National Institute for Health and Care Excellence

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Draft for consultation

Type 2 diabetes in adults: management

[F6] Evidence reviews for subsequent pharmacological management of type 2 diabetes

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

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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ISBN:

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K.1 Adding

K.1.1 Metformin

K.1.1.1 Adding metformin compared to adding placebo

Figure 1: All-cause mortality at end of follow up

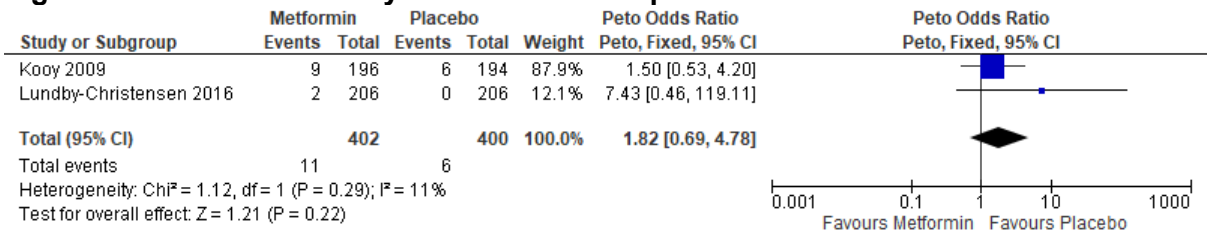


Figure 2: Hypoglycaemia episodes at end of follow up

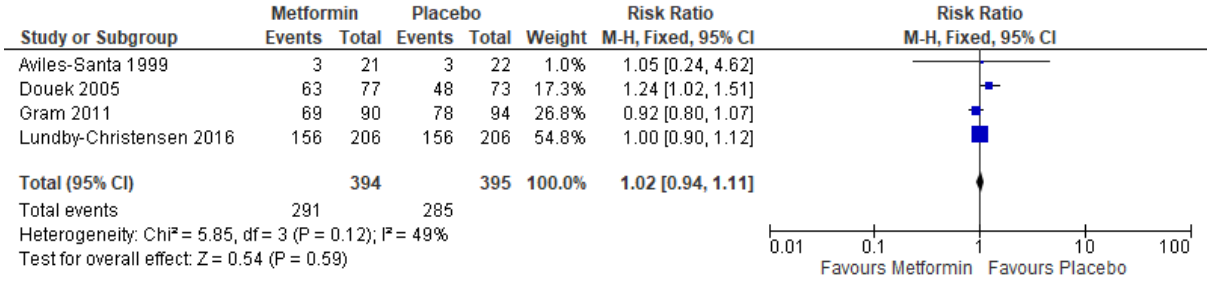


Figure 3: Severe hypoglycaemic episodes at end of follow up

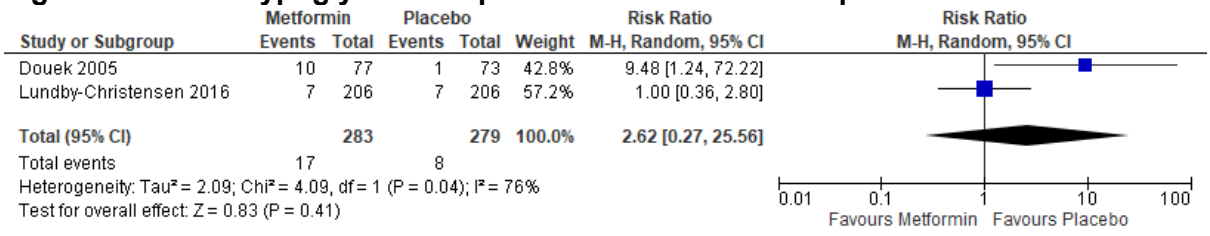
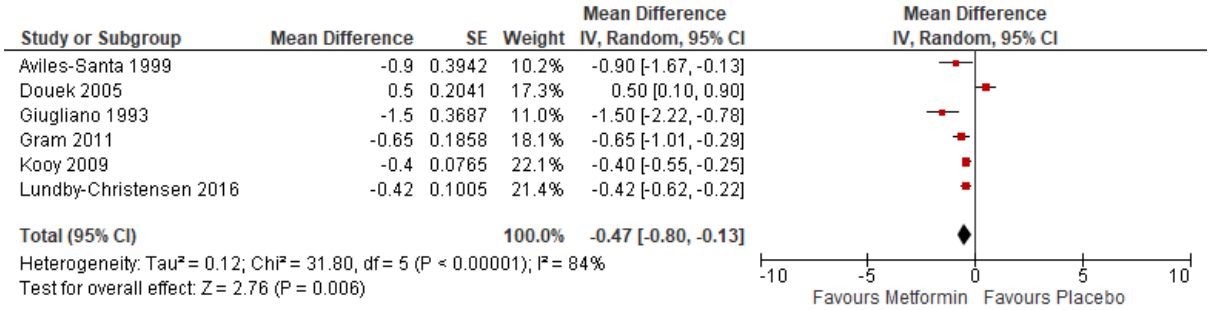
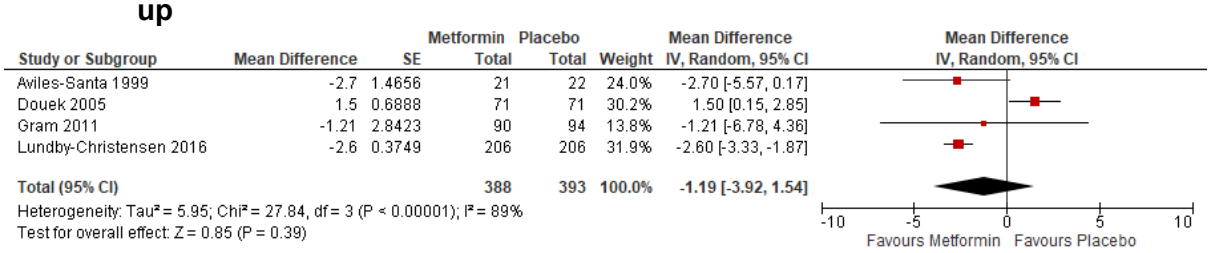


Figure 4: HbA1c change (%, lower values are better, mean difference) at end of follow up



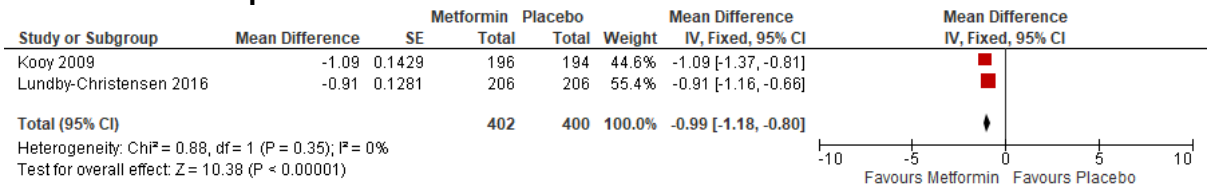
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by obesity and onset subgroups.

Figure 5: Weight change (kg, lower values are better, mean difference) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis. Subgroup analysis was not possible for any subgroup.

Figure 6: BMI change (kg/m^2, lower values are better, mean difference) at end of follow up



K.1.1.2 Adding metformin compared to adding insulin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.2 DPP-4 inhibitors

K.1.2.1 Adding alogliptin compared to adding placebo

Figure 7: All-cause mortality at end of follow up

Study or Subgroup	Alogliptin Events	Alogliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Nauck 2009A	1	423	0	104	25.5%	0.00 [-0.01, 0.02]
Pratley 2009A	1	397	0	97	23.8%	0.00 [-0.01, 0.02]
Pratley 2009B	0	401	0	99	24.2%	0.00 [-0.01, 0.01]
Rosenstock 2009B	1	260	0	130	26.5%	0.00 [-0.01, 0.02]
Total (95% CI)		**1481**		**430**	**100.0%**	**0.00 [-0.01, 0.01]**
Total events	3		0			

Heterogeneity: Chi² = 0.15, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)

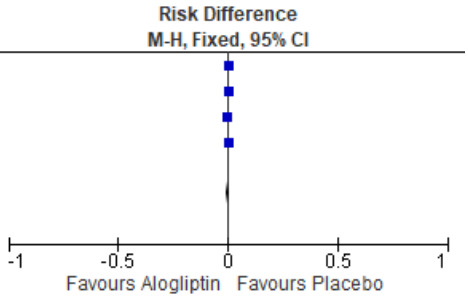


Figure 8: Cardiovascular mortality at end of follow up

Study or Subgroup	Alogliptin Events	Alogliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Nauck 2009A	1	423	0	104	33.5%	0.00 [-0.01, 0.02]
Pratley 2009B	0	401	0	99	31.8%	0.00 [-0.01, 0.01]
Rosenstock 2009B	1	260	0	130	34.7%	0.00 [-0.01, 0.02]
Total (95% CI)		**1084**		**333**	**100.0%**	**0.00 [-0.01, 0.01]**
Total events	2		0			

Heterogeneity: Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.50 (P = 0.61)

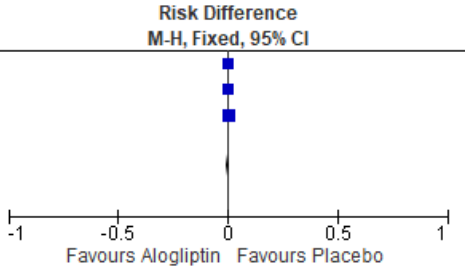


Figure 9: Hypoglycaemia episodes at end of follow up

Study or Subgroup	Alogliptin Events	Alogliptin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Nauck 2009A	2	423	3	104	6.7%	0.16 [0.03, 0.97]
Pratley 2009A	25	397	5	97	11.2%	1.22 [0.48, 3.11]
Pratley 2009B	51	401	11	99	24.5%	1.14 [0.62, 2.11]
Rosenstock 2009B	70	260	31	129	57.6%	1.12 [0.78, 1.62]
Total (95% CI)		**1481**		**429**	**100.0%**	**1.07 [0.80, 1.44]**
Total events	148		50			

Heterogeneity: Chi² = 4.47, df = 3 (P = 0.22); I² = 33%
Test for overall effect: Z = 0.48 (P = 0.63)

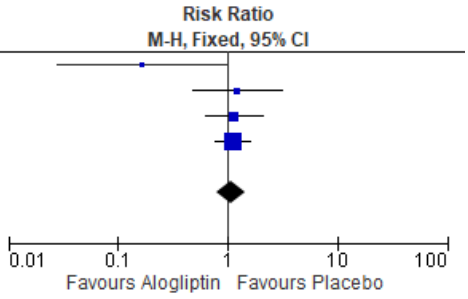


Figure 10: Severe hypoglycaemic episodes at end of follow up

Study or Subgroup	Alogliptin Events	Alogliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Nauck 2009A	0	423	0	104	33.5%	0.00 [-0.01, 0.01]
Pratley 2009B	2	401	1	99	31.8%	-0.01 [-0.03, 0.02]
Rosenstock 2009B	1	260	2	130	34.7%	-0.01 [-0.03, 0.01]
Total (95% CI)		**1084**		**333**	**100.0%**	**-0.01 [-0.02, 0.01]**
Total events	3		3			

Heterogeneity: Chi² = 0.93, df = 2 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.32)

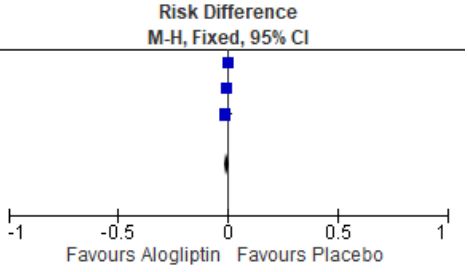
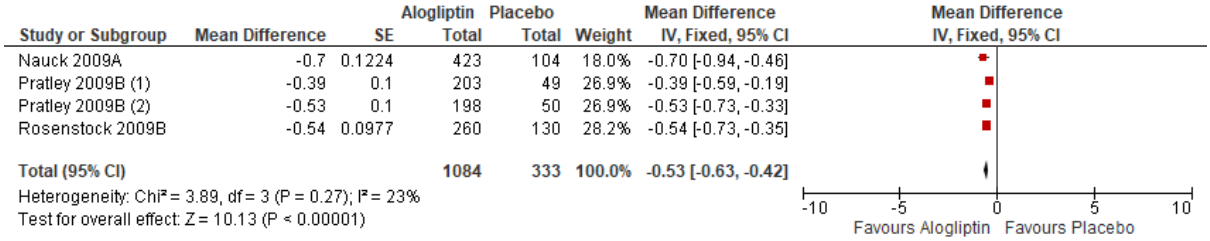
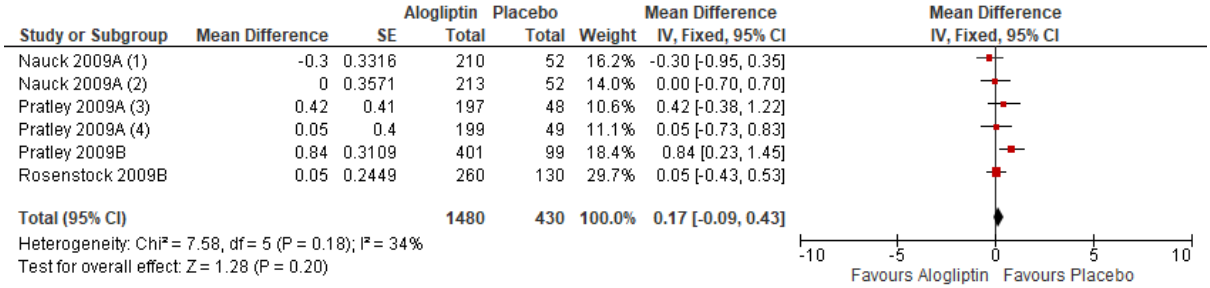


Figure 11: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) Data for alogliptin 12.5 mg. N for placebo arm has been halved.
(2) Data for alogliptin 25 mg. N for placebo arm has been halved.

Figure 12: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) Data for alogliptin 25 mg daily compared to placebo. N for placebo arm has been halved.
(2) Data for alogliptin 12.5 mg daily compared to placebo. N for placebo arm has been halved.
(3) Data for alogliptin 12.5 mg. N for placebo arm has been halved
(4) Data for alogliptin 25 mg. N for placebo arm has been halved

K.1.2.2 Adding linagliptin compared to adding placebo

Figure 13: All-cause mortality at end of follow up

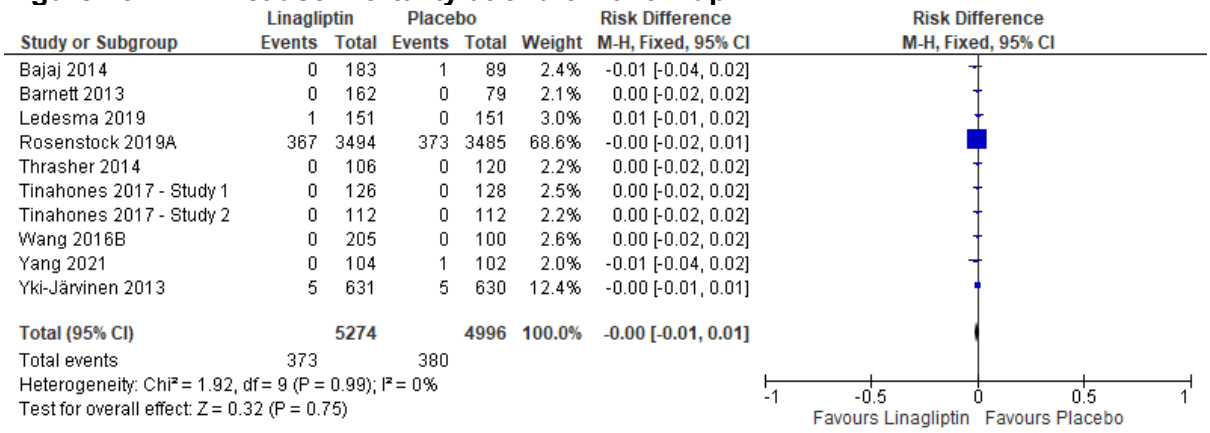


Figure 14: Cardiovascular mortality at end of follow up

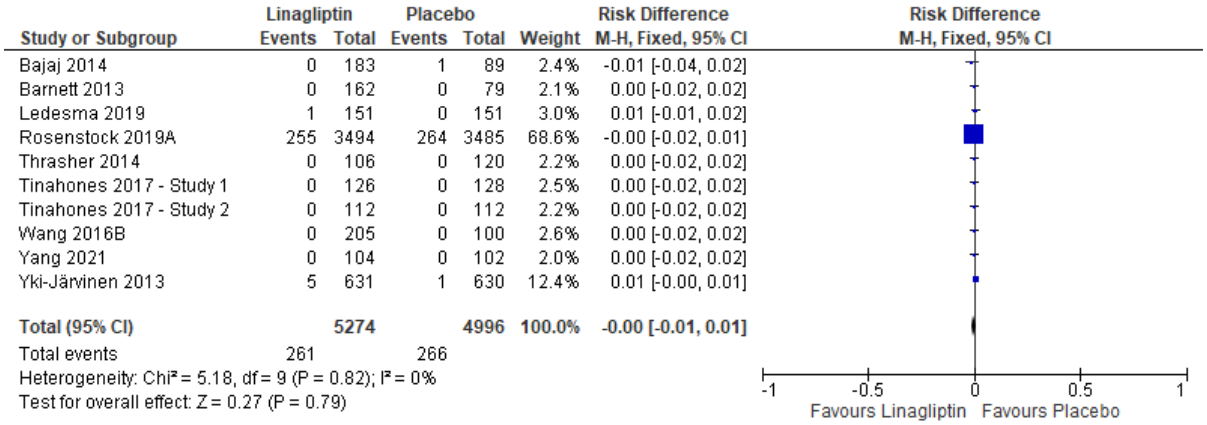


Figure 15: 4-point MACE at end of follow up

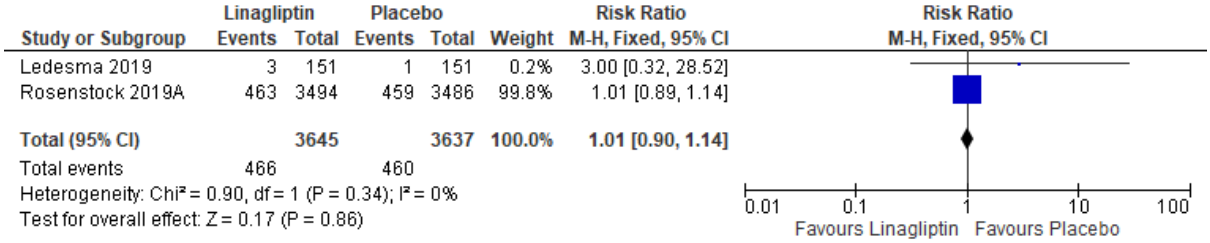


Figure 16: 5-point MACE at end of follow up

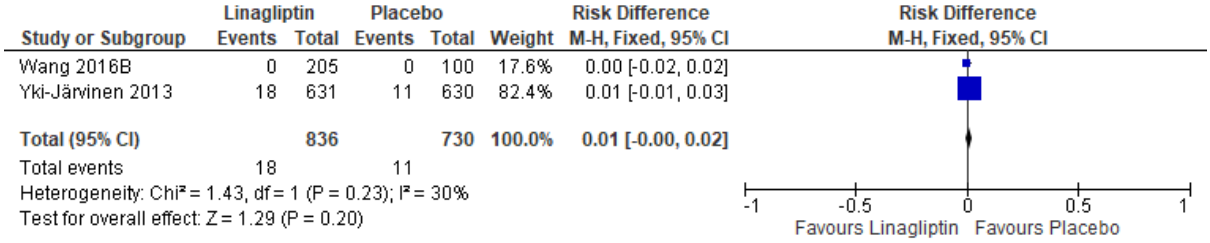


Figure 17: Non-fatal stroke at end of follow up

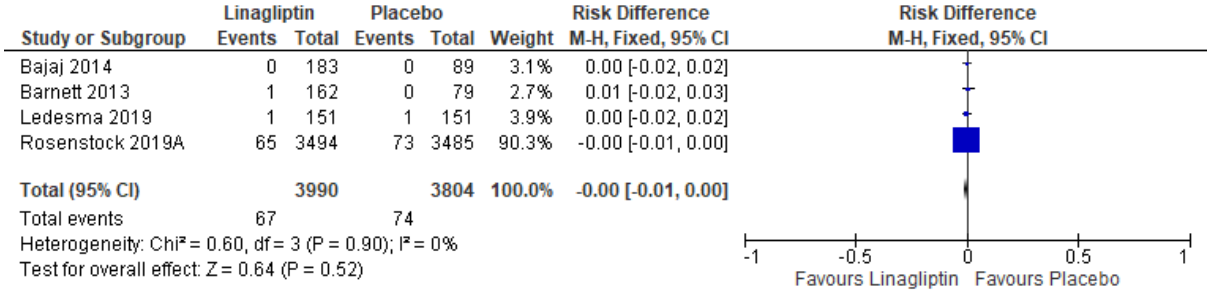


Figure 18: Non-fatal myocardial infarction at end of follow up

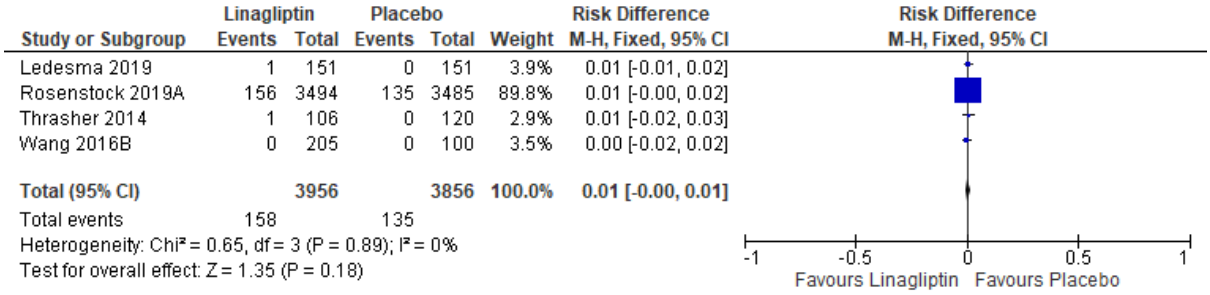


Figure 19: Unstable angina at end of follow up

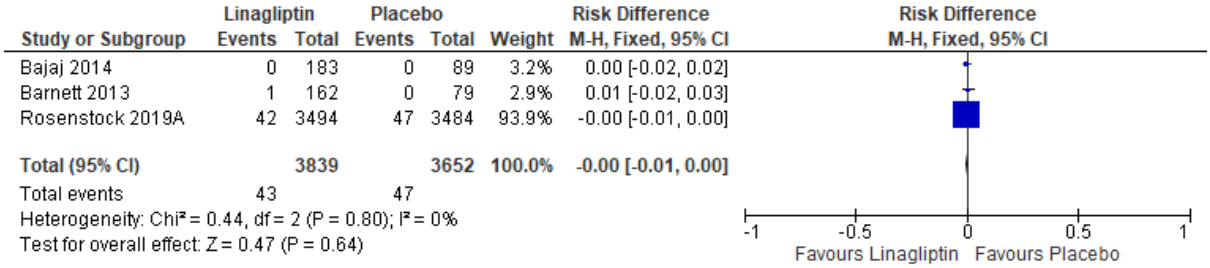


Figure 20: Hospitalisation for heart failure at end of follow up

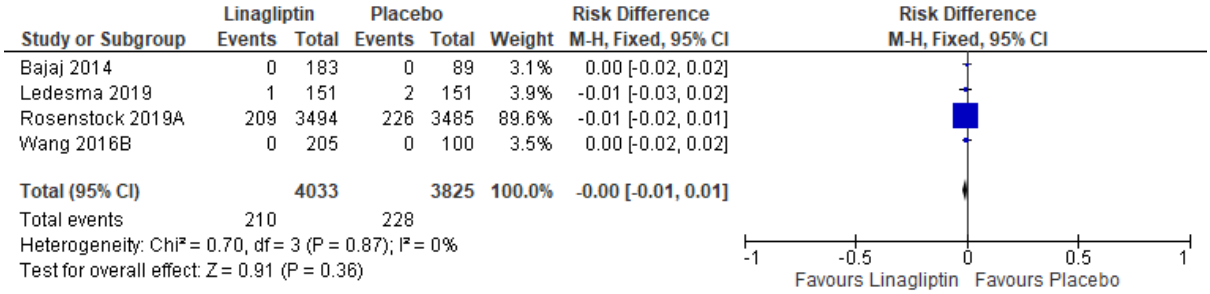


Figure 21: Development of end stage kidney disease at end of follow up

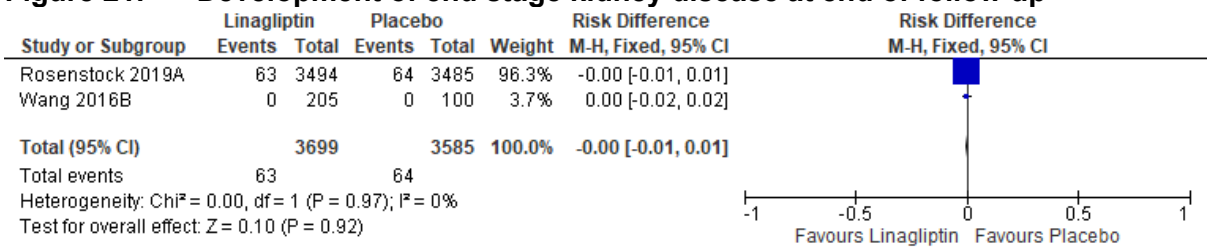


Figure 22: Diabetic ketoacidosis at end of follow up

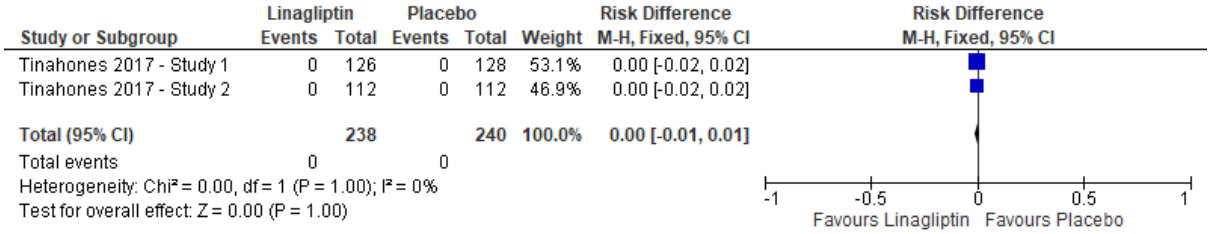
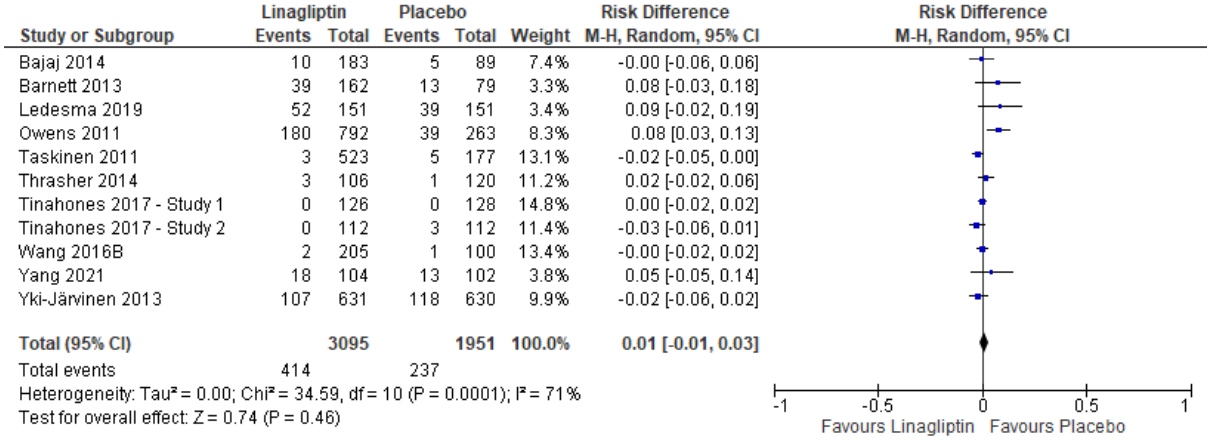


Figure 23: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 24: Severe hypoglycaemic episodes

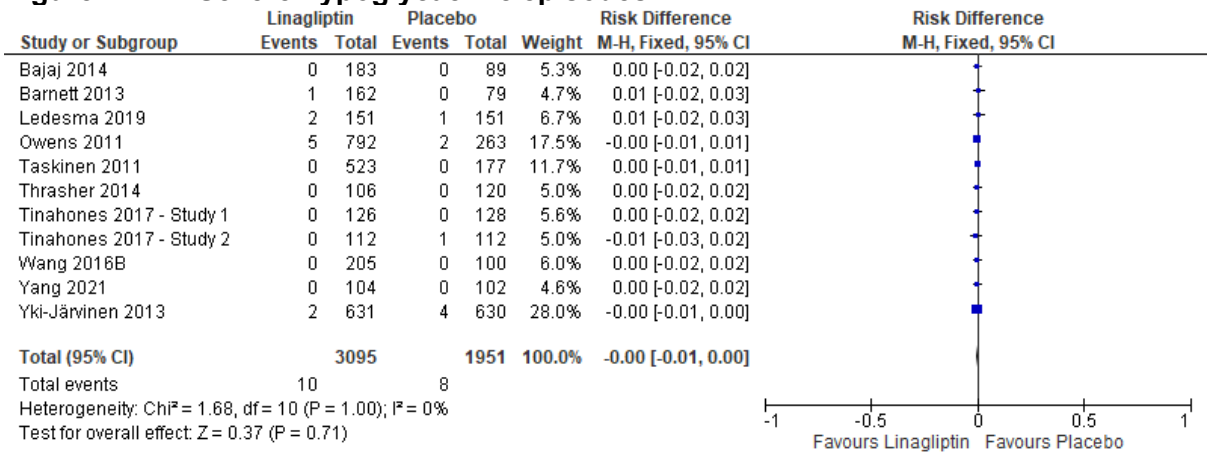
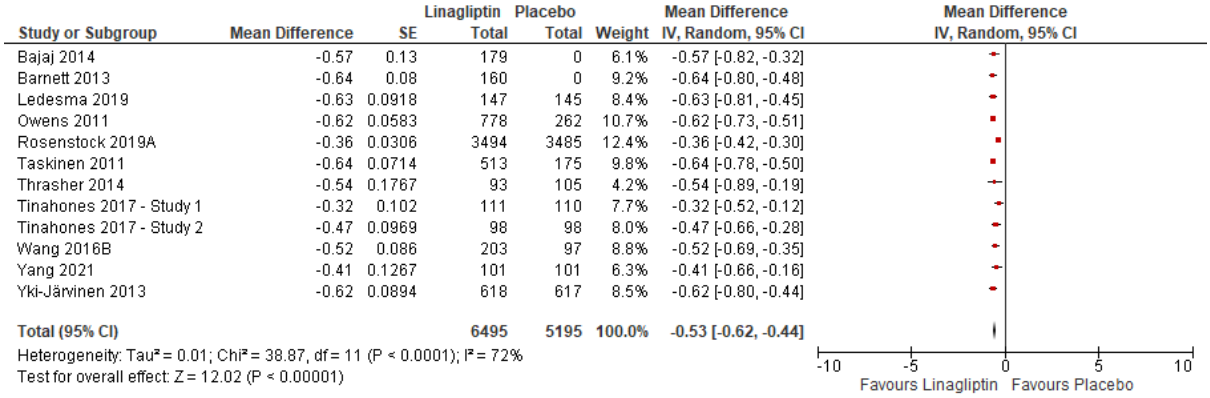
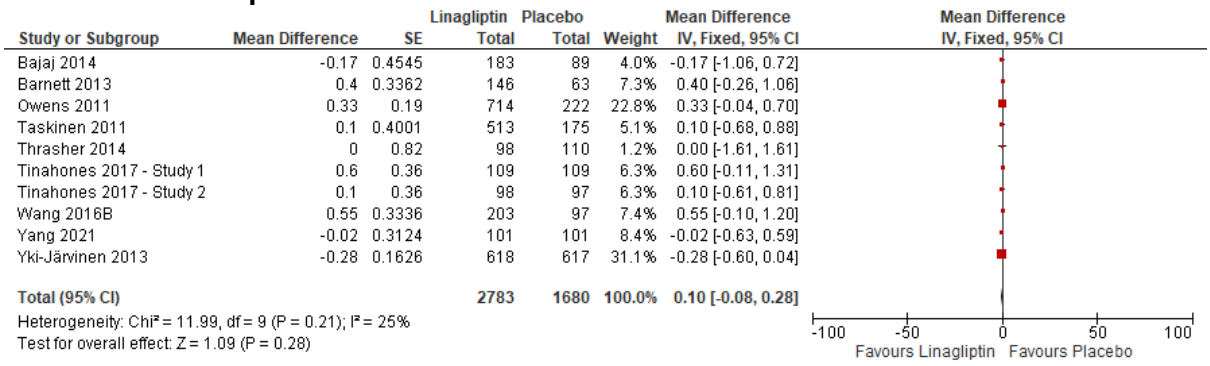


Figure 25: HbA1c change (%, lower values are better, change scores) at end of follow up



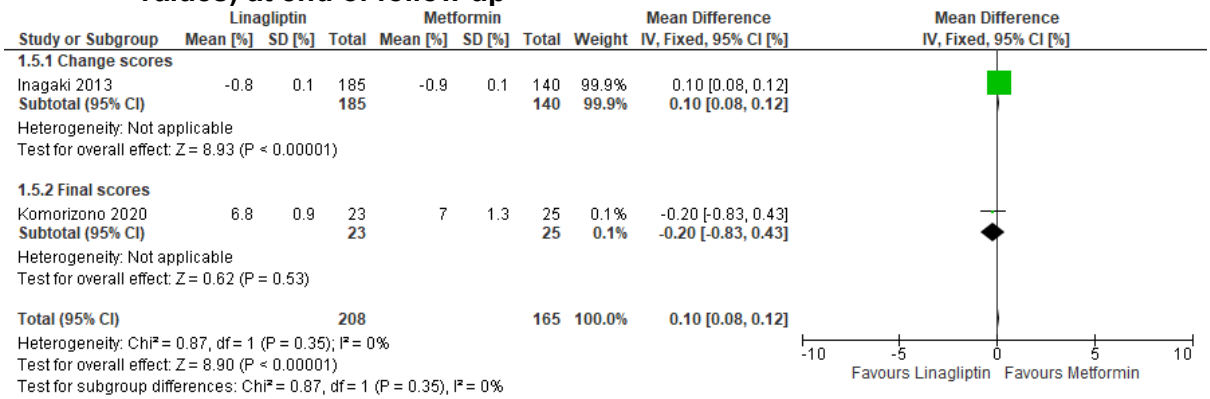
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 26: Weight change (%, lower values are better, change scores) at end of follow up



K.1.2.3 Adding linagliptin compared to adding metformin

Figure 27: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



K.1.2.4 Adding saxagliptin compared to adding placebo

Figure 28: All-cause mortality at end of follow up

Study or Subgroup	Saxagliptin Events	Saxagliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Barnett 2012	2	304	0	151	2.1%	0.01 [-0.01, 0.02]
Chen 2018A	1	232	1	230	2.4%	-0.00 [-0.01, 0.01]
DeFronzo 2009	0	564	1	179	2.9%	-0.01 [-0.02, 0.01]
Hollander 2009	2	381	0	184	2.6%	0.01 [-0.01, 0.02]
Matthaei 2015A	0	153	1	162	1.7%	-0.01 [-0.02, 0.01]
Moses 2014	0	129	0	128	1.4%	0.00 [-0.02, 0.02]
Scirica 2013	420	8280	378	8212	86.9%	0.00 [-0.00, 0.01]
Total (95% CI)		**10043**		**9246**	**100.0%**	**0.00 [-0.00, 0.01]**
Total events	425		381			

Heterogeneity: Chi² = 4.29, df = 6 (P = 0.64); I² = 0%
Test for overall effect: Z = 1.40 (P = 0.16)

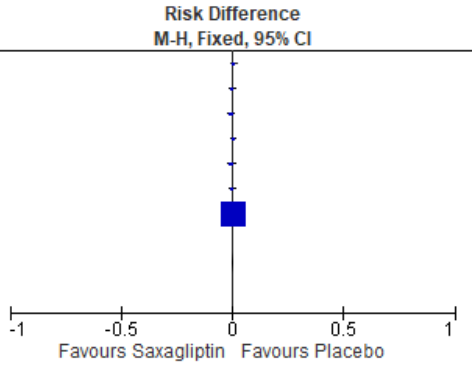


Figure 29: Cardiovascular mortality at end of follow up

Study or Subgroup	Saxagliptin Events	Saxagliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Chen 2018A	1	232	0	230	2.5%	0.00 [-0.01, 0.02]
DeFronzo 2009	0	564	1	179	3.0%	-0.01 [-0.02, 0.01]
Hollander 2009	1	381	0	184	2.7%	0.00 [-0.01, 0.01]
Moses 2014	0	129	0	128	1.4%	0.00 [-0.02, 0.02]
Scirica 2013	269	8280	260	8212	90.4%	0.00 [-0.00, 0.01]
Total (95% CI)		**9586**		**8933**	**100.0%**	**0.00 [-0.00, 0.01]**
Total events	271		261			

Heterogeneity: Chi² = 1.34, df = 4 (P = 0.85); I² = 0%
Test for overall effect: Z = 0.30 (P = 0.76)

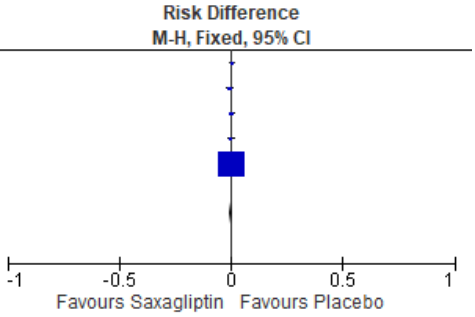


Figure 30: Non-fatal stroke at end of follow up

Study or Subgroup	Saxagliptin Events	Saxagliptin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Scirica 2013	157	8240	141	8173	99.3%	1.10 [0.88, 1.38]
Yang 2011	1	283	1	287	0.7%	1.01 [0.06, 16.13]
Total (95% CI)		**8523**		**8460**	**100.0%**	**1.10 [0.88, 1.38]**
Total events	158		142			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.86 (P = 0.39)

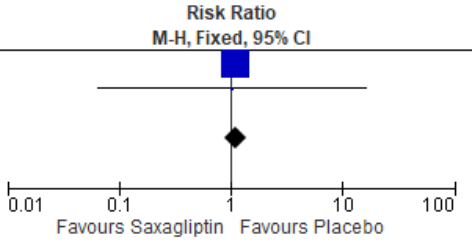


Figure 31: Non-fatal myocardial infarction at end of follow up

Study or Subgroup	Saxagliptin Events	Saxagliptin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chen 2018A	1	234	0	231	0.2%	2.96 [0.12, 72.33]
Scirica 2013	265	8240	278	8173	99.8%	0.95 [0.80, 1.12]
Total (95% CI)		**8474**		**8404**	**100.0%**	**0.95 [0.80, 1.12]**
Total events	266		278			

Heterogeneity: Chi² = 0.49, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.62 (P = 0.54)

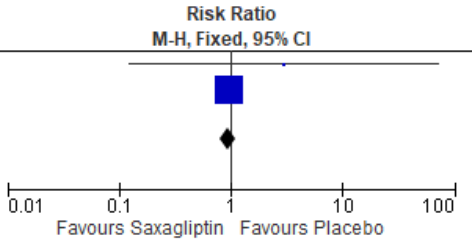
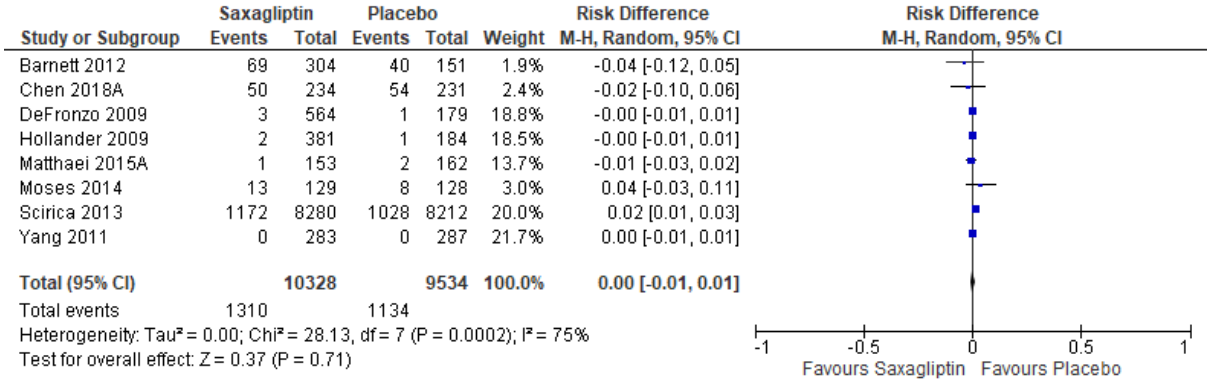


Figure 32: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 33: Severe hypoglycaemic episodes at end of follow up

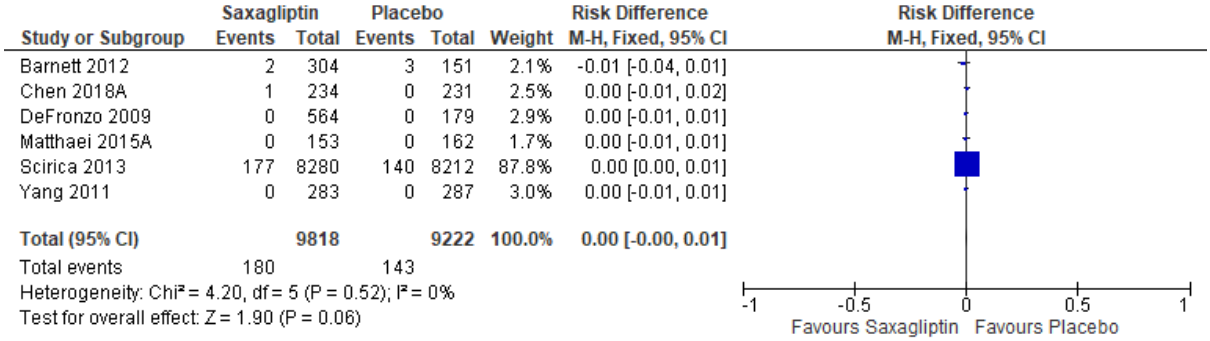
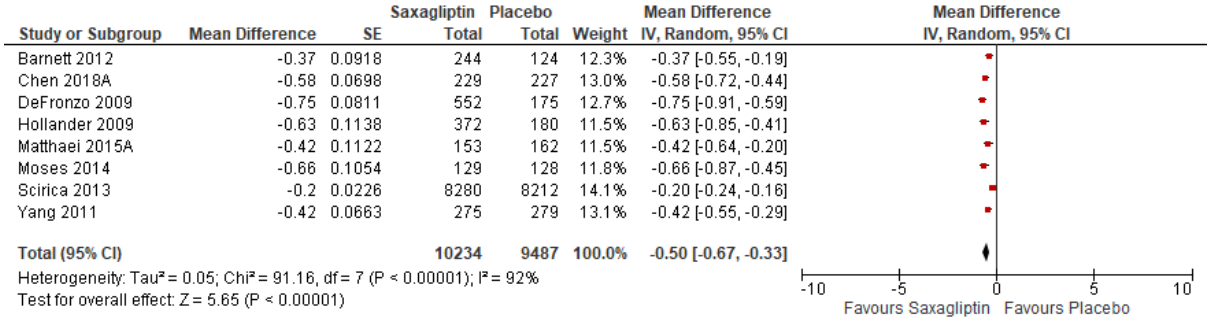
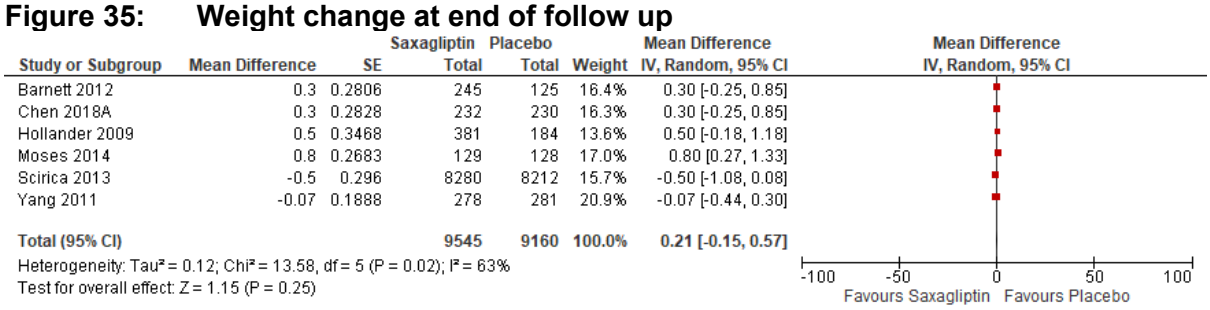


