              | Directly applicable | None specified      |
| Kim 2017   | Sitagliptin + Metformin v Glimepiride | Severe hypoglycaemic episodes                | High          | None specified                              | Directly applicable | None specified      |
| Kim 2017   | Sitagliptin + Metformin v Glimepiride | Weight change                                | High          | None specified                              | Directly applicable | None specified      |
| Kondo 2016 | Glimepiride v Sitagliptin             | BMI change                                   | High          | Concerns regarding allocation and attrition | Directly applicable | None specified      |
| Kondo 2016 | Glimepiride v Sitagliptin             | HbA1c change                                 | High          | Concerns regarding allocation and attrition | Directly applicable | None specified      |
| Kondo 2016 | Glimepiride v Sitagliptin             | Hypoglycaemia episodes                       | High          | Concerns regarding allocation and attrition | Directly applicable | None specified      |
| Kondo 2016 | Glimepiride v Sitagliptin             | Persistent signs of worsening kidney disease | High          | Concerns regarding allocation and attrition | Directly applicable | None specified      |
| Kondo 2016 | Glimepiride v Sitagliptin             | Severe hypoglycaemic episodes                | High          | Concerns regarding allocation and attrition | Directly applicable | None specified      |
| Kumar 2014 | Saxagliptin v Placebo                 | All-cause mortality                          | Some concerns | Problems with allocation concealment        | Directly applicable | None specified      |

| Study name      | Comparison details      | Outcome                         | Risk of bias  | Bias comments                                               | Directness          | Directness comments |
|-----------------|-------------------------|---------------------------------|---------------|-------------------------------------------------------------|---------------------|---------------------|
| Kumar 2014      | Saxagliptin v Placebo   | BMI change                      | Some concerns | Problems with allocation concealment                        | Directly applicable | None specified      |
| Kumar 2014      | Saxagliptin v Placebo   | Cardiovascular mortality        | Some concerns | Problems with allocation concealment                        | Directly applicable | None specified      |
| Kumar 2014      | Saxagliptin v Placebo   | HbA1c change                    | Some concerns | Problems with allocation concealment                        | Directly applicable | None specified      |
| Kumar 2014      | Saxagliptin v Placebo   | Hypoglycaemia episodes          | Some concerns | Problems with allocation concealment                        | Directly applicable | None specified      |
| Kumar 2014      | Saxagliptin v Placebo   | Weight change                   | Some concerns | Problems with allocation concealment                        | Directly applicable | None specified      |
| Lambadiari 2018 | Liraglutide v Metformin | BMI change                      | High          | None specified                                              | Directly applicable | None specified      |
| Lambadiari 2018 | Liraglutide v Metformin | HbA1c change                    | High          | None specified                                              | Directly applicable | None specified      |
| Lambadiari 2018 | Liraglutide v Metformin | Weight change                   | High          | None specified                                              | Directly applicable | None specified      |
| Lee 2013A       | Pioglitazone v Placebo  | All-cause mortality             | Some concerns | Lack of information on randomisation and single blind study | Directly applicable | None specified      |
| Lee 2013A       | Pioglitazone v Placebo  | Cardiovascular mortality        | Some concerns | Lack of information on randomisation and single blind study | Directly applicable | None specified      |
| Lee 2013A       | Pioglitazone v Placebo  | Non-fatal myocardial infarction | Some concerns | Lack of information on randomisation and single blind study | Directly applicable | None specified      |

| Study name | Comparison details                          | Outcome                       | Risk of bias  | Bias comments                                                                                                                                   | Directness          | Directness comments |
|------------|---------------------------------------------|-------------------------------|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Lee 2013A  | Pioglitazone v Placebo                      | Non-fatal stroke              | Some concerns | Lack of information on randomisation and single blind study                                                                                     | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin v Linagliptin                 | HbA1c change                  | Some concerns | Large amount of missing data, LOCF not sufficient to address this (16% attrition) - should not be assumed that this has corrected for bias.     | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Empagliflozin | All-cause mortality           | High          | None specified                                                                                                                                  | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Empagliflozin | Cardiovascular mortality      | High          | None specified                                                                                                                                  | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Empagliflozin | HbA1c change                  | High          | None specified                                                                                                                                  | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Empagliflozin | Hypoglycaemia episodes        | High          | None specified                                                                                                                                  | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Empagliflozin | Severe hypoglycaemic episodes | High          | None specified                                                                                                                                  | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Linagliptin   | All-cause mortality           | High          | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated" analysis to be inappropriate for | Directly applicable | None specified      |

| Study name | Comparison details                        | Outcome                  | Risk of bias | Bias comments                                                                                                                                                                                                                                                                                                                     | Directness          | Directness comments |
|------------|-------------------------------------------|--------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                                           |                          |              | per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data                                                                                                                                                 |                     |                     |
| Lewin 2015 | Empagliflozin v Linagliptin               | All-cause mortality      | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated" analysis to be inappropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Linagliptin | Cardiovascular mortality | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated" analysis to be                                                                                                                                                                                                     | Directly applicable | None specified      |

| Study name | Comparison details                        | Outcome                  | Risk of bias | Bias comments                                                                                                                                                                                                                                                                                                                     | Directness          | Directness comments |
|------------|-------------------------------------------|--------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                                           |                          |              | innapropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data                                                                                                                               |                     |                     |
| Lewin 2015 | Empagliflozin v Linagliptin               | Cardiovascular mortality | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated" analysis to be innapropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin + Linagliptin v Linagliptin | HbA1c change             | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated"                                                                                                                                                                                                                    | Directly applicable | None specified      |

| Study name | Comparison details                        | Outcome                | Risk of bias | Bias comments                                                                                                                                                                                                                                                                                                                     | Directness          | Directness comments |
|------------|-------------------------------------------|------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                                           |                        |              | analysis to be inappropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data                                                                                                                |                     |                     |
| Lewin 2015 | Empagliflozin + Linagliptin v Linagliptin | Hypoglycaemia episodes | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated" analysis to be inappropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin v Linagliptin               | Hypoglycaemia episodes | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use                                                                                                                                                                                                                                    | Directly applicable | None specified      |

| Study name | Comparison details                        | Outcome                       | Risk of bias | Bias comments                                                                                                                                                                                                                                                                                                                     | Directness          | Directness comments |
|------------|-------------------------------------------|-------------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                                           |                               |              | of "as treated" analysis to be inappropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data                                                                                                |                     |                     |
| Lewin 2015 | Empagliflozin + Linagliptin v Linagliptin | Severe hypoglycaemic episodes | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool states that the use of "as treated" analysis to be inappropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data | Directly applicable | None specified      |
| Lewin 2015 | Empagliflozin v Linagliptin               | Severe hypoglycaemic episodes | High         | Treated set used for analysis (received 1 or more doses of drug). RoB tool                                                                                                                                                                                                                                                        | Directly applicable | None specified      |



| Study name | Comparison details        | Outcome                       | Risk of bias | Bias comments                                                                                                                                                                                                                                          | Directness          | Directness comments            |
|------------|---------------------------|-------------------------------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|--------------------------------|
|            |                           |                               |              | states that the use of "as treated" analysis to be inappropriate for per-protocol analysis. Higher dropouts in the empagliflozin arm than linagliptin due to adverse events. LOCF not sufficient to account for any potential bias due to missing data |                     |                                |
| Li 2019A   | Glimepiride v Saxagliptin | BMI change                    | High         | Open-label trial, completer analysis                                                                                                                                                                                                                   | Directly applicable | Participants are T2D and NAFLD |
| Li 2019A   | Glimepiride v Saxagliptin | HbA1c change                  | High         | Open-label trial, completer analysis                                                                                                                                                                                                                   | Directly applicable | Participants are T2D and NAFLD |
| Liu 2020   | Exenatide v Insulin       | BMI change                    | High         | Open-label trial, possible selective reporting of results                                                                                                                                                                                              | Directly applicable | Participants are T2D and NAFLD |
| Liu 2020   | Exenatide v Insulin       | HbA1c change                  | High         | Open-label trial, possible selective reporting of results                                                                                                                                                                                              | Directly applicable | Participants are T2D and NAFLD |
| Liu 2020   | Exenatide v Insulin       | Hypoglycaemia episodes        | High         | Open-label trial, possible selective reporting of results                                                                                                                                                                                              | Directly applicable | Participants are T2D and NAFLD |
| Liu 2020   | Exenatide v Insulin       | Severe hypoglycaemic episodes | High         | Open-label trial, possible selective reporting of results                                                                                                                                                                                              | Directly applicable | Participants are T2D and NAFLD |
| Liu 2020   | Exenatide v Insulin       | Weight change                 | High         | Open-label trial, possible selective reporting of results                                                                                                                                                                                              | Directly applicable | Participants are T2D and NAFLD |