Figure 34: HbA1c change at end of follow up



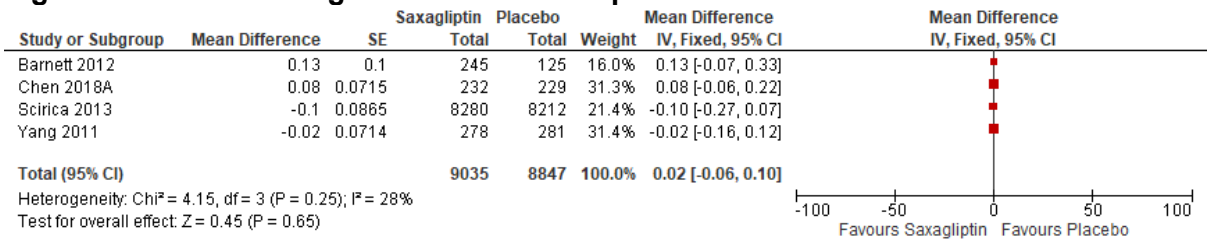
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 35: Weight change at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 36: BMI change at end of follow up



K.1.2.5 Adding sitagliptin compared to adding placebo

Figure 37: All-cause mortality at end of follow up

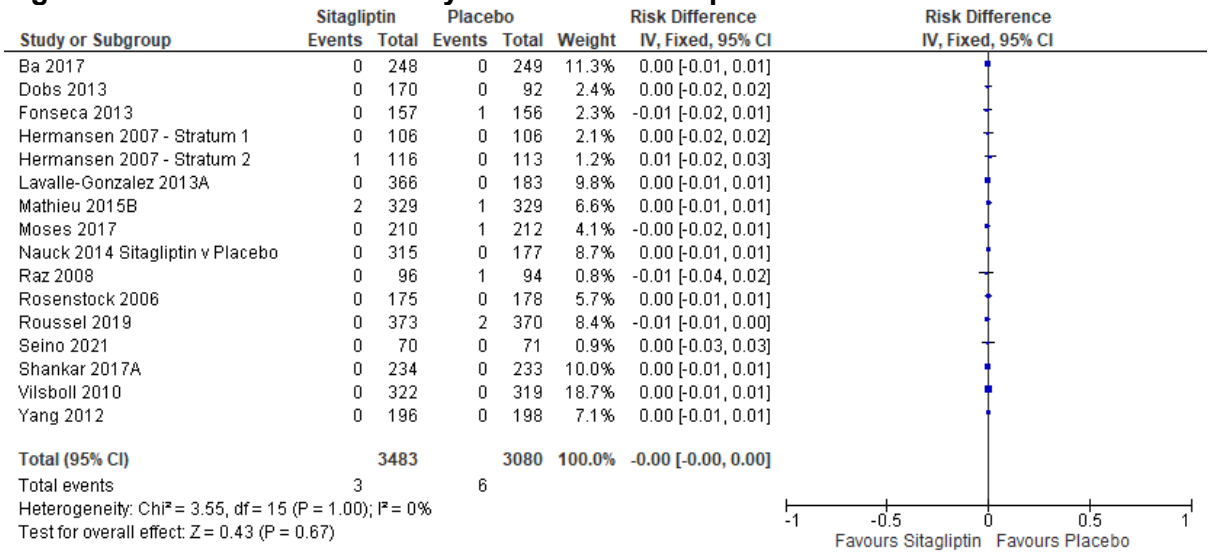


Figure 38: Cardiovascular mortality at end of follow up

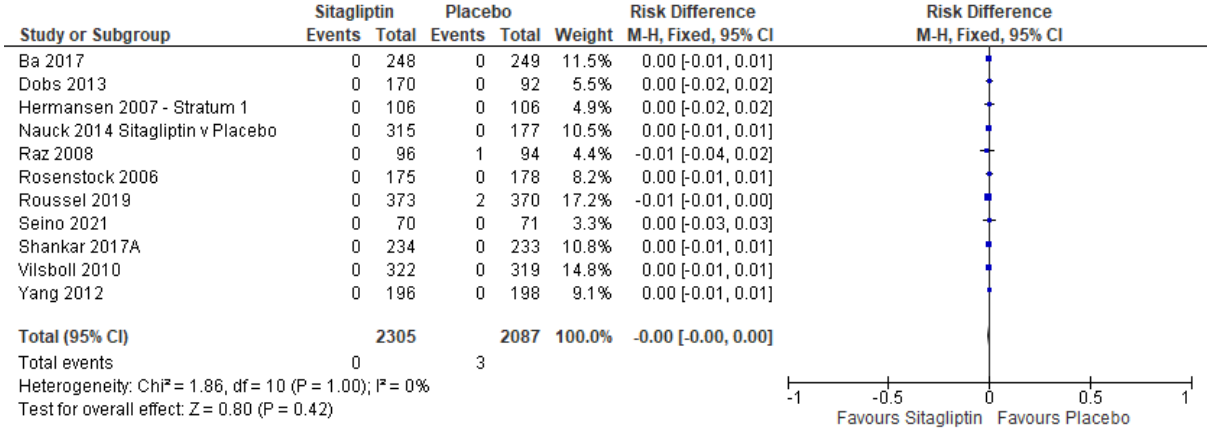


Figure 39: Non-fatal myocardial infarction at end of follow up

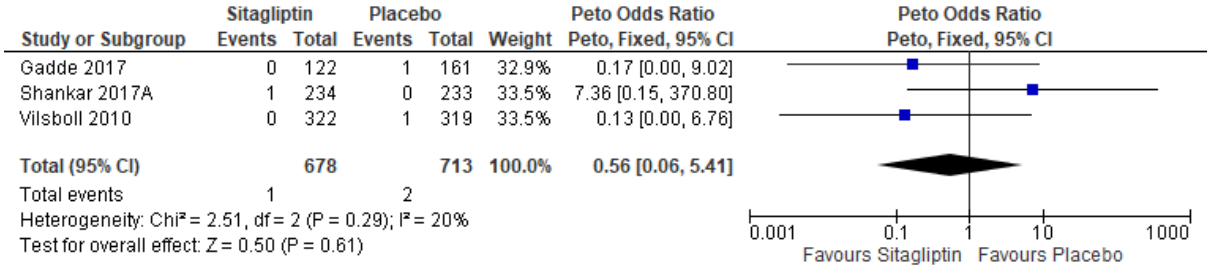


Figure 40: Unstable angina at end of follow up

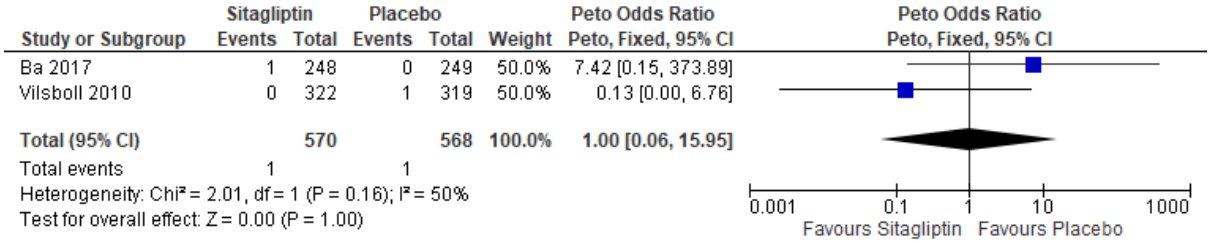
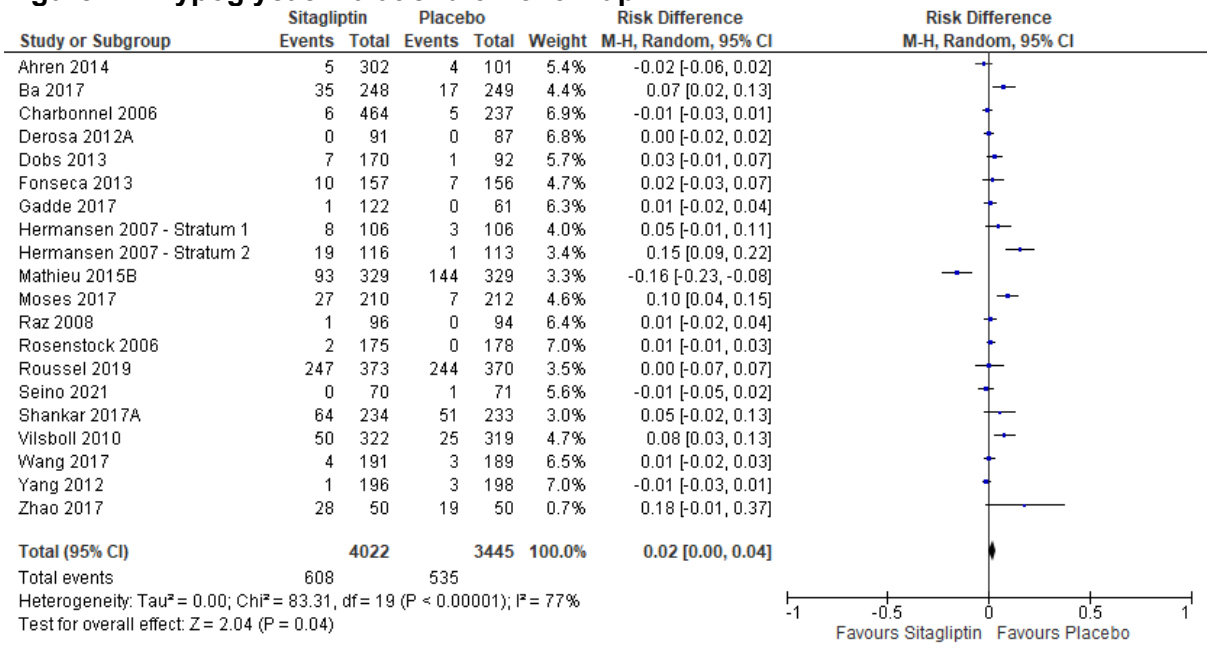


Figure 41: Hypoglycaemia at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 42: Severe hypoglycaemic episodes at end of follow up

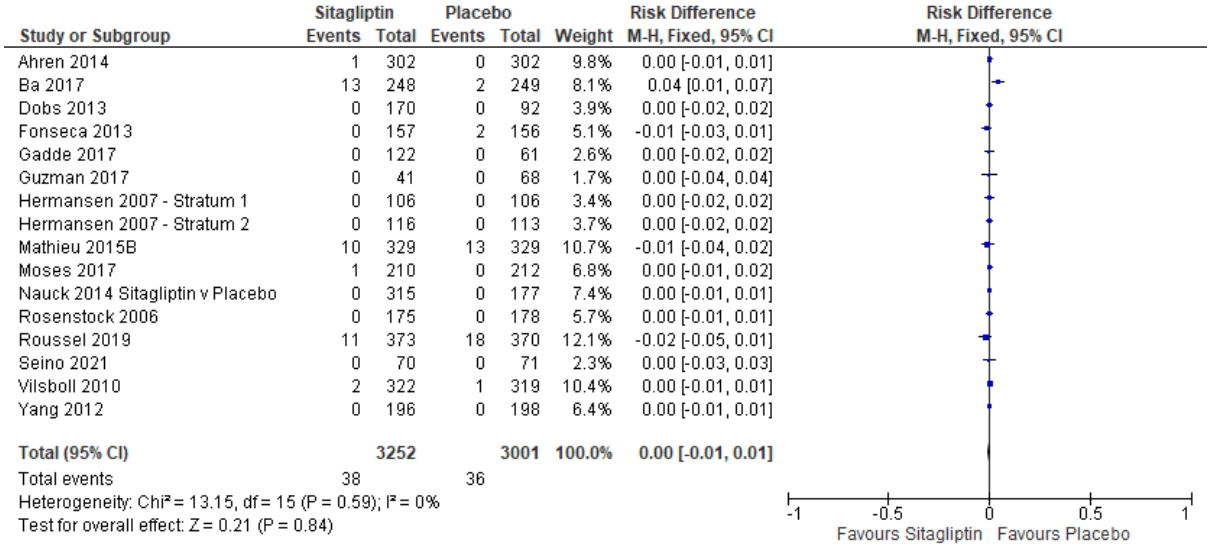
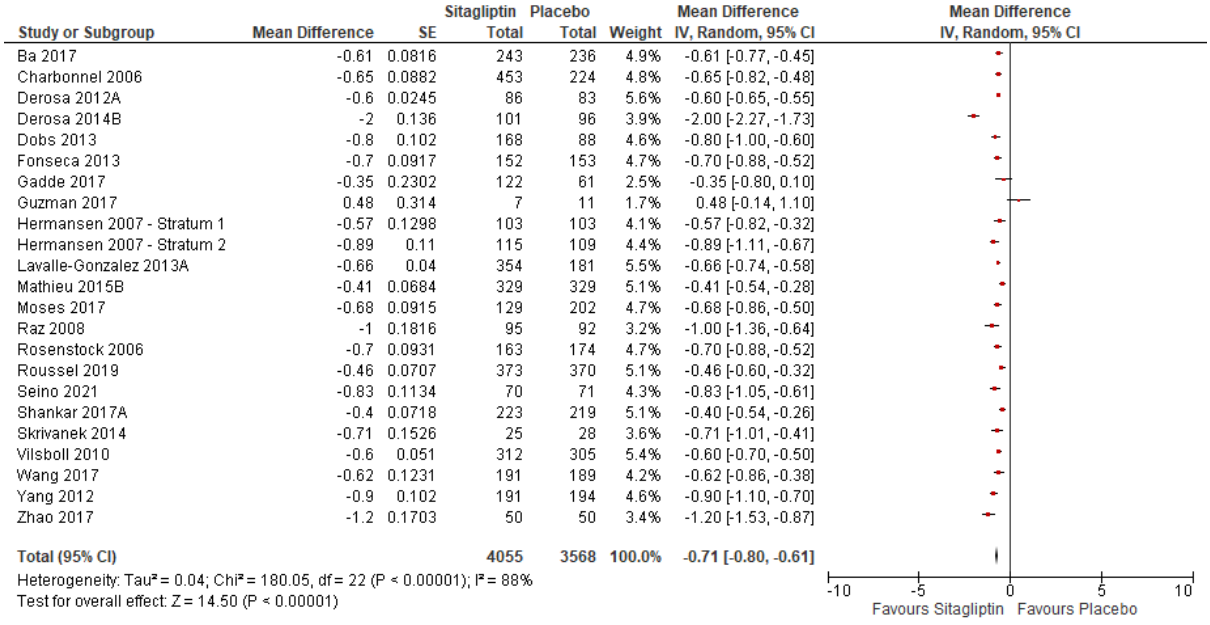
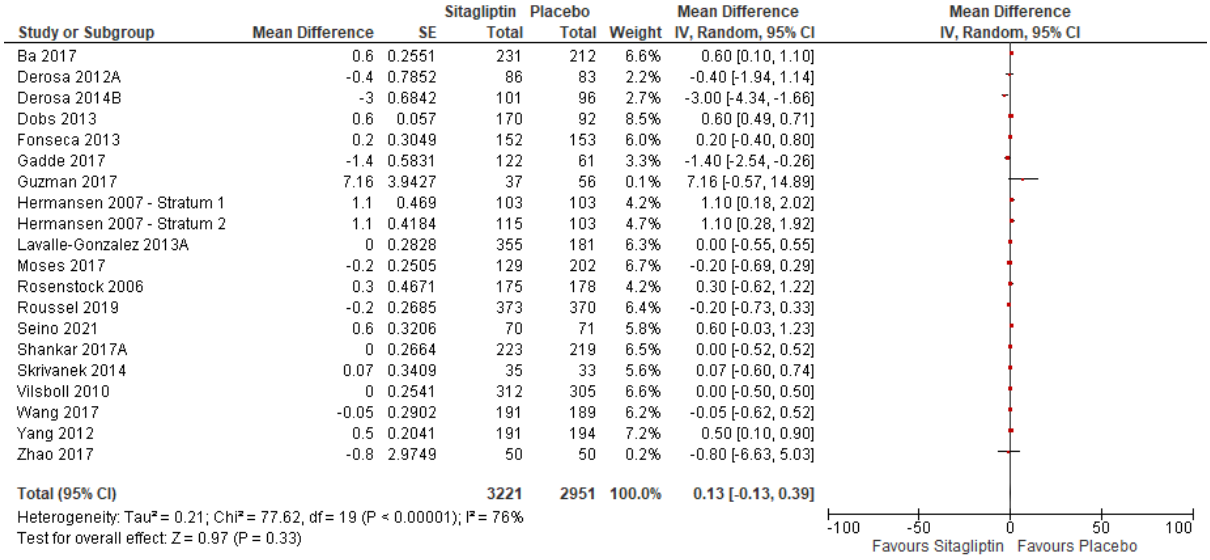


Figure 43: HbA1c change (%, lower values are better, mean difference) at end of follow up



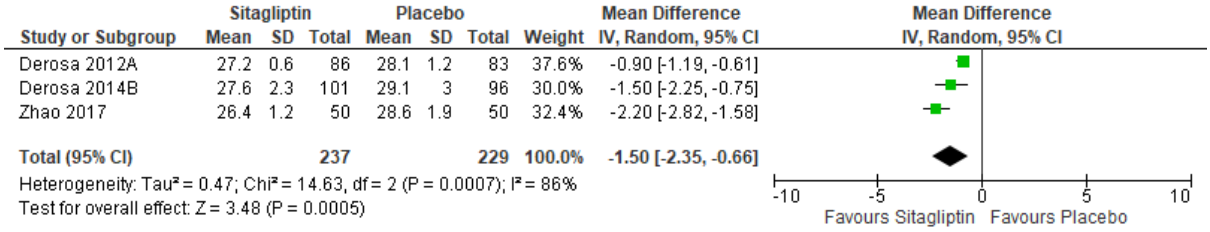
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 44: Weight change (kg, lower values are better, mean difference) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 45: BMI change (kg/m^2, lower values are better, final values) at end of follow up



K.1.2.6 Adding sitagliptin compared to adding metformin

Figure 46: HbA1c change (%, lower values are better, change and final scores) at end of follow up

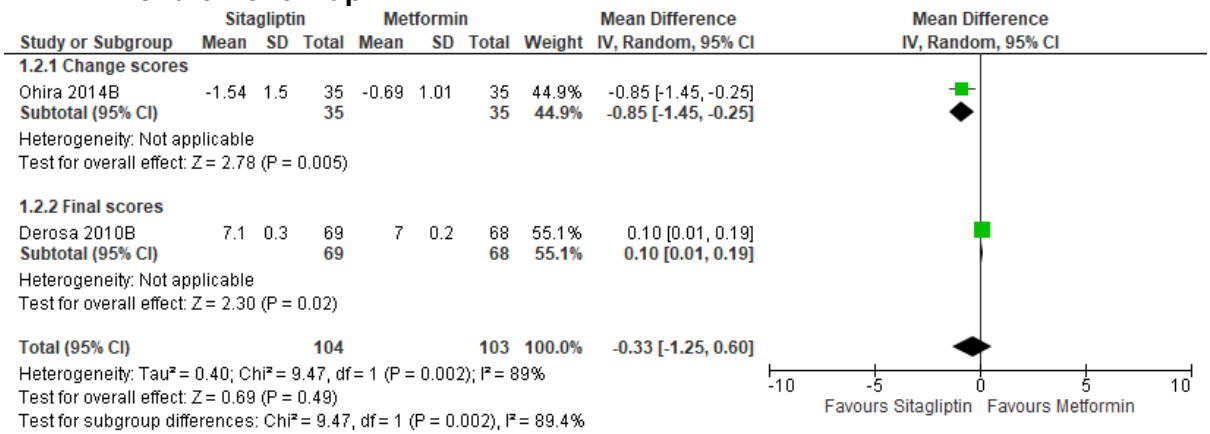


Figure 47: Weight change (kg, lower values are better, change and final scores) at end of follow up

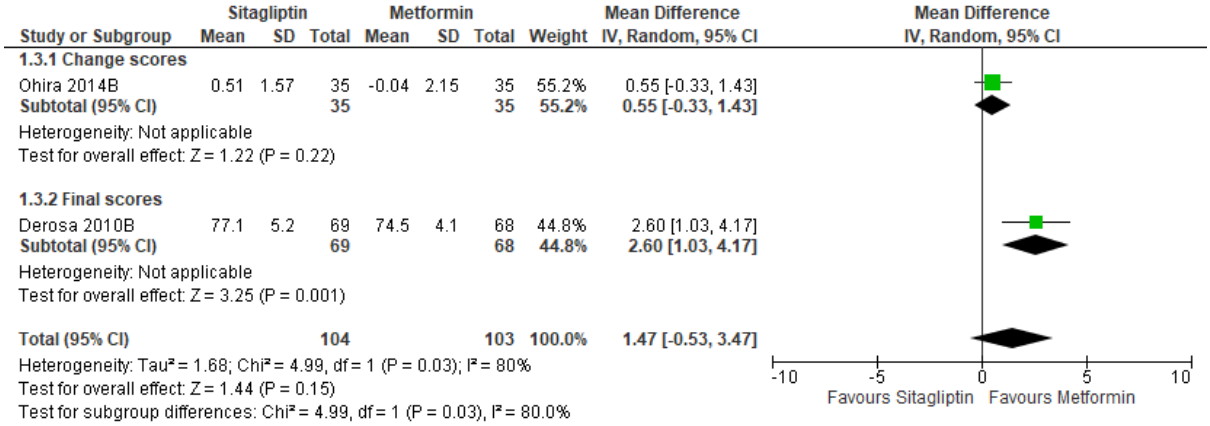
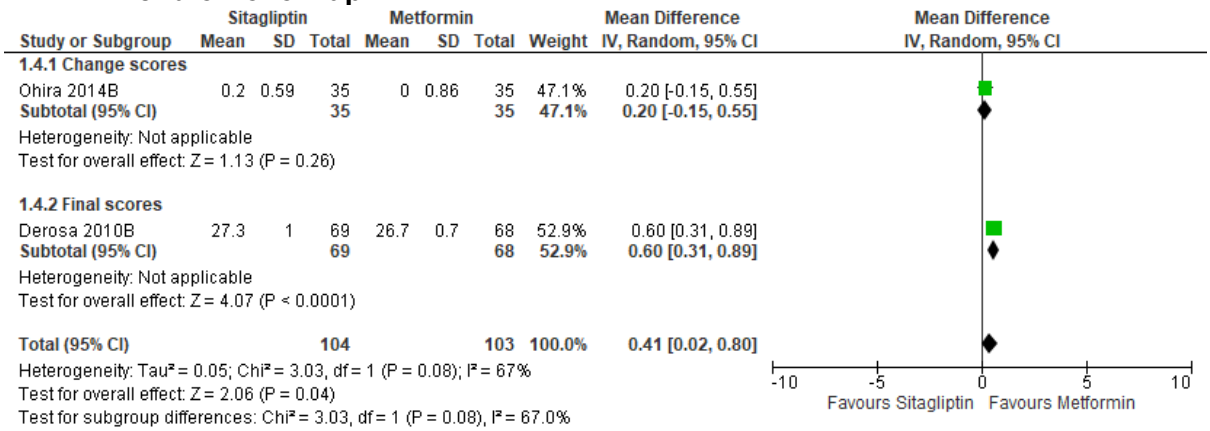


Figure 48: BMI change (kg/m^2, lower values are better, change and final scores) at end of follow up



K.1.2.7 Adding sitagliptin compared to adding insulin

Figure 49: All-cause mortality at end of follow up

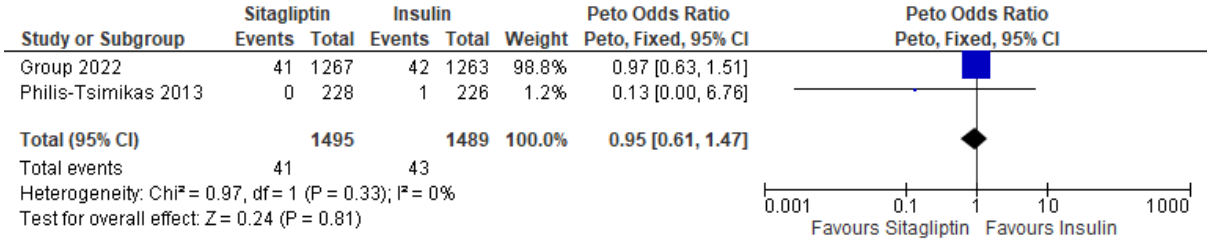


Figure 50: Unstable angina at end of follow up

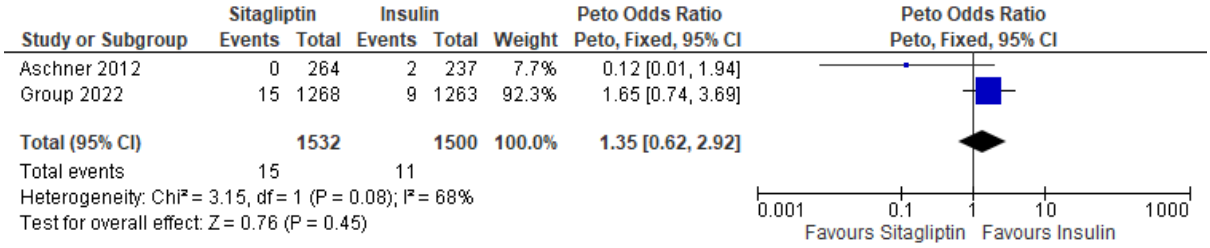
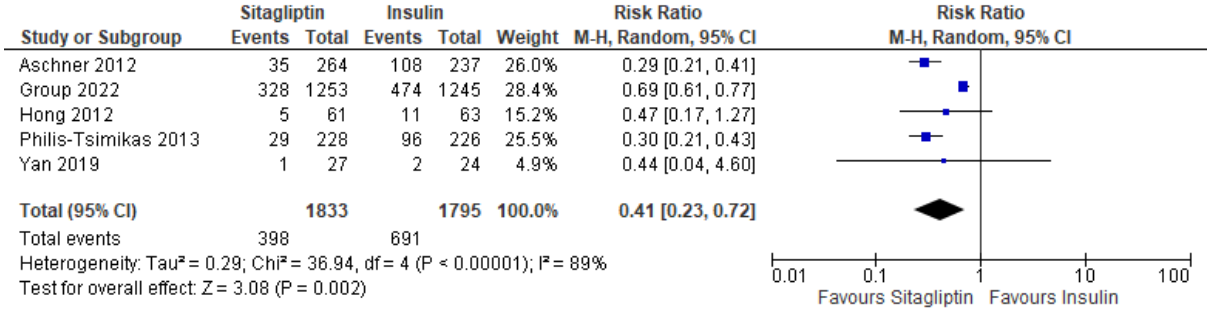


Figure 51: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 52: At night hypoglycaemic episodes at end of follow up

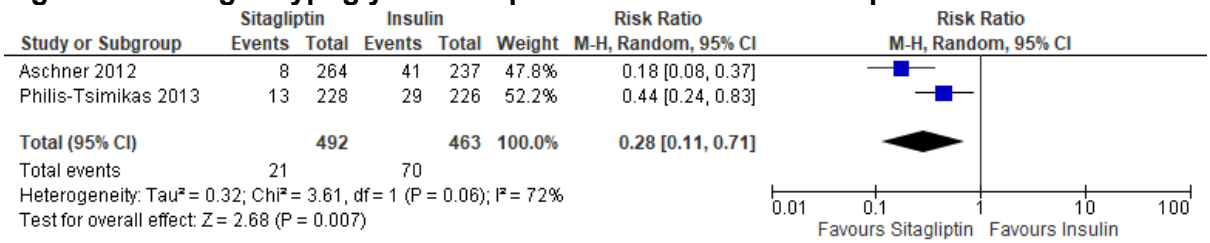


Figure 53: Severe hypoglycaemic episodes at end of follow up

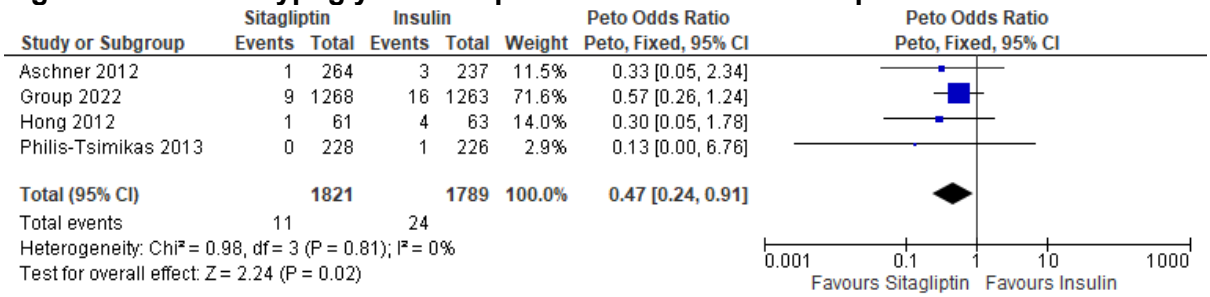
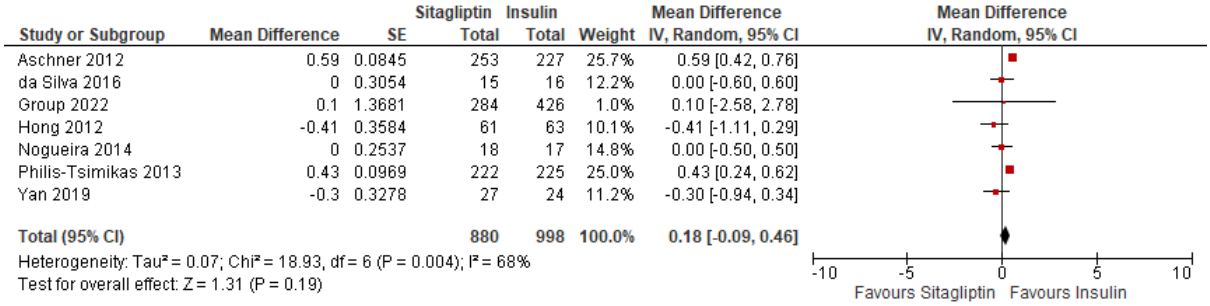
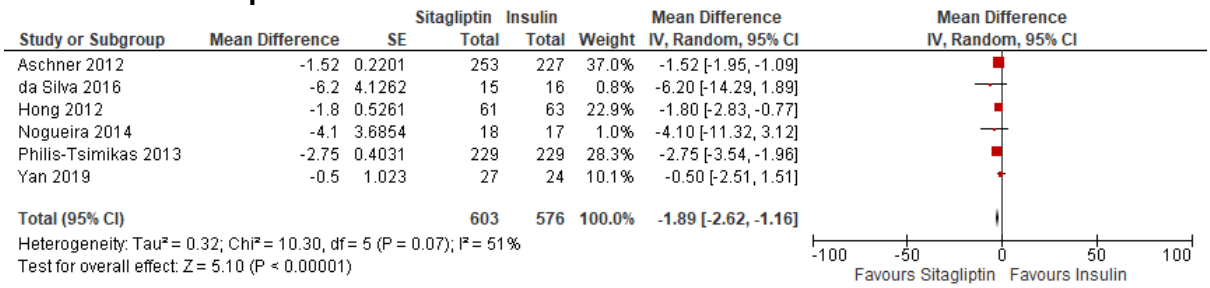


Figure 54: HbA1c change (%, lower values are better, mean difference) at end of follow up



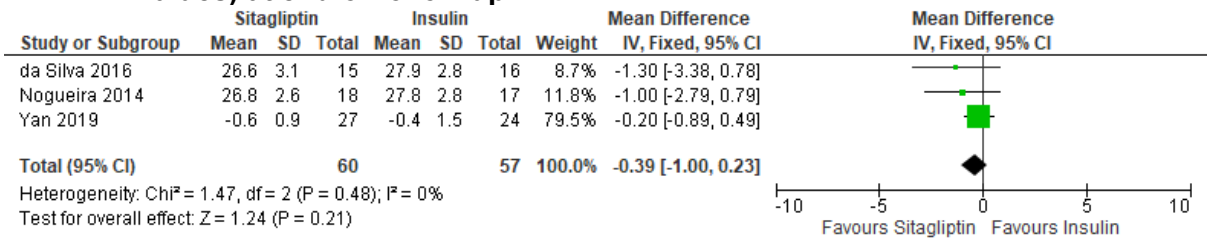
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 55: Weight change (kg, lower values are better, mean difference) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 56: BMI change (kg/m^2, lower values are better, change scores and final values) at end of follow up



K.1.2.8 Adding vildagliptin compared to adding placebo

Figure 57: All-cause mortality at end of follow up

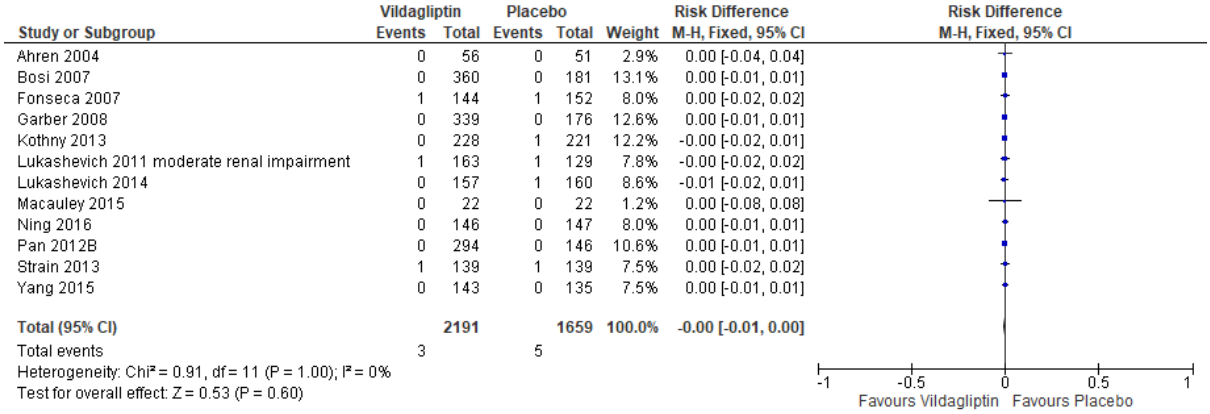


Figure 58: Cardiovascular mortality at end of follow up

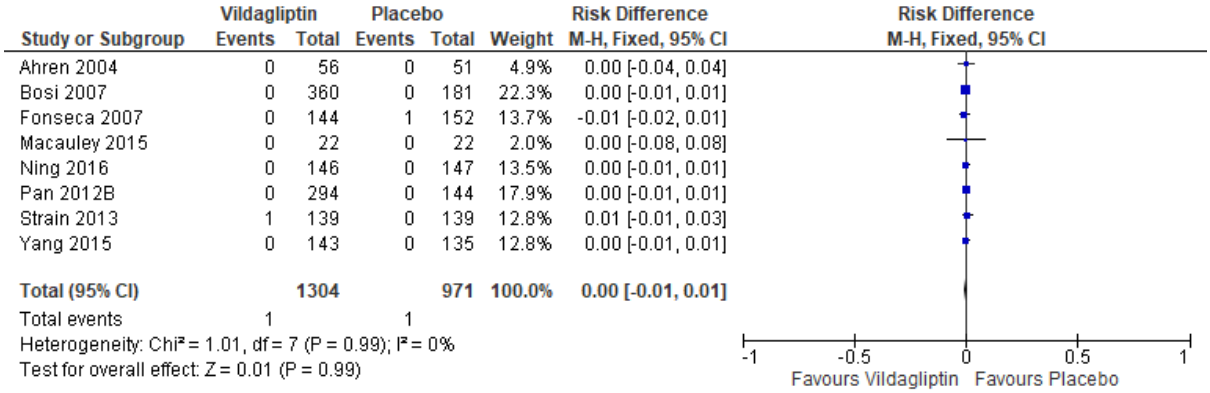


Figure 59: Non-fatal stroke at end of follow up

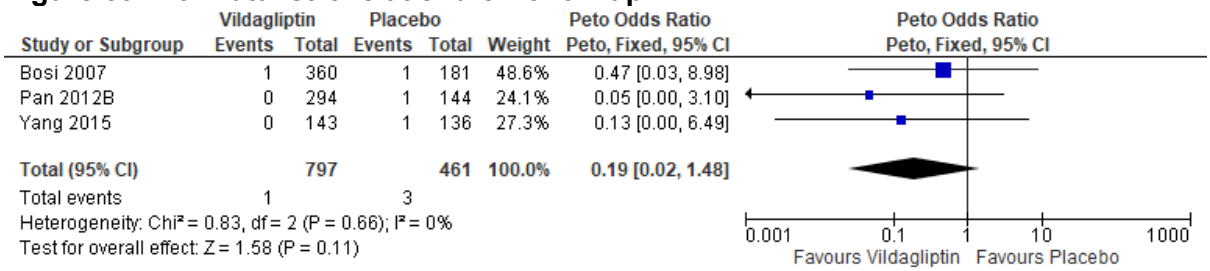


Figure 60: Hypoglycaemia episodes at end of follow up

Study or Subgroup	Vildagliptin Events	Vildagliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Bosi 2007	2	360	1	181	9.6%	0.00 [-0.01, 0.01]
Derosa 2012B	0	84	0	83	3.3%	0.00 [-0.02, 0.02]
Fonseca 2007	33	144	45	152	5.9%	-0.07 [-0.17, 0.03]
Garber 2007	1	305	3	158	8.3%	-0.02 [-0.04, 0.01]
Garber 2008	8	339	1	176	9.3%	0.02 [-0.00, 0.04]
Goodman 2009	2	248	0	122	6.5%	0.01 [-0.01, 0.02]
Kothny 2013	19	228	16	221	9.0%	0.01 [-0.04, 0.06]
Lukashevich 2011 moderate renal impairment	32	122	15	89	4.1%	0.09 [-0.02, 0.20]
Lukashevich 2014	8	157	3	160	6.3%	0.03 [-0.01, 0.07]
Macauley 2015	1	22	0	22	0.9%	0.05 [-0.07, 0.16]
Ning 2016	4	146	8	147	5.9%	-0.03 [-0.07, 0.02]
Pan 2012B	1	294	0	144	7.7%	0.00 [-0.01, 0.02]
Strain 2013	3	139	1	139	5.6%	0.01 [-0.01, 0.04]
Su 2014	2	300	0	300	12.0%	0.01 [-0.00, 0.02]
Yang 2015	0	143	0	135	5.6%	0.00 [-0.01, 0.01]
Total (95% CI)		**3031**		**2229**	**100.0%**	**0.00 [-0.01, 0.01]**
Total events	116		93			

Heterogeneity: Chi² = 15.48, df = 14 (P = 0.35); I² = 10%
Test for overall effect: Z = 0.85 (P = 0.39)

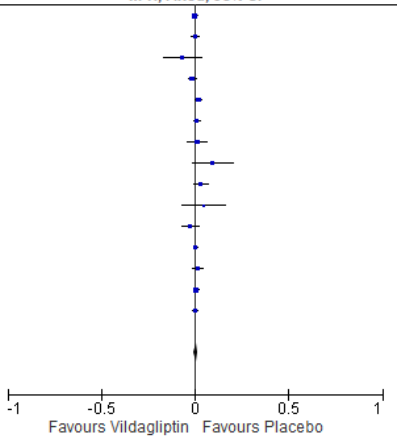


Figure 61: Severe hypoglycaemic episodes at end of follow up

Study or Subgroup	Vildagliptin Events	Vildagliptin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Bosi 2007	0	360	0	181	11.4%	0.00 [-0.01, 0.01]
Fonseca 2007	0	144	4	152	7.0%	-0.03 [-0.05, 0.00]
Garber 2007	0	305	0	158	9.9%	0.00 [-0.01, 0.01]
Garber 2008	0	339	1	176	11.0%	-0.01 [-0.02, 0.01]
Goodman 2009	0	248	0	122	7.7%	0.00 [-0.01, 0.01]
Kothny 2013	2	228	2	221	10.6%	-0.00 [-0.02, 0.02]
Li 2017	0	17	0	16	0.8%	0.00 [-0.11, 0.11]
Lukashevich 2011 moderate renal impairment	2	122	3	89	4.9%	-0.02 [-0.06, 0.03]
Lukashevich 2014	1	157	0	160	7.5%	0.01 [-0.01, 0.02]
Ning 2016	0	146	1	147	6.9%	-0.01 [-0.03, 0.01]
Pan 2012B	1	294	0	144	9.2%	0.00 [-0.01, 0.02]
Strain 2013	0	139	0	139	6.6%	0.00 [-0.01, 0.01]
Yang 2015	0	143	0	135	6.6%	0.00 [-0.01, 0.01]
Total (95% CI)		**2642**		**1840**	**100.0%**	**-0.00 [-0.01, 0.00]**
Total events	6		11			

Heterogeneity: Chi² = 6.94, df = 12 (P = 0.86); I² = 0%
Test for overall effect: Z = 1.20 (P = 0.23)

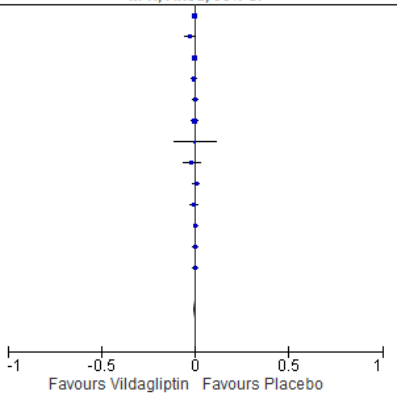
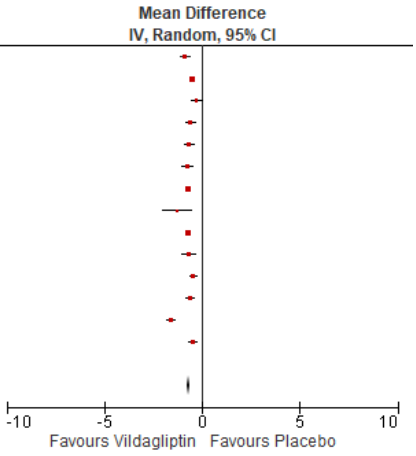


Figure 62: HbA1c change (%, lower values are better, mean difference) at end of follow up

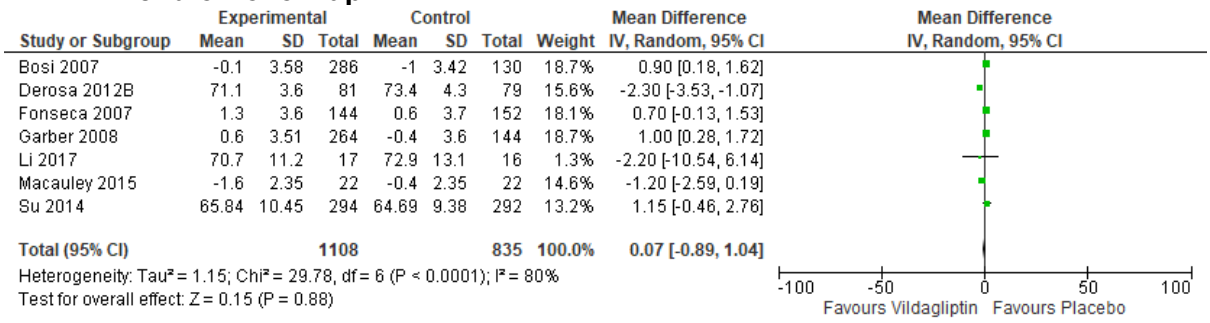
Study or Subgroup	Mean Difference	SE	Vildagliptin Total	Placebo Total	Weight	Mean Difference IV, Random, 95% CI
Bosi 2007	-0.9	0.1226	286	130	5.7%	-0.90 [-1.14, -0.66]
Derosa 2012B	-0.5	0.0251	81	79	12.9%	-0.50 [-0.55, -0.45]
Fonseca 2007	-0.3	0.1412	140	149	4.8%	-0.30 [-0.58, -0.02]
Garber 2007	-0.6	0.1228	305	158	5.7%	-0.60 [-0.84, -0.36]
Garber 2008	-0.675	0.1119	264	144	6.3%	-0.68 [-0.89, -0.46]
Goodman 2009	-0.77	0.1345	248	122	5.1%	-0.77 [-1.03, -0.51]
Kothny 2013	-0.7	0.0094	228	221	13.6%	-0.70 [-0.72, -0.68]
Li 2017	-1.3	0.3785	17	16	0.9%	-1.30 [-2.04, -0.56]
Macauley 2015	-0.7	0.0094	22	22	13.6%	-0.70 [-0.72, -0.68]
Ning 2016	-0.7	0.1697	146	147	3.7%	-0.70 [-1.03, -0.37]
Pan 2012B	-0.45	0.0981	292	144	7.2%	-0.45 [-0.64, -0.26]
Strain 2013	-0.6	0.1071	137	137	6.6%	-0.60 [-0.81, -0.39]
Su 2014	-1.61	0.1004	294	292	7.0%	-1.61 [-1.81, -1.41]
Yang 2015	-0.5	0.1	141	133	7.1%	-0.50 [-0.70, -0.30]
Total (95% CI)			**2601**	**1894**	**100.0%**	**-0.69 [-0.77, -0.62]**

Heterogeneity: Tau² = 0.01; Chi² = 167.84, df = 13 (P < 0.00001); I² = 92%
Test for overall effect: Z = 18.20 (P < 0.00001)



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, Frailty, NAFLD, obesity and early onset subgroups.

Figure 63: Weight change (kg, lower values are better, change and final scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, Frailty, NAFLD, obesity and early onset subgroups.

K.1.2.9 Adding vildagliptin compared to adding metformin

Figure 64: Hypoglycaemia episodes at end of follow up

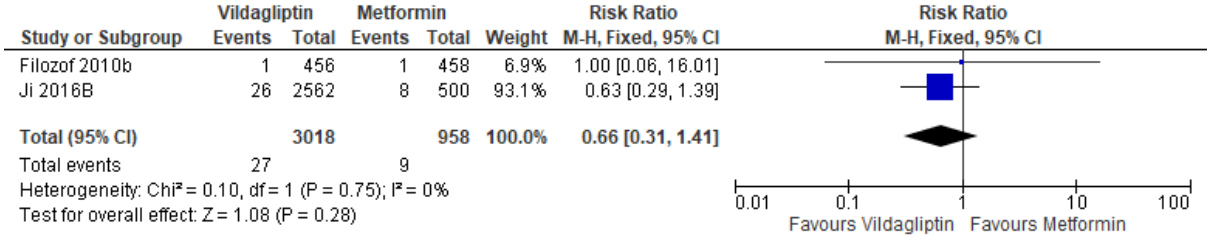
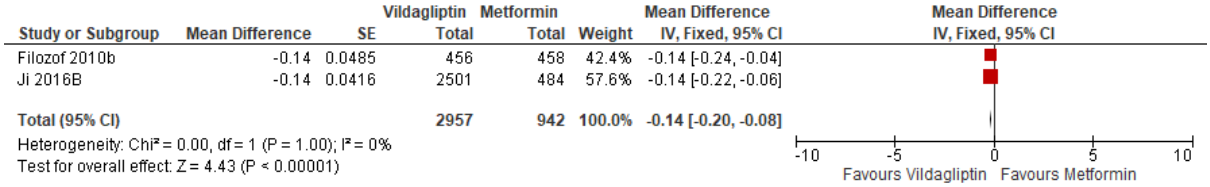


Figure 65: HbA1c change (%, lower values are better, change and final scores) at end of follow up



K.1.2.10 Adding vildagliptin compared to adding insulin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.2.11 Adding vildagliptin compared to adding saxagliptin

Figure 66: All-cause mortality at end of follow up

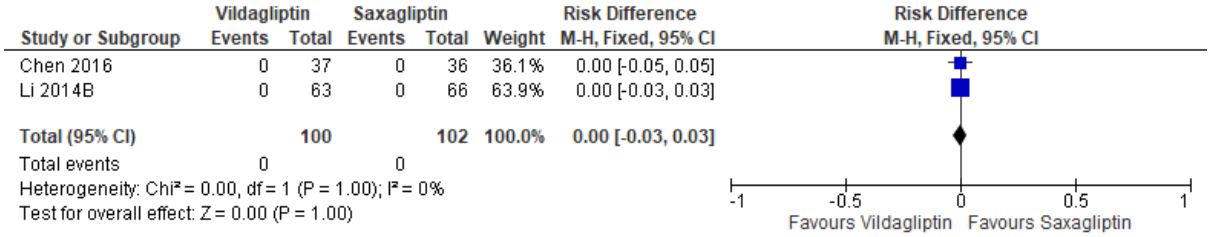


Figure 67: Cardiovascular mortality at end of follow up

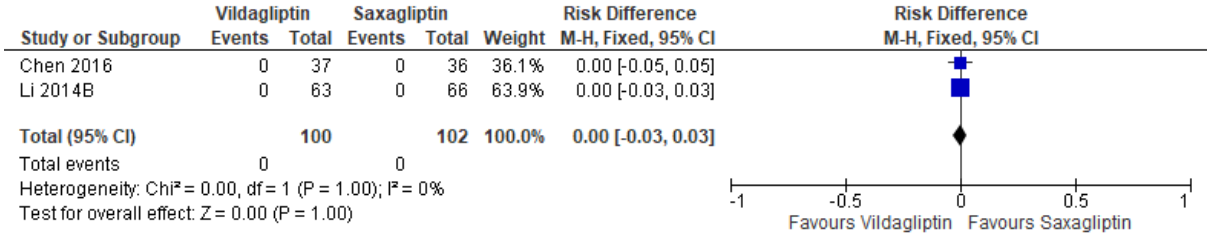


Figure 68: Hypoglycaemia episodes at end of follow up

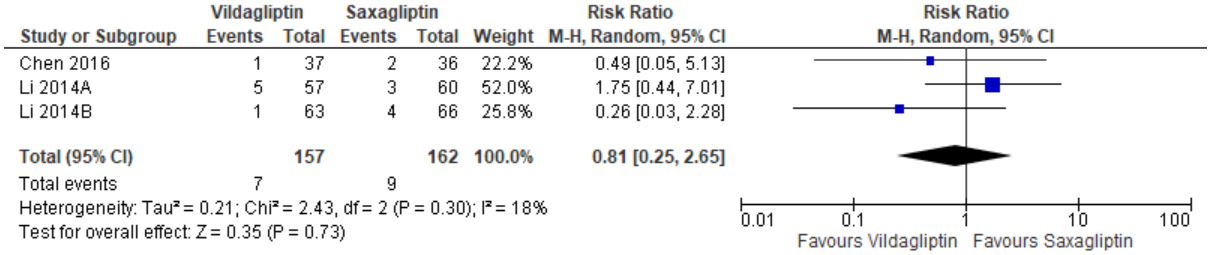


Figure 69: Severe hypoglycaemic episodes at end of follow up

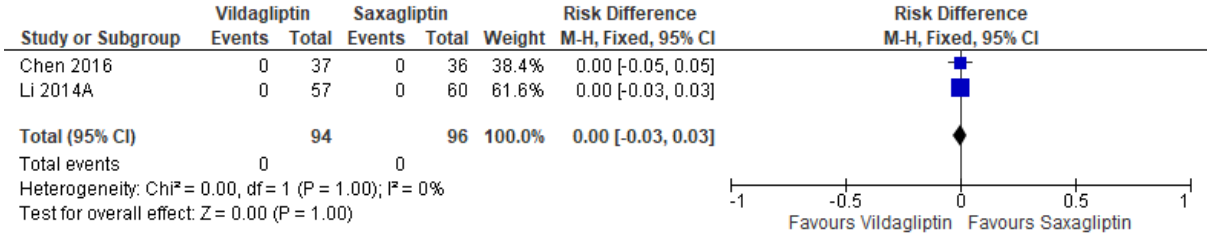


Figure 70: HbA1c change (%, lower values are better, change scores) at end of follow up

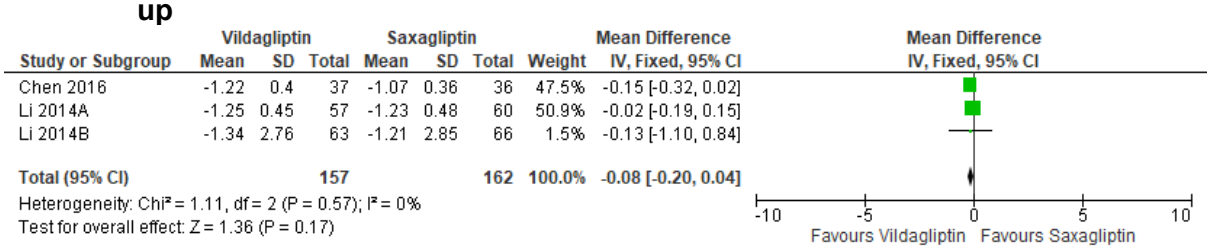
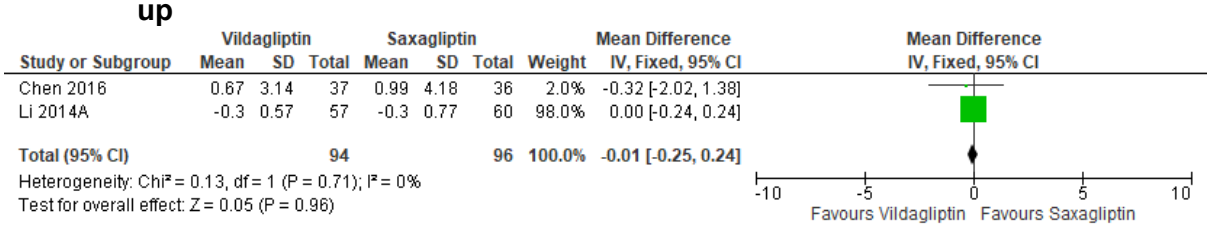


Figure 71: BMI change (kg/m^2, lower values are better, change scores) at end of follow up



K.1.3 GLP-1 receptor agonist

K.1.3.1 Adding dulaglutide compared to adding placebo

Figure 72: All-cause mortality at end of follow up

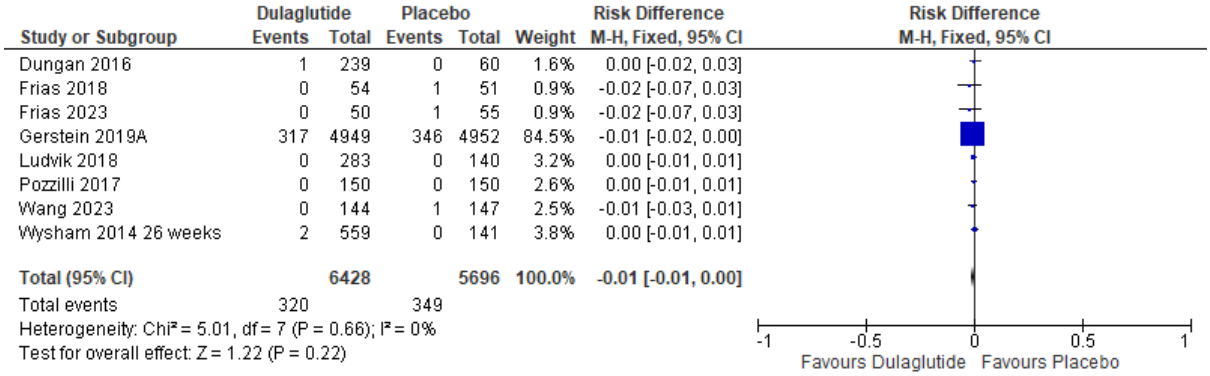


Figure 73: Cardiovascular mortality at end of follow up

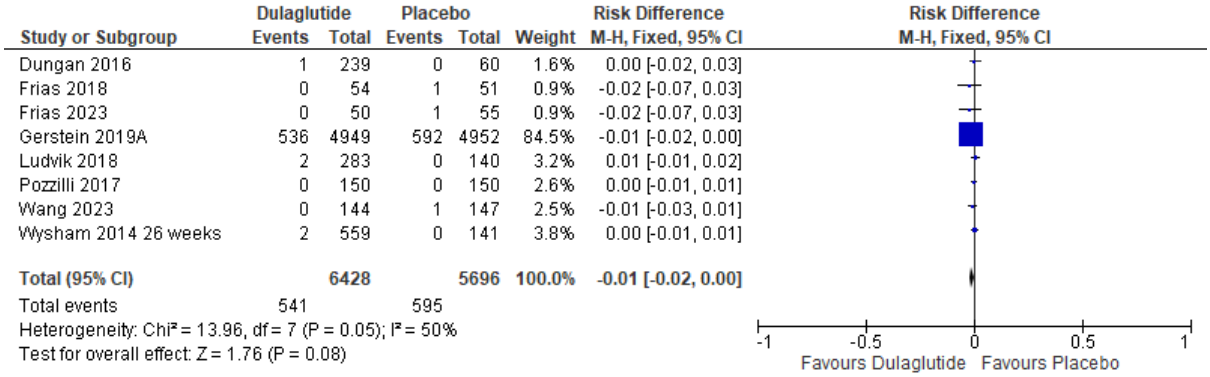


Figure 74: Non-fatal stroke at end of follow up

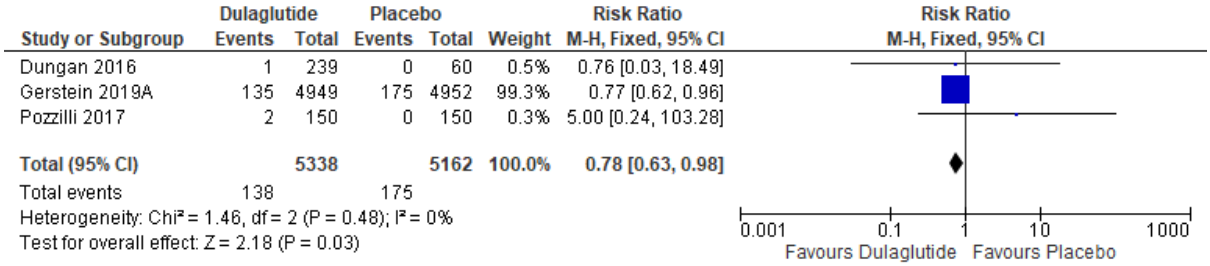


Figure 75: Non-fatal myocardial infarction at end of follow up

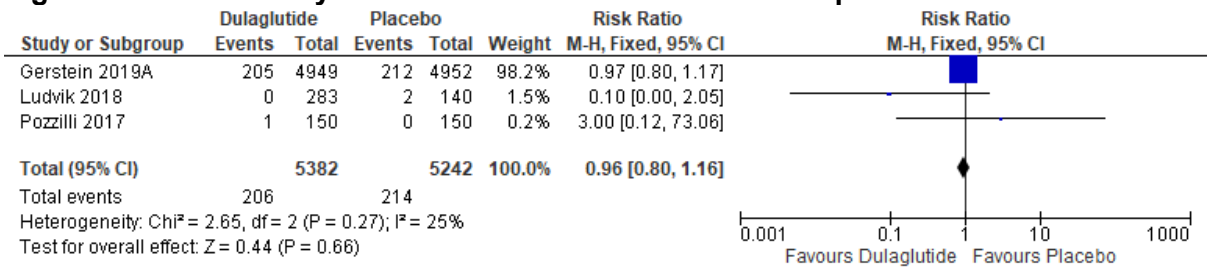


Figure 76: Unstable angina at end of follow up

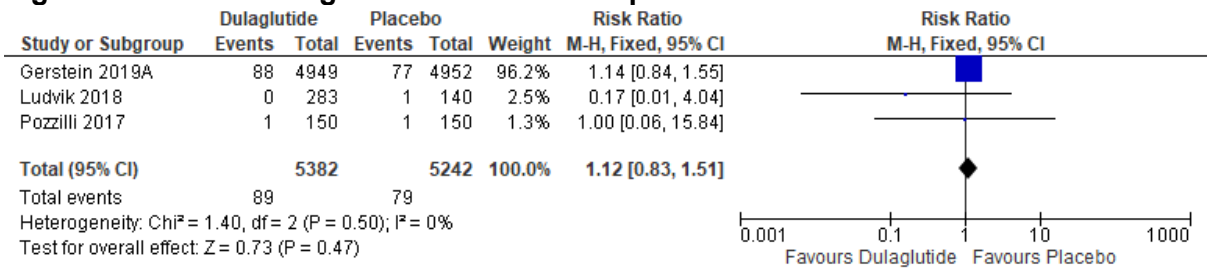


Figure 77: Acute kidney injury at end of follow up

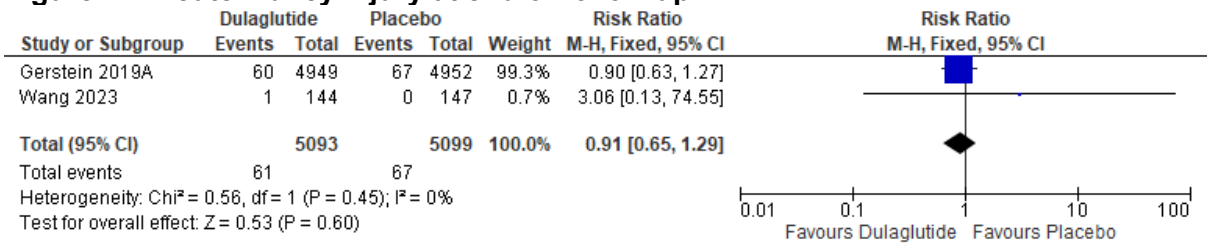


Figure 78: Cardiac arrhythmia at end of follow up

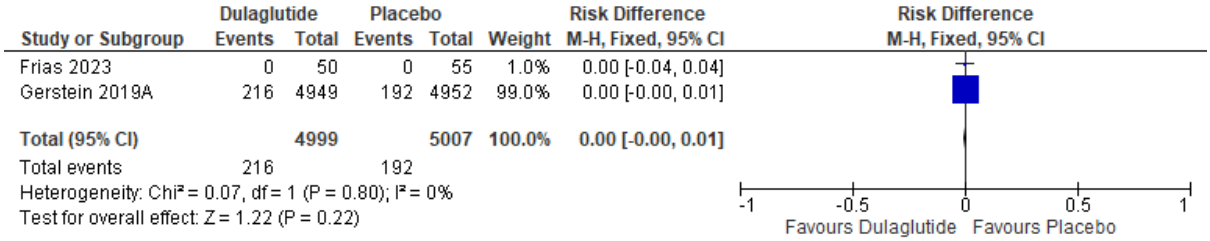


Figure 79: Diabetic ketoacidosis at end of follow up

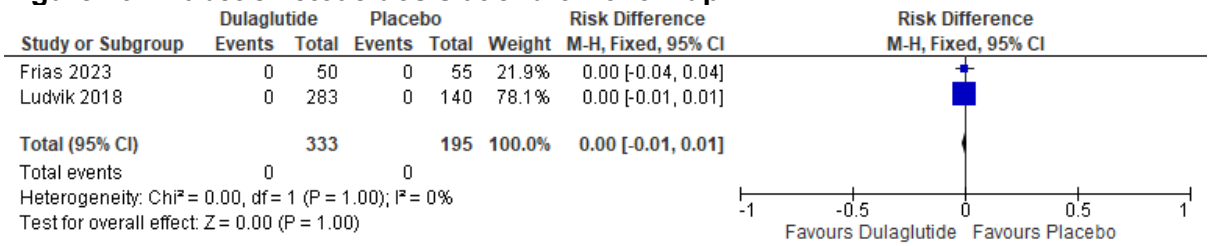


Figure 80: Hypoglycaemia episodes at end of follow up

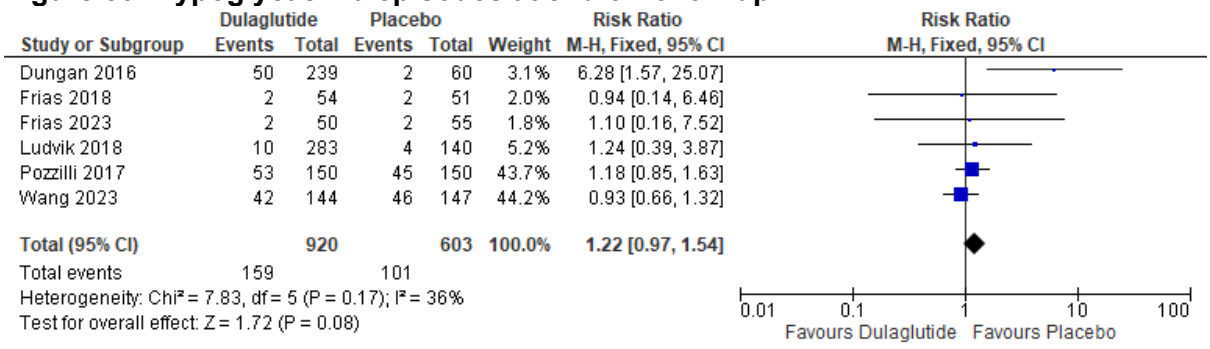


Figure 81: At night hypoglycaemic episodes at end of follow up

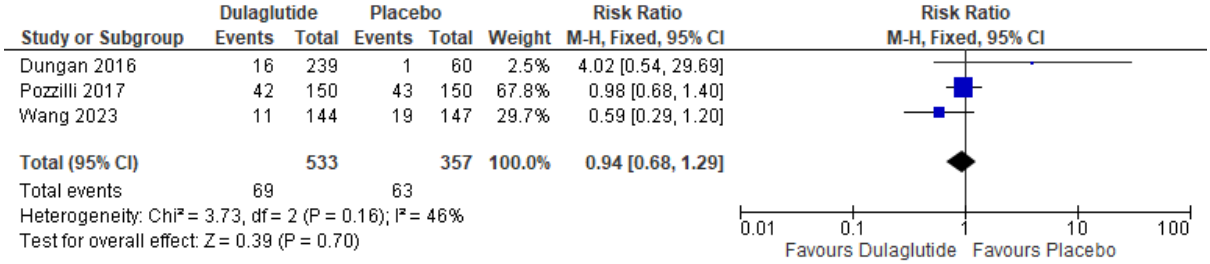


Figure 82: Severe hypoglycaemic episodes at end of follow up

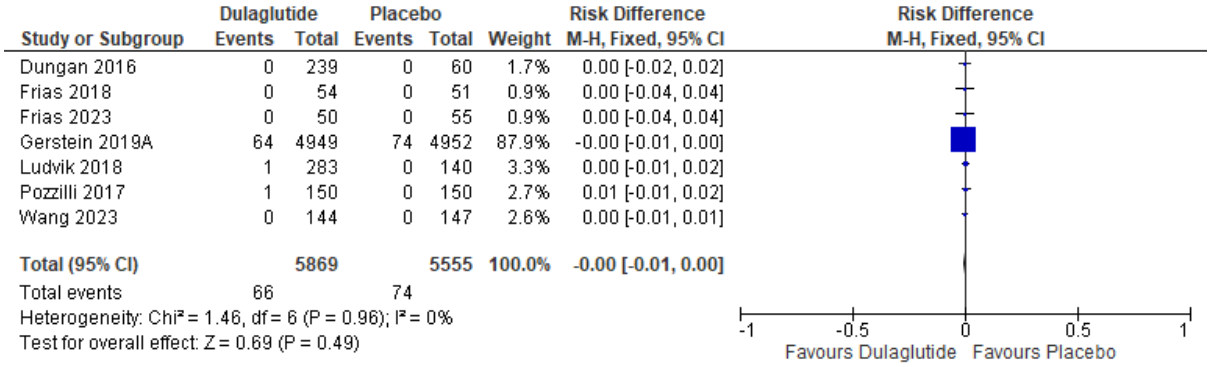
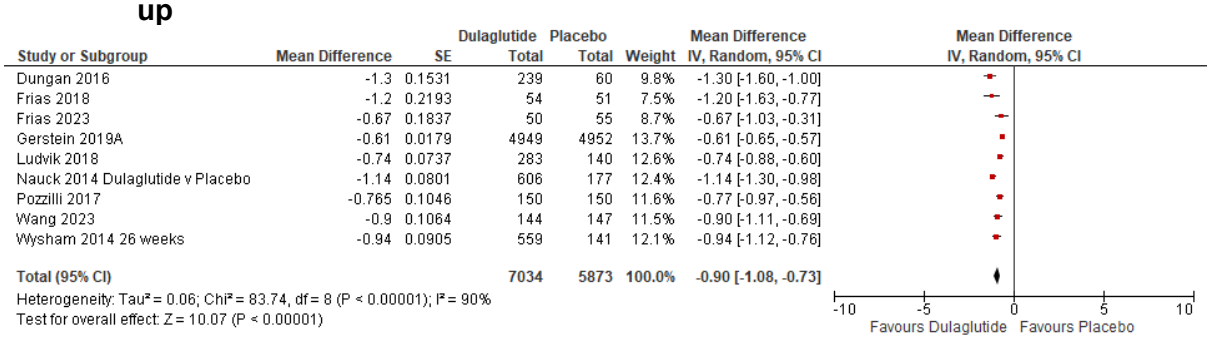


Figure 83: HbA1c change (%, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, obesity and early onset subgroups.

Figure 84: Weight change (kg, lower values are better, change scores) at end of follow up

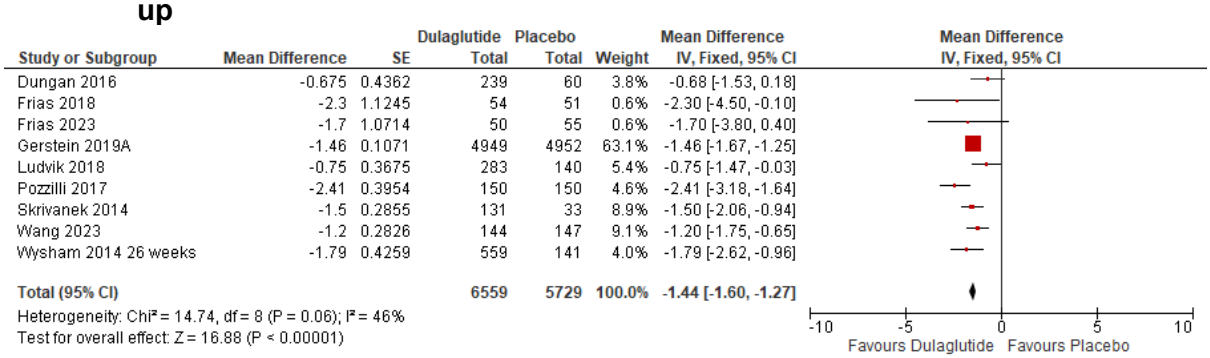
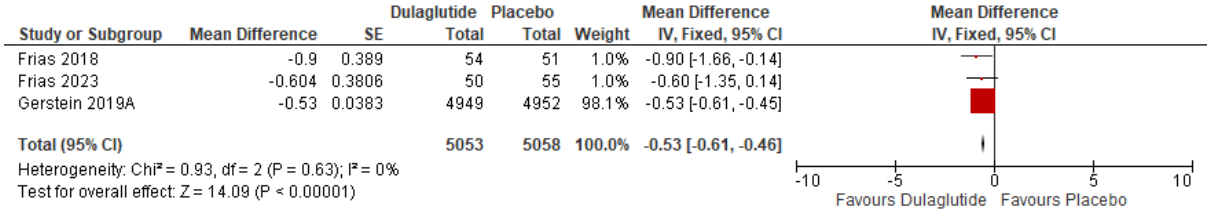


Figure 85: BMI change (kg/m^2, lower values are better, change scores) at end of follow up



K.1.3.2 Adding dulaglutide compared to adding insulin

Figure 86: All-cause mortality at end of follow up

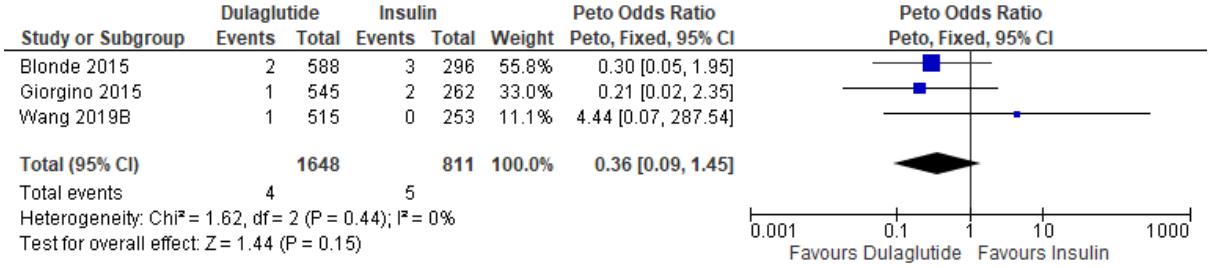


Figure 87: Hypoglycaemia episodes at end of follow up

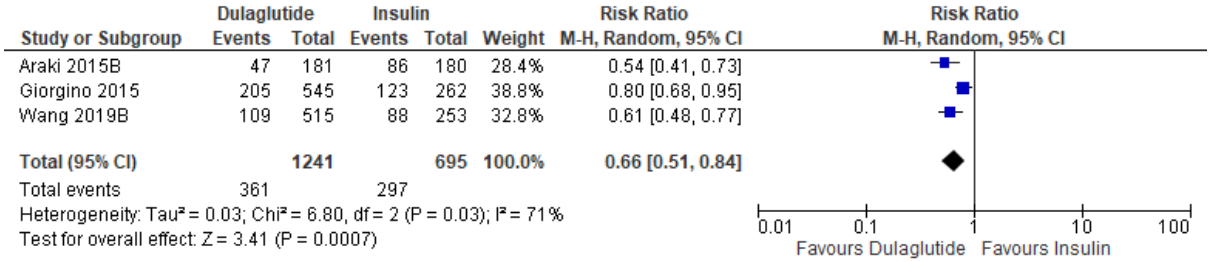


Figure 88: At night hypoglycaemic episodes at end of follow yp

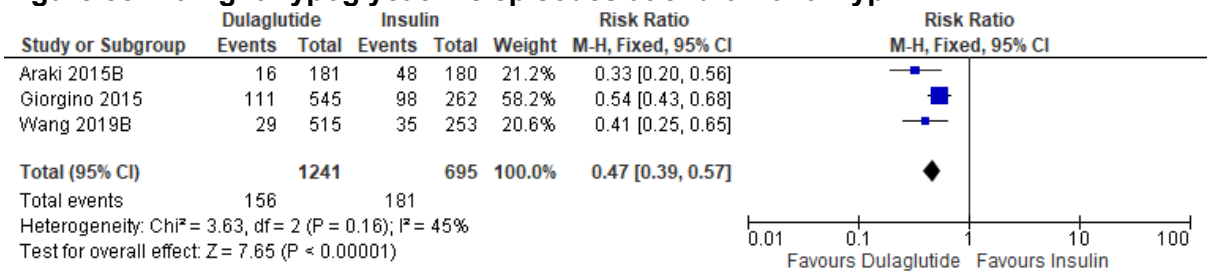
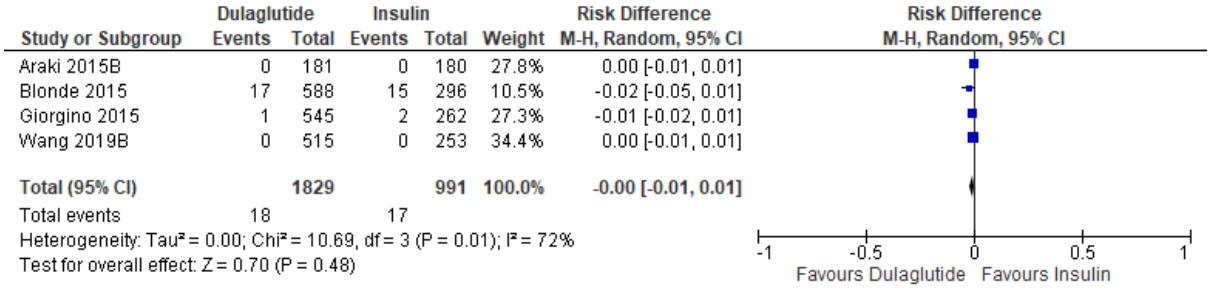
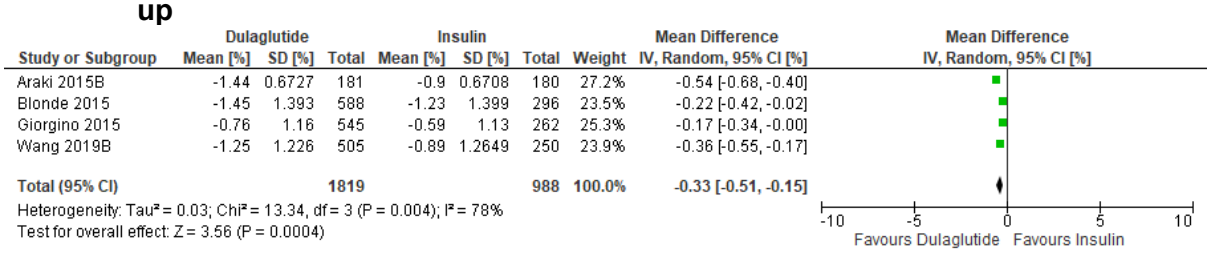


Figure 89: Severe hypoglycaemic episodes at end of follow up



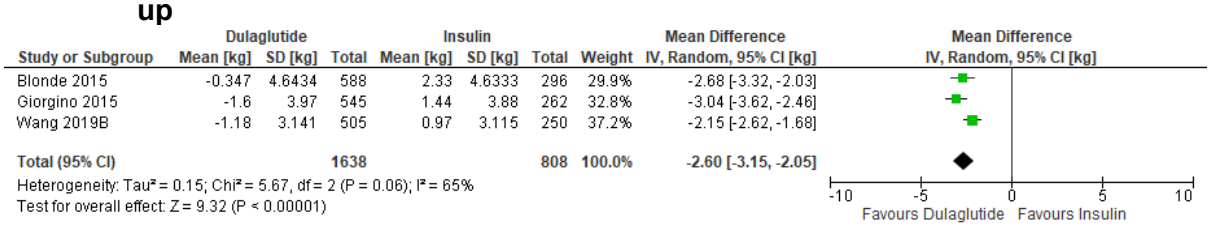
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 90: HbA1c change (%, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup.

Figure 91: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.3.3 Adding dulaglutide compared to adding exenatide

There are no forest plots for this comparison (all outcomes include a single study)

K.1.3.4 Adding dulaglutide compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.3.5 Adding exenatide compared to adding placebo

Figure 92: All-cause mortality at end of follow up

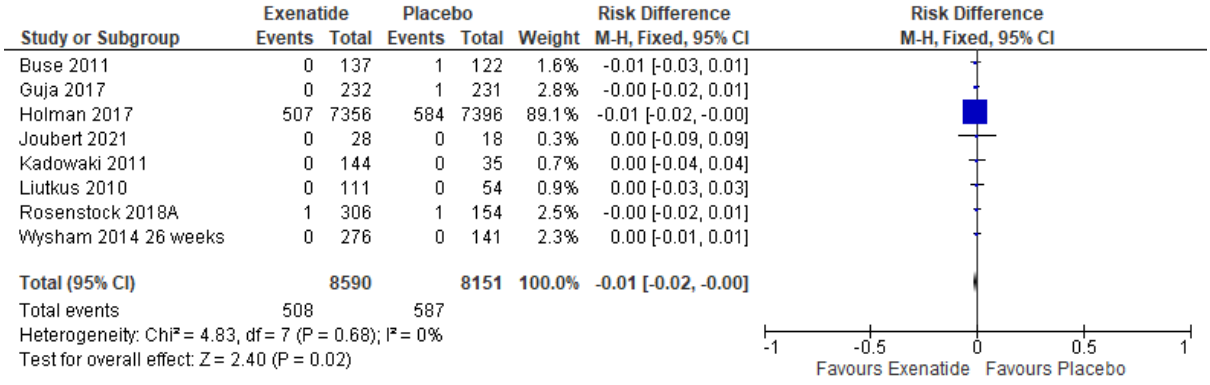


Figure 93: Cardiovascular mortality at end of follow up

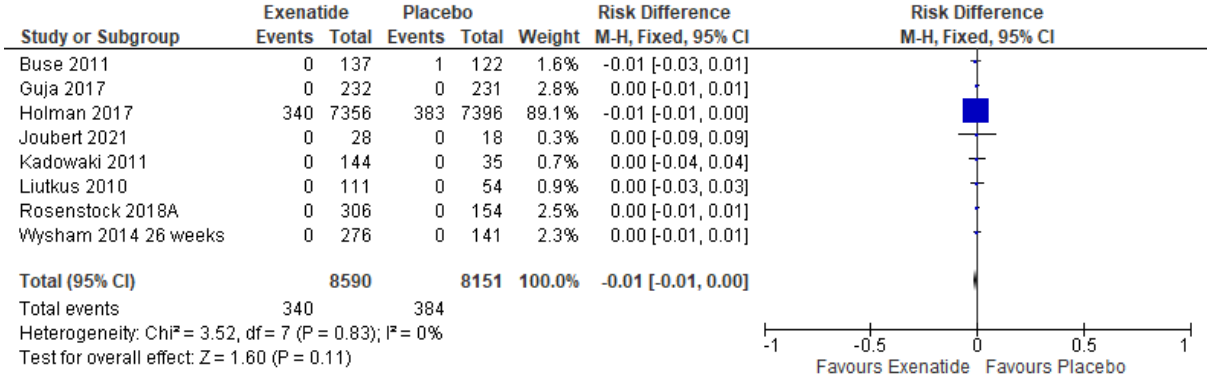


Figure 94: Non-fatal myocardial infarction at end of follow up

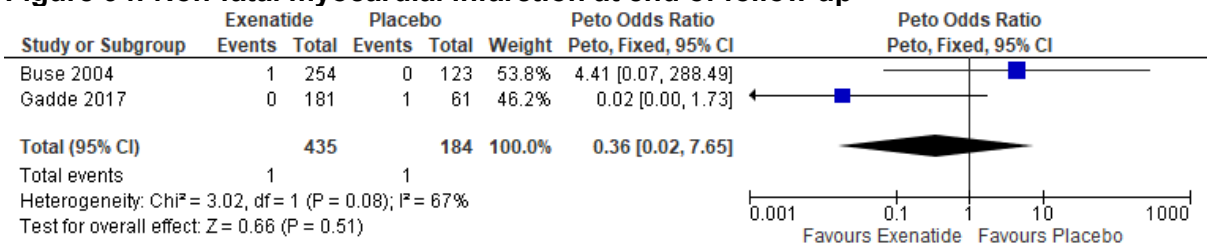


Figure 95: Hospitalisation for heart failure at end of follow up

Figure 96: Diabetic ketoacidosis at end of follow up

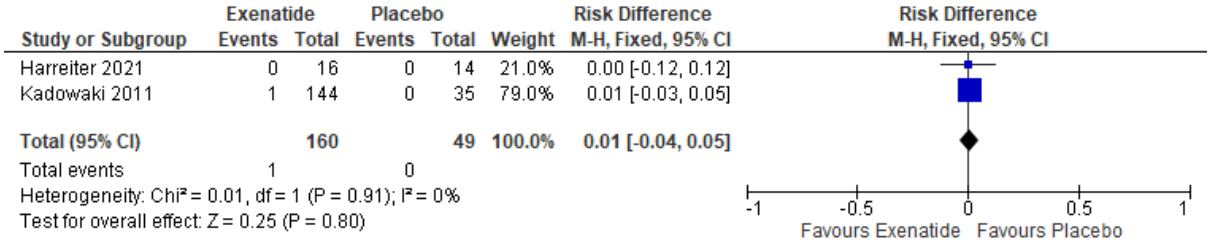
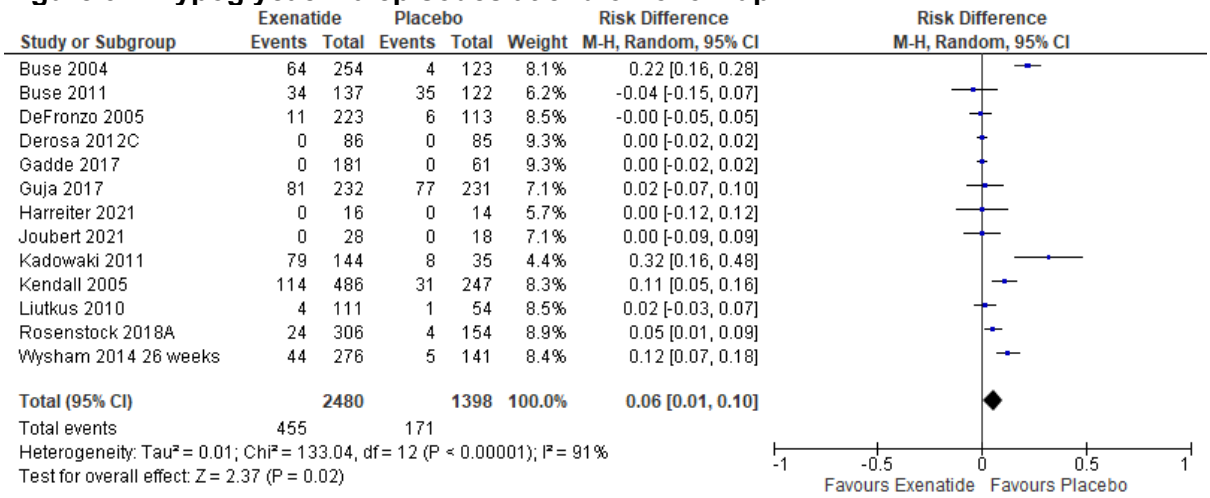


Figure 97: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis

Figure 98: Severe hypoglycaemic episodes at end of follow up

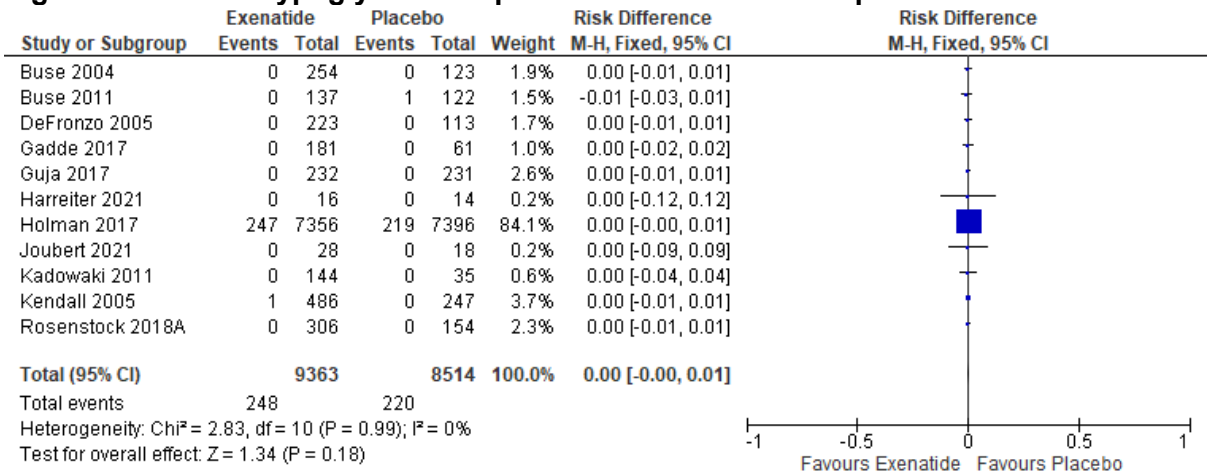
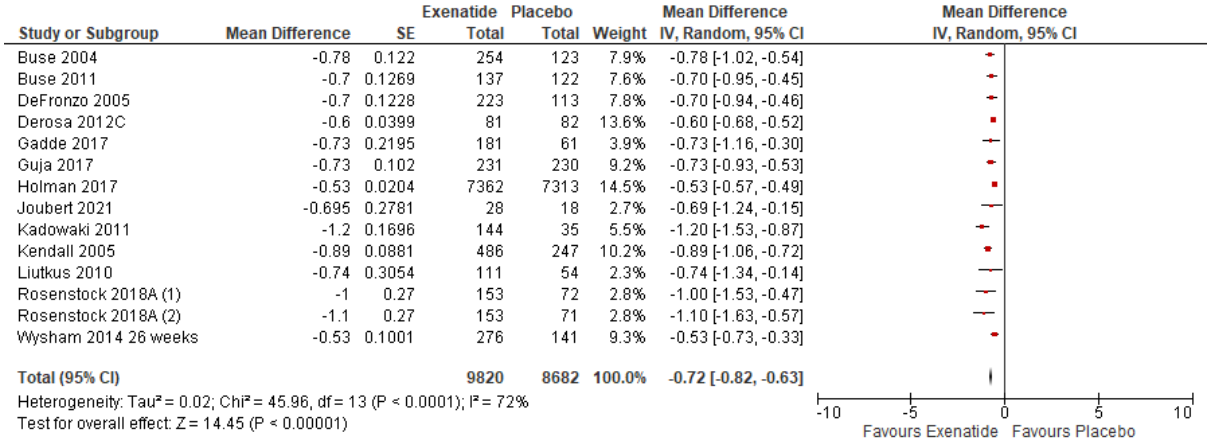


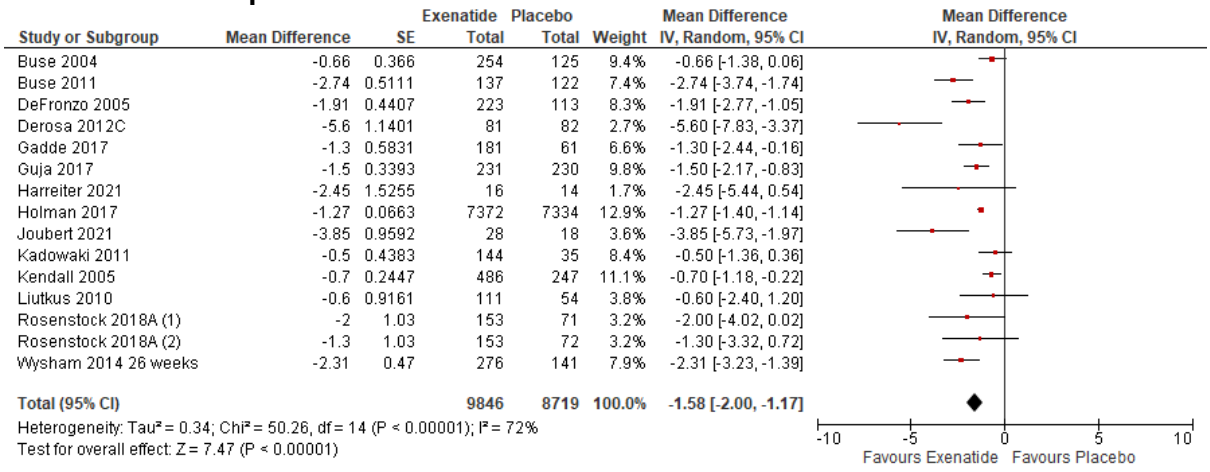
Figure 99: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) 40 mcg daily arm. N placebo was halved
(2) 60 mcg daily arm. N placebo was halved

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by obesity or eGFR subgroup

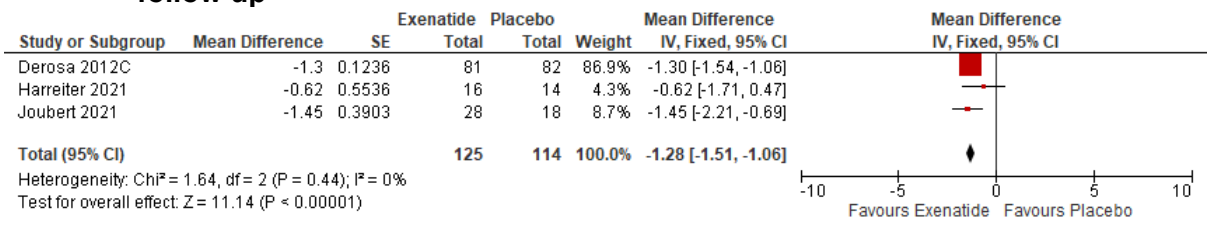
Figure 100: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 60 mcg daily arm. N for placebo arm was halved
(2) 40 mcg daily arm. N for placebo arm was halved.