| Study name           | Comparison details      | Outcome                       | Risk of bias | Bias comments                                                                | Directness          | Directness comments |
|----------------------|-------------------------|-------------------------------|--------------|------------------------------------------------------------------------------|---------------------|---------------------|
| Mari 2008            | Vildagliptin v Placebo  | All-cause mortality           | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mari 2008            | Vildagliptin v Placebo  | HbA1c change                  | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mari 2008            | Vildagliptin v Placebo  | Hypoglycaemia episodes        | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mari 2008            | Vildagliptin v Placebo  | Severe hypoglycaemic episodes | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mari 2008            | Vildagliptin v Placebo  | Weight change                 | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mari 2008 No obesity | Vildagliptin v Placebo  | HbA1c change                  | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mari 2008 Obesity    | Vildagliptin v Placebo  | HbA1c change                  | High         | Double-blind trial, no info about randomisation, analysis unclear            | Directly applicable | None specified      |
| Mita 2019            | Linagliptin v Metformin | BMI change                    | High         | Low attrition but lack of information on randomisation, and allocation. Some | Directly applicable | None specified      |

| Study name    | Comparison details      | Outcome                         | Risk of bias  | Bias comments                                                                                     | Directness          | Directness comments |
|---------------|-------------------------|---------------------------------|---------------|---------------------------------------------------------------------------------------------------|---------------------|---------------------|
|               |                         |                                 |               | baseline imbalances.                                                                              |                     |                     |
| Mita 2019     | Linagliptin v Metformin | HbA1c change                    | High          | Low attrition but lack of information on randomisation, and allocation. Some baseline imbalances. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo   | All-cause mortality             | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.                              | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo   | At night hypoglycaemic episodes | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.                              | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo   | At night hypoglycaemic episodes | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.                              | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo   | Cardiovascular mortality        | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.                              | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo   | Cardiovascular mortality        | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.                              | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo   | HbA1c change                    | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.                              | Directly applicable | None specified      |

| Study name    | Comparison details    | Outcome                                                         | Risk of bias  | Bias comments                                                                  | Directness          | Directness comments |
|---------------|-----------------------|-----------------------------------------------------------------|---------------|--------------------------------------------------------------------------------|---------------------|---------------------|
| Miyagawa 2015 | Dulaglutide v Placebo | Hypoglycaemia episodes                                          | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.           | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Hypoglycaemia episodes                                          | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.           | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Severe hypoglycaemic episodes                                   | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.           | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Severe hypoglycaemic episodes                                   | Some concerns | Double-blind trial with open label liraglutide. As-treated analysis.           | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | HbA1c change                                                    | Some concerns | Double-blind trial with open label liraglutide. mITT analysis.                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | All-cause mortality                                             | High          | Double-blind trial, no info about randomisation, analysis unclear              | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale blood glucose control | High          | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale blood glucose control | High          | Liraglutide open-label, dulaglutide and placebo double-                        | Directly applicable | None specified      |

| Study name    | Comparison details    | Outcome                                                     | Risk of bias | Bias comments                                                                  | Directness          | Directness comments |
|---------------|-----------------------|-------------------------------------------------------------|--------------|--------------------------------------------------------------------------------|---------------------|---------------------|
|               |                       |                                                             |              | blinded. mITT analysis.                                                        |                     |                     |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale convenience       | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale convenience       | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale ease of use       | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale ease of use       | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale emotional effects | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale emotional effects | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life -                            | High         | Liraglutide open-label, dulaglutide                                            | Directly applicable | None specified      |

| Study name    | Comparison details    | Outcome                                                           | Risk of bias | Bias comments                                                                  | Directness          | Directness comments |
|---------------|-----------------------|-------------------------------------------------------------------|--------------|--------------------------------------------------------------------------------|---------------------|---------------------|
|               |                       | subscale lifestyle impact                                         |              | and placebo double-blinded. mITT analysis.                                     |                     |                     |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale lifestyle impact        | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale perceived effectiveness | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale perceived effectiveness | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale role physical           | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Placebo | Health-related quality of life - subscale role physical           | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Dulaglutide v Placebo | Health-related quality of life - subscale satisfaction            | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |

| Study name    | Comparison details        | Outcome                                                           | Risk of bias | Bias comments                                                                  | Directness          | Directness comments |
|---------------|---------------------------|-------------------------------------------------------------------|--------------|--------------------------------------------------------------------------------|---------------------|---------------------|
| Miyagawa 2015 | Liraglutide v Placebo     | Health-related quality of life - subscale satisfaction            | High         | Liraglutide open-label, dulaglutide and placebo double-blinded. mITT analysis. | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | HbA1c change                                                      | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale blood glucose control   | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale convenience             | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale ease of use             | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale emotional effects       | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale lifestyle impact        | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale perceived effectiveness | High         | None specified                                                                 | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life -                                  | High         | None specified                                                                 | Directly applicable | None specified      |



| Study name    | Comparison details        | Outcome                                                | Risk of bias  | Bias comments                                                                                       | Directness          | Directness comments |
|---------------|---------------------------|--------------------------------------------------------|---------------|-----------------------------------------------------------------------------------------------------|---------------------|---------------------|
|               |                           | subscale role physical                                 |               |                                                                                                     |                     |                     |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Health-related quality of life - subscale satisfaction | High          | None specified                                                                                      | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | All-cause mortality                                    | Some concerns | None specified                                                                                      | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | At night hypoglycaemic episodes                        | Some concerns | None specified                                                                                      | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Cardiovascular mortality                               | Some concerns | None specified                                                                                      | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Hypoglycaemia episodes                                 | Some concerns | None specified                                                                                      | Directly applicable | None specified      |
| Miyagawa 2015 | Liraglutide v Dulaglutide | Severe hypoglycaemic episodes                          | Some concerns | None specified                                                                                      | Directly applicable | None specified      |
| Miyazaki 2002 | Pioglitazone v Placebo    | BMI change                                             | High          | No info on randomisation and imbalance in baseline characteristics eg age between placebo and other | Directly applicable | None specified      |
| Miyazaki 2002 | Pioglitazone v Placebo    | HbA1c change                                           | High          | No info on randomisation and imbalance in baseline characteristics eg age between placebo and other | Directly applicable | None specified      |

| Study name    | Comparison details                    | Outcome                       | Risk of bias  | Bias comments                                                                                       | Directness          | Directness comments |
|---------------|---------------------------------------|-------------------------------|---------------|-----------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Miyazaki 2002 | Pioglitazone v Placebo                | Weight change                 | High          | No info on randomisation and imbalance in baseline characteristics eg age between placebo and other | Directly applicable | None specified      |
| Moretto 2008  | Exenatide v Placebo                   | All-cause mortality           | Some concerns | Double-blind trial with mITT analysis                                                               | Directly applicable | None specified      |
| Moretto 2008  | Exenatide v Placebo                   | Cardiovascular mortality      | Some concerns | Double-blind trial with mITT analysis                                                               | Directly applicable | None specified      |
| Moretto 2008  | Exenatide v Placebo                   | HbA1c change                  | Some concerns | Double-blind trial with mITT analysis                                                               | Directly applicable | None specified      |
| Moretto 2008  | Exenatide v Placebo                   | Hypoglycaemia episodes        | Some concerns | Double-blind trial with mITT analysis                                                               | Directly applicable | None specified      |
| Moretto 2008  | Exenatide v Placebo                   | Severe hypoglycaemic episodes | Some concerns | Double-blind trial with mITT analysis                                                               | Directly applicable | None specified      |
| Moretto 2008  | Exenatide v Placebo                   | Weight change                 | Some concerns | Double-blind trial with mITT analysis                                                               | Directly applicable | None specified      |
| Mu 2017       | Linagliptin + Metformin v Linagliptin | 4-point MACE                  | High          | None specified                                                                                      | Directly applicable | None specified      |
| Mu 2017       | Linagliptin + Metformin v Metformin   | 4-point MACE                  | High          | None specified                                                                                      | Directly applicable | None specified      |
| Mu 2017       | Linagliptin v Metformin               | 4-point MACE                  | High          | None specified                                                                                      | Directly applicable | None specified      |
| Mu 2017       | Linagliptin + Metformin v Linagliptin | HbA1c change                  | High          | None specified                                                                                      | Directly applicable | None specified      |