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR subgroup

Figure 101: BMI change (kg/m², lower values are better, change scores) at end of follow up



K.1.3.6 Adding exenatide compared to adding insulin

Figure 102: Health-related quality of life – overall (EQ5D, -0.59-1.0, higher values are better, change scores) at end of follow up

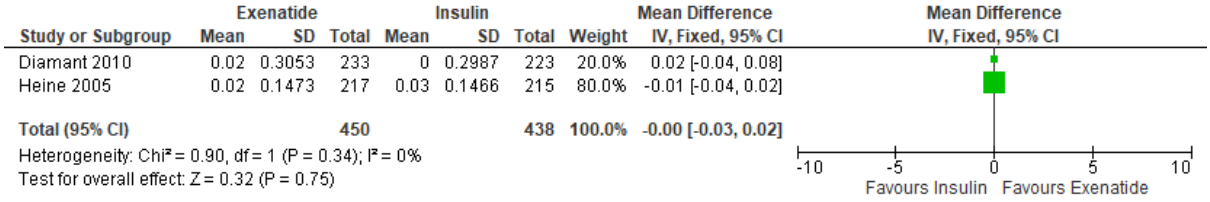


Figure 103: Health-related quality of life – overall (IWQoL, 0-100, higher values are better, change scores) at end of follow up

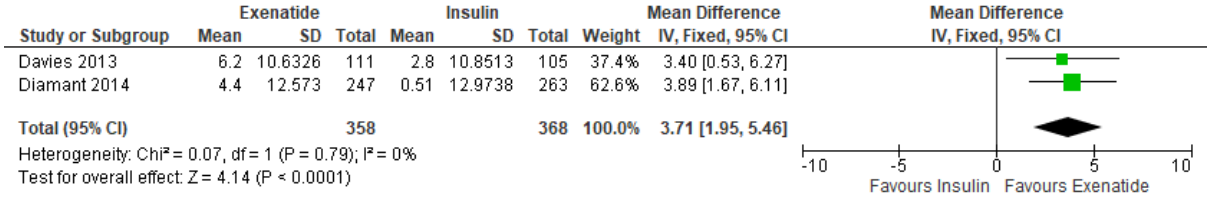


Figure 104: All-cause mortality at end of follow up

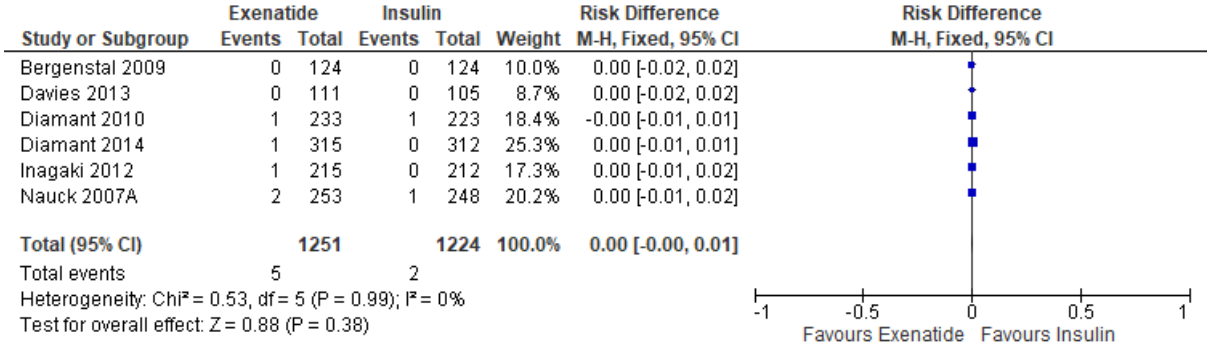


Figure 105: Cardiovascular mortality at end of follow up

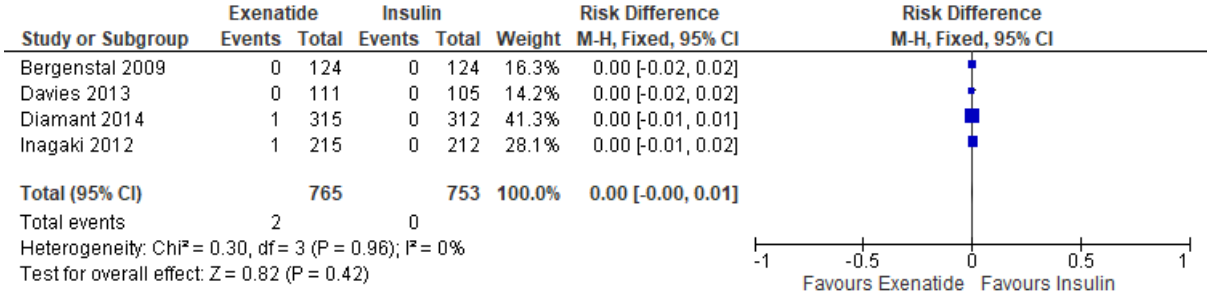


Figure 106: Hypoglycaemia episodes at end of follow up

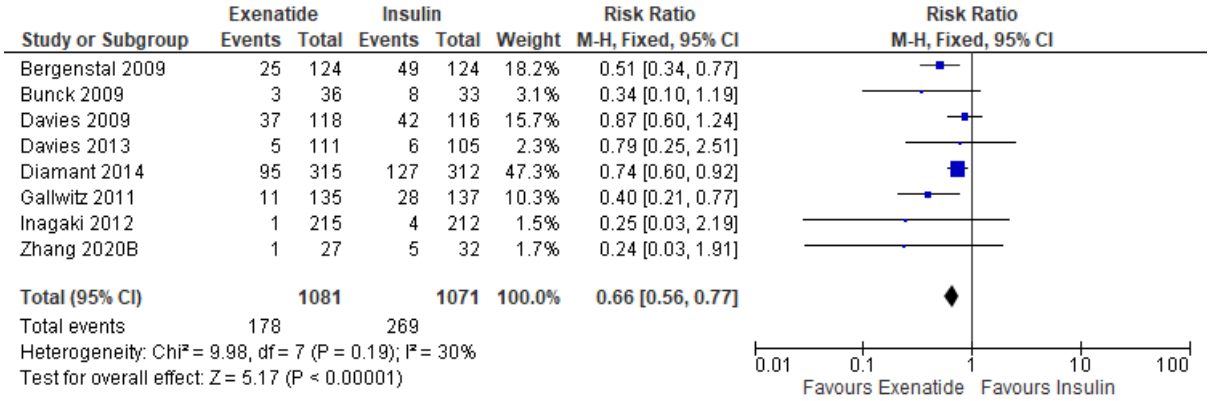
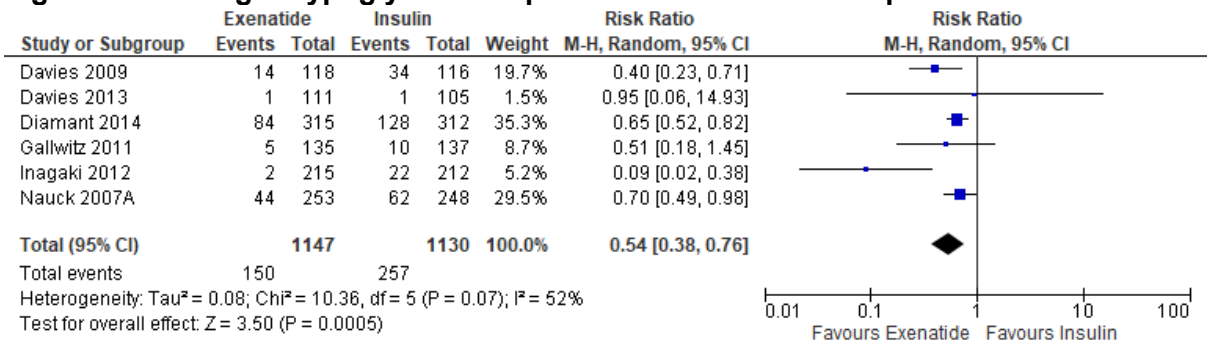


Figure 107: At night hypoglycaemic episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by obesity subgroup.

Figure 108: Severe hypoglycaemic episodes at end of follow up

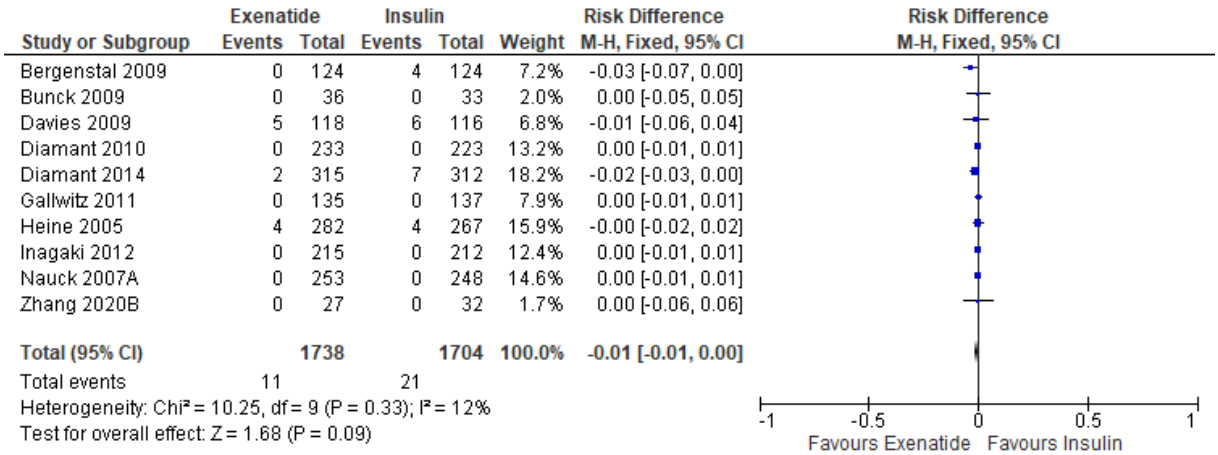
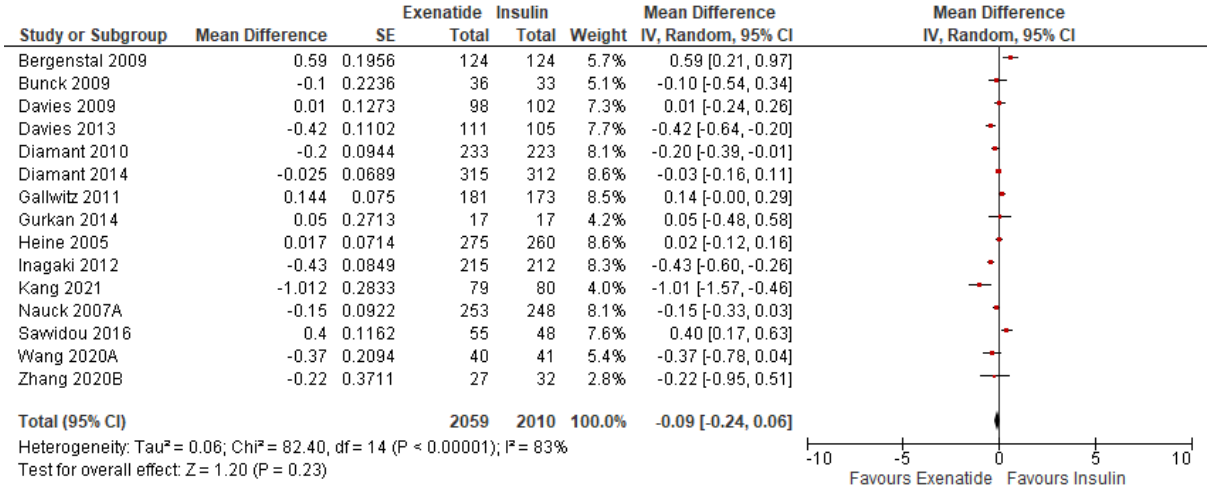
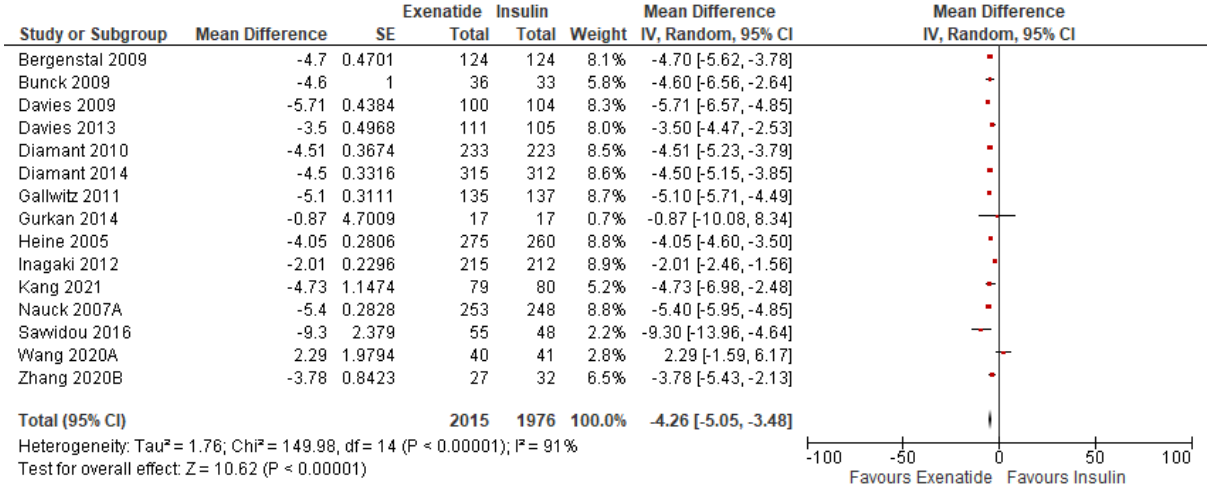


Figure 109: HbA1c change (%, lower values are better, change and final scores) at end of follow up



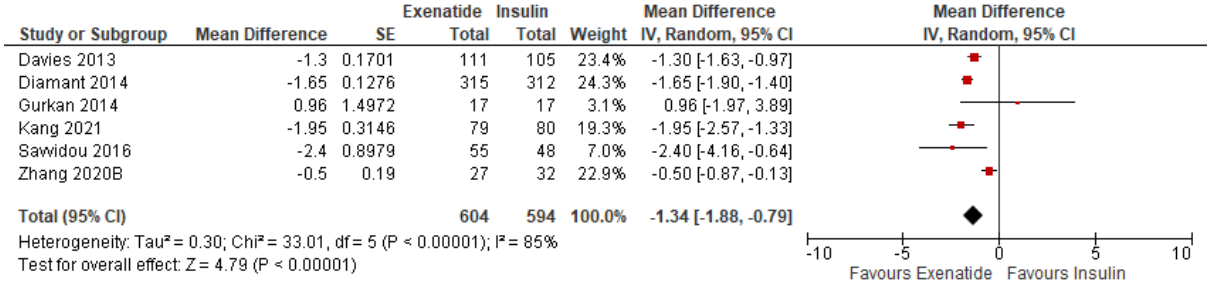
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by obesity subgroup.

Figure 110: Weight change (kg, lower values are better, change and final scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by obesity subgroup.

Figure 111: BMI change (kg/m^2, lower values are better, change and final scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis. Subgroup analysis was not possible for this outcome.

K.1.3.7 Adding exenatide compared to adding liraglutide

Figure 112: Hypoglycaemia episodes at end of follow up

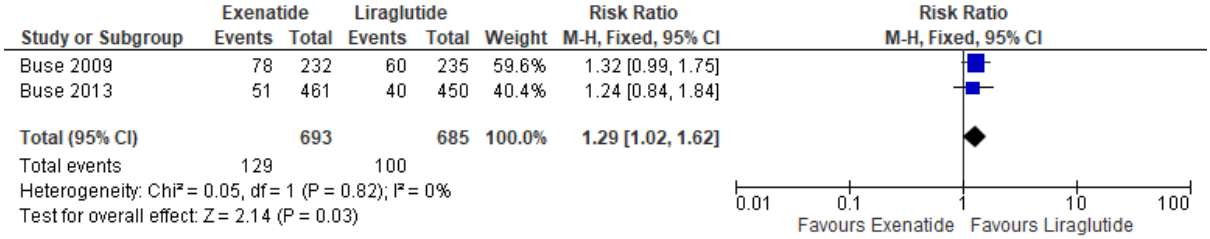


Figure 113: Severe hypoglycaemic episodes at end of follow up

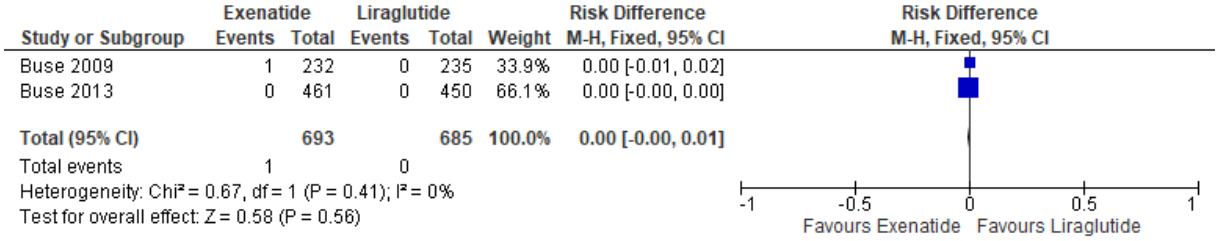


Figure 114: HbA1c change (%, lower values are better, change scores) at end of follow up

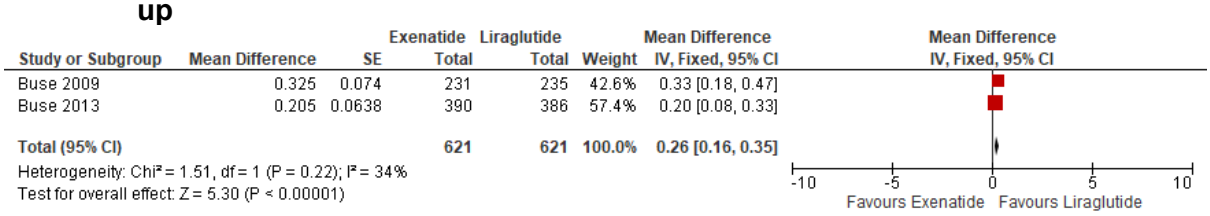
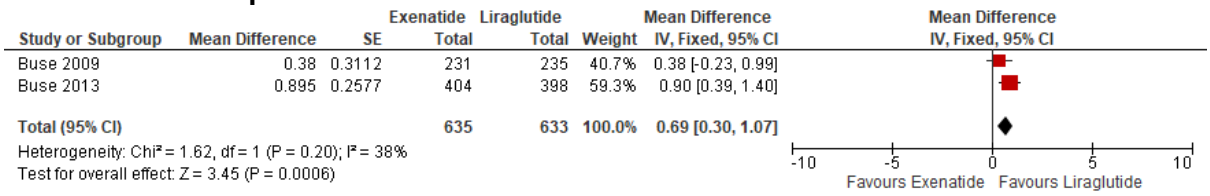


Figure 115: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.3.8 Adding exenatide compared to adding sitagliptin

Figure 116: Hypoglycaemia episodes at end of follow up

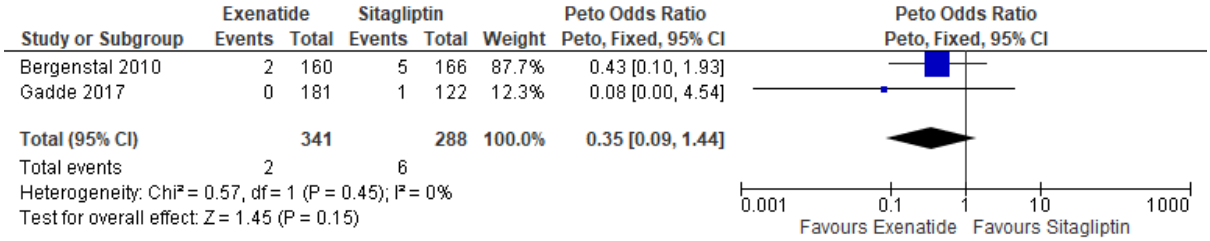


Figure 117: Severe hypoglycaemic episodes at end of follow up

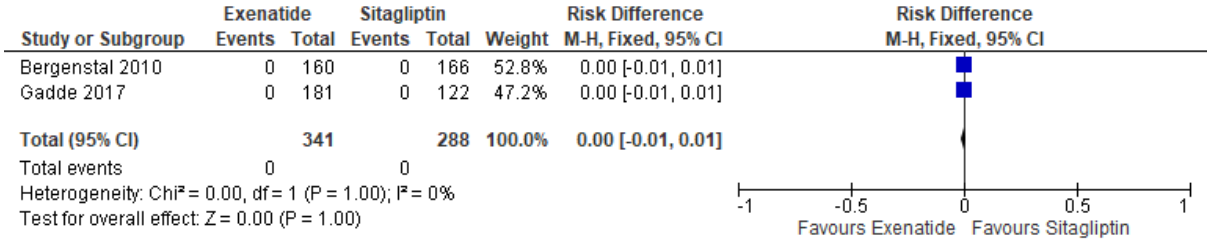


Figure 118: HbA1c change (%, lower values are better, change scores) at end of follow up

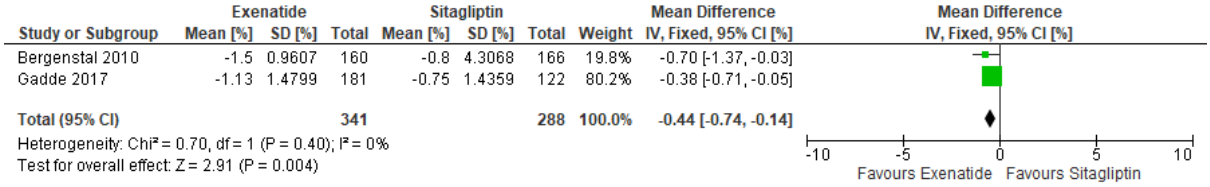
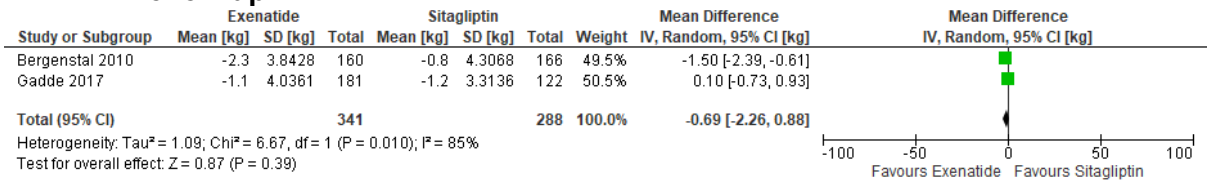


Figure 119: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.3.9 Adding liraglutide compared to adding placebo

Figure 120: Health-related quality of life – subscale physical functioning (SF-36 physical function subscale, higher value are better, change scores) at end of follow-up

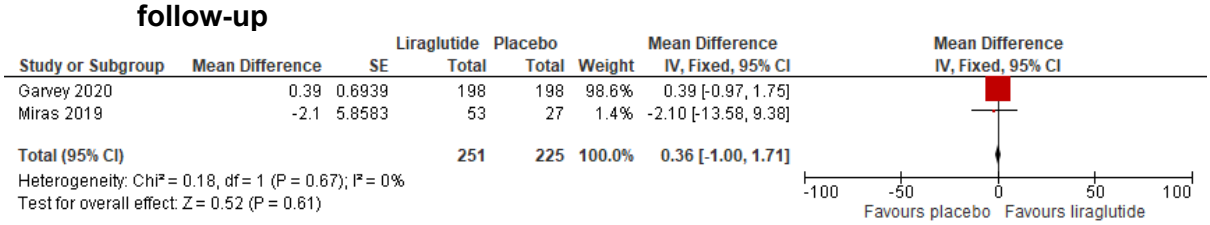
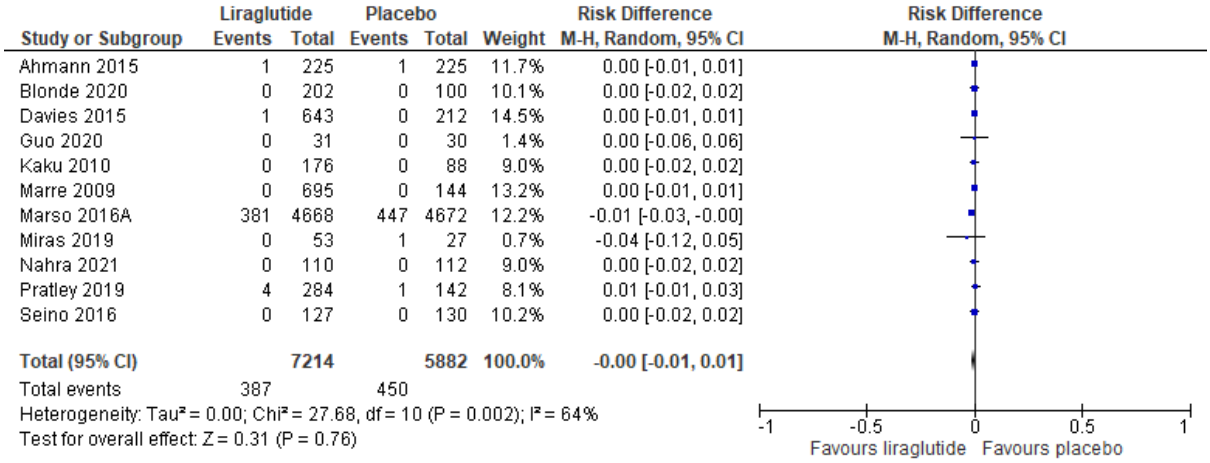
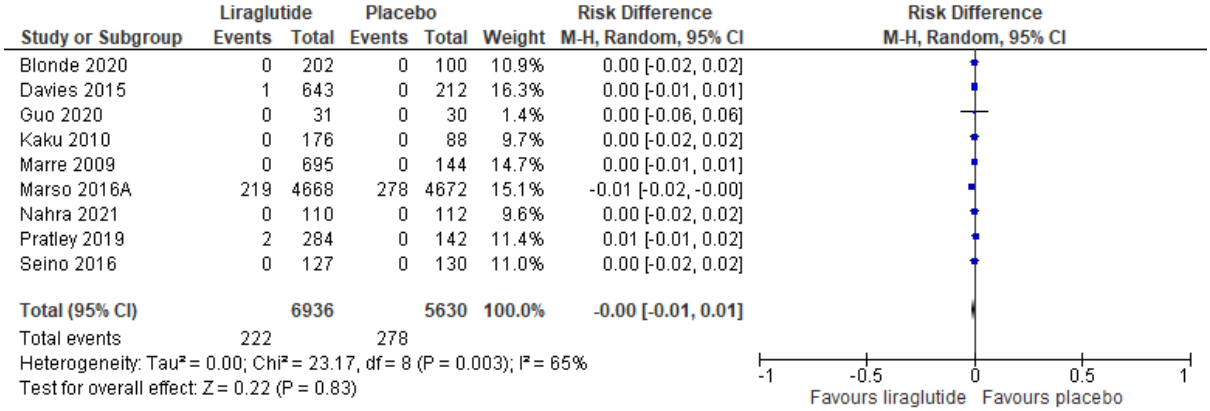


Figure 121: All-cause mortality at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD and obesity subgroups.

Figure 122: Cardiovascular mortality at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD and obesity subgroups.

Figure 123: Non-fatal stroke at end of follow-up

Figure 124: Non-fatal myocardial infarction at end of follow-up

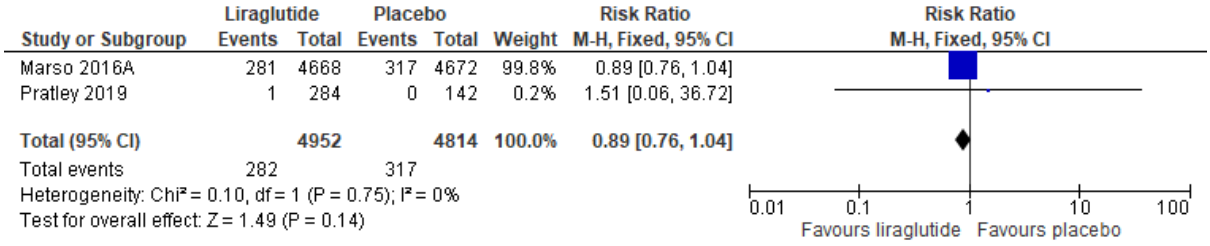


Figure 125: Unstable angina at end of follow-up

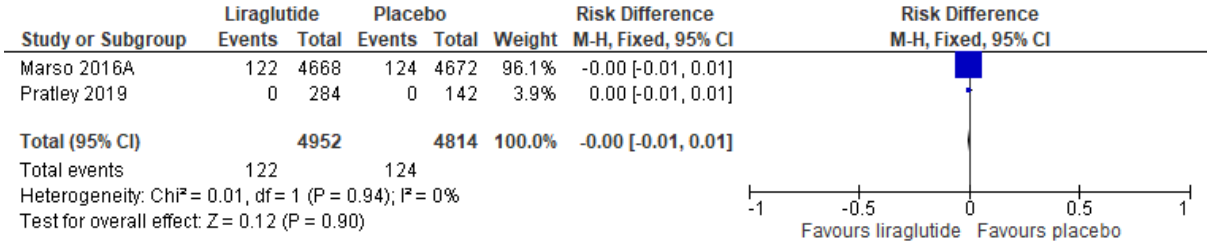


Figure 126: Acute kidney injury at end of follow-up

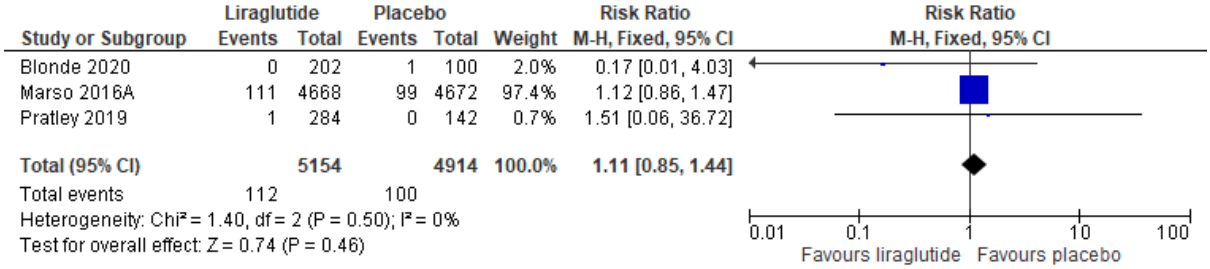


Figure 127: Persistent signs of kidney disease at end of follow-up

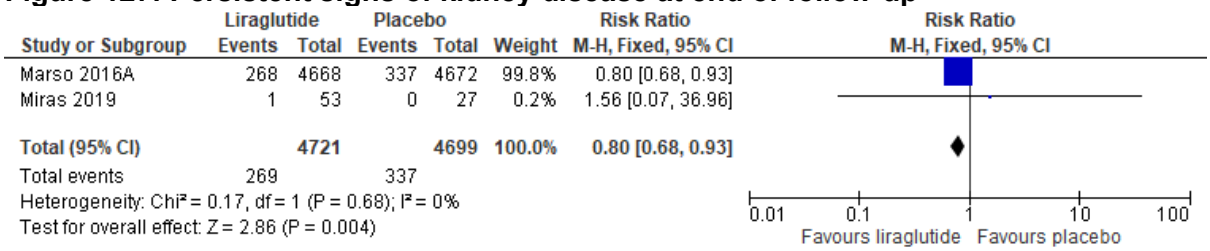


Figure 128: Development of end stage kidney disease at end of follow-up

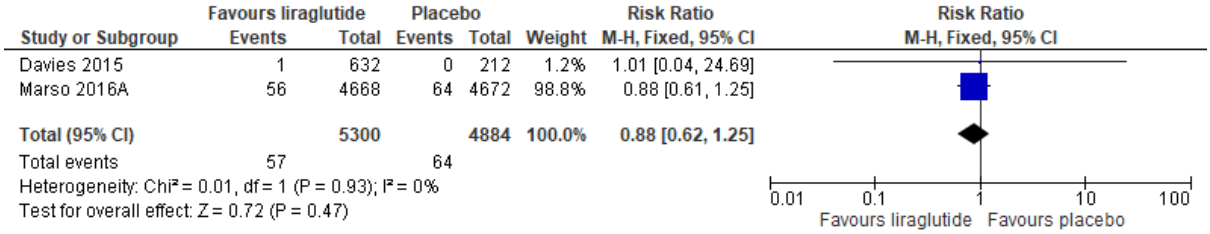


Figure 129: Death from renal cause at end of follow-up

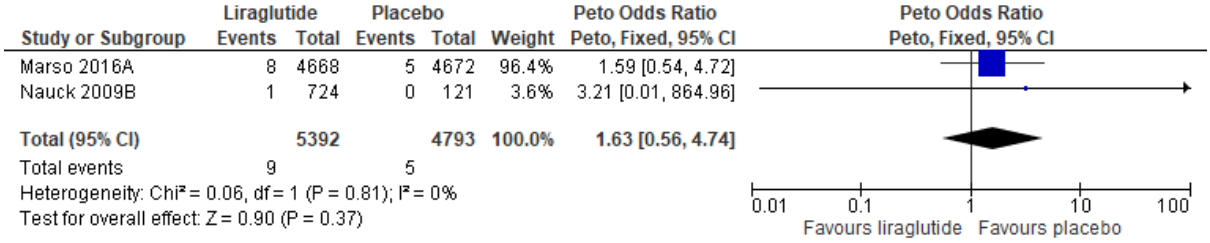
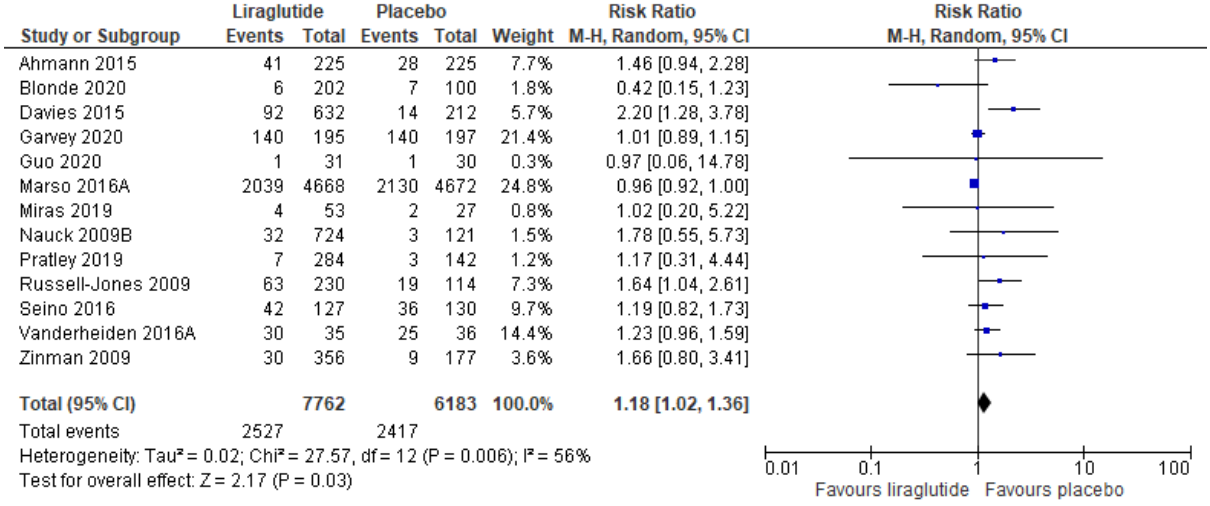


Figure 130: Hypoglycaemia episodes at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD and obesity subgroups.

Figure 131: At night hypoglycaemic episodes at end of follow up

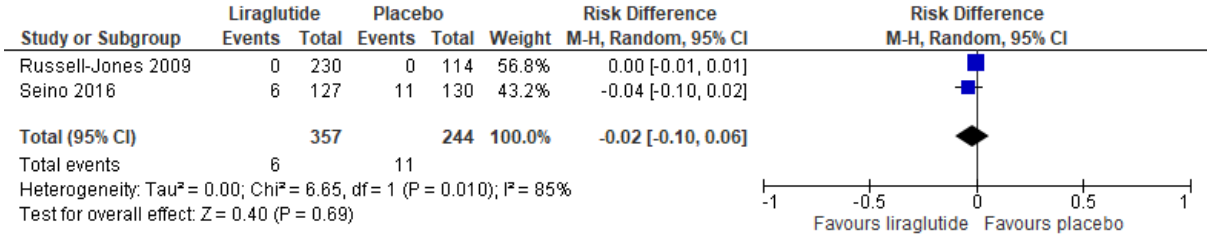


Figure 132: Severe hypoglycaemic episodes at end of follow up

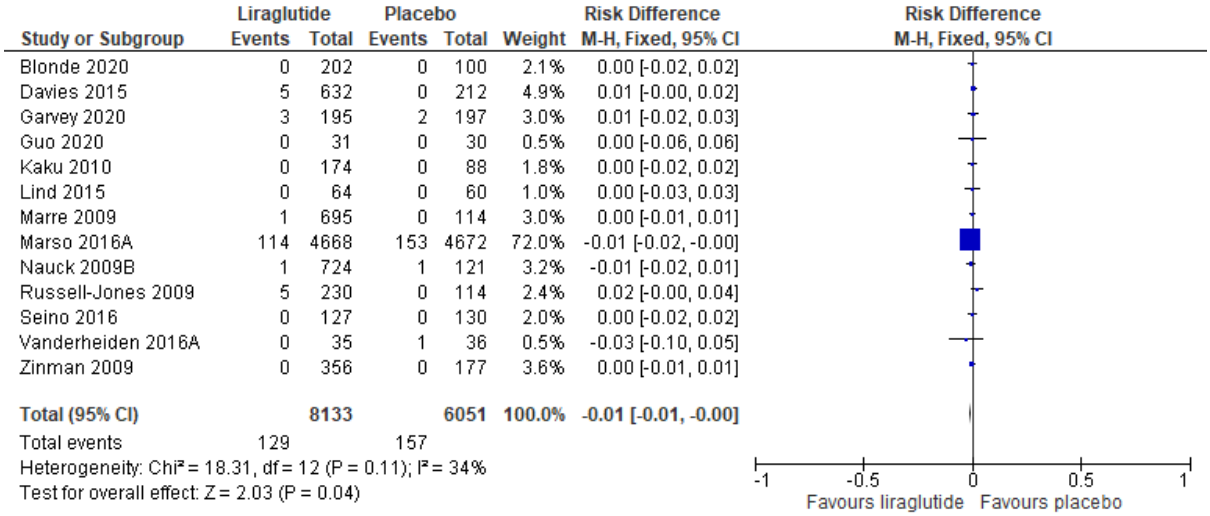
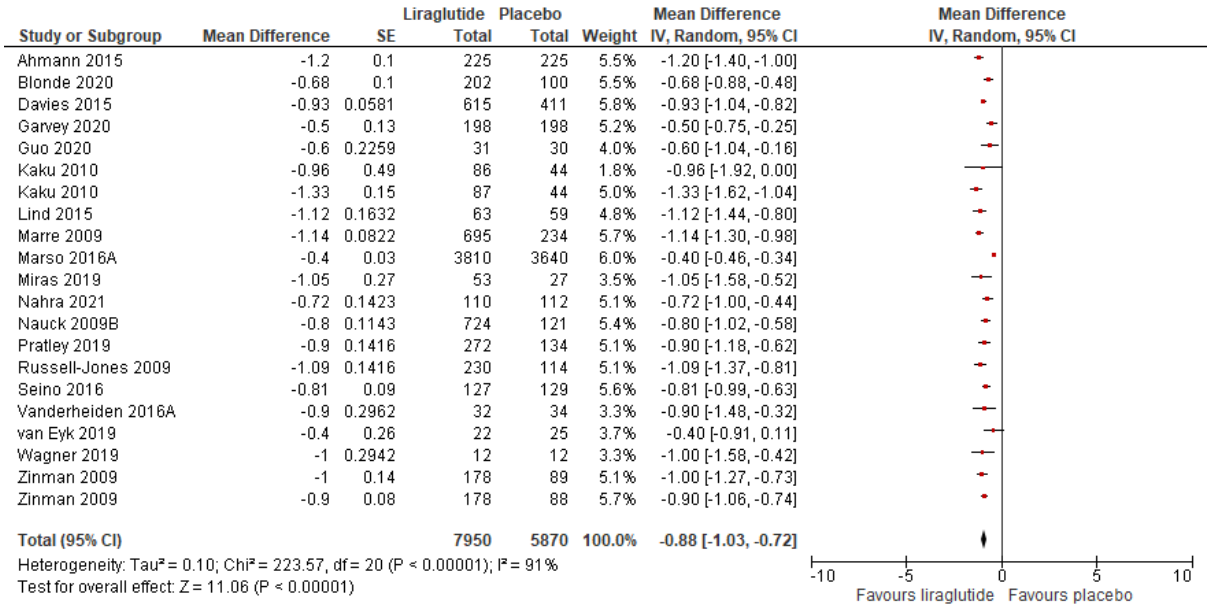
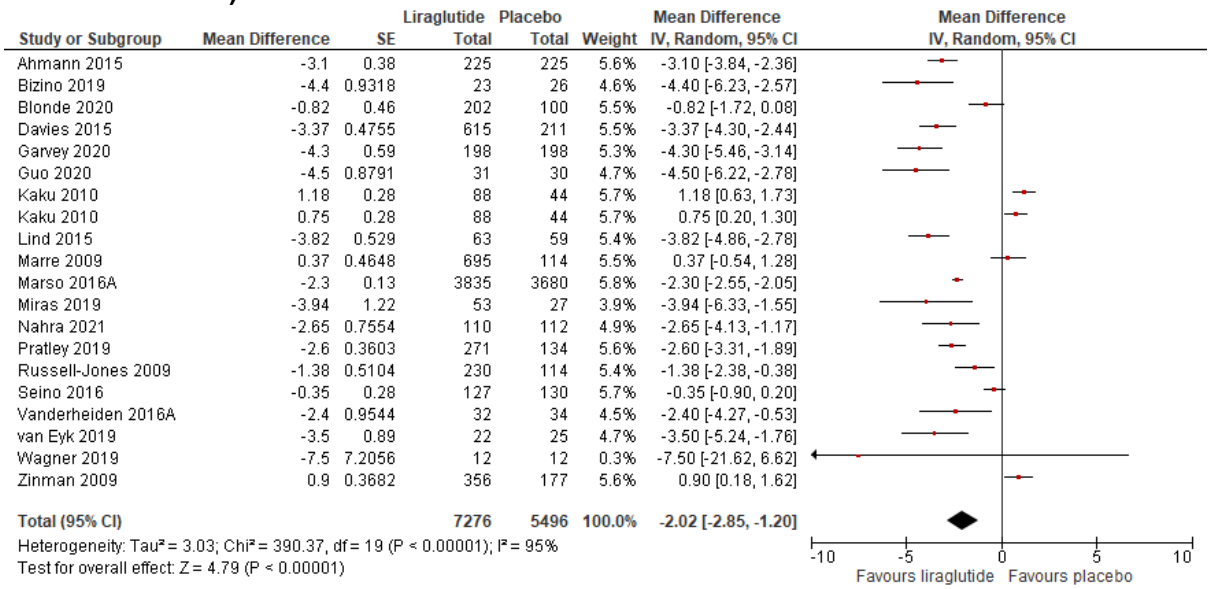


Figure 133: HbA1c change (% lower values are better, change scores and final values) at end of follow up



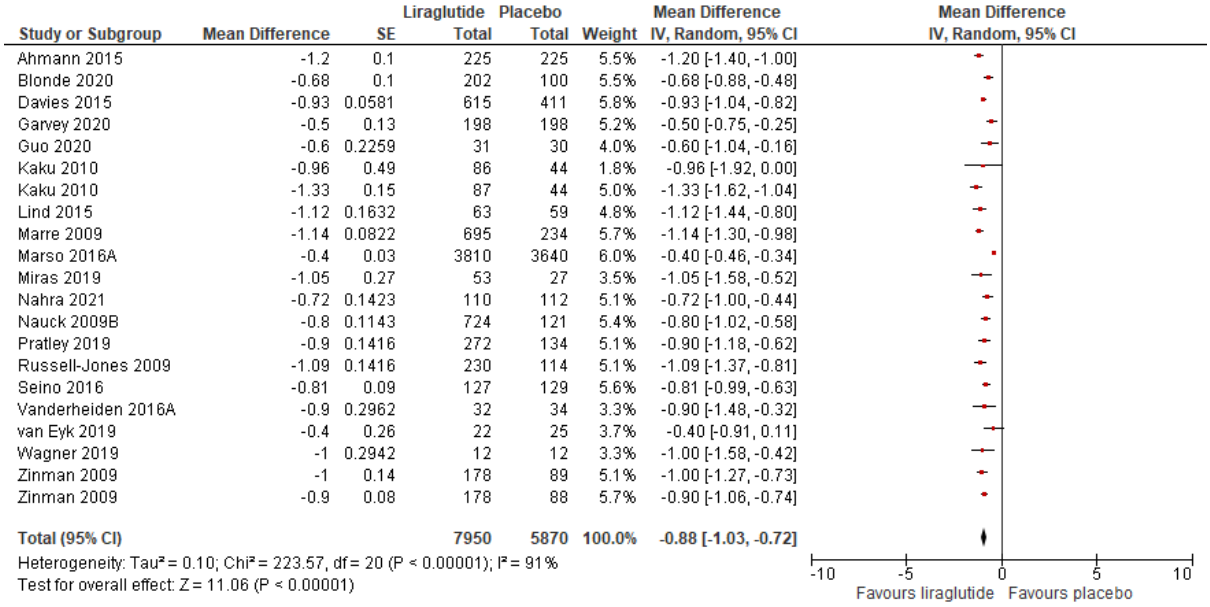
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD and obesity subgroups.

Figure 134: Weight change (kg, lower values are better, change scores and final values)



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD and obesity subgroups.

Figure 135: BMI change (kg/m^2, lower values are better, change scores and final values) at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD and obesity subgroups.

K.1.3.10 Adding liraglutide compared to adding insulin

Figure 136: Health-related quality of life - subscale mental component (SF-36, 0-100. higher values are better, change scores) at end of follow-up

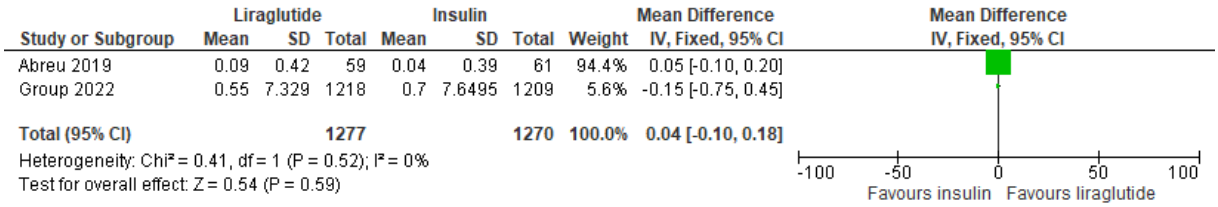


Figure 137: Health-related quality of life -subscale physical component (SF-36, 0, 100, higher values are better, change scores) at end of follow-up

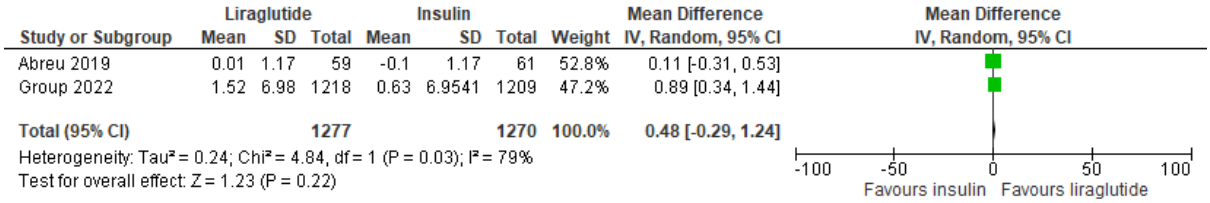
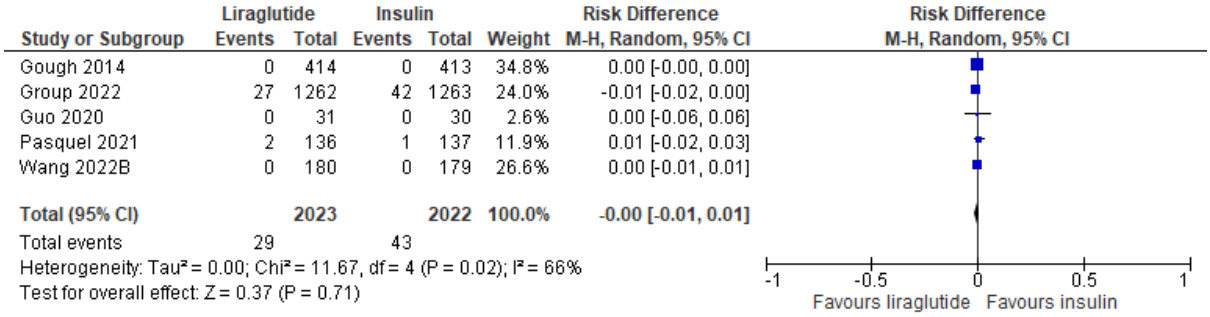
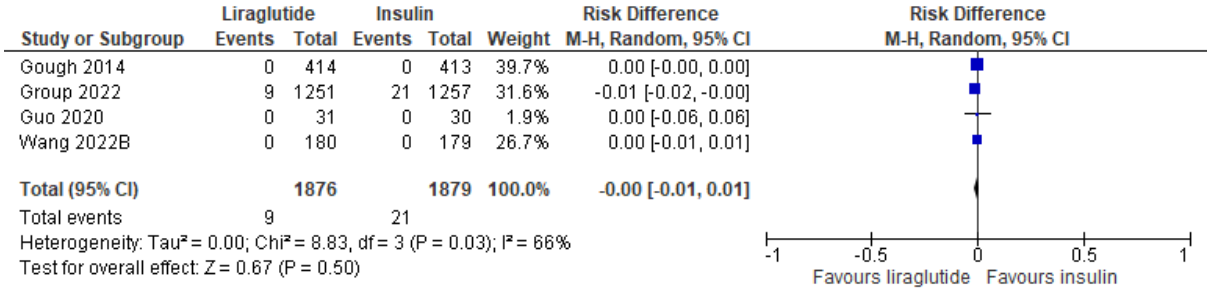


Figure 138: All-cause mortality at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 139: Cardiovascular mortality at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 140: 3-point MACE at end of follow-up

Figure 141: Unstable angina at end of follow-up

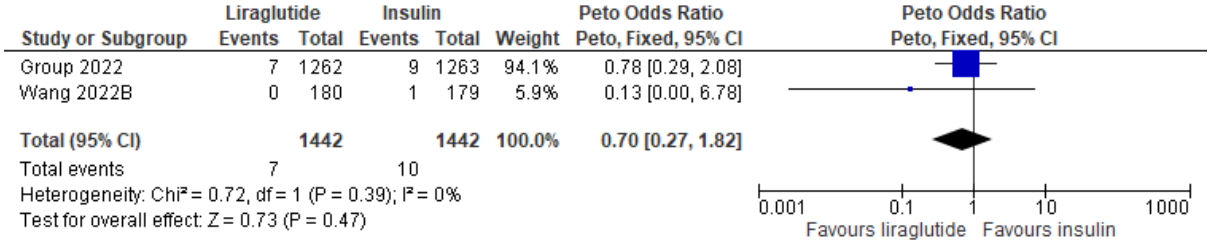


Figure 142: Non-fatal stroke at end of follow-up

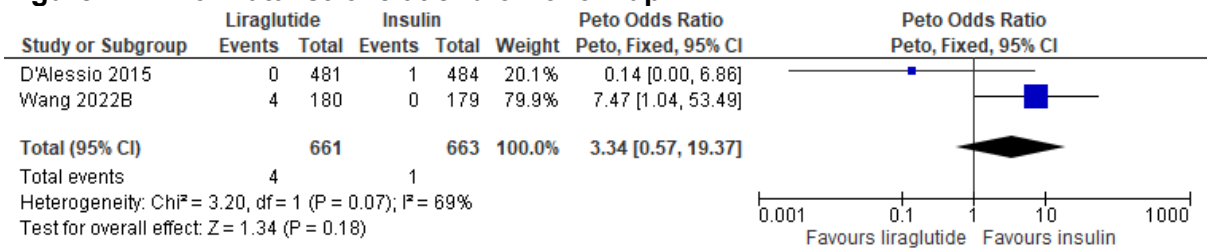
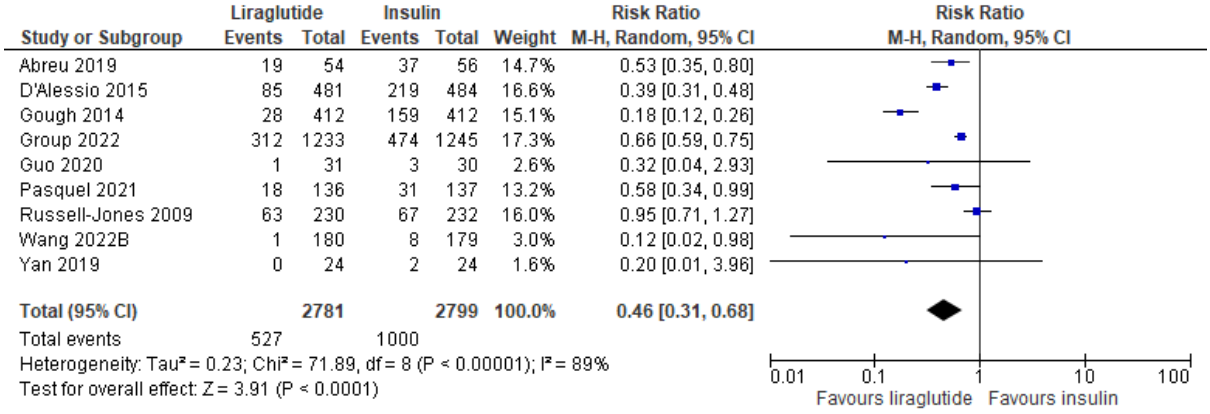


Figure 143: Hypoglycaemia episodes at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 144: At night hypoglycaemic episodes

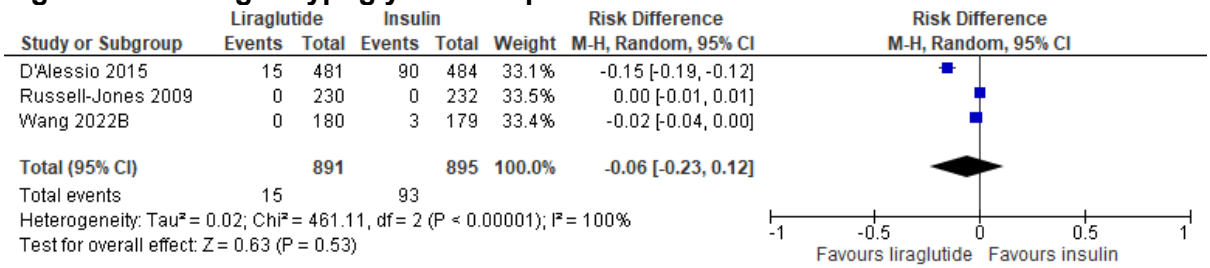


Figure 145: Severe hypoglycaemic episodes at end of follow up

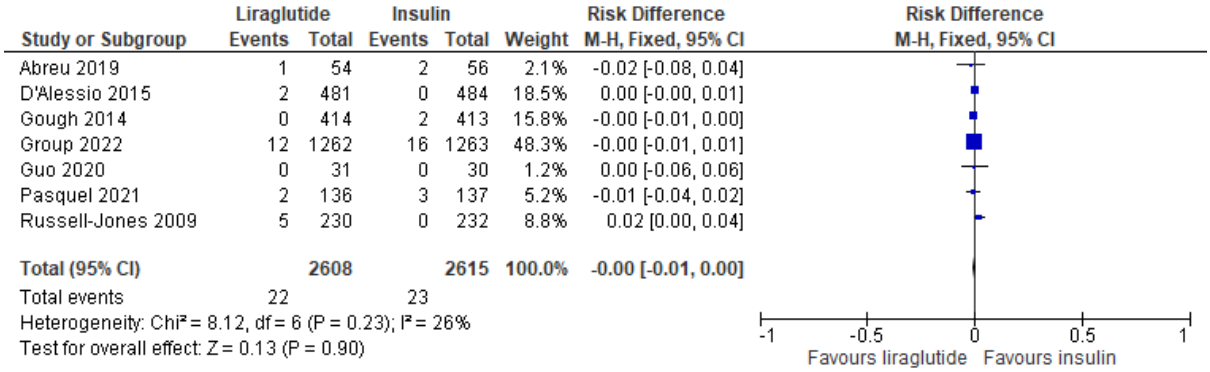
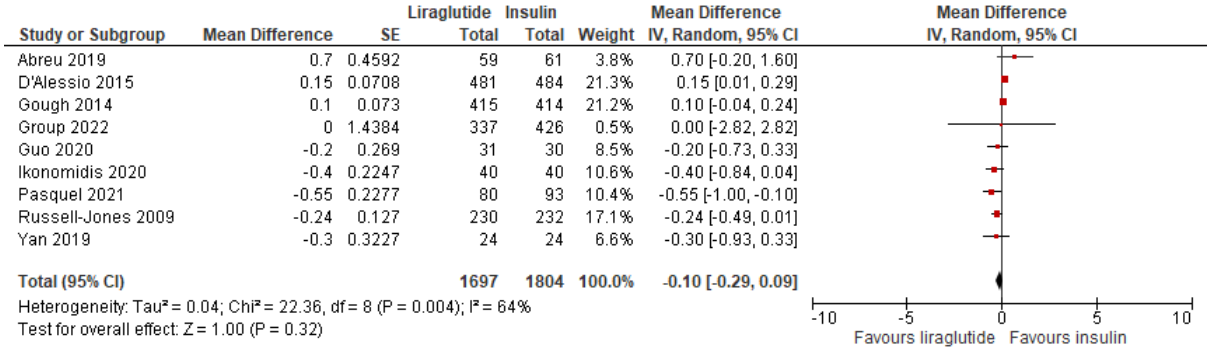


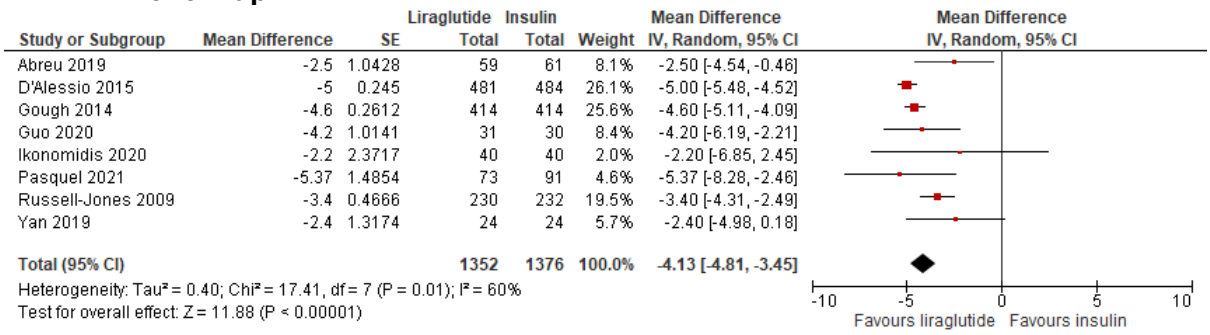
Figure 146: HbA1c change (%, lower values are better, change scores and final values) at end of follow-up

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgrou



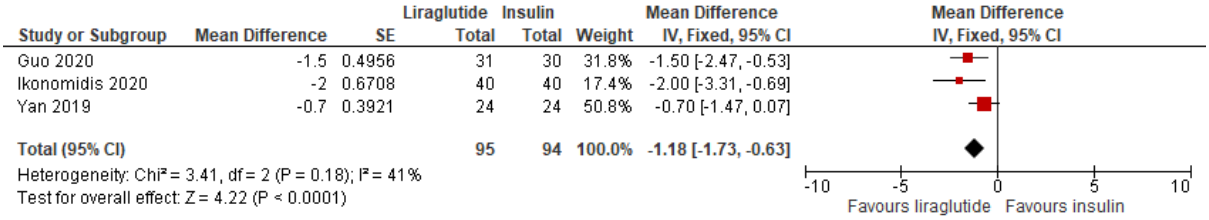
ps.

Figure 147: Weight change (kg, lower values are better, change scores) at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 148: BMI change (kg/m^2, lower values are better, change scores and final values) at end of follow-up



K.1.3.11 Adding liraglutide compared to adding dulaglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.3.12 Adding liraglutide compared to adding saxagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.3.13 Adding liraglutide compared to adding sitagliptin

Figure 149: All-cause mortality at end of follow up

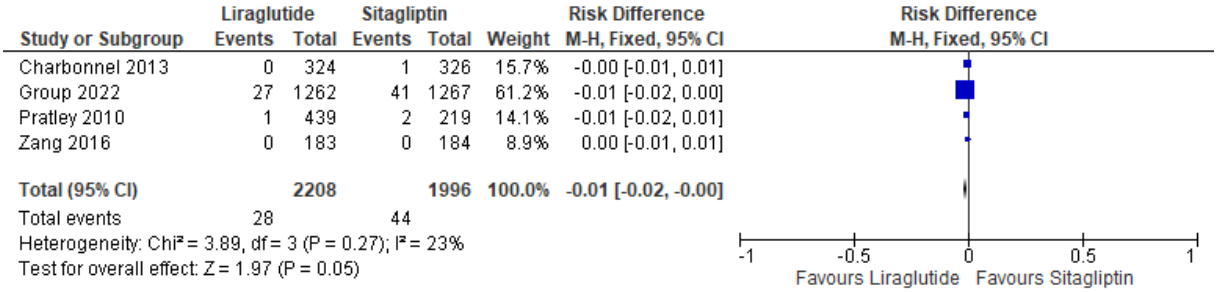


Figure 150: Cardiovascular mortality at end of follow up

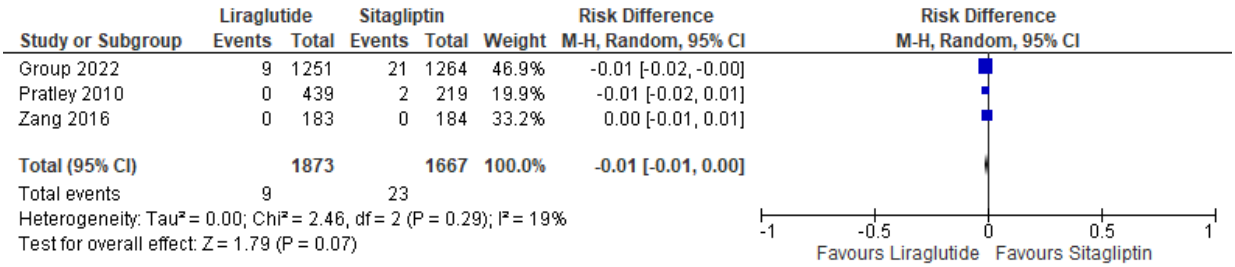
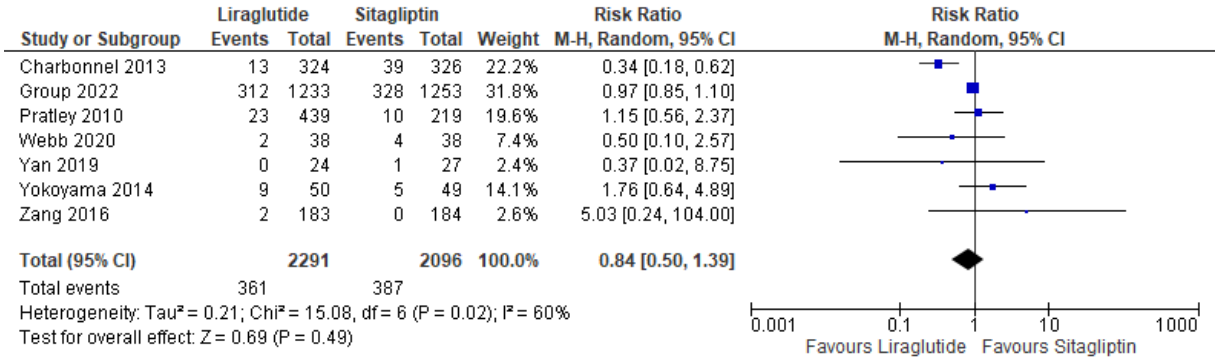


Figure 151: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 152: Severe hypoglycaemic episodes at end of follow up

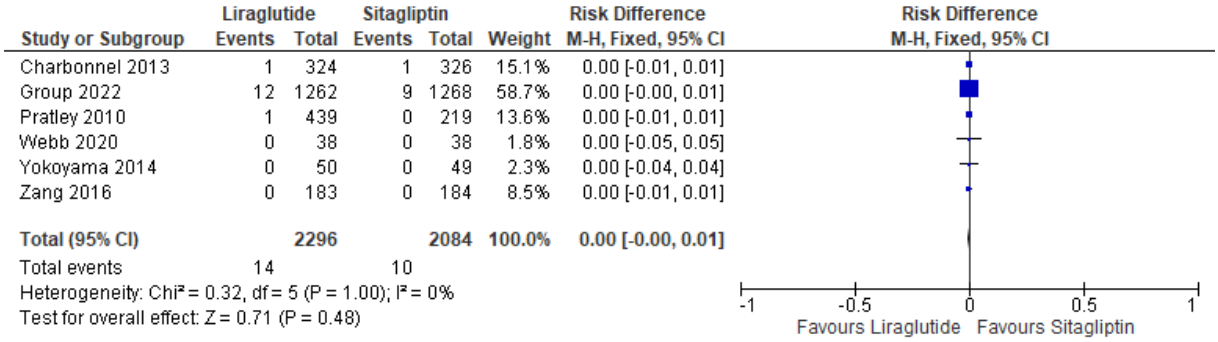
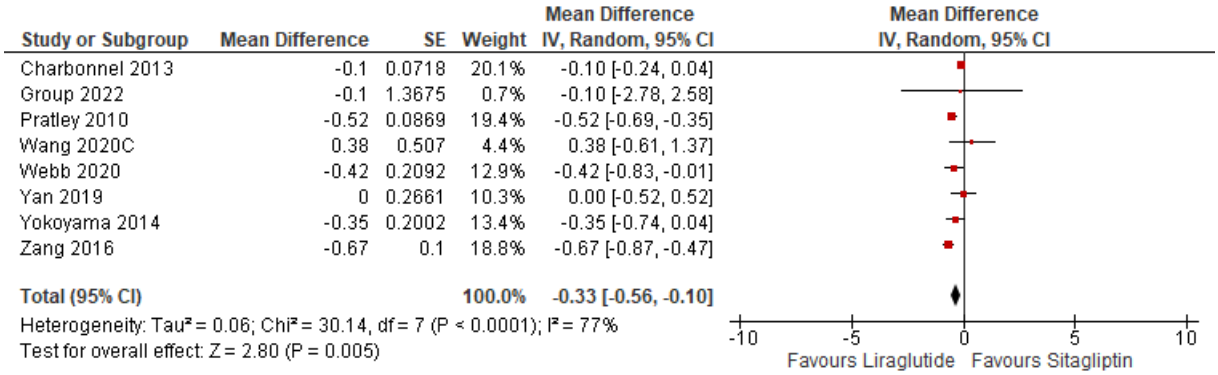
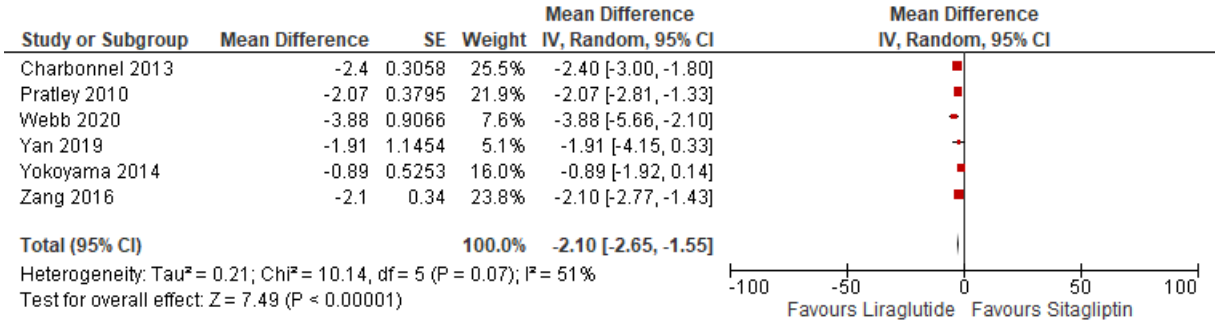


Figure 153: HbA1c change (%, lower values are better, mean difference) at end of follow up



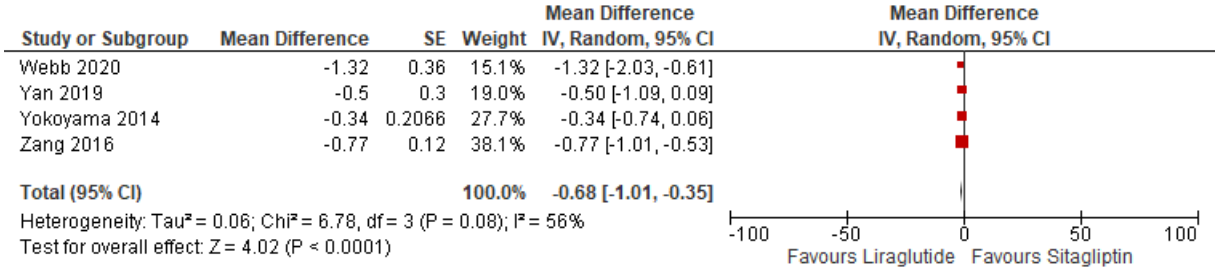
Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

Figure 154: Weight change (kg, lower values are better, mean difference) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, mixed population, NAFLD, obesity and not stated/ unclear subgroup.

Figure 155: BMI change (kg/m^2, lower values are better, mean difference) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

K.1.3.14 Adding liraglutide compared to adding vildagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.3.15 Adding lixisenatide compared to adding placebo

Figure 156: All-cause mortality at end of follow up

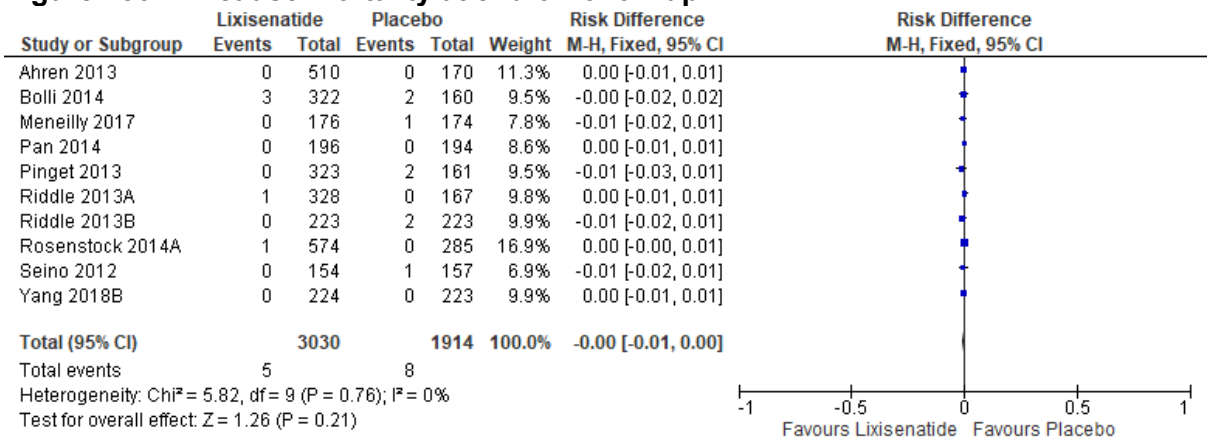


Figure 157: Cardiovascular mortality at end of follow up

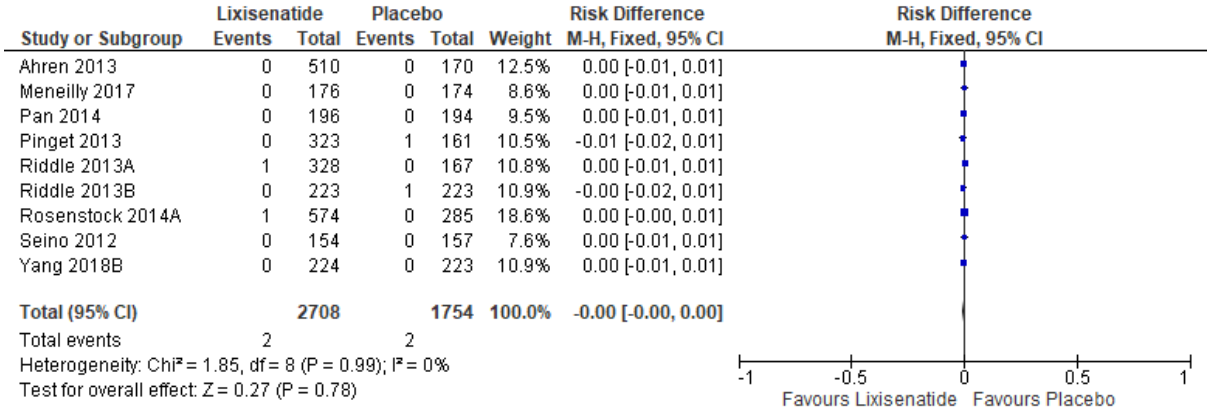


Figure 158: Non-fatal stroke at end of follow up

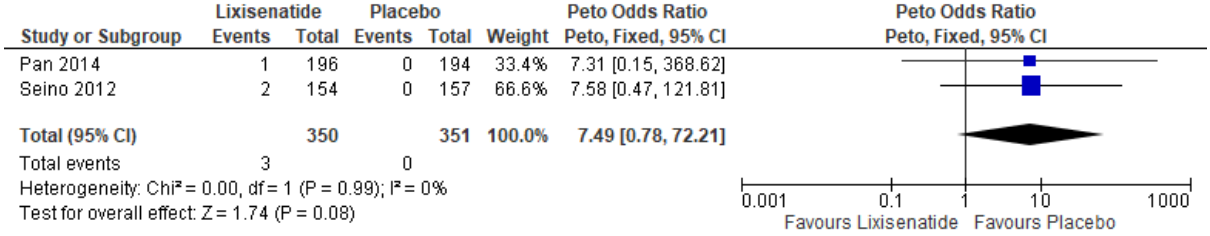


Figure 159: Hypoglycaemia episodes at end of follow up

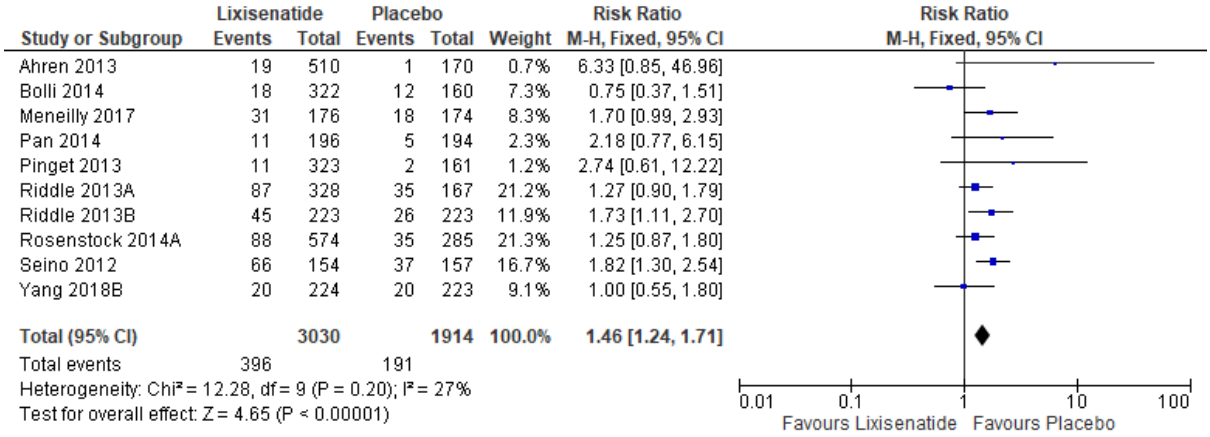


Figure 160: Severe hypoglycaemic episodes at end of follow up

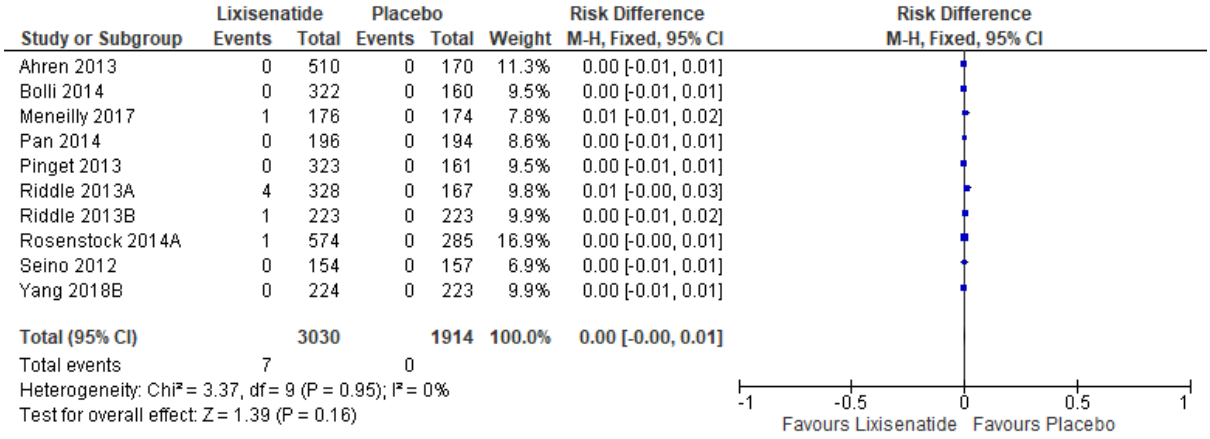
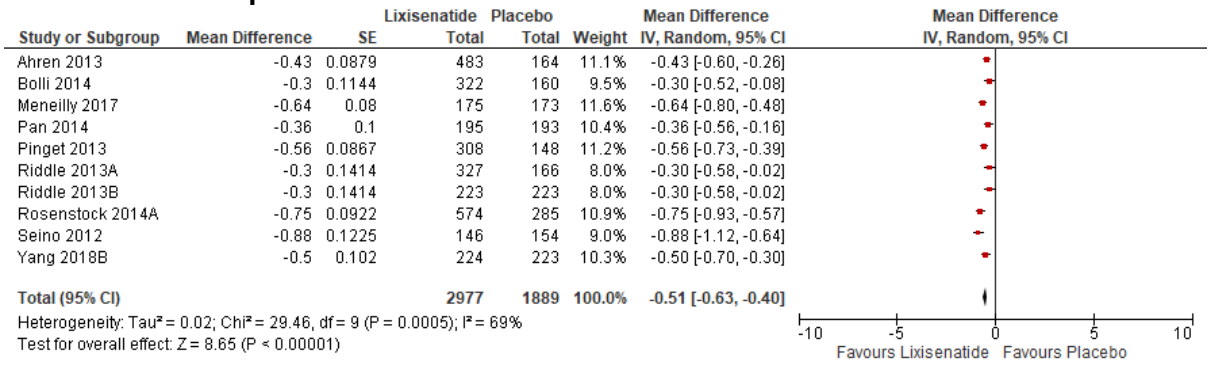
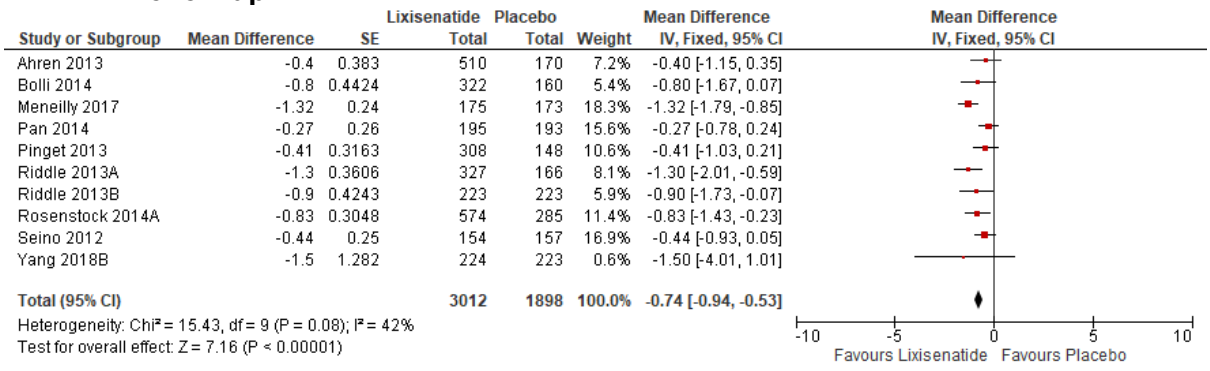


Figure 161: HbA1c change (%, lower values are better, mean difference) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by frailty subgroup.

Figure 162: Weight change (kg, lower values are better, mean difference) at end of follow up



K.1.3.16 Adding lixisenatide compared to adding insulin

Figure 163: All-cause mortality at end of follow up

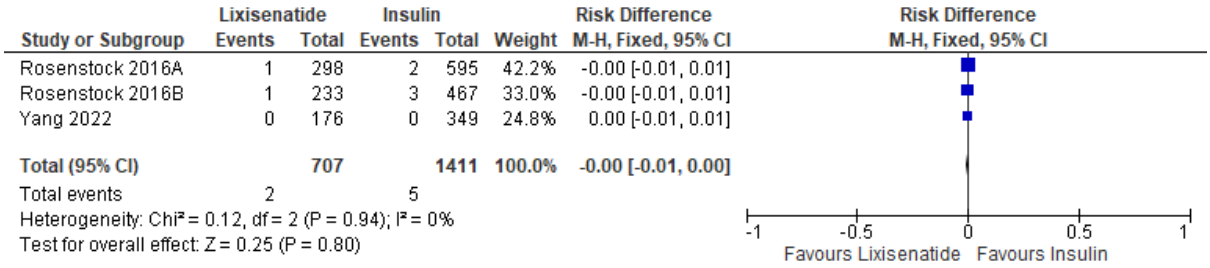


Figure 164: Cardiovascular mortality at end of follow up

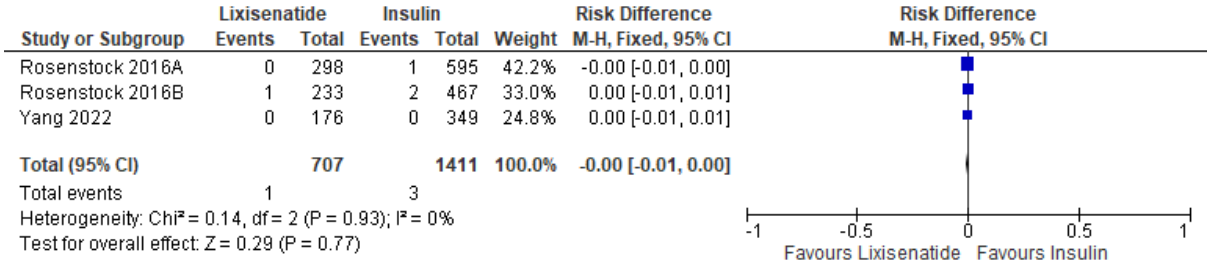


Figure 165: Hypoglycaemia episodes at end of follow up

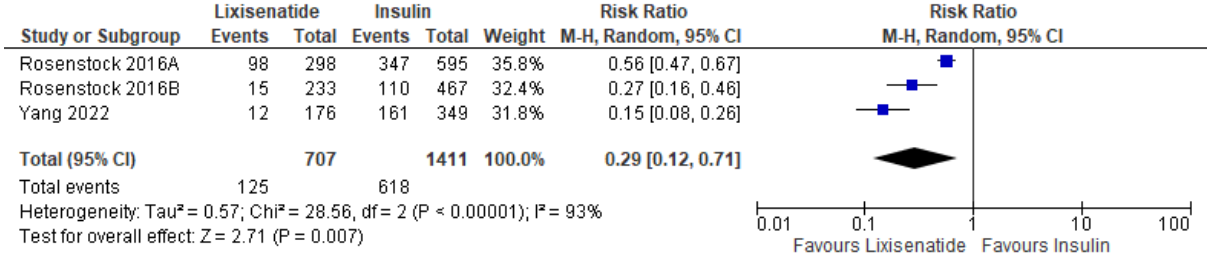


Figure 166: Severe hypoglycaemic episodes at end of follow up

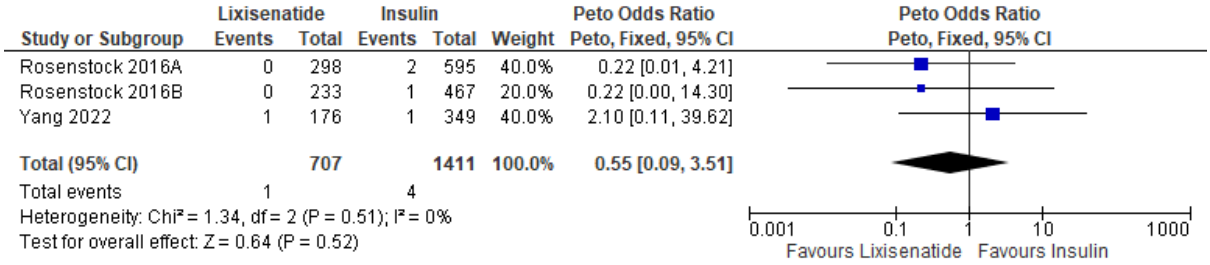


Figure 167: HbA1c change (%, lower values are better, change scores) at end of follow up

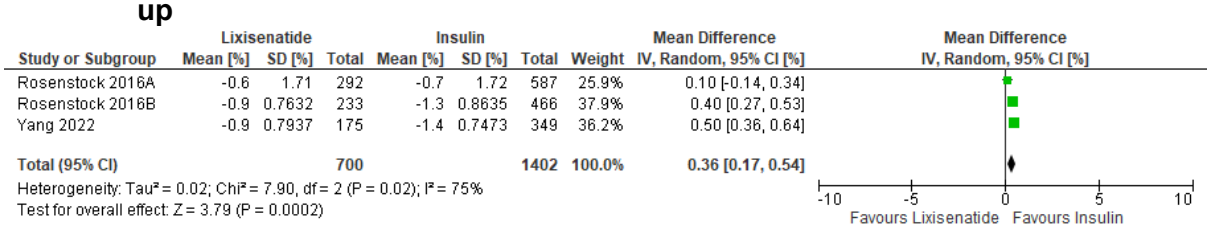
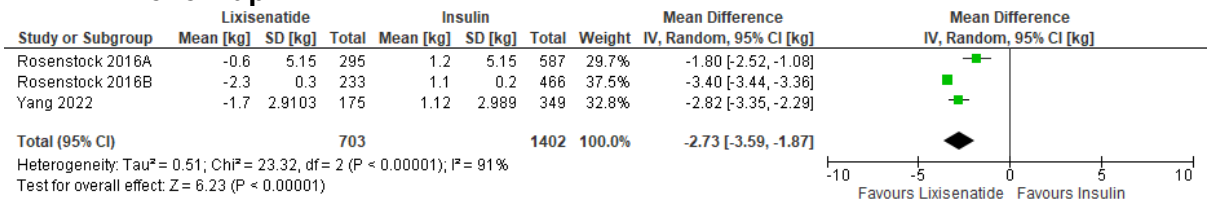


Figure 168: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.3.17 Adding lixisenatide compared to adding exenatide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.3.18 Adding lixisenatide compared to adding liraglutide

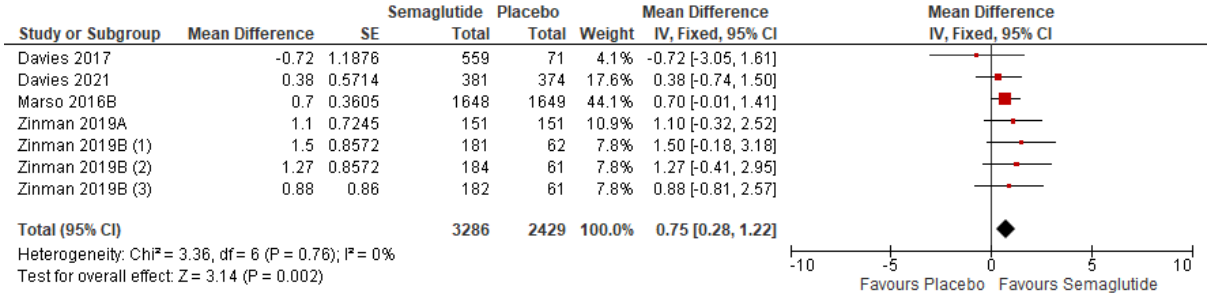
There are no forest plots for this comparison (all outcomes include a single study).