| Study name | Comparison details                    | Outcome                           | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|---------------------------------------|-----------------------------------|--------------|----------------|---------------------|---------------------|
| Mu 2017    | Linagliptin + Metformin v Metformin   | HbA1c change                      | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin v Metformin               | HbA1c change                      | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Linagliptin | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Metformin   | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin v Metformin               | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Linagliptin | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Metformin   | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin v Metformin               | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Linagliptin | Severe hypoglycaemic episodes     | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Metformin   | Severe hypoglycaemic episodes     | High         | None specified | Directly applicable | None specified      |
| Mu 2017    | Linagliptin v Metformin               | Severe hypoglycaemic episodes     | High         | None specified | Directly applicable | None specified      |

| Study name | Comparison details                        | Outcome                       | Risk of bias  | Bias comments                                        | Directness          | Directness comments |
|------------|-------------------------------------------|-------------------------------|---------------|------------------------------------------------------|---------------------|---------------------|
| Mu 2017    | Linagliptin + Metformin v Linagliptin     | Weight change                 | High          | None specified                                       | Directly applicable | None specified      |
| Mu 2017    | Linagliptin + Metformin v Metformin       | Weight change                 | High          | None specified                                       | Directly applicable | None specified      |
| Mu 2017    | Linagliptin v Metformin                   | Weight change                 | High          | None specified                                       | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Linagliptin  | 4-point MACE                  | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Pioglitazone | 4-point MACE                  | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Linagliptin  | HbA1c change                  | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Pioglitazone | HbA1c change                  | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Linagliptin  | Hypoglycaemia episodes        | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Pioglitazone | Hypoglycaemia episodes        | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Linagliptin  | Severe hypoglycaemic episodes | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Pioglitazone | Severe hypoglycaemic episodes | Some concerns | Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |

| Study name | Comparison details                        | Outcome                       | Risk of bias  | Bias comments                                                                     | Directness          | Directness comments |
|------------|-------------------------------------------|-------------------------------|---------------|-----------------------------------------------------------------------------------|---------------------|---------------------|
| Nauck 2016 | Pioglitazone + Linagliptin v Linagliptin  | Weight change                 | Some concerns | Double-blind, double-dummy trial with mITT analysis.                              | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone + Linagliptin v Pioglitazone | Weight change                 | Some concerns | Double-blind, double-dummy trial with mITT analysis.                              | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone v Linagliptin                | 4-point MACE                  | Some concerns | None specified                                                                    | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone v Linagliptin                | HbA1c change                  | Some concerns | None specified                                                                    | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone v Linagliptin                | Hypoglycaemia episodes        | Some concerns | None specified                                                                    | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone v Linagliptin                | Severe hypoglycaemic episodes | Some concerns | None specified                                                                    | Directly applicable | None specified      |
| Nauck 2016 | Pioglitazone v Linagliptin                | Weight change                 | Some concerns | None specified                                                                    | Directly applicable | None specified      |
| Pan 2012A  | Saxagliptin v Placebo                     | All-cause mortality           | High          | Lack of info about allocation concealment. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Pan 2012A  | Saxagliptin v Placebo                     | Cardiovascular mortality      | High          | Lack of info about allocation concealment. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Pan 2012A  | Saxagliptin v Placebo                     | HbA1c change                  | High          | Lack of info about allocation concealment. Double-blind trial with mITT analysis. | Directly applicable | None specified      |

| Study name | Comparison details                      | Outcome                       | Risk of bias  | Bias comments                                                                                            | Directness          | Directness comments |
|------------|-----------------------------------------|-------------------------------|---------------|----------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Pan 2012A  | Saxagliptin v Placebo                   | Hypoglycaemia episodes        | High          | Lack of info about allocation concealment. Double-blind trial with mITT analysis.                        | Directly applicable | None specified      |
| Pan 2012A  | Saxagliptin v Placebo                   | Severe hypoglycaemic episodes | High          | Lack of info about allocation concealment. Double-blind trial with mITT analysis.                        | Directly applicable | None specified      |
| Pan 2012A  | Saxagliptin v Placebo                   | Weight change                 | High          | Lack of info about allocation concealment. Double-blind trial with mITT analysis.                        | Directly applicable | None specified      |
| Pavo 2003  | Pioglitazone v Metformin                | HbA1c change                  | Some concerns | Lack of information around whether participants were analysed in the group to which they were allocated. | Directly applicable | None specified      |
| Pavo 2003  | Pioglitazone v Metformin                | Weight change                 | Some concerns | Lack of information around whether participants were analysed in the group to which they were allocated. | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Metformin    | All-cause mortality           | High          | None specified                                                                                           | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Pioglitazone | All-cause mortality           | High          | None specified                                                                                           | Directly applicable | None specified      |

| Study name | Comparison details                      | Outcome                         | Risk of bias | Bias comments  | Directness          | Directness comments |
|------------|-----------------------------------------|---------------------------------|--------------|----------------|---------------------|---------------------|
| Perez 2009 | Pioglitazone v Metformin                | All-cause mortality             | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Metformin    | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Pioglitazone | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone v Metformin                | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Metformin    | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Pioglitazone | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone v Metformin                | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Metformin    | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Pioglitazone | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone v Metformin                | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Metformin    | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Perez 2009 | Pioglitazone + Metformin v Pioglitazone | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |



| Study name     | Comparison details                    | Outcome                         | Risk of bias | Bias comments  | Directness          | Directness comments |
|----------------|---------------------------------------|---------------------------------|--------------|----------------|---------------------|---------------------|
| Perez 2009     | Pioglitazone v Metformin              | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Metformin   | All-cause mortality             | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Saxagliptin | All-cause mortality             | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin v Metformin               | All-cause mortality             | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Metformin   | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Saxagliptin | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin v Metformin               | Cardiovascular mortality        | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Metformin   | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Saxagliptin | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin v Metformin               | HbA1c change                    | High         | None specified | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Metformin   | Hypoglycaemia episodes          | High         | None specified | Directly applicable | None specified      |

| Study name     | Comparison details                    | Outcome                       | Risk of bias  | Bias comments                               | Directness          | Directness comments |
|----------------|---------------------------------------|-------------------------------|---------------|---------------------------------------------|---------------------|---------------------|
| Pfützner 2011A | Saxagliptin + Metformin v Saxagliptin | Hypoglycaemia episodes        | High          | None specified                              | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin v Metformin               | Hypoglycaemia episodes        | High          | None specified                              | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Metformin   | Severe hypoglycaemic episodes | High          | None specified                              | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin + Metformin v Saxagliptin | Severe hypoglycaemic episodes | High          | None specified                              | Directly applicable | None specified      |
| Pfützner 2011A | Saxagliptin v Metformin               | Severe hypoglycaemic episodes | High          | None specified                              | Directly applicable | None specified      |
| Pistrosch 2013 | Metformin v Insulin                   | HbA1c change                  | High          | Open label study                            | Directly applicable | None specified      |
| Pistrosch 2013 | Metformin v Insulin                   | Hypoglycaemia episodes        | High          | Open label study                            | Directly applicable | None specified      |
| Pistrosch 2013 | Metformin v Insulin                   | Severe hypoglycaemic episodes | High          | Open label study                            | Directly applicable | None specified      |
| Pi-Sunyer 2007 | Vildagliptin v Placebo                | HbA1c change                  | Some concerns | No info about randomisation. mITT analysis. | Directly applicable | None specified      |
| Pi-Sunyer 2007 | Vildagliptin v Placebo                | Weight change                 | Some concerns | No info about randomisation. mITT analysis. | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin + Metformin v Alogliptin   | All-cause mortality           | High          | None specified                              | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin + Metformin v Metformin    | All-cause mortality           | High          | None specified                              | Directly applicable | None specified      |

| Study name   | Comparison details                  | Outcome                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------|-------------------------------------|--------------------------|--------------|----------------|---------------------|---------------------|
| Pratley 2014 | Alogliptin + Metformin v Placebo    | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Placebo                | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Metformin v Placebo                 | All-cause mortality      | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Alogliptin | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Metformin  | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Placebo    | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Placebo                | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Metformin v Placebo                 | Cardiovascular mortality | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Alogliptin | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Metformin  | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Placebo    | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | HbA1c change             | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Placebo                | HbA1c change             | High         | None specified | Directly applicable | None specified      |

| Study name   | Comparison details                  | Outcome                           | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------|-------------------------------------|-----------------------------------|--------------|----------------|---------------------|---------------------|
| Pratley 2014 | Metformin v Placebo                 | HbA1c change                      | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Alogliptin | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Metformin  | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Placebo    | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Placebo                | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Metformin v Placebo                 | Hospitalisation for heart failure | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Alogliptin | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Metformin  | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Placebo    | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Placebo                | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Metformin v Placebo                 | Hypoglycaemia episodes            | High         | None specified | Directly applicable | None specified      |

| Study name   | Comparison details                  | Outcome                         | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------|-------------------------------------|---------------------------------|--------------|----------------|---------------------|---------------------|
| Pratley 2014 | Alogliptin + Metformin v Alogliptin | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Metformin  | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Placebo    | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Placebo                | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Metformin v Placebo                 | Non-fatal myocardial infarction | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Alogliptin | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Metformin  | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin + Metformin v Placebo    | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |
| Pratley 2014 | Alogliptin v Metformin              | Severe hypoglycaemic episodes   | High         | None specified | Directly applicable | None specified      |

| Study name     | Comparison details                  | Outcome                       | Risk of bias  | Bias comments                                                                          | Directness          | Directness comments |
|----------------|-------------------------------------|-------------------------------|---------------|----------------------------------------------------------------------------------------|---------------------|---------------------|
| Pratley 2014   | Alogliptin v Placebo                | Severe hypoglycaemic episodes | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Metformin v Placebo                 | Severe hypoglycaemic episodes | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin + Metformin v Alogliptin | Weight change                 | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin + Metformin v Metformin  | Weight change                 | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin + Metformin v Placebo    | Weight change                 | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin v Metformin              | Weight change                 | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Alogliptin v Placebo                | Weight change                 | High          | None specified                                                                         | Directly applicable | None specified      |
| Pratley 2014   | Metformin v Placebo                 | Weight change                 | High          | None specified                                                                         | Directly applicable | None specified      |
| Roden 2005 1.1 | Pioglitazone v Metformin            | Weight change                 | High          | Allocation concealment unclear, unclear reporting of attrition and methods of analysis | Directly applicable | None specified      |
| Roden 2015     | Empagliflozin v Placebo             | All-cause mortality           | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis.           | Directly applicable | None specified      |
| Roden 2015     | Empagliflozin v Sitagliptin         | All-cause mortality           | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis.           | Directly applicable | None specified      |

| Study name | Comparison details          | Outcome                       | Risk of bias  | Bias comments                                                                | Directness          | Directness comments |
|------------|-----------------------------|-------------------------------|---------------|------------------------------------------------------------------------------|---------------------|---------------------|
| Roden 2015 | Empagliflozin v Placebo     | Cardiovascular mortality      | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Sitagliptin | Cardiovascular mortality      | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Placebo     | HbA1c change                  | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Sitagliptin | HbA1c change                  | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Placebo     | Hypoglycaemia episodes        | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Sitagliptin | Hypoglycaemia episodes        | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Placebo     | Severe hypoglycaemic episodes | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Roden 2015 | Empagliflozin v Sitagliptin | Severe hypoglycaemic episodes | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis. | Directly applicable | None specified      |



| Study name       | Comparison details                         | Outcome                       | Risk of bias  | Bias comments                                                                                 | Directness          | Directness comments |
|------------------|--------------------------------------------|-------------------------------|---------------|-----------------------------------------------------------------------------------------------|---------------------|---------------------|
| Roden 2015       | Empagliflozin v Placebo                    | Weight change                 | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis.                  | Directly applicable | None specified      |
| Roden 2015       | Empagliflozin v Sitagliptin                | Weight change                 | Some concerns | Extension study, high attrition rate. Double-blind trial with mITT analysis.                  | Directly applicable | None specified      |
| Roden 2015       | Sitagliptin v Placebo                      | All-cause mortality           | Some concerns | None specified                                                                                | Directly applicable | None specified      |
| Roden 2015       | Sitagliptin v Placebo                      | Cardiovascular mortality      | Some concerns | None specified                                                                                | Directly applicable | None specified      |
| Roden 2015       | Sitagliptin v Placebo                      | HbA1c change                  | Some concerns | None specified                                                                                | Directly applicable | None specified      |
| Roden 2015       | Sitagliptin v Placebo                      | Hypoglycaemia episodes        | Some concerns | None specified                                                                                | Directly applicable | None specified      |
| Roden 2015       | Sitagliptin v Placebo                      | Severe hypoglycaemic episodes | Some concerns | None specified                                                                                | Directly applicable | None specified      |
| Roden 2015       | Sitagliptin v Placebo                      | Weight change                 | Some concerns | None specified                                                                                | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone + Vildagliptin v Vildagliptin | HbA1c change                  | High          | Baseline difference on free fatty acids. Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone v Vildagliptin                | HbA1c change                  | High          | Baseline difference on free fatty acids. Double-blind, double-dummy trial with mITT analysis. | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone + Vildagliptin v Vildagliptin | Hypoglycaemia episodes        | High          | Baseline difference on free fatty acids. Double-blind,                                        | Directly applicable | None specified      |

| Study name       | Comparison details                         | Outcome                | Risk of bias | Bias comments                                                                                          | Directness          | Directness comments |
|------------------|--------------------------------------------|------------------------|--------------|--------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|                  |                                            |                        |              | double-dummy trial with mITT analysis.                                                                 |                     |                     |
| Rosenstock 2007A | Pioglitazone v Vildagliptin                | Hypoglycaemia episodes | High         | Baseline difference on free fatty acids. Double-blind, double-dummy trial with mITT analysis.          | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone + Vildagliptin v Vildagliptin | Weight change          | High         | Baseline difference on free fatty acids. Double-blind, double-dummy trial with mITT analysis.          | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone v Vildagliptin                | Weight change          | High         | Baseline difference on free fatty acids. Double-blind, double-dummy trial with mITT analysis.          | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone + Vildagliptin v Pioglitazone | HbA1c change           | High         | None specified                                                                                         | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone + Vildagliptin v Pioglitazone | Hypoglycaemia episodes | High         | None specified                                                                                         | Directly applicable | None specified      |
| Rosenstock 2007A | Pioglitazone + Vildagliptin v Pioglitazone | Weight change          | High         | None specified                                                                                         | Directly applicable | None specified      |
| Rosenstock 2009A | Saxagliptin v Placebo                      | All-cause mortality    | High         | No adherence monitoring included - intention to treat analysis inappropriate given lack of information | Directly applicable | None specified      |

| Study name       | Comparison details                       | Outcome                  | Risk of bias  | Bias comments                                                                                          | Directness          | Directness comments |
|------------------|------------------------------------------|--------------------------|---------------|--------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Rosenstock 2009A | Saxagliptin v Placebo                    | Cardiovascular mortality | High          | No adherence monitoring included - intention to treat analysis inappropriate given lack of information | Directly applicable | None specified      |
| Rosenstock 2009A | Saxagliptin v Placebo                    | Hypoglycaemia episodes   | High          | No adherence monitoring included - intention to treat analysis inappropriate given lack of information | Directly applicable | None specified      |
| Rosenstock 2010  | Pioglitazone + Alogliptin v Pioglitazone | HbA1c change             | Some concerns | No details on randomisation or concealment. No standard baseline data reported                         | Directly applicable | None specified      |
| Rosenstock 2010  | Pioglitazone v Alogliptin                | HbA1c change             | Some concerns | No details on randomisation or concealment. No standard baseline data reported                         | Directly applicable | None specified      |
| Rosenstock 2010  | Pioglitazone + Alogliptin v Pioglitazone | Weight change            | Some concerns | No details on randomisation or concealment. No standard baseline data reported                         | Directly applicable | None specified      |
| Rosenstock 2010  | Pioglitazone v Alogliptin                | Weight change            | Some concerns | No details on randomisation or concealment. No standard baseline data reported                         | Directly applicable | None specified      |