K.1.3.19 Adding lixisenatide compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

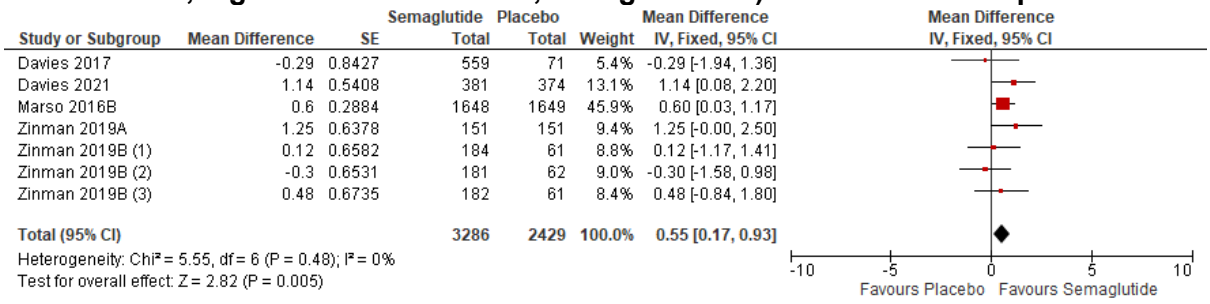
K.1.3.20 Adding semaglutide compared to adding placebo

Figure 169: Health-related quality of life - subscale mental component (SF-36, 0-100, higher values are better, change scores) at end of follow-up



Footnotes
(1) 14 mg semaglutide v placebo
(2) 3 mg semaglutide v placebo
(3) 7 mg semaglutide v placebo

Figure 170: Health-related quality of life - subscale physical component (SF-36, 0-100, higher values are better, change scores) at end of follow-up



Footnotes
(1) 3 mg semagluitde v placebo
(2) 14 mg semaglutide v placebo
(3) 7 mg semaglutide v placebo

Figure 171: All-cause mortality at end of follow up

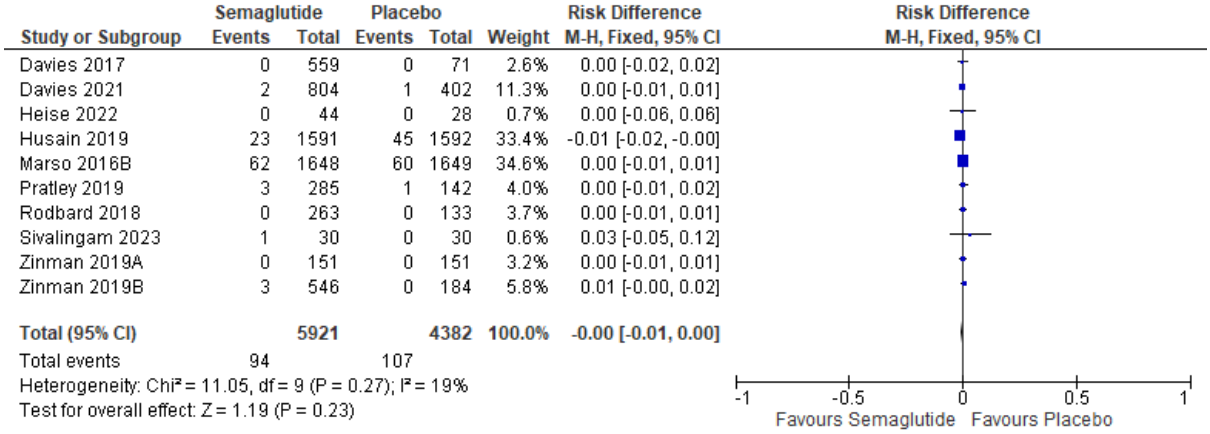


Figure 172: All-cause mortality at end of follow up

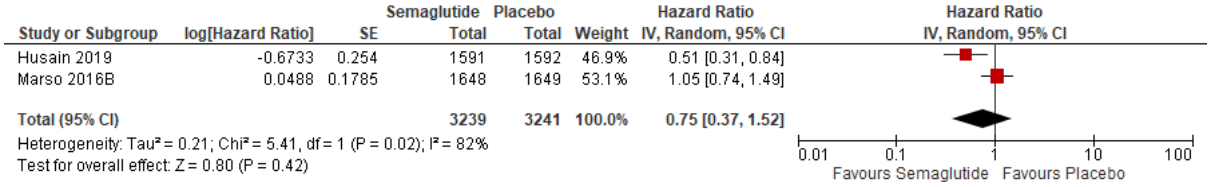


Figure 173: Cardiovascular mortality at end of follow-up

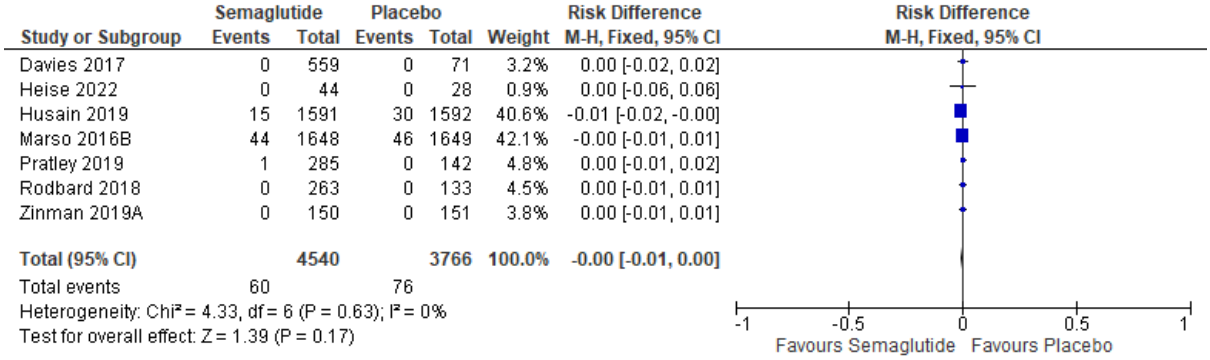


Figure 174: Cardiovascular mortality at end of follow-up

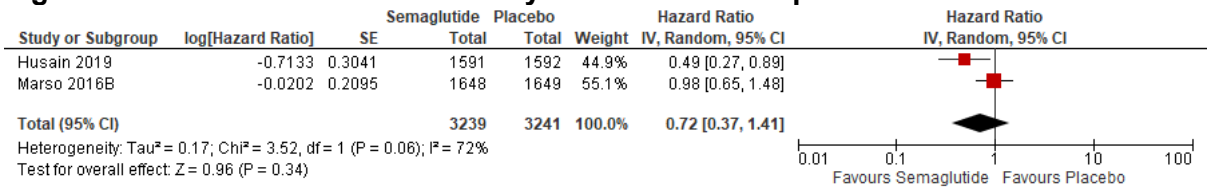


Figure 175: 3-point MACE at end of follow-up

Figure 176: 3-point MACE at end of follow-up

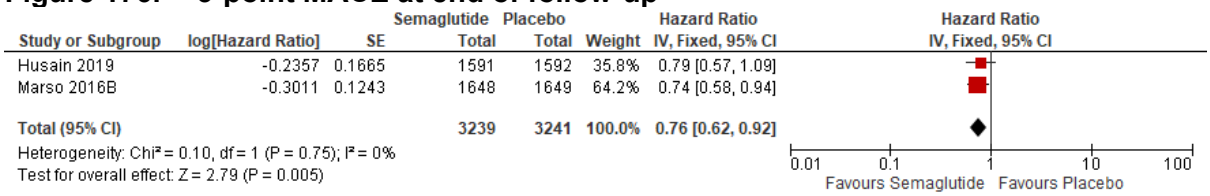


Figure 177: 5-point MACE at end of follow-up

Figure 178: 5-point MACE at end of follow-up

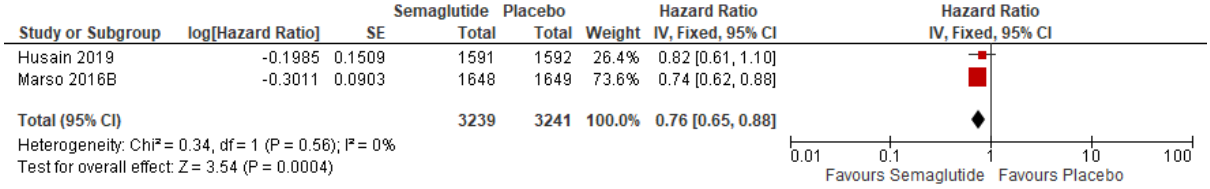


Figure 179: Non-fatal stroke at end of follow-up

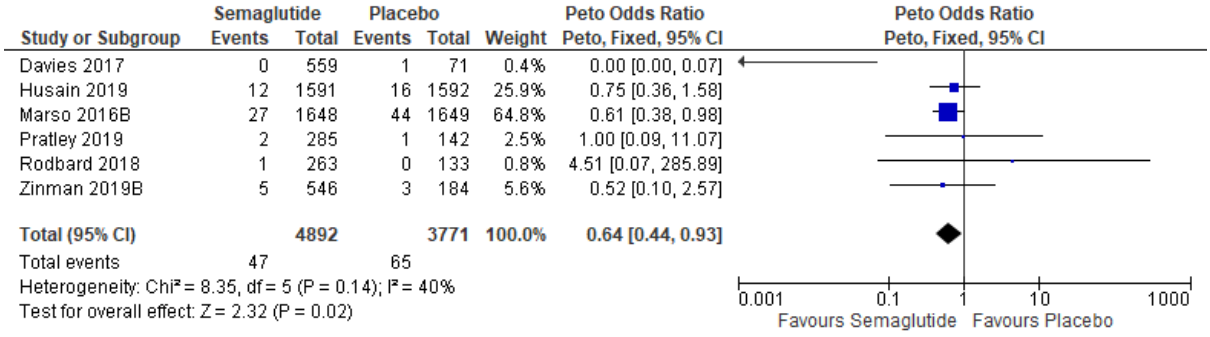


Figure 180: Non-fatal stroke at end of follow-up

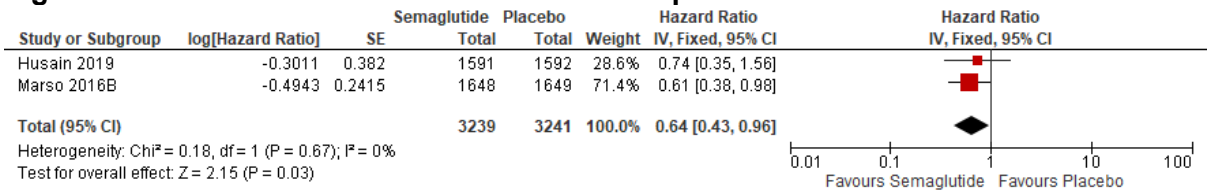


Figure 181: Non-fatal myocardial infarction at end of follow-up

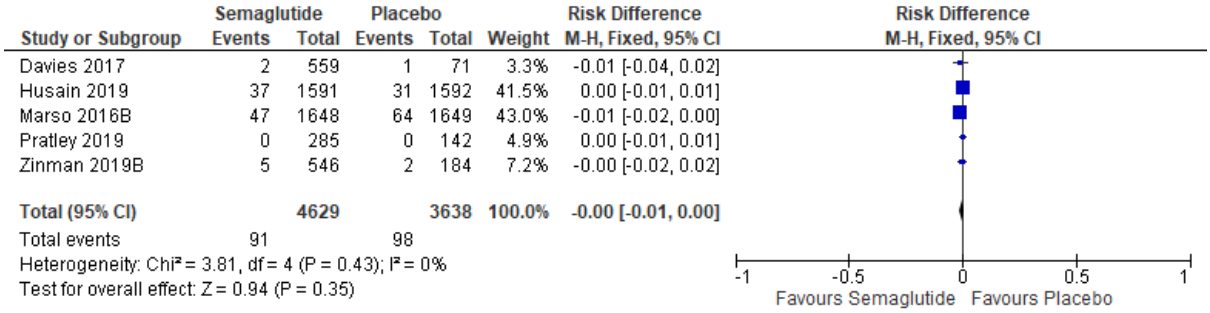


Figure 182: Non-fatal myocardial infarction at end of follow-up

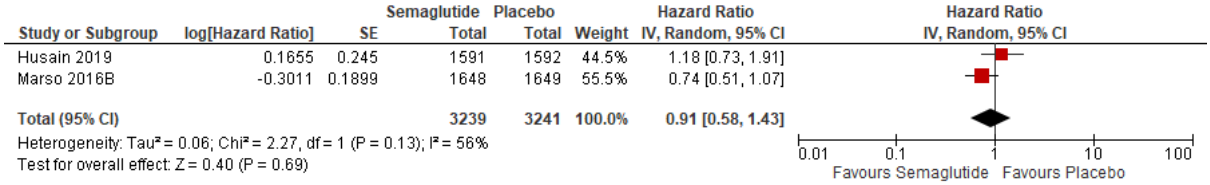


Figure 183: Unstable angina at end of follow-up

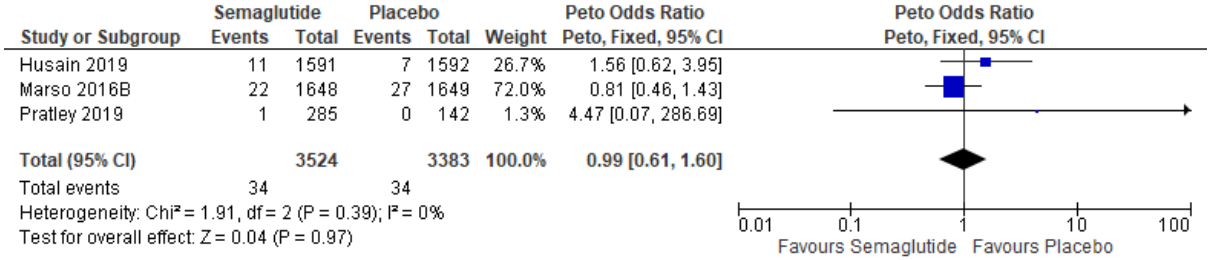


Figure 184: Unstable angina at end of follow-up

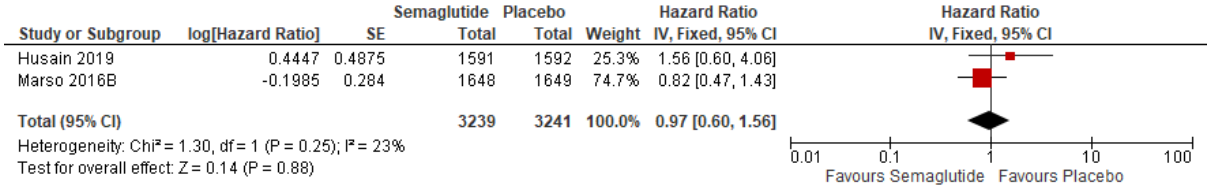


Figure 185: Hospitalisation for heart failure at end of follow-up

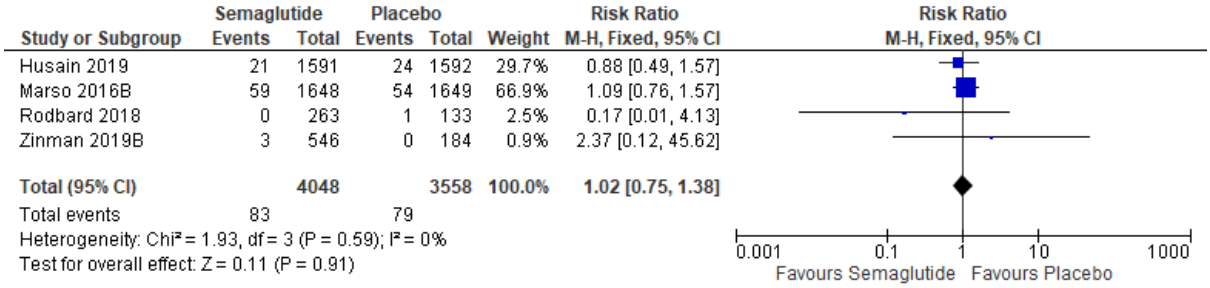


Figure 186: Hospitalisation for heart failure at end of follow-up

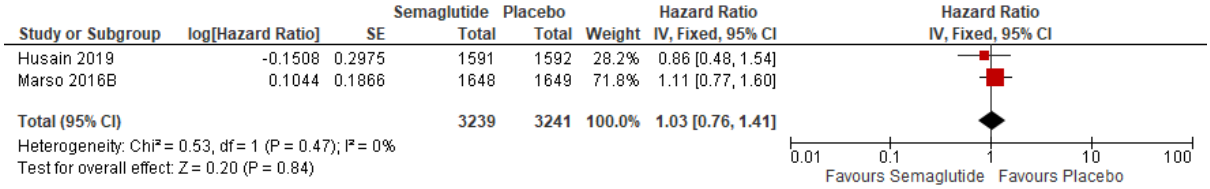


Figure 187: Acute kidney injury at end of follow-up

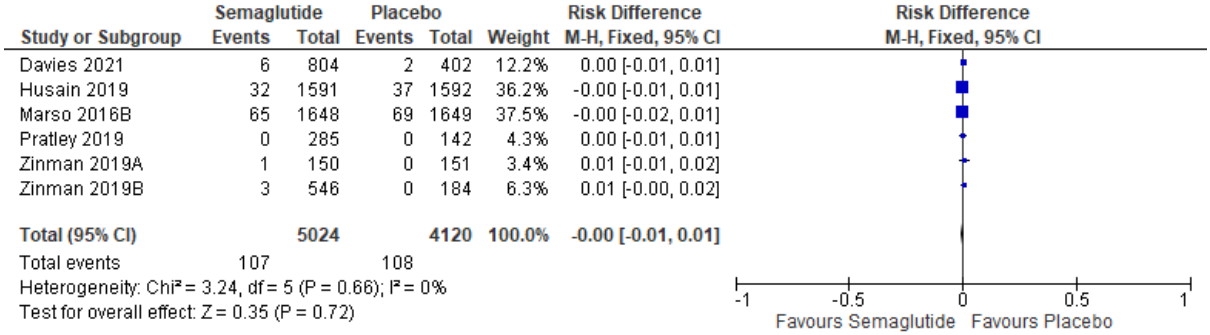
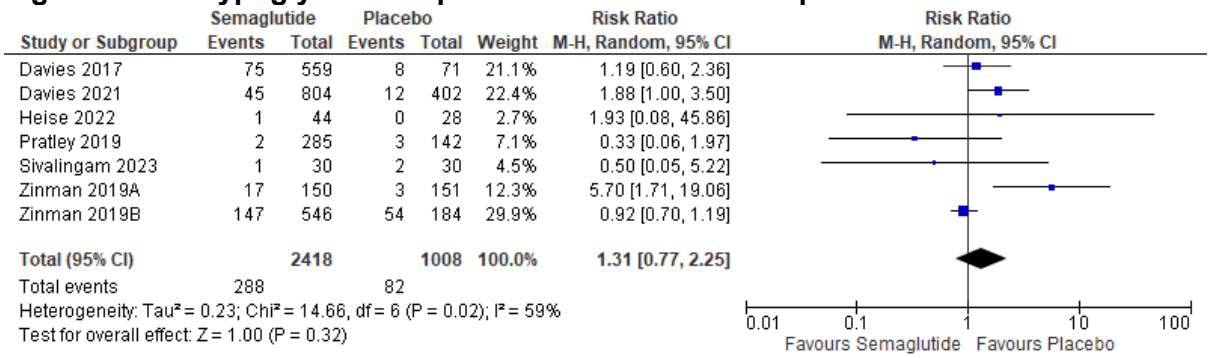


Figure 188: Hypoglycaemia episodes at end of follow-up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, NAFLD, and obesity subgroups.

Figure 189: Severe hypoglycaemic episodes at end of follow-up

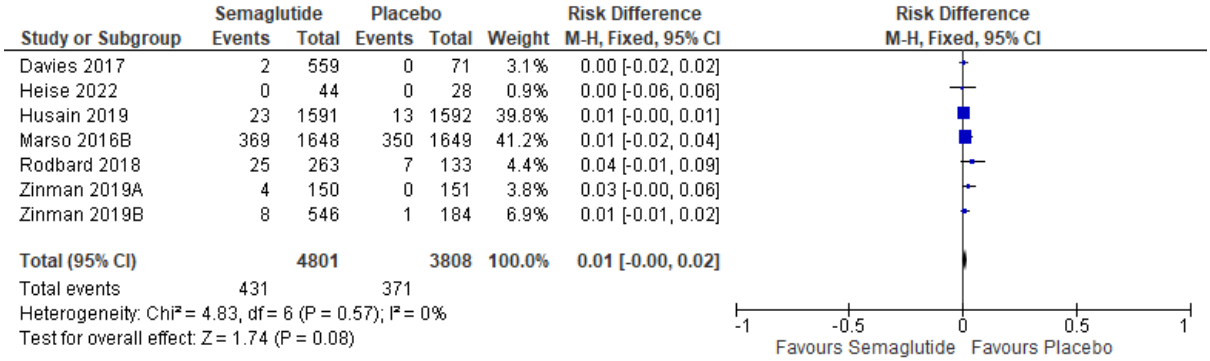
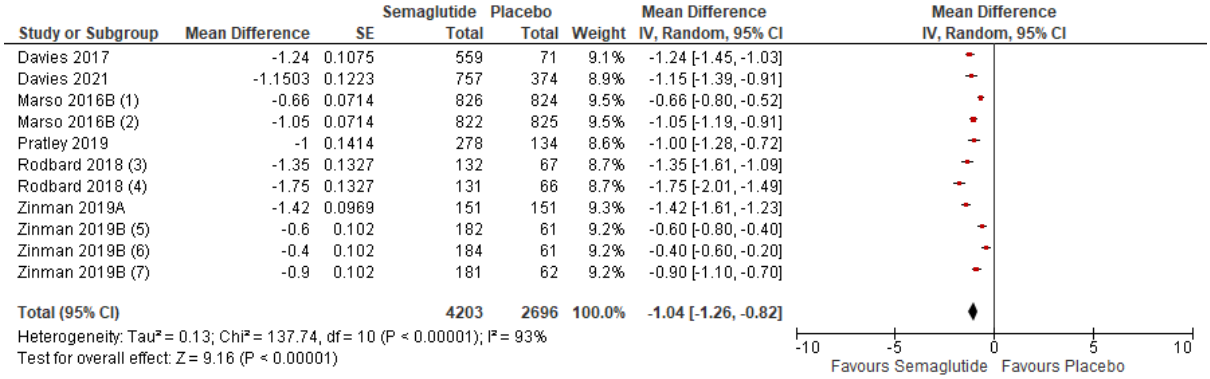


Figure 190: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg semaglutide v placebo
(2) 1.0 mg semaglutide v placebo
(3) 0.5 mg semaglutide v placebo
(4) 1.0 mg semaglutide v placebo
(5) 7 mg semaglutide v placebo
(6) 3 mg semaglutide v placebo
(7) 14 mg semaglutide v placebo

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, NAFLD, and obesity subgroups.

Figure 191: HbA1c change (mmol/mol, lower values are better, change scores) at end of follow up

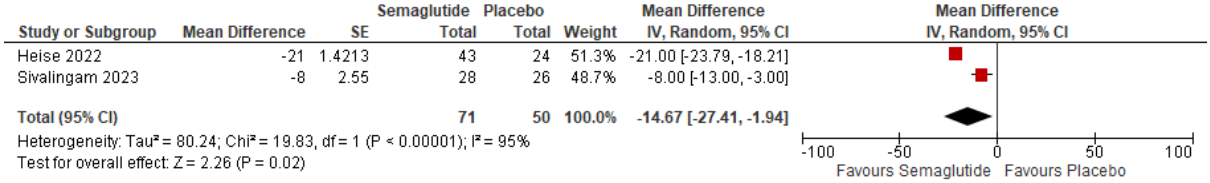
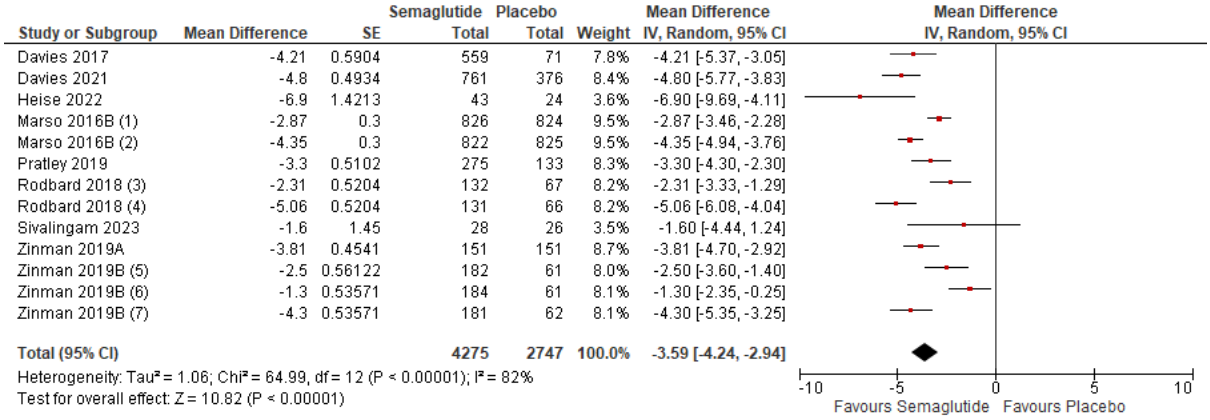


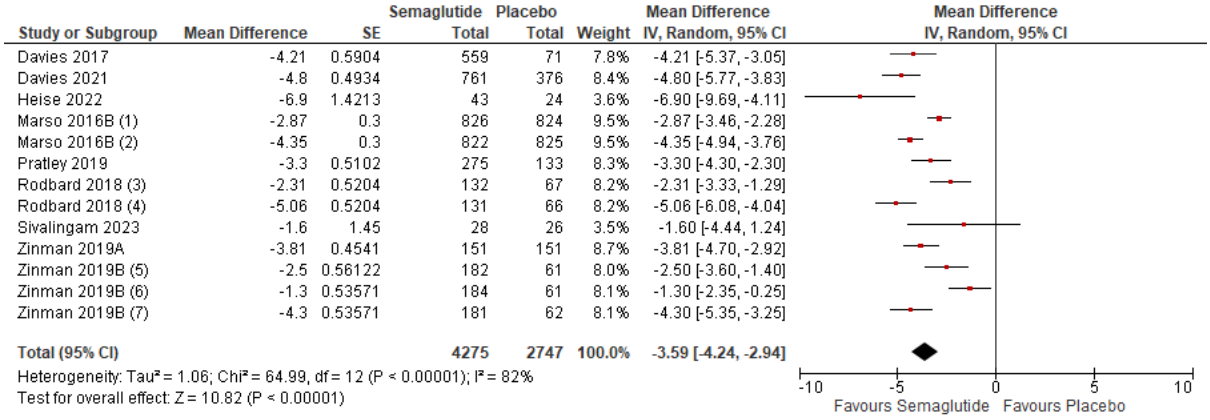
Figure 192: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg semaglutide v placebo
(2) 1.0 mg semaglutide v placebo
(3) 0.5 mg semaglutide v placebo
(4) 1.0 mg semaglutide v placebo
(5) 7 mg semaglutide v placebo
(6) 3 mg semaglutide v placebo
(7) 14 mg semaglutide v placebo

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, and NAFLD subgroups.

Figure 193: BMI change (kg/m^2, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg semaglutide v placebo
(2) 1.0 mg semaglutide v placebo
(3) 0.5 mg semaglutide v placebo
(4) 1.0 mg semaglutide v placebo
(5) 7 mg semaglutide v placebo
(6) 3 mg semaglutide v placebo
(7) 14 mg semaglutide v placebo

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR, NAFLD, and obesity subgroups.

K.1.3.21 Adding semaglutide compared to adding insulin

Figure 194: All-cause mortality at end of follow up

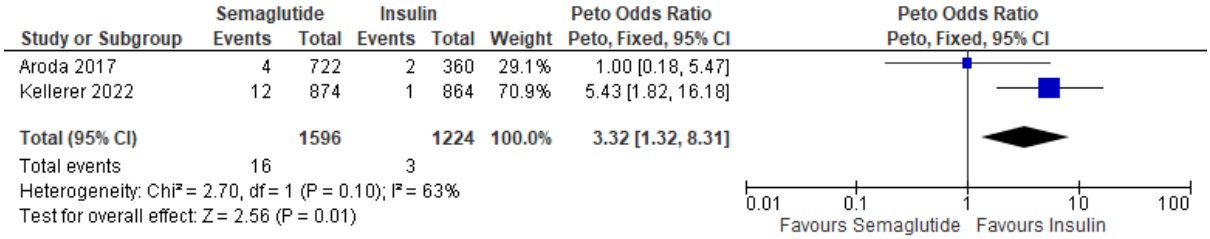


Figure 195: Severe hypoglycaemic episodes at end of follow up

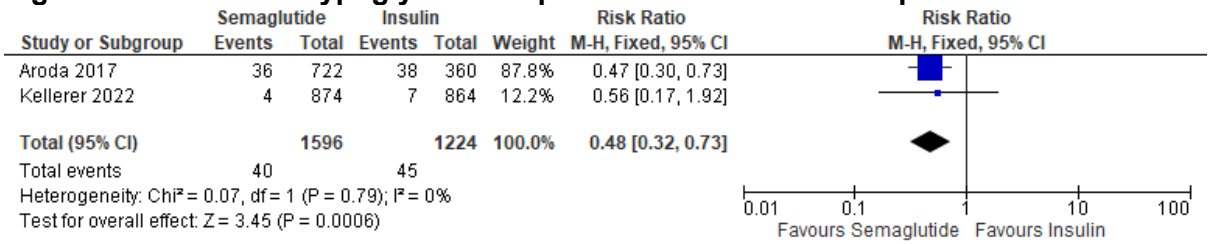
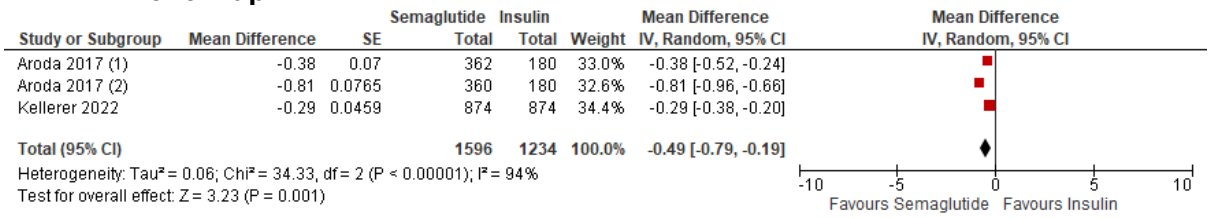
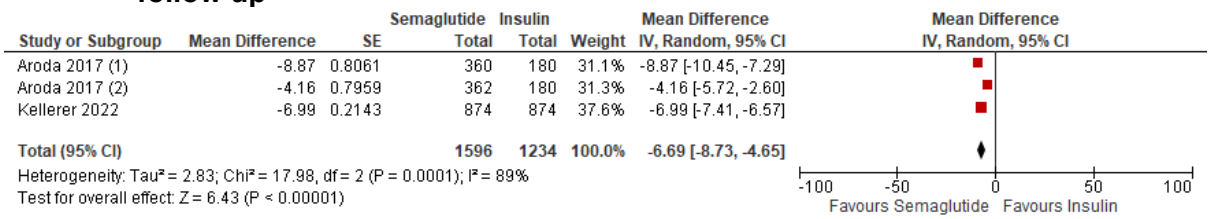


Figure 196: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg semaglutide v placebo
(2) 1.0 mg semaglutide v insulin

Figure 197: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 1.0 mg semaglutide v insulin
(2) 0.5 mg semaglutide v insulin

K.1.3.22 Adding semaglutide compared to adding dulaglutide

Figure 198: All-cause mortality at end of follow up

Study or Subgroup	Semaglutide Events	Semaglutide Total	Dulaglutide Events	Dulaglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Pratley 2018B	2	601	4	598	84.3%	-0.00 [-0.01, 0.00]
Yabe 2020	0	393	0	65	15.7%	0.00 [-0.02, 0.02]
Total (95% CI)		**994**		**663**	**100.0%**	**-0.00 [-0.01, 0.00]**
Total events	2		4			

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 0.74 (P = 0.46)

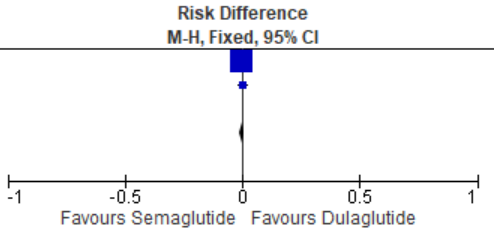


Figure 199: Cardiovascular mortality at end of follow up

Study or Subgroup	Semaglutide Events	Semaglutide Total	Dulaglutide Events	Dulaglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Pratley 2018B	1	601	2	598	84.3%	-0.00 [-0.01, 0.00]
Yabe 2020	0	393	0	65	15.7%	0.00 [-0.02, 0.02]
Total (95% CI)		**994**		**663**	**100.0%**	**-0.00 [-0.01, 0.00]**
Total events	1		2			

Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.48 (P = 0.63)

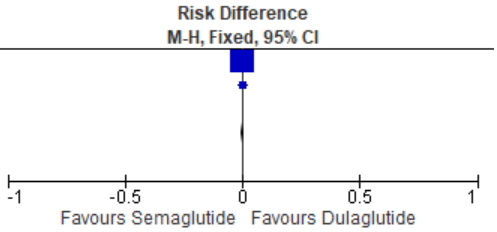


Figure 200: Hypoglycaemia episodes at end of follow up

Study or Subgroup	Semaglutide Events	Semaglutide Total	Dulaglutide Events	Dulaglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Iijima 2023	0	16	0	16	12.5%	0.00 [-0.11, 0.11]
Yabe 2020	67	393	13	65	87.5%	-0.03 [-0.13, 0.07]
Total (95% CI)		**409**		**81**	**100.0%**	**-0.03 [-0.12, 0.07]**
Total events	67		13			

Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.55 (P = 0.58)

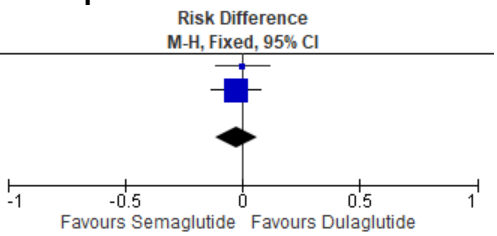


Figure 201: Severe hypoglycaemic episodes at end of follow up

Study or Subgroup	Semaglutide Events	Semaglutide Total	Dulaglutide Events	Dulaglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Pratley 2018B	7	601	8	598	84.3%	-0.00 [-0.01, 0.01]
Yabe 2020	0	393	0	65	15.7%	0.00 [-0.02, 0.02]
Total (95% CI)		**994**		**663**	**100.0%**	**-0.00 [-0.01, 0.01]**
Total events	7		8			

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.26 (P = 0.80)

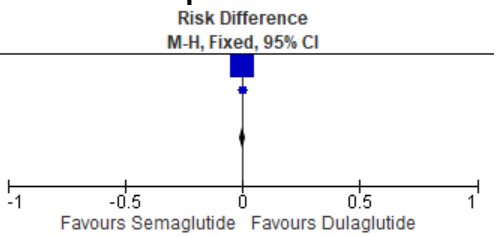


Figure 202: HbA1c change (%, lower values are better, change scores) at end of follow up

Study or Subgroup	Semaglutide Mean [%]	Semaglutide SD [%]	Semaglutide Total	Dulaglutide Mean [%]	Dulaglutide SD [%]	Dulaglutide Total	Weight	Mean Difference IV, Random, 95% CI [%]
Iijima 2023	-0.42	0.49	16	0	0.34	16	29.4%	-0.42 [-0.71, -0.13]
Pratley 2018B	-1.65	1.04	601	-1.25	1	598	37.8%	-0.40 [-0.52, -0.28]
Yabe 2020	-1.33	1.19	393	-1.4	0.81	65	32.7%	0.07 [-0.16, 0.30]
Total (95% CI)			**1010**			**679**	**100.0%**	**-0.25 [-0.56, 0.06]**

Heterogeneity: Tau² = 0.06; Chi² = 13.40, df = 2 (P = 0.001); I² = 85%
Test for overall effect: Z = 1.60 (P = 0.11)

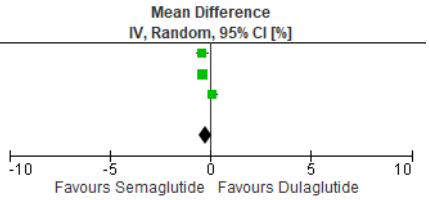


Figure 203: Weight change (kg, lower values are better, change scores) at end of follow up

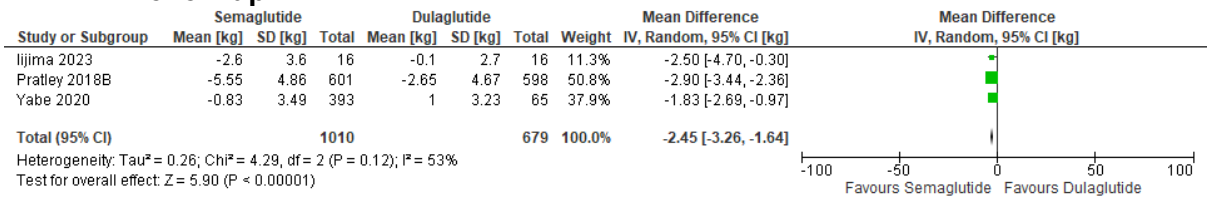
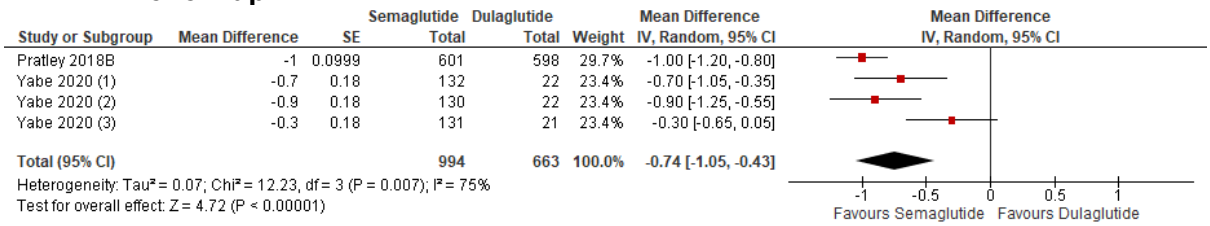


Figure 204: BMI change (kg/m^2, lower values are better, change scores) at end of follow up



Footnotes
(1) 7 mg semaglutide v dulaglutide
(2) 14 mg semaglutide v dulaglutide
(3) 3 mg semaglutide v dulaglutide

K.1.3.23 Adding semaglutide compared to adding exenatide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.3.24 Adding semaglutide compared to adding liraglutide

Figure 205: All-cause mortality at end of follow up

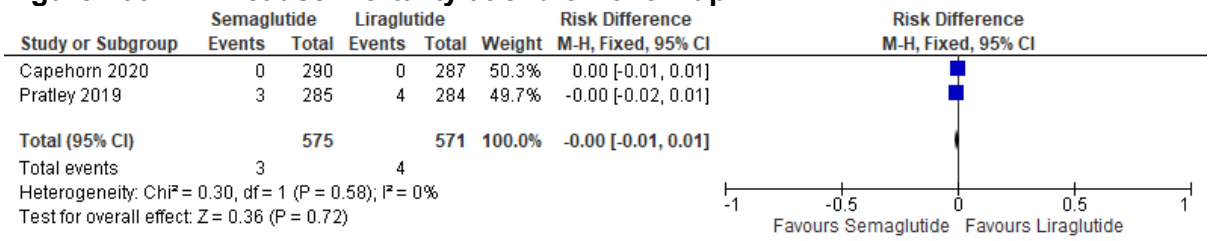


Figure 206: Cardiovascular mortality at end of follow up

Figure 207: Hypoglycaemia episodes at end of follow up

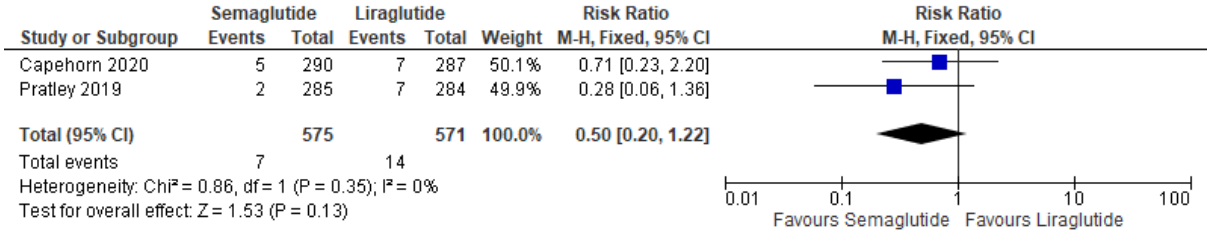


Figure 208: HbA1c change (%, lower values are better, change scores) at end of follow up

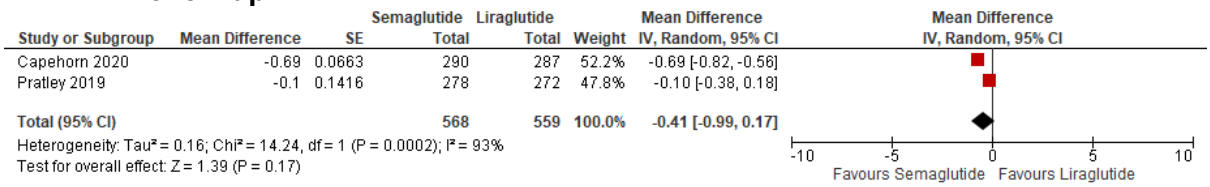


Figure 209: Weight change (kg, lower values are better, change scores) at end of follow up

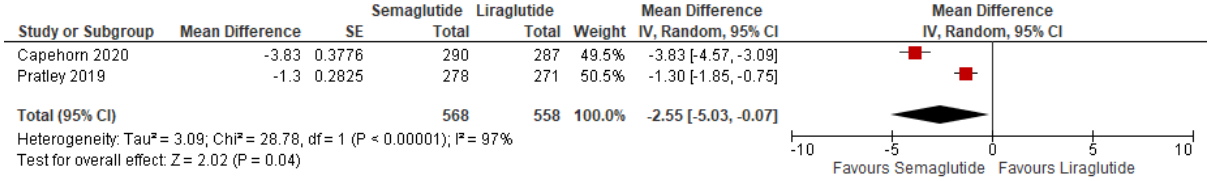
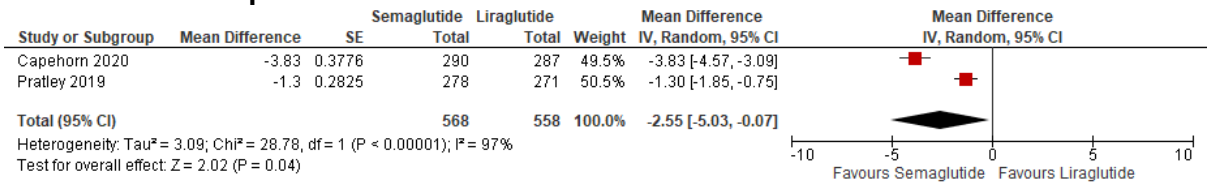
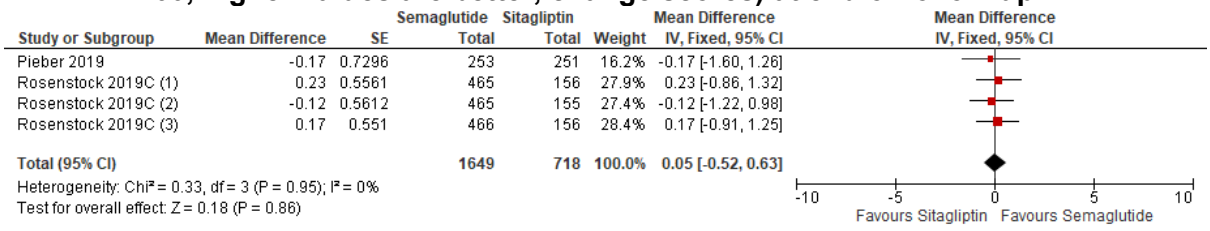


Figure 210: BMI change (kg/m², lower values are better, change scores) at end of follow up



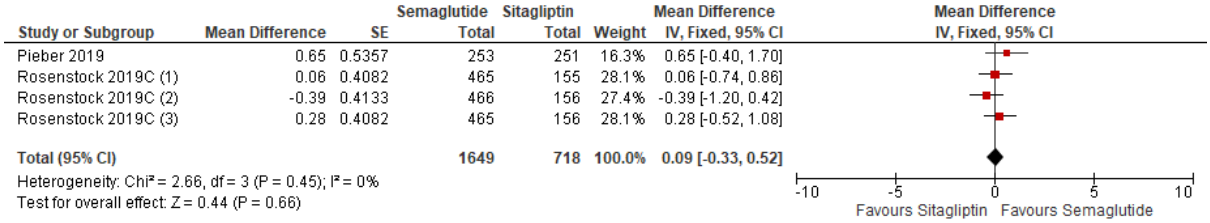
K.1.3.25 Adding semaglutide compared to adding sitagliptin

Figure 211: Health-related quality of life - subscale mental component (SF36 v2, 0-100, higher values are better, change scores) at end of follow-up



Footnotes
(1) 7 mg semaglutide v sitagliptin
(2) 14 mg semaglutide v sitagliptin
(3) 3 mg semaglutide v sitagliptin

Figure 212: Health-related quality of life - subscale physical component (SF36 v2, 0-100, higher values are better, change scores) at end of follow-up



Footnotes
(1) 14 mg semaglutide v sitagliptin
(2) 3 mg semaglutide v sitagliptin
(3) 7 mg semaglutide v sitagliptin

Figure 213: All-cause mortality at end of follow up

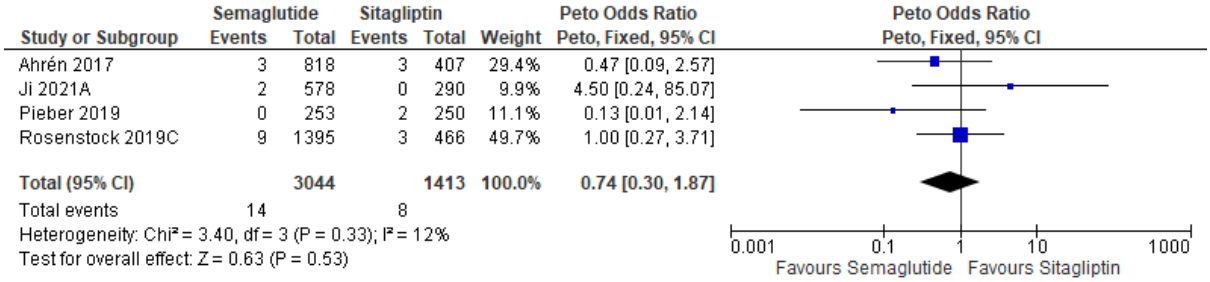


Figure 214: Cardiovascular mortality at end of follow up

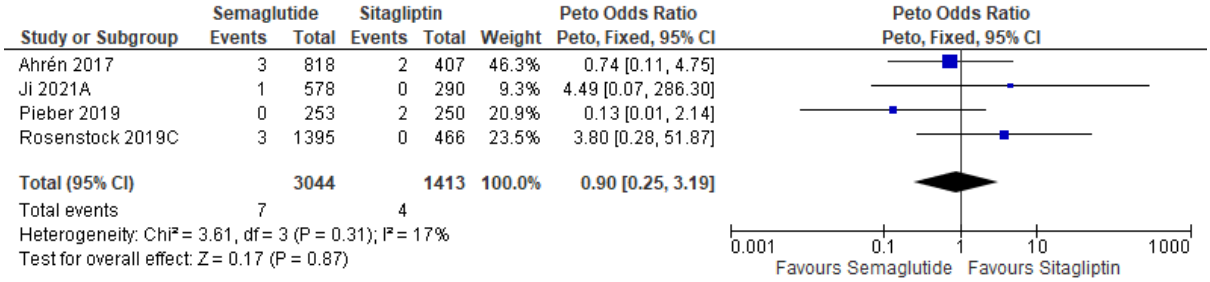


Figure 215: Hospitalisation for heart failure at end of follow up

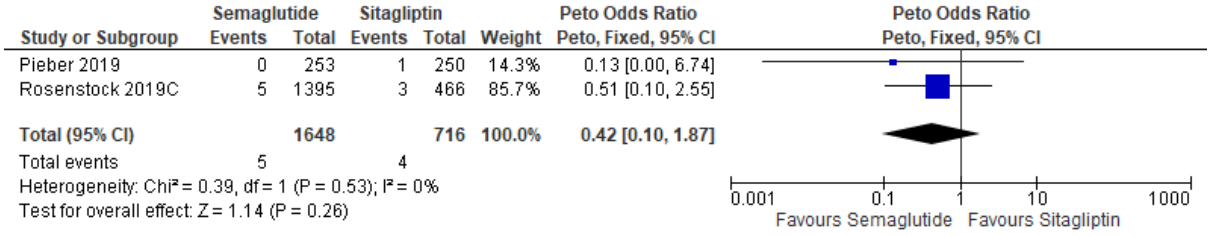


Figure 216: Acute kidney injury at end of follow up

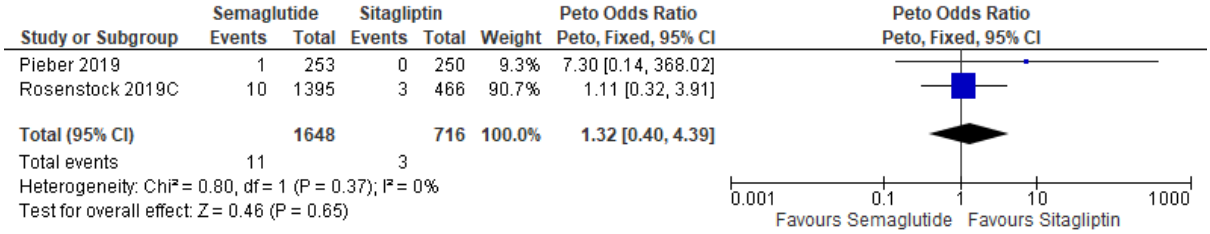


Figure 217: Hypoglycaemia episodes at end of follow up

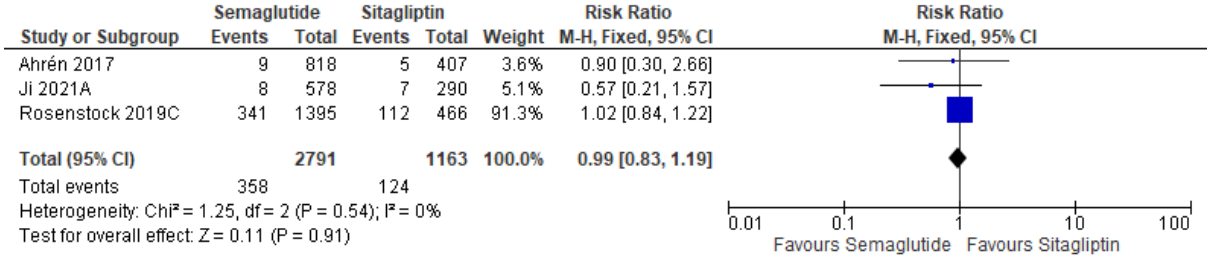


Figure 218: At night hypoglycaemic episodes at end of follow up

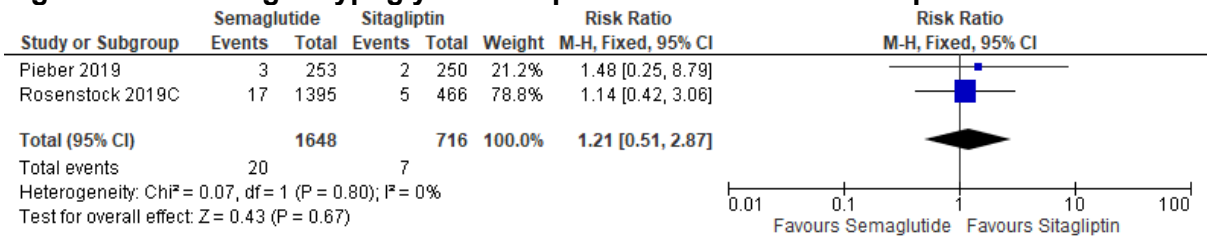


Figure 219: Severe hypoglycaemic episodes at end of follow up

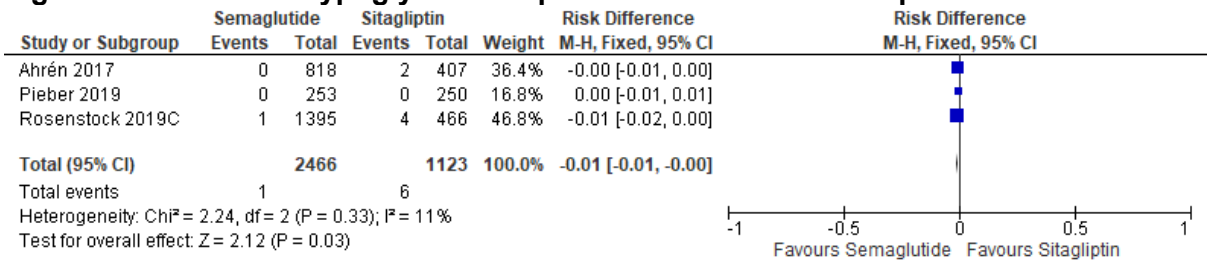
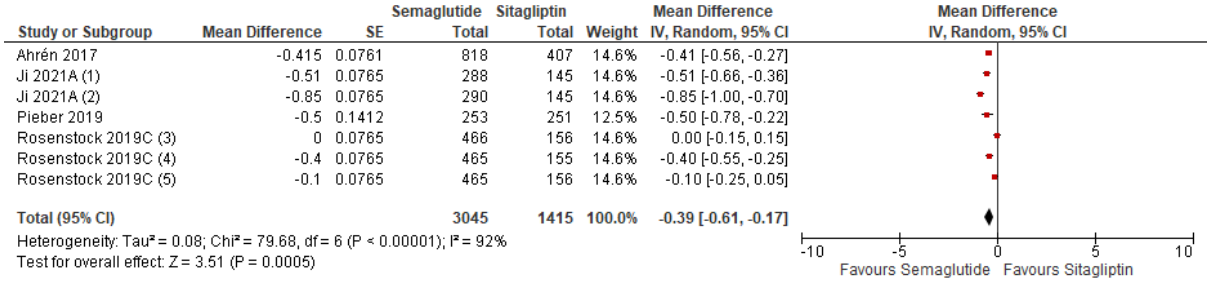


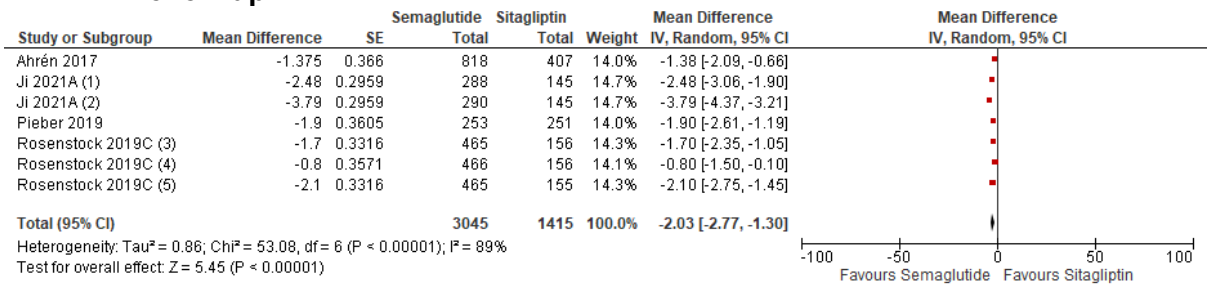
Figure 220: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg semaglutide v sitagliptin
(2) 1.0 mg semaglutide v sitagliptin
(3) 3 mg semaglutide v sitagliptin
(4) 14 mg semaglutide v sitagliptin
(5) 7 mg semaglutide v sitagliptin

Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR subgroup.

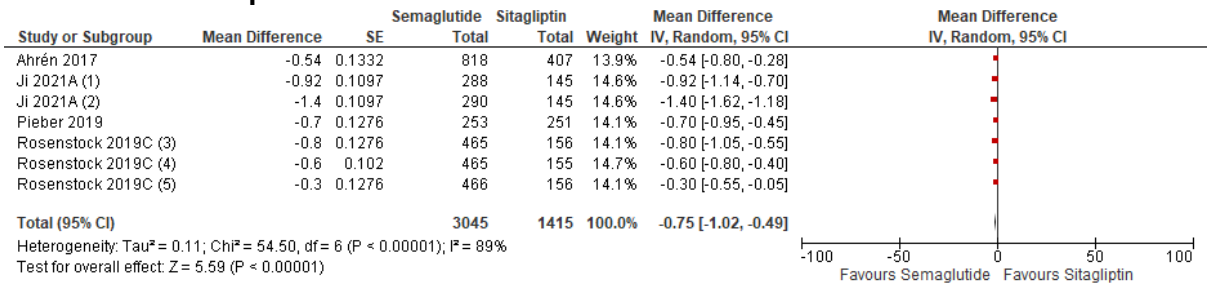
Figure 221: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg semaglutide v sitagliptin
(2) 1.0 mg semaglutide v sitagliptin
(3) 7 mg semaglutide v sitagliptin
(4) 3 mg semaglutide v sitagliptin
(5) 14 mg semaglutide v sitagliptin

Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR subgroup.

Figure 222: BMI change (kg/m^2, lower values are better, change scores) at end of follow up



Footnotes
(1) 0.5 mg v sitagliptin
(2) 1.0 mg semaglutide v sitagliptin
(3) 14 mg semaglutide v sitagliptin
(4) 7 mg semaglutide v sitagliptin
(5) 3 mg semaglutide v sitagliptin

Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR subgroup.

K.1.3.26 Adding subcutaneous semaglutide compared to adding oral semaglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.4 Dual GIP/GLP-1 receptor co-agonists

K.1.4.1 Adding tirzepatide compared to adding placebo

Figure 223: All-cause mortality at end of follow up

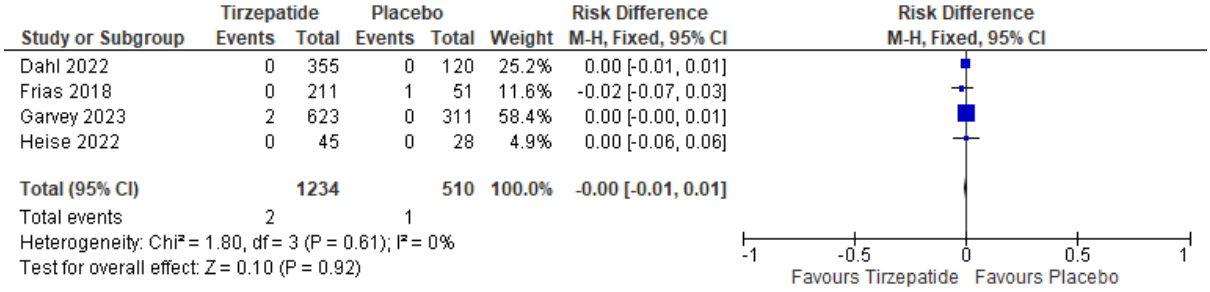


Figure 224: Cardiovascular mortality at end of follow up

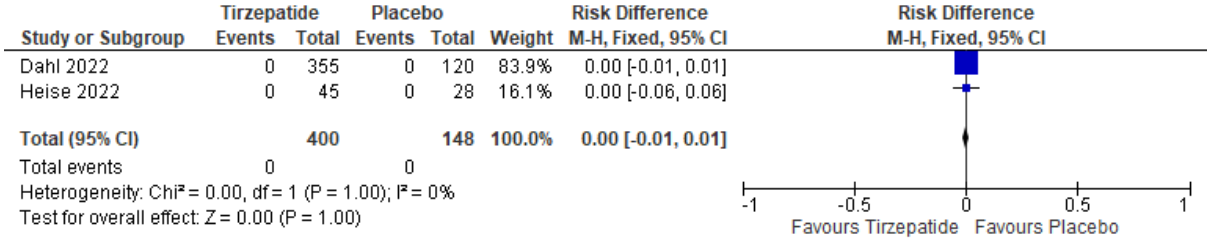
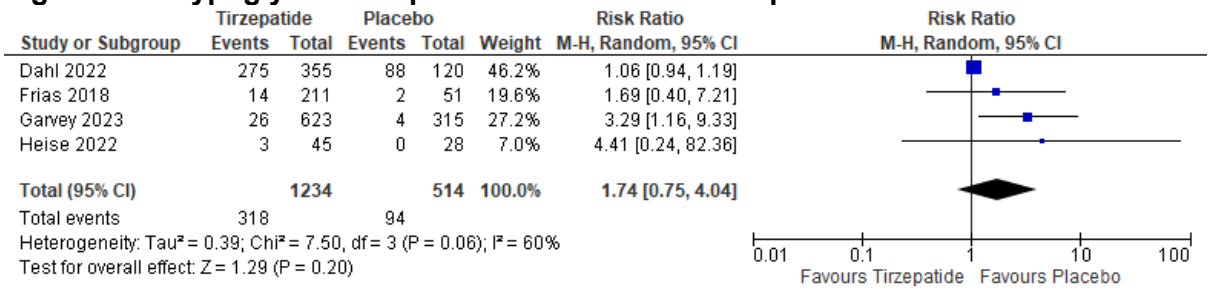


Figure 225: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR, NAFLD, Obesity, and early onset subgroups.

Figure 226: Severe hypoglycaemia episodes at end of follow up

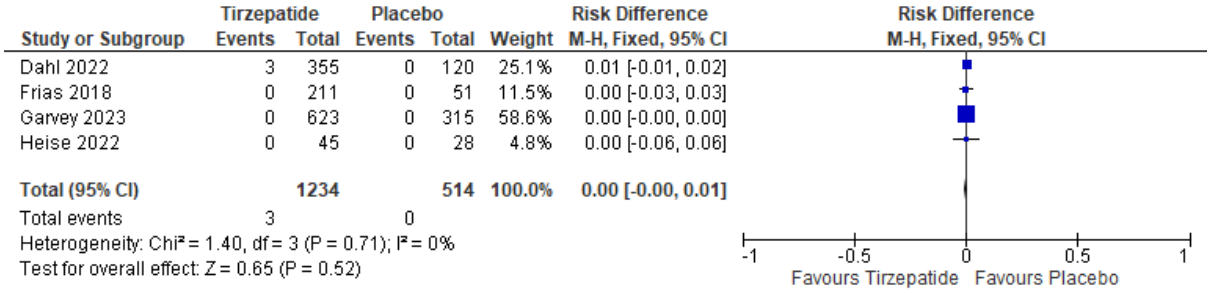


Figure 227: HbA1c change (%, lowr values are better, change scores) at end of follow up

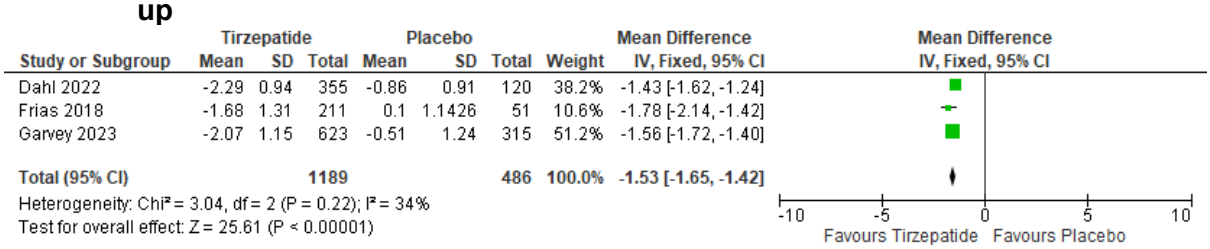
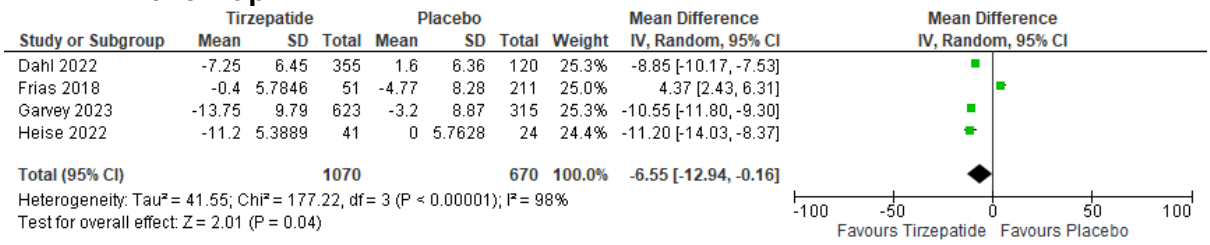
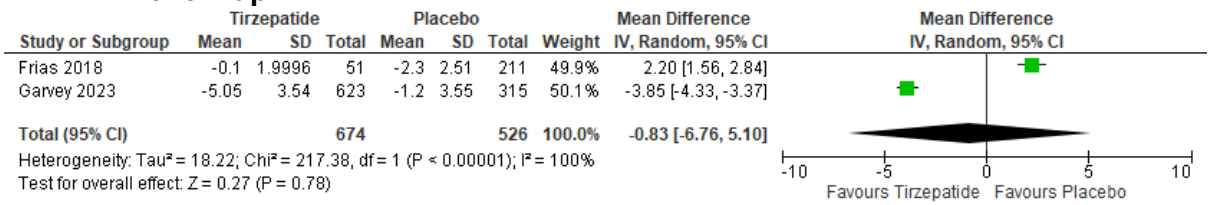


Figure 228: Weight change (kg, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR, NAFLD, Obesity, and early onset subgroups.

Figure 229: BMI change (kg/m^2, lower values are better, change scores) at end of follow-up



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K.1.4.2 Adding tirzepatide compared to adding insulin

Figure 230: All-cause mortality at end of follow up

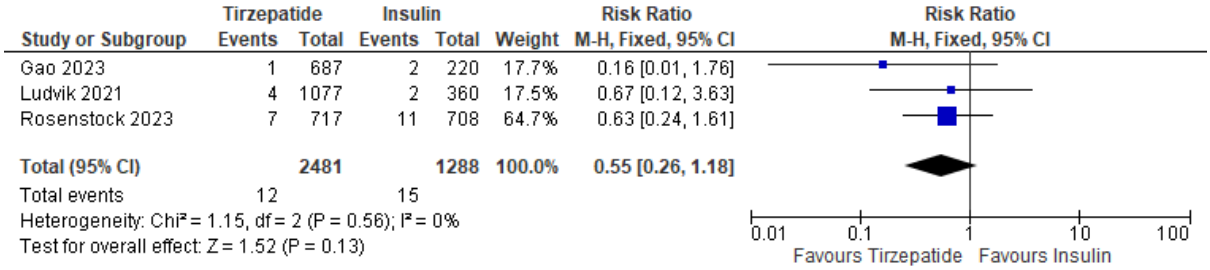


Figure 231: Cardiovascular mortality at end of follow up

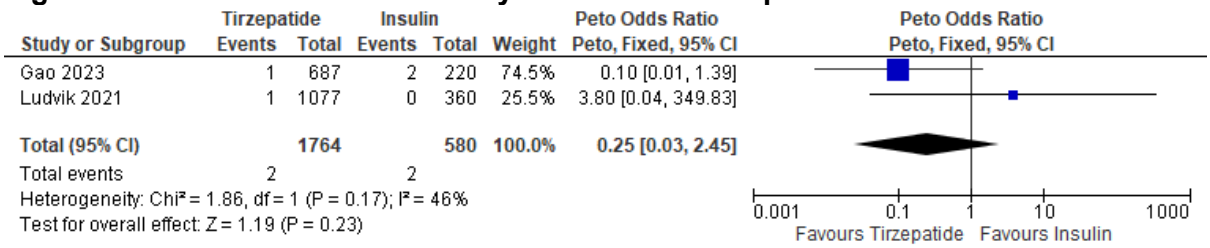


Figure 232: 4-point MACE at end of follow up

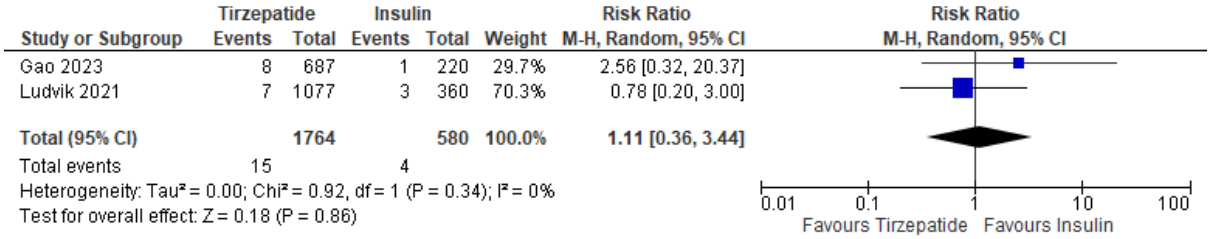


Figure 233: Hypoglycaemia episodes at end of follow up

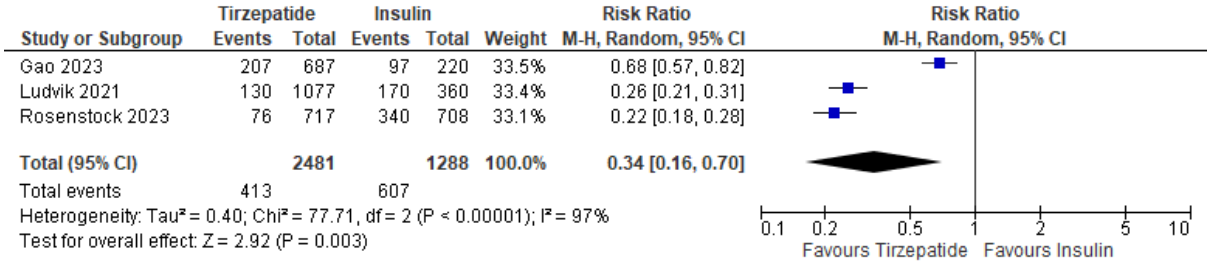


Figure 234: Severe hypoglycaemic episodes at end of follow up

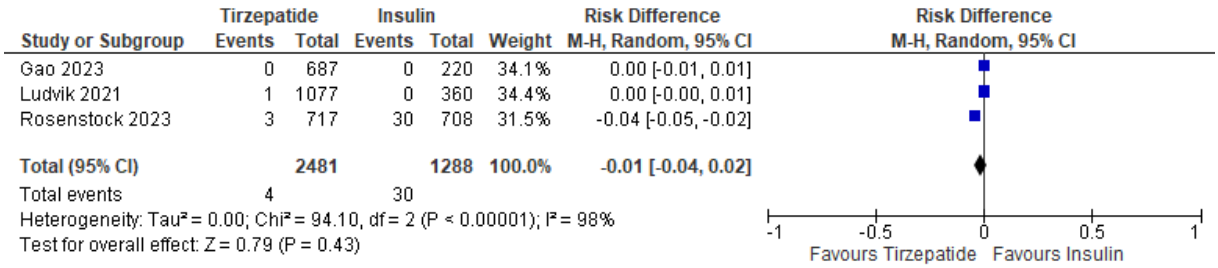


Figure 235: HbA1c change (%, lower values are better, change scores) at end of follow up

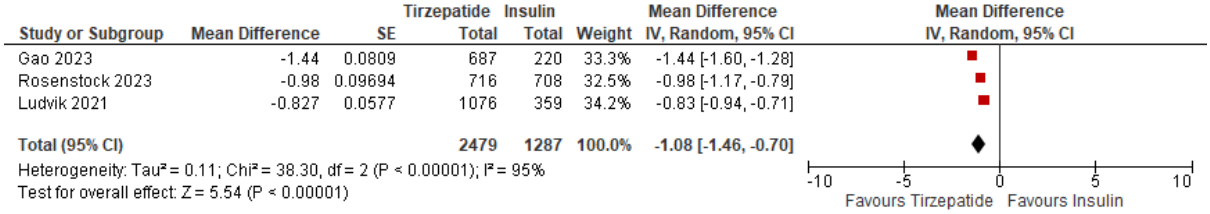
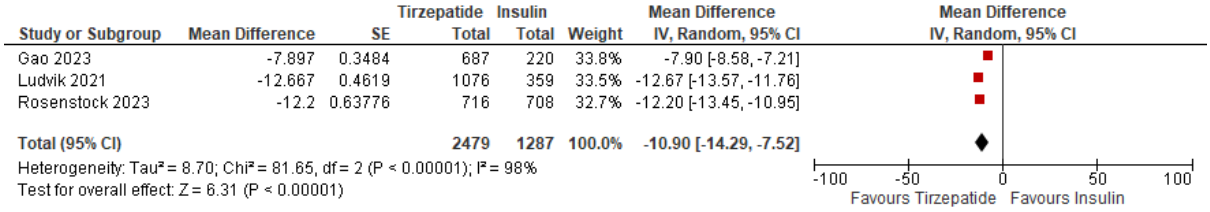


Figure 236: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.4.3 Adding tirzepatide compared to adding dulaglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.4.4 Adding tirzepatide compared to adding semaglutide

Figure 237: All-cause mortality at end of follow up

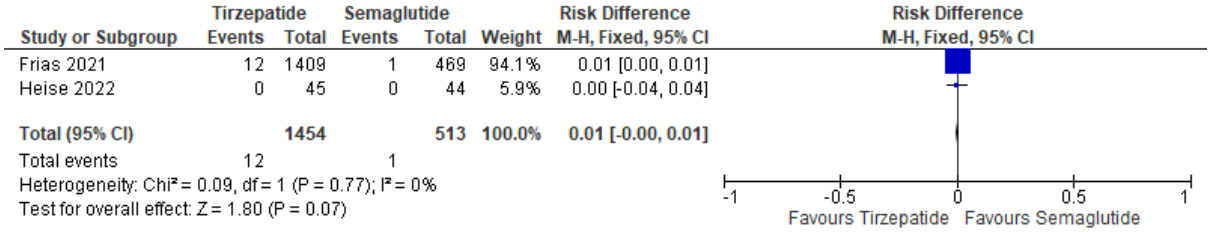


Figure 238: Cardiovascular mortality at end of follow up

Study or Subgroup	Tirzepatide Events	Tirzepatide Total	Semaglutide Events	Semaglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Frias 2021	5	1410	0	469	94.1%	0.00 [-0.00, 0.01]
Heise 2022	0	45	0	44	5.9%	0.00 [-0.04, 0.04]
Total (95% CI)		**1455**		**513**	**100.0%**	**0.00 [-0.00, 0.01]**
Total events	5		0			

Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z = 1.34 (P = 0.18)

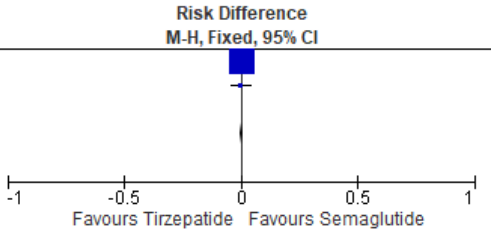


Figure 239: Hypoglycaemia episodes at end of follow up

Study or Subgroup	Tirzepatide Events	Tirzepatide Total	Semaglutide Events	Semaglutide Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Frias 2021	12	1409	2	469	73.0%	1.78 [0.53, 5.98]
Heise 2022	3	45	1	44	27.0%	2.75 [0.37, 20.22]
Total (95% CI)		**1454**		**513**	**100.0%**	**2.00 [0.71, 5.64]**
Total events	15		3			

Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.31 (P = 0.19)

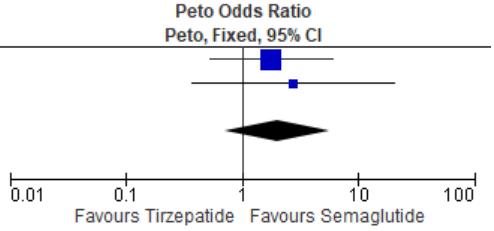


Figure 240: Severe hypoglycaemic episodes at end of follow up

Study or Subgroup	Tirzepatide Events	Tirzepatide Total	Semaglutide Events	Semaglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Frias 2021	2	1409	0	469	94.1%	0.00 [-0.00, 0.01]
Heise 2022	0	45	0	44	5.9%	0.00 [-0.04, 0.04]
Total (95% CI)		**1454**		**513**	**100.0%**	**0.00 [-0.00, 0.01]**
Total events	2		0			

Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)

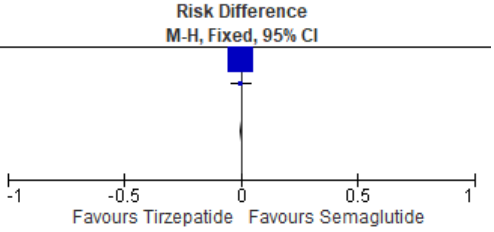
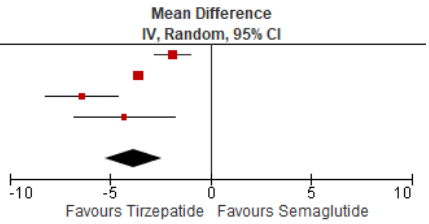


Figure 241: Weight change (kg, lower values are better, mean difference) at end of follow up

Study or Subgroup	Mean Difference	SE	Tirzepatide Total	Semaglutide Total	Weight	Mean Difference IV, Random, 95% CI
Frias 2021 (1)	-1.9	0.4592	470	156	29.2%	-1.90 [-2.80, -1.00]
Frias 2021 (2)	-3.6	0.0612	469	156	33.0%	-3.60 [-3.72, -3.48]
Frias 2021 (3)	-6.4	0.9184	469	156	21.5%	-6.40 [-8.20, -4.60]
Heise 2022	-4.3	1.2728	41	43	16.3%	-4.30 [-6.79, -1.81]
Total (95% CI)			**1449**	**511**	**100.0%**	**-3.82 [-5.24, -2.41]**

Heterogeneity: Tau² = 1.58; Chi² = 23.24, df = 3 (P < 0.0001); I² = 87%
Test for overall effect: Z = 5.29 (P < 0.00001)



Footnotes
(1) Tirzepatide 5 mg daily
(2) Tirzepatide 10 mg daily
(3) Tirzepatide 15 mg daily

Note: Heterogeneity for this outcome was not explored due to the small number of studies (2 studies, 3 different dose comparisons for 1 study).

K.1.5 SGLT2 inhibitors

K.1.5.1 Adding canagliflozin compared to adding placebo

Figure 242: All-cause mortality at end of follow up

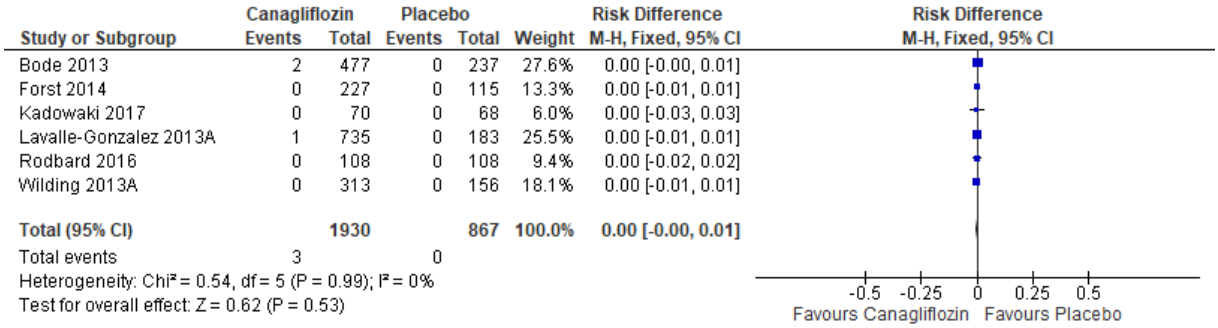


Figure 243: Cardiovascular mortality at end of follow up

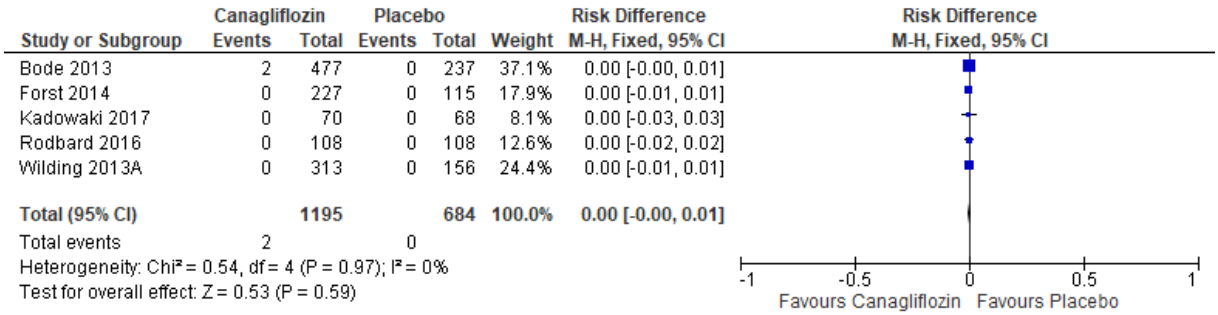


Figure 244: Diabetic ketoacidosis at end of follow up

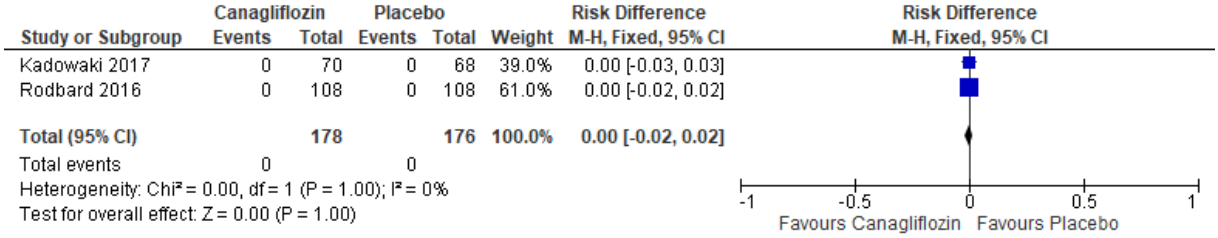
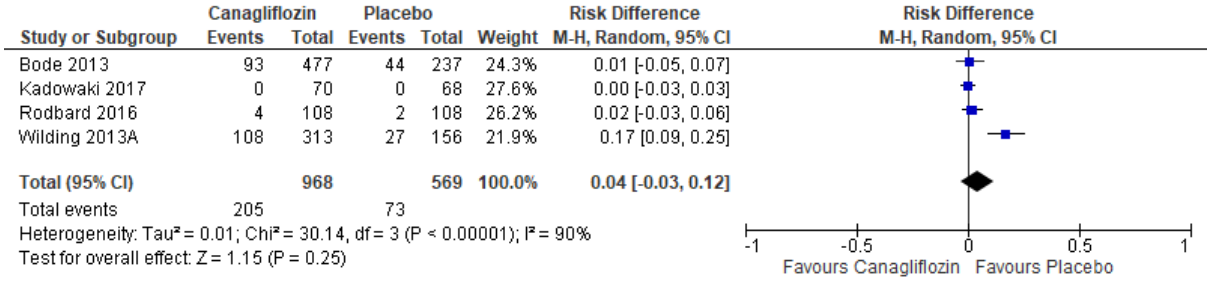


Figure 245: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR subgroup.

Figure 246: Severe hypoglycaemia at end of follow up

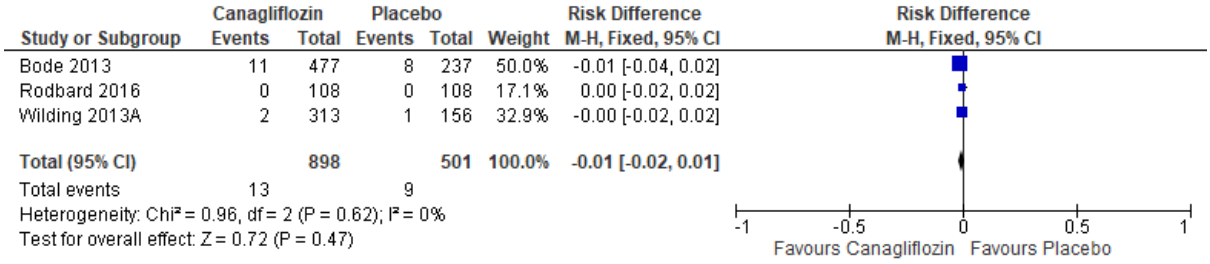
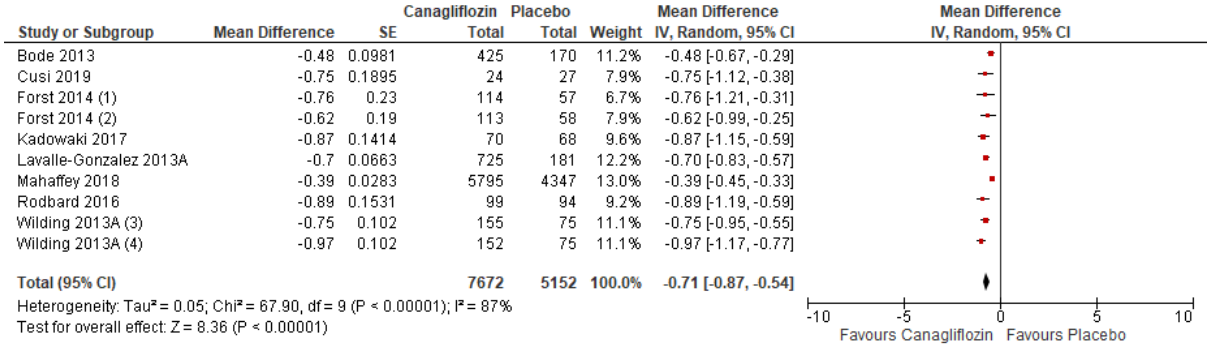


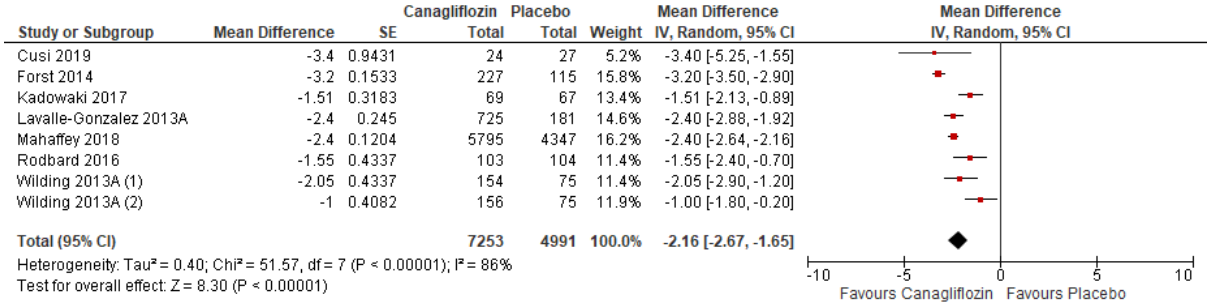
Figure 247: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) 300 mg canagliflozin daily. Number of participants in placebo arm has been halved.
(2) 100mg canagliflozin daily. Number of participants in placebo arm has been halved.
(3) 100mg canagliflozin daily. Number of participants in placebo arm has been halved.
(4) 300mg canagliflozin daily. Number of participants in placebo arm has been halved.