| Study name      | Comparison details                        | Outcome                  | Risk of bias  | Bias comments  | Directness          | Directness comments |
|-----------------|-------------------------------------------|--------------------------|---------------|----------------|---------------------|---------------------|
| Rosenstock 2010 | Pioglitazone + Alogliptin v Alogliptin    | HbA1c change             | Some concerns | None specified | Directly applicable | None specified      |
| Rosenstock 2010 | Pioglitazone + Alogliptin v Alogliptin    | Weight change            | Some concerns | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | All-cause mortality      | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | All-cause mortality      | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | All-cause mortality      | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Cardiac arrhythmia       | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Cardiac arrhythmia       | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Cardiac arrhythmia       | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Cardiovascular mortality | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Cardiovascular mortality | High          | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Cardiovascular mortality | High          | None specified | Directly applicable | None specified      |

| Study name      | Comparison details                        | Outcome                | Risk of bias | Bias comments  | Directness          | Directness comments |
|-----------------|-------------------------------------------|------------------------|--------------|----------------|---------------------|---------------------|
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Diabetic ketoacidosis  | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Diabetic ketoacidosis  | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Diabetic ketoacidosis  | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | HbA1c change           | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | HbA1c change           | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | HbA1c change           | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Hypoglycaemia episodes | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Hypoglycaemia episodes | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Hypoglycaemia episodes | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Non-fatal stroke       | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Non-fatal stroke       | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Non-fatal stroke       | High         | None specified | Directly applicable | None specified      |

| Study name      | Comparison details                        | Outcome                                      | Risk of bias | Bias comments  | Directness          | Directness comments |
|-----------------|-------------------------------------------|----------------------------------------------|--------------|----------------|---------------------|---------------------|
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Persistent signs of worsening kidney disease | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Persistent signs of worsening kidney disease | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Persistent signs of worsening kidney disease | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Severe hypoglycaemic episodes                | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Unstable angina                              | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Unstable angina                              | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin v Metformin                 | Unstable angina                              | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Canagliflozin | Weight change                                | High         | None specified | Directly applicable | None specified      |
| Rosenstock 2016 | Canagliflozin + Metformin v Metformin     | Weight change                                | High         | None specified | Directly applicable | None specified      |

| Study name         | Comparison details                    | Outcome                           | Risk of bias  | Bias comments  | Directness          | Directness comments |
|--------------------|---------------------------------------|-----------------------------------|---------------|----------------|---------------------|---------------------|
| Rosenstock 2016    | Canagliflozin v Metformin             | Weight change                     | High          | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | All-cause mortality               | Low           | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | Cardiovascular mortality          | Low           | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | HbA1c change                      | Low           | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | Hospitalisation for heart failure | Low           | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | Hypoglycaemia episodes            | Low           | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | Severe hypoglycaemic episodes     | Low           | None specified | Directly applicable | None specified      |
| Ross 2015          | Linagliptin + Metformin v Linagliptin | Weight change                     | Some concerns | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Metformin                 | All-cause mortality               | Low           | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Sitagliptin               | All-cause mortality               | Low           | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Exenatide              | All-cause mortality               | Low           | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Metformin              | All-cause mortality               | Low           | None specified | Directly applicable | None specified      |



| Study name         | Comparison details         | Outcome                                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------------|----------------------------|------------------------------------------|--------------|----------------|---------------------|---------------------|
| Russell-Jones 2012 | Pioglitazone v Sitagliptin | All-cause mortality                      | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Sitagliptin v Metformin    | All-cause mortality                      | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Metformin      | Cardiovascular mortality                 | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Sitagliptin    | Cardiovascular mortality                 | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Exenatide   | Cardiovascular mortality                 | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Metformin   | Cardiovascular mortality                 | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Sitagliptin | Cardiovascular mortality                 | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Sitagliptin v Metformin    | Cardiovascular mortality                 | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Metformin      | HbA1c change                             | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Sitagliptin    | HbA1c change                             | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Exenatide   | HbA1c change                             | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Metformin   | HbA1c change                             | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Sitagliptin | HbA1c change                             | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Sitagliptin v Metformin    | HbA1c change                             | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Metformin      | Health-related quality of life - overall | Low          | None specified | Directly applicable | None specified      |

| Study name         | Comparison details         | Outcome                                  | Risk of bias | Bias comments  | Directness          | Directness comments |
|--------------------|----------------------------|------------------------------------------|--------------|----------------|---------------------|---------------------|
| Russell-Jones 2012 | Exenatide v Sitagliptin    | Health-related quality of life - overall | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Exenatide   | Health-related quality of life - overall | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Metformin   | Health-related quality of life - overall | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Sitagliptin | Health-related quality of life - overall | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Sitagliptin v Metformin    | Health-related quality of life - overall | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Metformin      | Hypoglycaemia episodes                   | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Sitagliptin    | Hypoglycaemia episodes                   | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Exenatide   | Hypoglycaemia episodes                   | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Metformin   | Hypoglycaemia episodes                   | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Sitagliptin | Hypoglycaemia episodes                   | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Sitagliptin v Metformin    | Hypoglycaemia episodes                   | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Metformin      | Weight change                            | Low          | None specified | Directly applicable | None specified      |
| Russell-Jones 2012 | Exenatide v Sitagliptin    | Weight change                            | Low          | None specified | Directly applicable | None specified      |

| Study name         | Comparison details                                  | Outcome                  | Risk of bias | Bias comments                                                                                                                                                 | Directness          | Directness comments |
|--------------------|-----------------------------------------------------|--------------------------|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Russell-Jones 2012 | Pioglitazone v Exenatide                            | Weight change            | Low          | None specified                                                                                                                                                | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Metformin                            | Weight change            | Low          | None specified                                                                                                                                                | Directly applicable | None specified      |
| Russell-Jones 2012 | Pioglitazone v Sitagliptin                          | Weight change            | Low          | None specified                                                                                                                                                | Directly applicable | None specified      |
| Russell-Jones 2012 | Sitagliptin v Metformin                             | Weight change            | Low          | None specified                                                                                                                                                | Directly applicable | None specified      |
| Scherbaum 2002     | Pioglitazone v Placebo                              | HbA1c change             | High         | Patients excluded after randomisation and not imputed                                                                                                         | Directly applicable | None specified      |
| Scherbaum 2002     | Pioglitazone v Placebo                              | Weight change            | High         | Patients excluded after randomisation and not imputed                                                                                                         | Directly applicable | None specified      |
| Schernthaner 2004  | Pioglitazone v Metformin                            | All-cause mortality      | Low          | None specified                                                                                                                                                | Directly applicable | None specified      |
| Schernthaner 2004  | Pioglitazone v Metformin                            | Cardiovascular mortality | Low          | None specified                                                                                                                                                | Directly applicable | None specified      |
| Schwartz 2006      | Metformin slow release v Metformin standard release | HbA1c change             | High         | Excluding patients from ITT analysis without imputation is not correct practice and introduces bias as this exclusion could be related to patients true value | Directly applicable | None specified      |
| Schweizer 2007     | Vildagliptin v Metformin                            | All-cause mortality      | High         | None specified                                                                                                                                                | Directly applicable | None specified      |
| Schweizer 2007     | Vildagliptin v Metformin                            | Cardiovascular mortality | High         | None specified                                                                                                                                                | Directly applicable | None specified      |
| Schweizer 2007     | Vildagliptin v Metformin                            | HbA1c change             | High         | None specified                                                                                                                                                | Directly applicable | None specified      |

| Study name     | Comparison details       | Outcome                         | Risk of bias  | Bias comments                                                                             | Directness           | Directness comments |
|----------------|--------------------------|---------------------------------|---------------|-------------------------------------------------------------------------------------------|----------------------|---------------------|
| Schweizer 2007 | Vildagliptin v Metformin | Hypoglycaemia episodes          | High          | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2007 | Vildagliptin v Metformin | Non-fatal myocardial infarction | High          | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2007 | Vildagliptin v Metformin | Severe hypoglycaemic episodes   | High          | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2007 | Vildagliptin v Metformin | Weight change                   | High          | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | All-cause mortality             | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | Cardiac arrhythmia              | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | Cardiovascular mortality        | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | HbA1c change                    | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | Hypoglycaemia episodes          | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | Severe hypoglycaemic episodes   | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | Weight change                   | Some concerns | None specified                                                                            | Directly applicable  | None specified      |
| Schweizer 2009 | Vildagliptin v Metformin | Non-fatal myocardial infarction | Some concerns | Outcome indirectness - acute coronary syndrome was reported. Included in this outcome but | Partially applicable | None specified      |

| Study name   | Comparison details         | Outcome                       | Risk of bias  | Bias comments                                                                             | Directness          | Directness comments |
|--------------|----------------------------|-------------------------------|---------------|-------------------------------------------------------------------------------------------|---------------------|---------------------|
|              |                            |                               |               | downgraded for indirectness.                                                              |                     |                     |
| Seino 2018   | Semaglutide v Sitagliptin  | BMI change                    | Low           | Open label trial clearly reported.                                                        | Directly applicable | None specified      |
| Seino 2018   | Semaglutide v Sitagliptin  | HbA1c change                  | Low           | Open label trial clearly reported.                                                        | Directly applicable | None specified      |
| Seino 2018   | Semaglutide v Sitagliptin  | Severe hypoglycaemic episodes | Low           | Open label trial clearly reported.                                                        | Directly applicable | None specified      |
| Seino 2018   | Semaglutide v Sitagliptin  | Weight change                 | Low           | Open label trial clearly reported.                                                        | Directly applicable | None specified      |
| Shihara 2011 | Pioglitazone v Glimepiride | BMI change                    | High          | Method of analysis and effect of this unclear, selective reporting of continuous outcomes | Directly applicable | None specified      |
| Shihara 2011 | Pioglitazone v Glimepiride | Weight change                 | High          | Method of analysis and effect of this unclear, selective reporting of continuous outcomes | Directly applicable | None specified      |
| Shihara 2011 | Pioglitazone v Glimepiride | Hypoglycaemia episodes        | Some concerns | Method of analysis unclear.                                                               | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo      | All-cause mortality           | High          | Baseline imbalance on weight. Double-blind trial with mITT analysis.                      | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo      | BMI change                    | High          | Baseline imbalance on weight. Double-blind trial with mITT analysis.                      | Directly applicable | None specified      |

| Study name   | Comparison details      | Outcome                         | Risk of bias | Bias comments                                                        | Directness          | Directness comments |
|--------------|-------------------------|---------------------------------|--------------|----------------------------------------------------------------------|---------------------|---------------------|
| Sorli 2017   | Semaglutide v Placebo   | Cardiovascular mortality        | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo   | HbA1c change                    | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo   | Hypoglycaemia episodes          | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo   | Non-fatal myocardial infarction | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo   | Non-fatal stroke                | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo   | Severe hypoglycaemic episodes   | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Sorli 2017   | Semaglutide v Placebo   | Weight change                   | High         | Baseline imbalance on weight. Double-blind trial with mITT analysis. | Directly applicable | None specified      |
| Stenlöf 2013 | Canagliflozin v Placebo | All-cause mortality             | Low          | None specified                                                       | Directly applicable | None specified      |
| Stenlöf 2013 | Canagliflozin v Placebo | Cardiovascular mortality        | Low          | None specified                                                       | Directly applicable | None specified      |

| Study name   | Comparison details        | Outcome       | Risk of bias  | Bias comments                                                                                                                                                                                   | Directness          | Directness comments |
|--------------|---------------------------|---------------|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Stenlöf 2013 | Canagliflozin v Placebo   | HbA1c change  | Some concerns | Overall 14% attrition, some differences in attrition between two arms: 11% in CANA arm and 17% in placebo . LOCF was used, this is inappropriate to account for any bias caused by missing data | Directly applicable | None specified      |
| Stenlöf 2013 | Canagliflozin v Placebo   | Weight change | Some concerns | Overall 14% attrition, some differences in attrition between two arms: 11% in CANA arm and 17% in placebo . LOCF was used, this is inappropriate to account for any bias caused by missing data | Directly applicable | None specified      |
| Suzuki 2014  | Liraglutide v Sitagliptin | HbA1c change  | High          | None specified                                                                                                                                                                                  | Directly applicable | None specified      |
| Suzuki 2014  | Liraglutide v Sitagliptin | Weight change | High          | None specified                                                                                                                                                                                  | Directly applicable | None specified      |
| Tan 2005     | Pioglitazone v Gliclazide | HbA1c change  | High          | Allocation concealment unclear, method of analysis and effect of this unclear,                                                                                                                  | Directly applicable | None specified      |



| Study name | Comparison details                    | Outcome       | Risk of bias | Bias comments                                                                                                 | Directness           | Directness comments |
|------------|---------------------------------------|---------------|--------------|---------------------------------------------------------------------------------------------------------------|----------------------|---------------------|
|            |                                       |               |              | selective reporting of outcome                                                                                |                      |                     |
| Tan 2005   | Pioglitazone v Gliclazide             | Weight change | High         | Allocation concealment unclear, method of analysis and effect of this unclear, selective reporting of outcome | Directly applicable  | None specified      |
| Tao 2018   | Saxagliptin v Metformin               | BMI change    | High         | None specified                                                                                                | Partially applicable | None specified      |
| Tao 2018   | Saxagliptin v Metformin               | HbA1c change  | High         | None specified                                                                                                | Partially applicable | None specified      |
| Tao 2018   | Saxagliptin v Metformin               | Weight change | High         | None specified                                                                                                | Partially applicable | None specified      |
| Tao 2018   | Saxagliptin + Metformin v Metformin   | BMI change    | High         | Population indirectness - people with polycystic ovary syndrome and type 2 diabetes                           | Partially applicable | None specified      |
| Tao 2018   | Saxagliptin + Metformin v Saxagliptin | BMI change    | High         | Population indirectness - people with polycystic ovary syndrome and type 2 diabetes                           | Partially applicable | None specified      |
| Tao 2018   | Saxagliptin + Metformin v Metformin   | HbA1c change  | High         | Population indirectness - people with polycystic ovary syndrome and type 2 diabetes                           | Partially applicable | None specified      |

| Study name    | Comparison details                    | Outcome                       | Risk of bias | Bias comments                                                                       | Directness           | Directness comments |
|---------------|---------------------------------------|-------------------------------|--------------|-------------------------------------------------------------------------------------|----------------------|---------------------|
| Tao 2018      | Saxagliptin + Metformin v Saxagliptin | HbA1c change                  | High         | Population indirectness - people with polycystic ovary syndrome and type 2 diabetes | Partially applicable | None specified      |
| Tao 2018      | Saxagliptin + Metformin v Metformin   | Weight change                 | High         | Population indirectness - people with polycystic ovary syndrome and type 2 diabetes | Partially applicable | None specified      |
| Tao 2018      | Saxagliptin + Metformin v Saxagliptin | Weight change                 | High         | Population indirectness - people with polycystic ovary syndrome and type 2 diabetes | Partially applicable | None specified      |
| Terauchi 2017 | Glimepiride v Sitagliptin             | All-cause mortality           | High         | Concerns with allocation concealment, blinding, method of analysis and attrition.   | Directly applicable  | None specified      |
| Terauchi 2017 | Glimepiride v Sitagliptin             | Severe hypoglycaemic episodes | High         | Concerns with allocation concealment, blinding, method of analysis and attrition.   | Directly applicable  | None specified      |
| Terauchi 2017 | Glimepiride v Sitagliptin             | Weight change                 | High         | Concerns with allocation concealment, blinding, method of                           | Directly applicable  | None specified      |

| Study name     | Comparison details                     | Outcome                       | Risk of bias  | Bias comments                                                                                           | Directness          | Directness comments |
|----------------|----------------------------------------|-------------------------------|---------------|---------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|                |                                        |                               |               | analysis and attrition.                                                                                 |                     |                     |
| Terauchi 2017  | Glimepiride v Sitagliptin              | HbA1c change                  | High          | Concerns with allocation concealment, blinding, method of analysis, attrition and selection of outcome. | Directly applicable | None specified      |
| Umpierrez 2014 | Dulaglutide v Metformin                | All-cause mortality           | Some concerns | Concerns due to attrition                                                                               | Directly applicable | None specified      |
| Umpierrez 2014 | Dulaglutide v Metformin                | Cardiovascular mortality      | Some concerns | Concerns due to attrition                                                                               | Directly applicable | None specified      |
| Umpierrez 2014 | Dulaglutide v Metformin                | HbA1c change                  | Some concerns | Concerns due to attrition                                                                               | Directly applicable | None specified      |
| Umpierrez 2014 | Dulaglutide v Metformin                | Hypoglycaemia episodes        | Some concerns | Concerns due to attrition                                                                               | Directly applicable | None specified      |
| Umpierrez 2014 | Dulaglutide v Metformin                | Severe hypoglycaemic episodes | Some concerns | Concerns due to attrition                                                                               | Directly applicable | None specified      |
| Umpierrez 2014 | Dulaglutide v Metformin                | Weight change                 | Some concerns | Concerns due to attrition                                                                               | Directly applicable | None specified      |
| Wainstein 2012 | Sitagliptin + Metformin v Pioglitazone | HbA1c change                  | High          | Allocation concealment unclear, attrition rate high                                                     | Directly applicable | None specified      |
| Wainstein 2012 | Sitagliptin + Metformin v Pioglitazone | Hypoglycaemia episodes        | High          | Allocation concealment unclear, attrition rate high                                                     | Directly applicable | None specified      |
| Wainstein 2012 | Sitagliptin + Metformin v Pioglitazone | Severe hypoglycaemic episodes | High          | Allocation concealment                                                                                  | Directly applicable | None specified      |

| Study name | Comparison details      | Outcome       | Risk of bias | Bias comments                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Directness          | Directness comments |
|------------|-------------------------|---------------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|            |                         |               |              | unclear, attrition rate high                                                                                                                                                                                                                                                                                                                                                                                                                                             |                     |                     |
| Wang 2013  | Gliclazide v Metformin  | HbA1c change  | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Directly applicable | None specified      |
| Wang 2013  | Gliclazide v Metformin  | Weight change | High         | None specified                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Directly applicable | None specified      |
| Wang 2016A | Dapagliflozin v Placebo | HbA1c change  | High         | Baseline differences statistically significant in the number of males (higher in the DAPA group vs. PCB) and higher fasting glucose levels in the DAPA group vs. PCB. Lack of information on analysis methods, blinding and allocation concealment. Subsidiary study (Li 2016) reports blinding . Lack of information on discontinuation, no consort diagram or reporting of number of patients who withdrew/not. But presentation of results suggests that all patients | Directly applicable | None specified      |

| Study name   | Comparison details                    | Outcome                | Risk of bias | Bias comments                                                                                         | Directness          | Directness comments |
|--------------|---------------------------------------|------------------------|--------------|-------------------------------------------------------------------------------------------------------|---------------------|---------------------|
|              |                                       |                        |              | were included in analysis                                                                             |                     |                     |
| Wang 2022A   | Sitagliptin + Metformin v Metformin   | BMI change             | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wang 2022A   | Sitagliptin + Metformin v Sitagliptin | BMI change             | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wang 2022A   | Sitagliptin v Metformin               | BMI change             | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wang 2022A   | Sitagliptin + Metformin v Metformin   | HbA1c change           | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wang 2022A   | Sitagliptin + Metformin v Sitagliptin | HbA1c change           | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wang 2022A   | Sitagliptin v Metformin               | HbA1c change           | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wolever 2000 | Metformin v Placebo                   | HbA1c change           | High         | None specified                                                                                        | Directly applicable | None specified      |
| Wu 2015      | Linagliptin v Placebo                 | HbA1c change           | High         | No statistical test info at baseline; trial not registered. Double-blind trial, likely mITT analysis. | Directly applicable | None specified      |
| Wu 2015      | Linagliptin v Placebo                 | Hypoglycaemia episodes | High         | No statistical test info at baseline; trial not registered. Double-blind trial, likely mITT analysis. | Directly applicable | None specified      |
| Wu 2015      | Linagliptin v Placebo                 | Weight change          | High         | No statistical test info at baseline; trial not registered.                                           | Directly applicable | None specified      |

| Study name | Comparison details       | Outcome                       | Risk of bias | Bias comments                                                      | Directness          | Directness comments |
|------------|--------------------------|-------------------------------|--------------|--------------------------------------------------------------------|---------------------|---------------------|
|            |                          |                               |              | Double-blind trial, likely mITT analysis.                          |                     |                     |
| Xu 2015    | Pioglitazone v Insulin   | All-cause mortality           | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Insulin   | BMI change                    | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Insulin   | Cardiovascular mortality      | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Insulin   | HbA1c change                  | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Insulin   | Hypoglycaemia episodes        | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Insulin   | Severe hypoglycaemic episodes | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Insulin   | Weight change                 | High         | None specified                                                     | Directly applicable | None specified      |
| Xu 2015    | Exenatide v Insulin      | All-cause mortality           | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Exenatide | All-cause mortality           | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Exenatide v Insulin      | BMI change                    | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Exenatide | BMI change                    | High         | Open-label trial with mITT analysis.                               | Directly applicable | None specified      |

| Study name | Comparison details       | Outcome                       | Risk of bias | Bias comments                                                      | Directness          | Directness comments |
|------------|--------------------------|-------------------------------|--------------|--------------------------------------------------------------------|---------------------|---------------------|
|            |                          |                               |              | Possible selective reporting.                                      |                     |                     |
| Xu 2015    | Exenatide v Insulin      | Cardiovascular mortality      | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Exenatide | Cardiovascular mortality      | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Exenatide v Insulin      | HbA1c change                  | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Exenatide | HbA1c change                  | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Exenatide v Insulin      | Hypoglycaemia episodes        | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Exenatide | Hypoglycaemia episodes        | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Exenatide v Insulin      | Severe hypoglycaemic episodes | High         | Open-label trial with mITT analysis. Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015    | Pioglitazone v Exenatide | Severe hypoglycaemic episodes | High         | Open-label trial with mITT analysis.                               | Directly applicable | None specified      |



| Study name  | Comparison details       | Outcome                         | Risk of bias | Bias comments                                                         | Directness          | Directness comments |
|-------------|--------------------------|---------------------------------|--------------|-----------------------------------------------------------------------|---------------------|---------------------|
|             |                          |                                 |              | Possible selective reporting.                                         |                     |                     |
| Xu 2015     | Exenatide v Insulin      | Weight change                   | High         | Open-label trial with mITT analysis.<br>Possible selective reporting. | Directly applicable | None specified      |
| Xu 2015     | Pioglitazone v Exenatide | Weight change                   | High         | Open-label trial with mITT analysis.<br>Possible selective reporting. | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Acute kidney injury             | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | All-cause mortality             | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | BMI change                      | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Cardiac arrhythmia              | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Cardiovascular mortality        | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | HbA1c change                    | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Hypoglycaemia episodes          | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Non-fatal myocardial infarction | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Non-fatal stroke                | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo    | Severe hypoglycaemic episodes   | High         | Double-blind trial with mITT analysis.                                | Directly applicable | None specified      |

| Study name  | Comparison details        | Outcome                                                    | Risk of bias | Bias comments                                                  | Directness          | Directness comments |
|-------------|---------------------------|------------------------------------------------------------|--------------|----------------------------------------------------------------|---------------------|---------------------|
| Yamada 2020 | Liraglutide v Placebo     | Unstable angina                                            | High         | Double-blind trial with mITT analysis.                         | Directly applicable | None specified      |
| Yamada 2020 | Liraglutide v Placebo     | Weight change                                              | High         | Double-blind trial with mITT analysis.                         | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Acute kidney injury                                        | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | All-cause mortality                                        | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | BMI change                                                 | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Cardiac arrhythmia                                         | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Cardiovascular mortality                                   | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | HbA1c change                                               | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Health-related quality of life - subscale mental component | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |

| Study name  | Comparison details        | Outcome                                                      | Risk of bias | Bias comments                                                  | Directness          | Directness comments |
|-------------|---------------------------|--------------------------------------------------------------|--------------|----------------------------------------------------------------|---------------------|---------------------|
| Yamada 2020 | Semaglutide v Liraglutide | Health-related quality of life - subscale physical component | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Hypoglycaemia episodes                                       | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Non-fatal myocardial infarction                              | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Non-fatal stroke                                             | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Severe hypoglycaemic episodes                                | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Unstable angina                                              | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Liraglutide | Weight change                                                | High         | Double-blind trial with open-label liraglutide. mITT analysis. | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Placebo     | Acute kidney injury                                          | High         | None specified                                                 | Directly applicable | None specified      |
| Yamada 2020 | Semaglutide v Placebo     | All-cause mortality                                          | High         | None specified                                                 | Directly applicable | None specified      |

| Study name      | Comparison details      | Outcome                                                      | Risk of bias | Bias comments  | Directness          | Directness comments |
|-----------------|-------------------------|--------------------------------------------------------------|--------------|----------------|---------------------|---------------------|
| Yamada 2020     | Semaglutide v Placebo   | BMI change                                                   | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Cardiac arrhythmia                                           | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Cardiovascular mortality                                     | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | HbA1c change                                                 | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Health-related quality of life - subscale mental component   | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Health-related quality of life - subscale physical component | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Hypoglycaemia episodes                                       | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Non-fatal myocardial infarction                              | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Non-fatal stroke                                             | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Severe hypoglycaemic episodes                                | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Unstable angina                                              | High         | None specified | Directly applicable | None specified      |
| Yamada 2020     | Semaglutide v Placebo   | Weight change                                                | High         | None specified | Directly applicable | None specified      |
| Yamanouchi 2005 | Glimepiride v Metformin | BMI change                                                   | High         | None specified | Directly applicable | None specified      |

| Study name      | Comparison details                        | Outcome                  | Risk of bias | Bias comments                                                                                | Directness          | Directness comments |
|-----------------|-------------------------------------------|--------------------------|--------------|----------------------------------------------------------------------------------------------|---------------------|---------------------|
| Yamanouchi 2005 | Pioglitazone v Glimepiride                | BMI change               | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Pioglitazone v Metformin                  | BMI change               | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Glimepiride v Metformin                   | HbA1c change             | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Pioglitazone v Glimepiride                | HbA1c change             | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Pioglitazone v Metformin                  | HbA1c change             | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Glimepiride v Metformin                   | Hypoglycaemia episodes   | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Pioglitazone v Glimepiride                | Hypoglycaemia episodes   | High         | None specified                                                                               | Directly applicable | None specified      |
| Yamanouchi 2005 | Pioglitazone v Metformin                  | Hypoglycaemia episodes   | High         | None specified                                                                               | Directly applicable | None specified      |
| Yoon 2011A      | Glimepiride v Metformin                   | HbA1c change             | High         | None specified                                                                               | Directly applicable | None specified      |
| Yoon 2011A      | Glimepiride v Metformin                   | Hypoglycaemia episodes   | High         | None specified                                                                               | Directly applicable | None specified      |
| Yoon 2012       | Pioglitazone + Sitagliptin v Pioglitazone | All-cause mortality      | High         | No randomisation info, high attrition rate. Double-blind trial with open label pioglitazone. | Directly applicable | None specified      |
| Yoon 2012       | Pioglitazone + Sitagliptin v Pioglitazone | Cardiovascular mortality | High         | No randomisation info, high attrition rate. Double-blind trial with open label pioglitazone. | Directly applicable | None specified      |

| Study name  | Comparison details                        | Outcome                       | Risk of bias | Bias comments                                                                                | Directness          | Directness comments |
|-------------|-------------------------------------------|-------------------------------|--------------|----------------------------------------------------------------------------------------------|---------------------|---------------------|
| Yoon 2012   | Pioglitazone + Sitagliptin v Pioglitazone | HbA1c change                  | High         | No randomisation info, high attrition rate. Double-blind trial with open label pioglitazone. | Directly applicable | None specified      |
| Yoon 2012   | Pioglitazone + Sitagliptin v Pioglitazone | Hypoglycaemia episodes        | High         | No randomisation info, high attrition rate. Double-blind trial with open label pioglitazone. | Directly applicable | None specified      |
| Yoon 2012   | Pioglitazone + Sitagliptin v Pioglitazone | Severe hypoglycaemic episodes | High         | No randomisation info, high attrition rate. Double-blind trial with open label pioglitazone. | Directly applicable | None specified      |
| Yoon 2012   | Pioglitazone + Sitagliptin v Pioglitazone | Weight change                 | High         | No randomisation info, high attrition rate. Double-blind trial with open label pioglitazone. | Directly applicable | None specified      |
| Yuan 2012   | Exenatide v Metformin                     | BMI change                    | High         | None specified                                                                               | Directly applicable | None specified      |
| Yuan 2012   | Exenatide v Metformin                     | HbA1c change                  | High         | None specified                                                                               | Directly applicable | None specified      |
| Yuan 2012   | Exenatide v Metformin                     | Hypoglycaemia episodes        | High         | None specified                                                                               | Directly applicable | None specified      |
| Yuan 2012   | Exenatide v Metformin                     | Severe hypoglycaemic episodes | High         | None specified                                                                               | Directly applicable | None specified      |
| Yuan 2012   | Exenatide v Metformin                     | Weight change                 | High         | None specified                                                                               | Directly applicable | None specified      |
| Zhang 2020A | Pioglitazone v Liraglutide                | BMI change                    | High         | Unclear reporting, trial not registered                                                      | Directly applicable | T2DM and NAFLD      |

| Study name  | Comparison details                                  | Outcome                       | Risk of bias | Bias comments                                                                                                                                                                                                                                                                     | Directness          | Directness comments |
|-------------|-----------------------------------------------------|-------------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Zhang 2020A | Pioglitazone v Liraglutide                          | HbA1c change                  | High         | Unclear reporting, trial not registered                                                                                                                                                                                                                                           | Directly applicable | T2DM and NAFLD      |
| Zhang 2020A | Pioglitazone v Liraglutide                          | Severe hypoglycaemic episodes | High         | Unclear reporting, trial not registered                                                                                                                                                                                                                                           | Directly applicable | T2DM and NAFLD      |
| Zhang 2020A | Pioglitazone v Liraglutide                          | Weight change                 | High         | Unclear reporting, trial not registered                                                                                                                                                                                                                                           | Directly applicable | T2DM and NAFLD      |
| Zhang 2020A | Pioglitazone v Liraglutide                          | Hypoglycaemia episodes        | High         | Unclear reporting, trial not registered. Possible                                                                                                                                                                                                                                 | Directly applicable | T2DM and NAFLD      |
| Zhou 2021   | Glimepiride + Metformin v Canagliflozin + Metformin | Weight change                 | High         | Suspicious methods and reporting - HbA1c outcome data could not be used due to median and IQR for canagliflozin (mean and SD reported for glimepiride). Additionally some data that should have been included in the baseline table was not included (total and HDL cholesterol). | Directly applicable | None specified      |
| Zhou 2022   | Dapagliflozin + Metformin v Metformin               | BMI change                    | High         | None specified                                                                                                                                                                                                                                                                    | Directly applicable | None specified      |
| Zhou 2022   | Dapagliflozin + Metformin v Metformin               | HbA1c change                  | High         | None specified                                                                                                                                                                                                                                                                    | Directly applicable | None specified      |



| Study name     | Comparison details                    | Outcome                | Risk of bias | Bias comments                                                                                                                                                                                                | Directness          | Directness comments |
|----------------|---------------------------------------|------------------------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|
| Zhou 2022      | Dapagliflozin + Metformin v Metformin | Hypoglycaemia episodes | High         | None specified                                                                                                                                                                                               | Directly applicable | None specified      |
| Zougrafou 2015 | Vildagliptin + Metformin v Metformin  | BMI change             | High         | No statement about allocation concealment, limited information about what happened to participants during the study (attrition, adherence), some outcomes could have been influenced by the lack of blinding | Directly applicable | None specified      |
| Zougrafou 2015 | Vildagliptin + Metformin v Metformin  | HbA1c change           | High         | No statement about allocation concealment, limited information about what happened to participants during the study (attrition, adherence), some outcomes could have been influenced by the lack of blinding | Directly applicable | None specified      |
| Zougrafou 2015 | Vildagliptin + Metformin v Metformin  | Weight change          | High         | No statement about allocation concealment, limited information about what happened to participants during the study (attrition, adherence), some                                                             | Directly applicable | None specified      |

| Study name | Comparison details | Outcome | Risk of bias | Bias comments                                               | Directness | Directness comments |
|------------|--------------------|---------|--------------|-------------------------------------------------------------|------------|---------------------|
|            |                    |         |              | outcomes could have been influenced by the lack of blinding |            |                     |