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, and NAFLD subgroups.

Figure 248: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 300 mg canagliflozin daily. Number of participants in placebo arm has been halved.
(2) 100mg canagliflozin daily. Number of participants in placebo arm has been halved.

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, and NAFLD subgroups.

K.1.5.2 Adding canagliflozin compared to adding semaglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.3 Adding canagliflozin compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.4 Adding dapagliflozin compared to adding placebo

Figure 249: Health-related quality of life - overall (EQ-5D, -0.59-1.0, higher values are better, change scores) at end of follow up

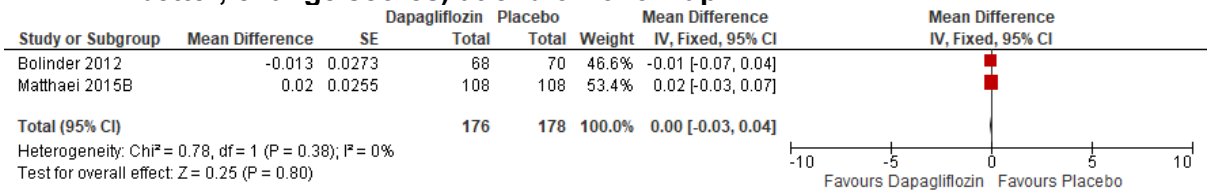


Figure 250: All-cause mortality at end of follow up

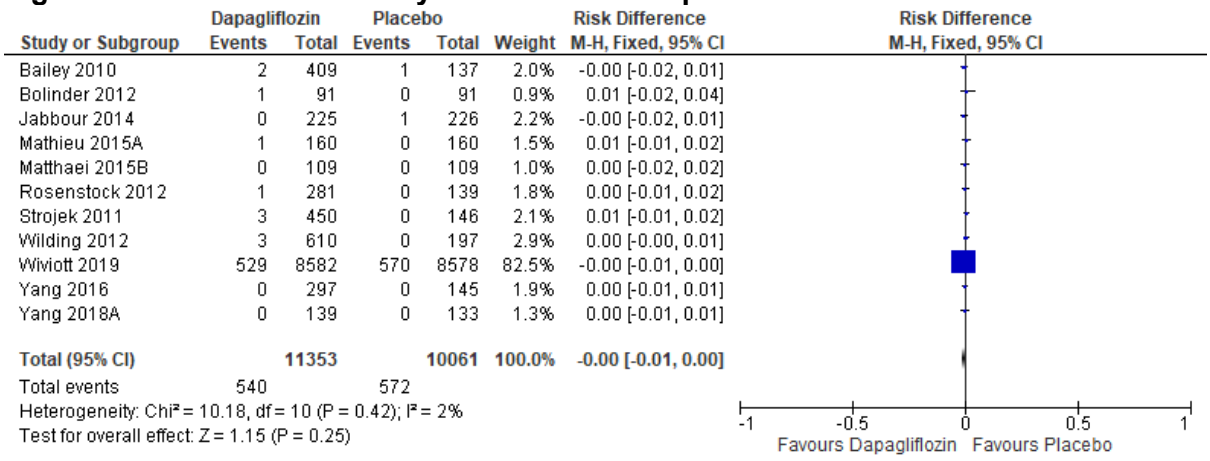


Figure 251: Cardiovascular mortality at end of follow up

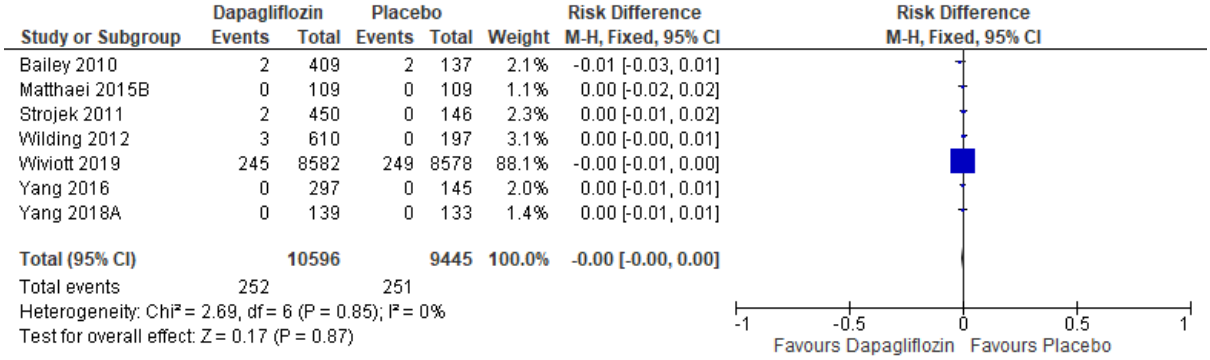


Figure 252: Non-fatal stroke at end of follow up

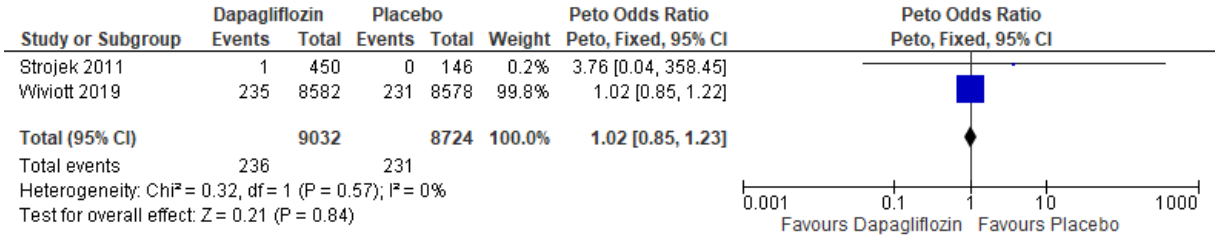


Figure 253: Persistent signs of worsening kidney disease at end of follow up

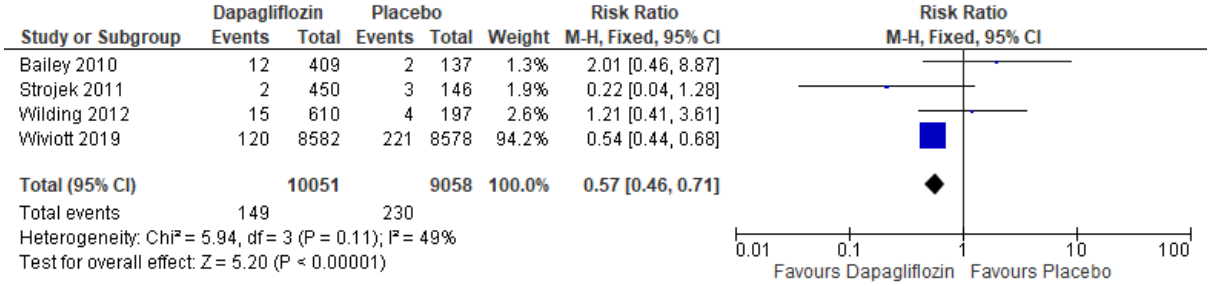


Figure 254: Development of end stage kidney disease at end of follow up

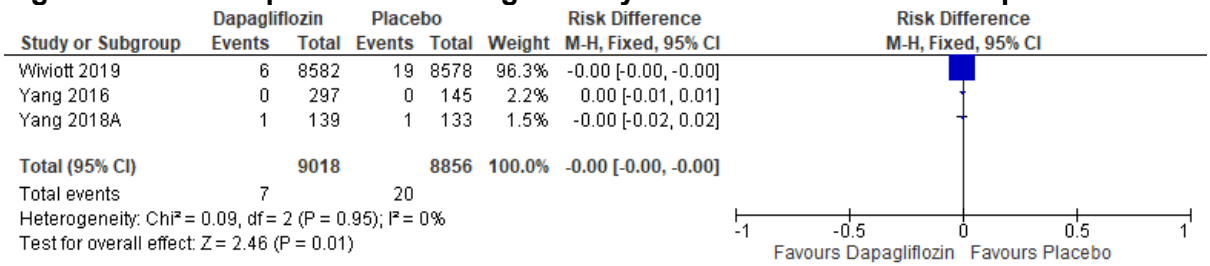


Figure 255: Diabetic ketoacidosis at end of follow up

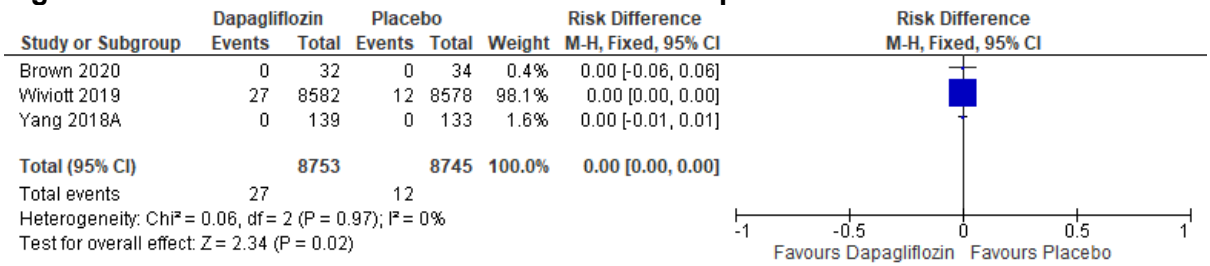
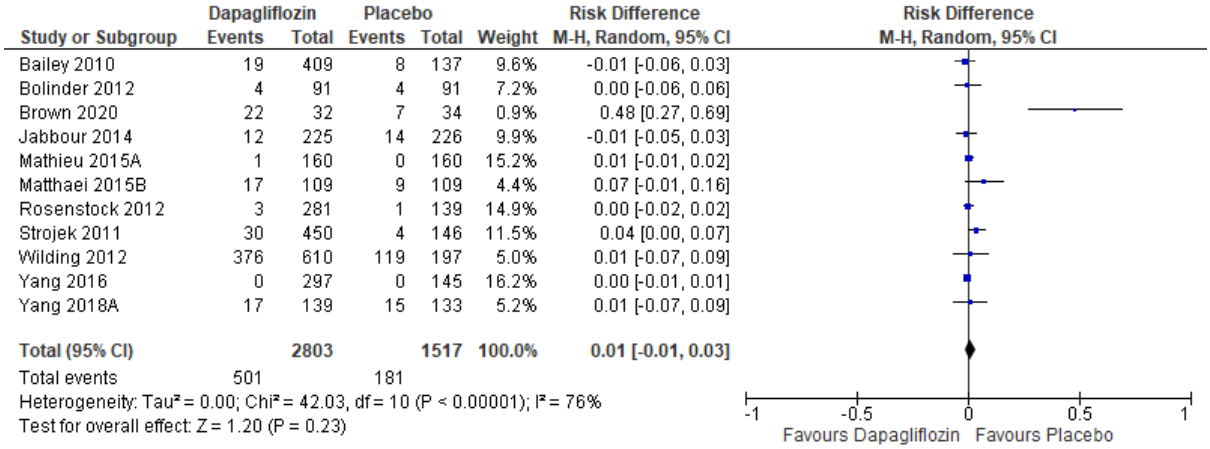


Figure 256: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, NAFLD, and obesity subgroups.

Figure 257: Severe hypoglycaemic episodes at end of follow up

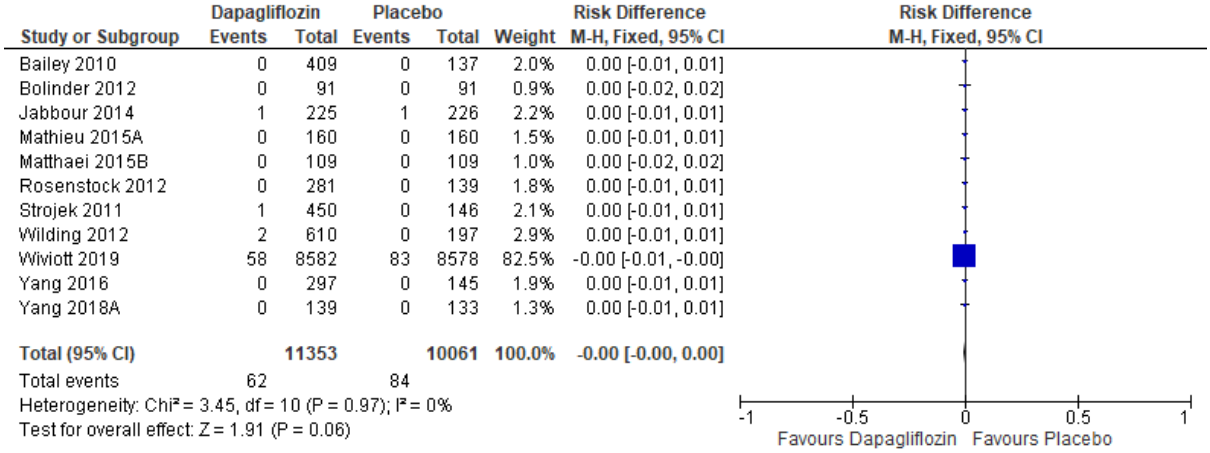
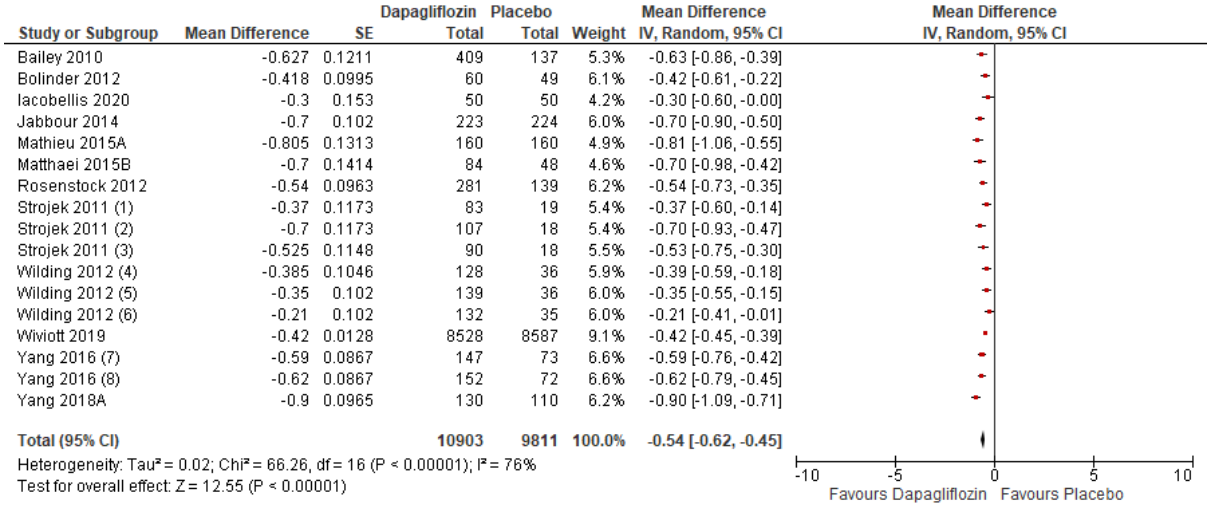


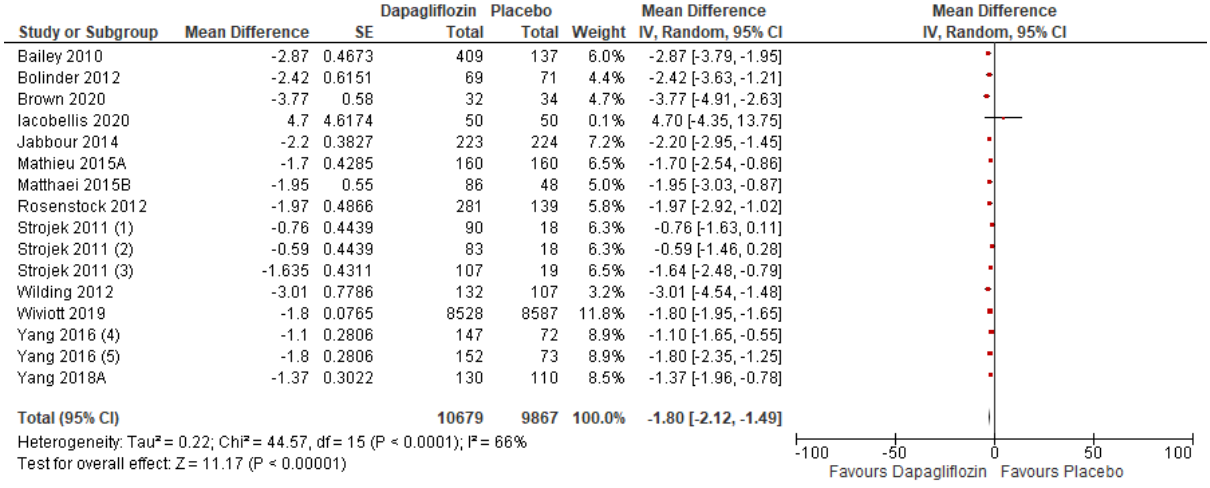
Figure 258: HbA1c change (%, lower values are better, change scores) at end of follow up



Footnotes
(1) 2.5 mg dapagliflozin daily. Number of participants for placebo arm has been divided by 3.
(2) 10 mg dapagliflozin daily. See above.
(3) 5 mg dapagliflozin daily. See above.
(4) 5/10 mg dapagliflozin daily. Number of participants for placebo arm has been divided by 3.
(5) 10 mg dapagliflozin daily. Number of participants for placebo arm has been divided by 3
(6) 2.5 mg dapagliflozin daily. Number of participants for placebo arm has been divided by 3.
(7) 5 mg dapagliflozin daily. See above.
(8) 10 mg dapagliflozin daily. Number of participants for placebo arm is halved.

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by ACR, eGFR, NAFLD, and obesity subgroups.

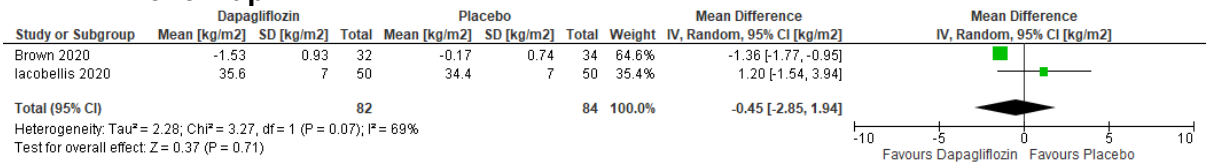
Figure 259: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 5 mg dapagliflozin daily. See above.
(2) 2.5 mg dapagliflozin daily. See above.
(3) 10mg dapagliflozin daily. Number of participants for placebo arm has been divided by 3.
(4) 5mg dapagliflozin daily. Number of participants for placebo arm is halved.
(5) 10mg dapagliflozin daily. Number of participants for placebo arm is halved.

Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by ACR, eGFR, NAFLD, and Obesity subgroups.

Figure 260: BMI change (kg/m^2, lower values are better, change scores) at end of follow up



K.1.5.5 Adding dapagliflozin compared to adding exenatide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.6 Adding dapagliflozin compared to adding liraglutide

Figure 261: Severe hypoglycaemic episodes at end of follow up

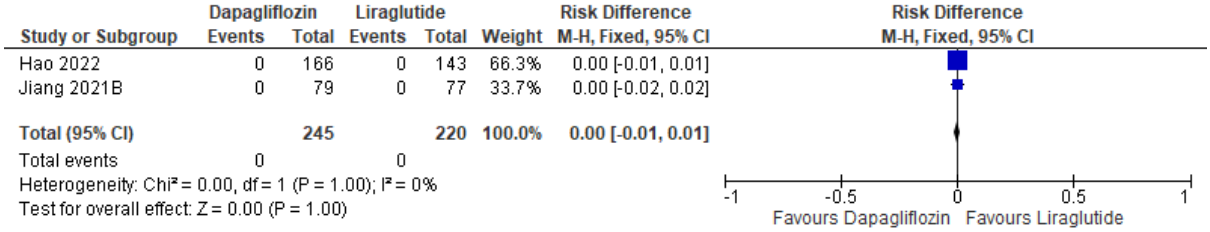
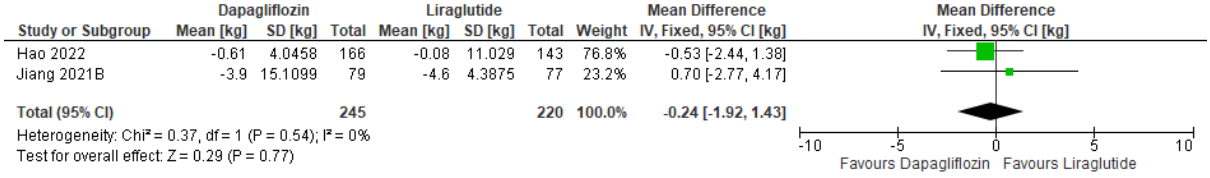


Figure 262: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.5.7 Adding dapagliflozin compared to adding saxagliptin

Figure 263: All-cause mortality at end of follow up

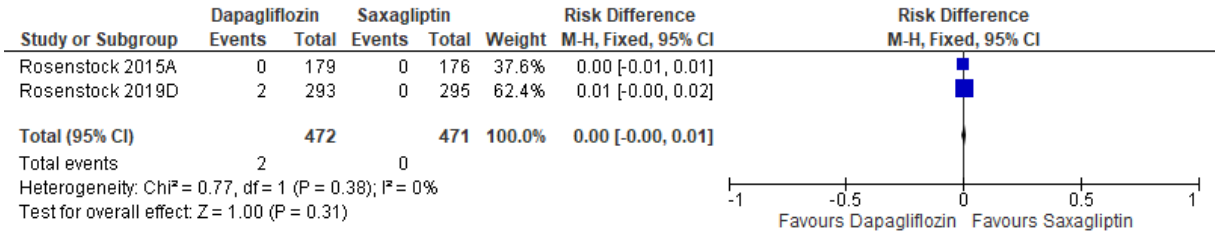


Figure 264: Cardiovascular mortality at end of follow up

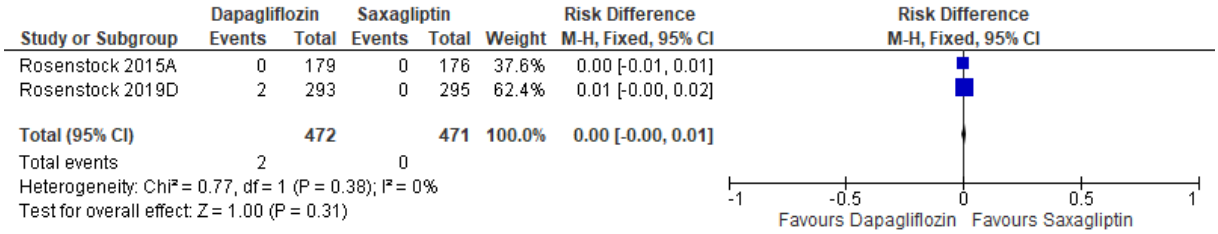


Figure 265: Hypoglycaemia episodes at end of follow up

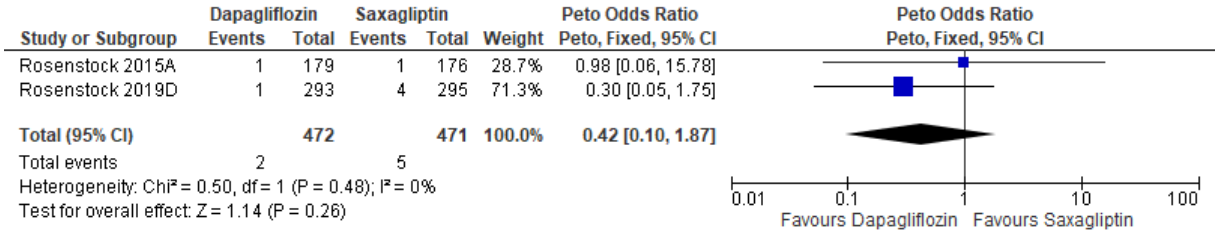


Figure 266: Severe hypoglycaemic episodes at end of follow up

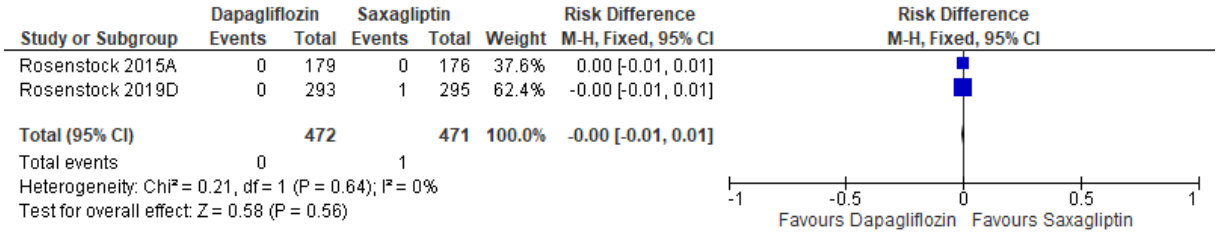
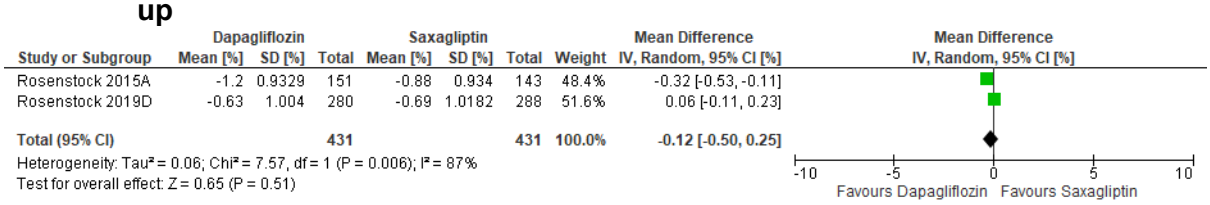


Figure 267: HbA1c change (%, lower values are better, change scores) at end of follow up



K.1.5.8 Adding dapagliflozin compared to adding sitagliptin

Figure 268: Hypoglycaemia episodes at end of follow up

Figure 269: Severe hypoglycaemic episodes at end of follow up

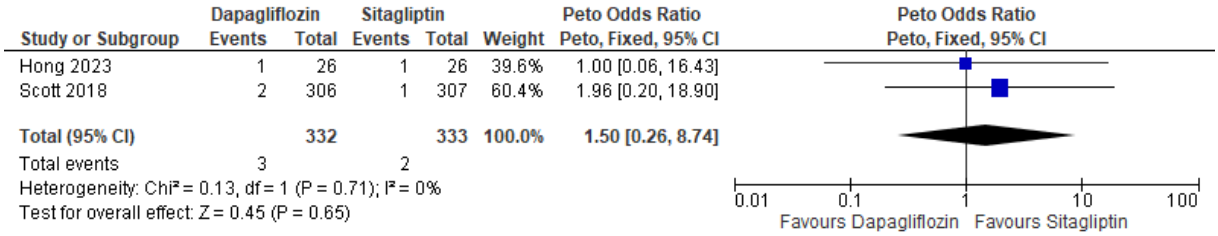
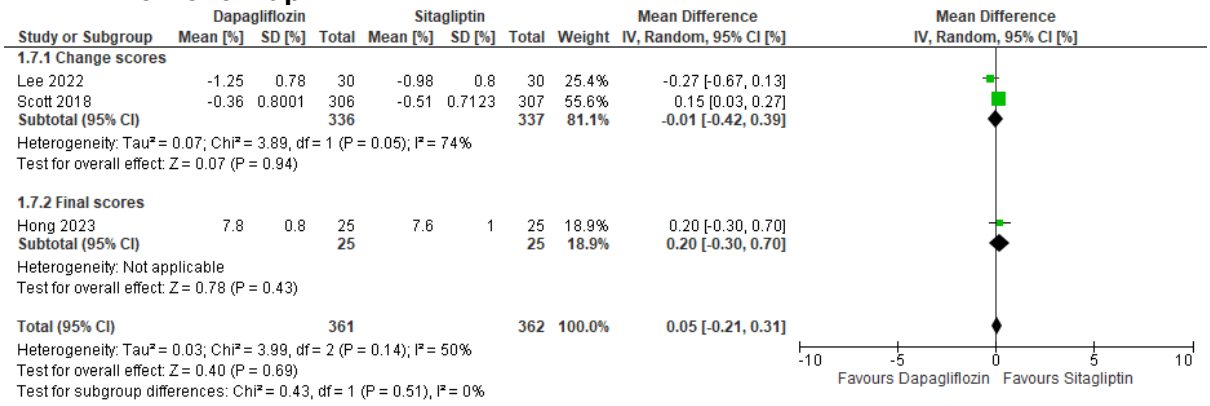


Figure 270: HbA1c change (%, lower values are better, change and final scores) at end of follow up



K.1.5.9 Adding empagliflozin compared to adding placebo

Figure 271: All-cause mortality at end of follow up

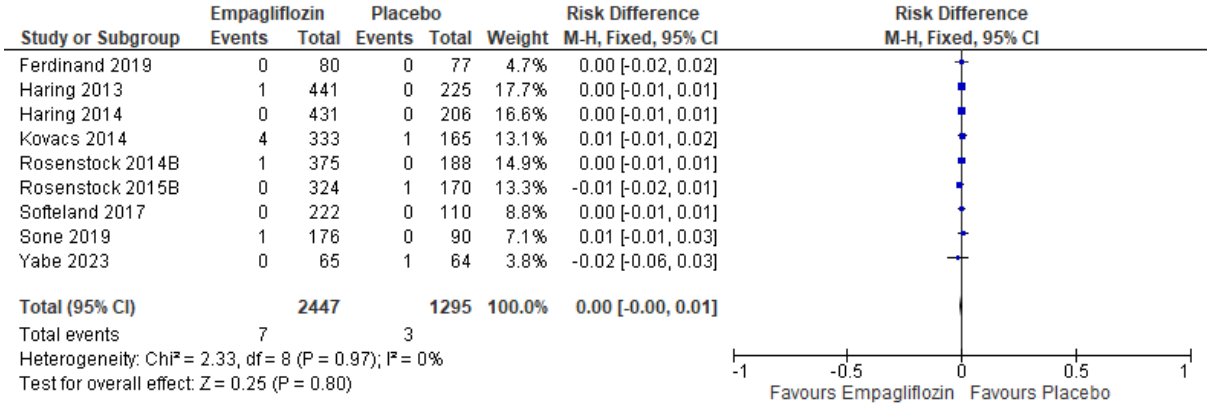


Figure 272: Cardiovascular mortality at end of follow up

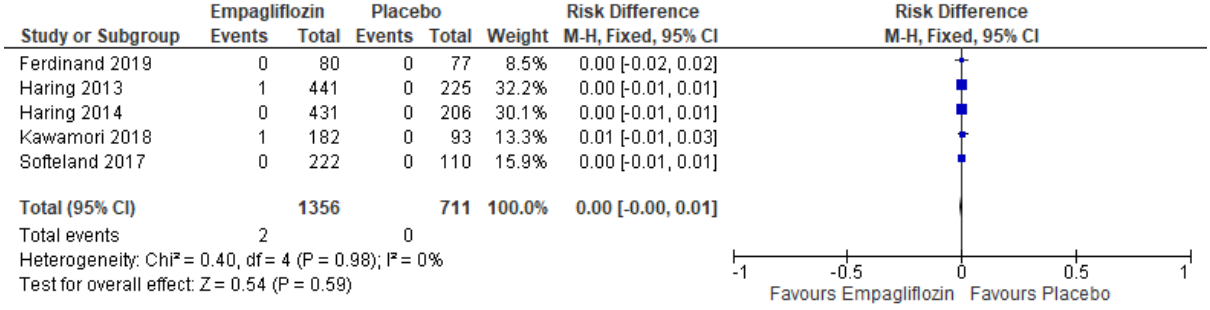


Figure 273: Acute kidney injury at end of follow up

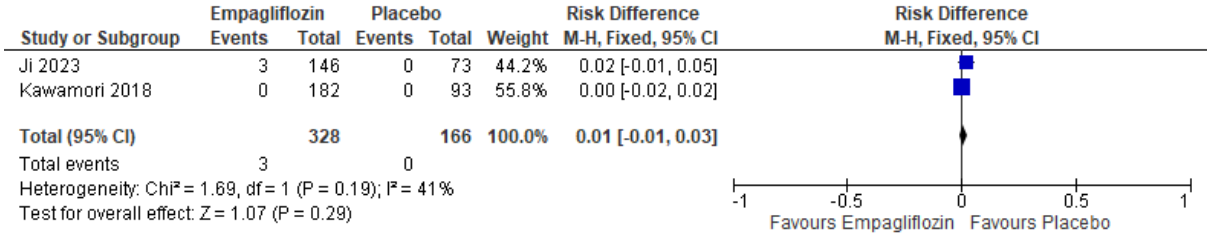


Figure 274: Persistent signs of worsening kidney disease at end of follow up

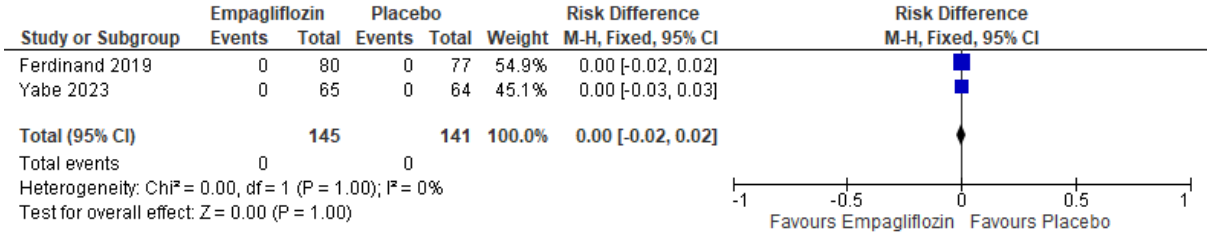


Figure 275: Diabetic ketoacidosis at end of follow up

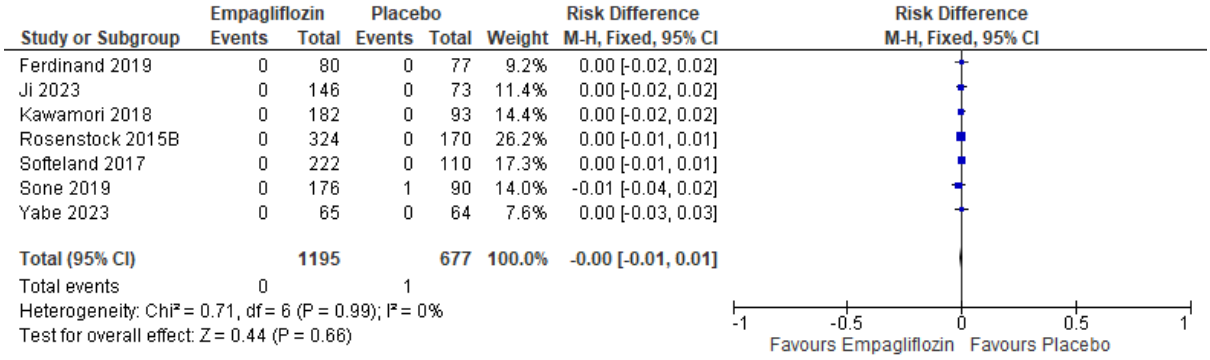


Figure 276: Hypoglycaemia episodes at end of follow up

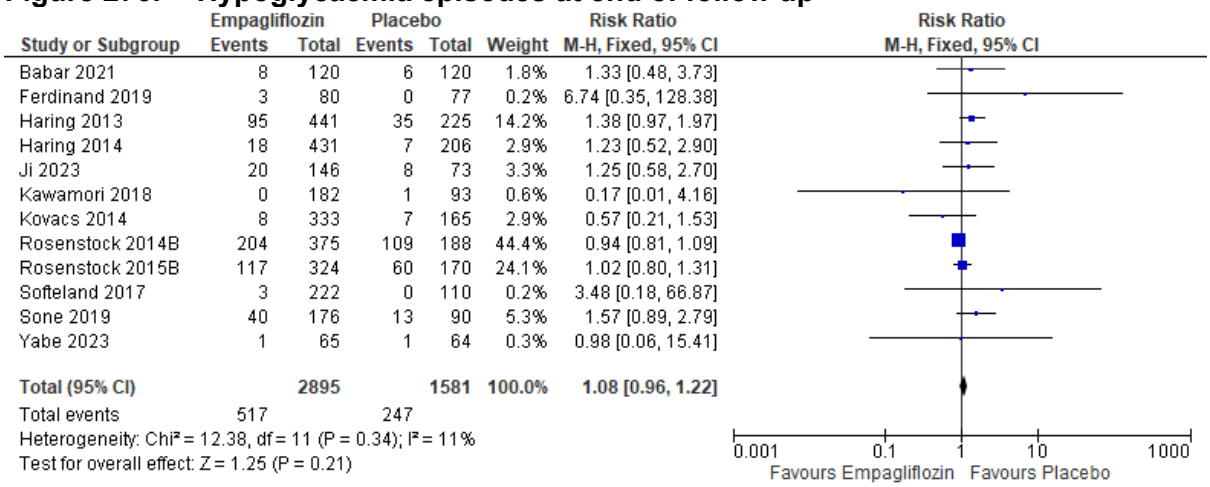


Figure 277: Severe hypoglycaemic episodes at end of follow up

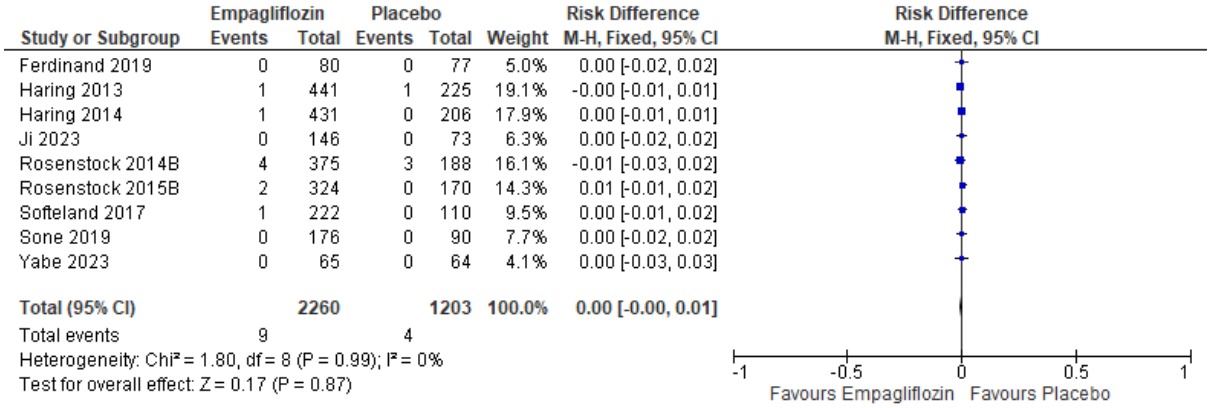
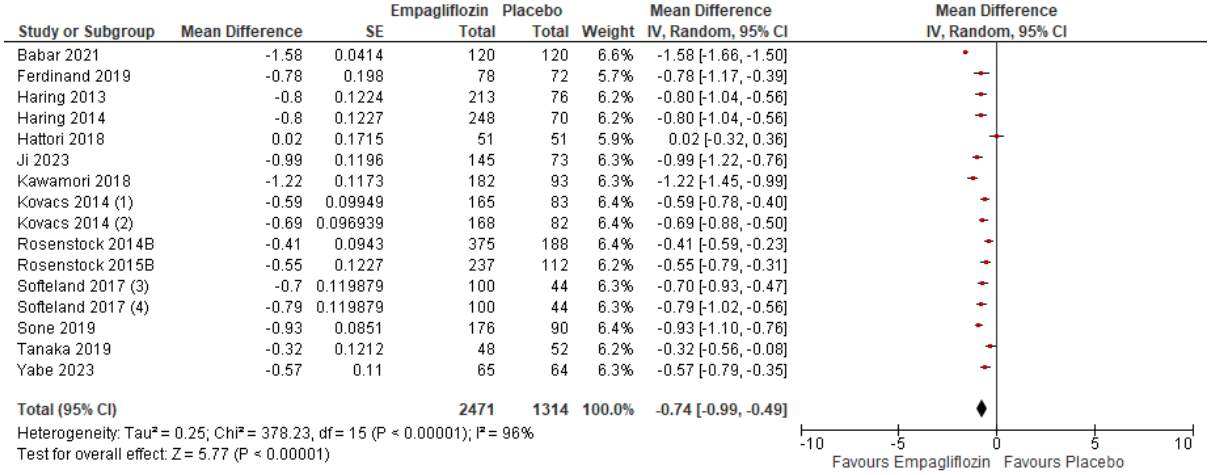


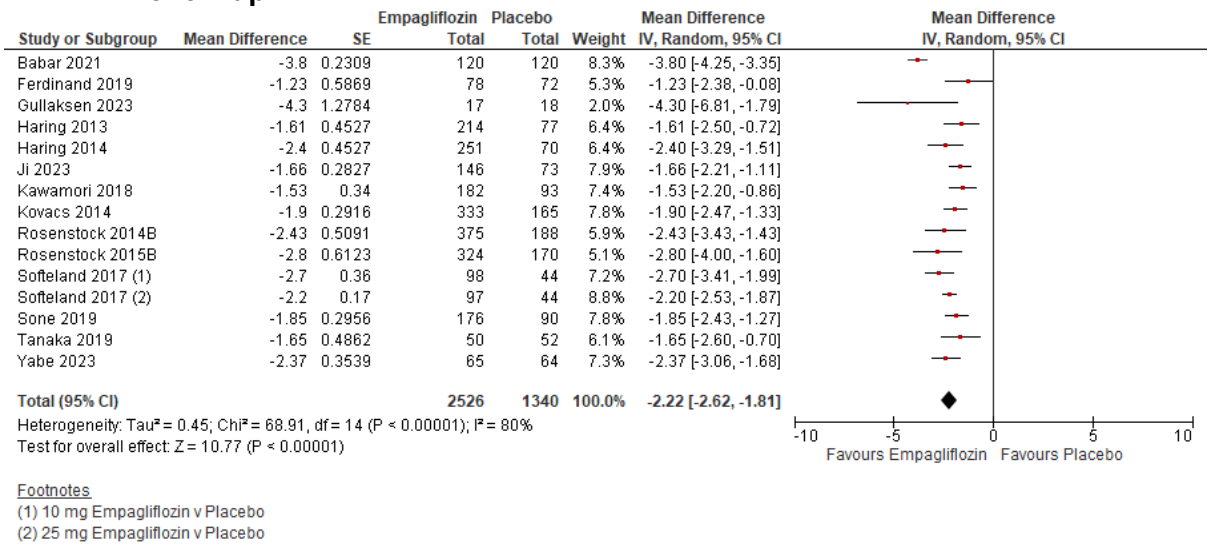
Figure 278: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



Footnotes
(1) 10 mg Empagliflozin v Placebo
(2) 25 mg Empagliflozin v Placebo
(3) 25 mg Empagliflozin v Placebo
(4) 10 mg Empagliflozin v Placebo

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR and obesity subgroups.

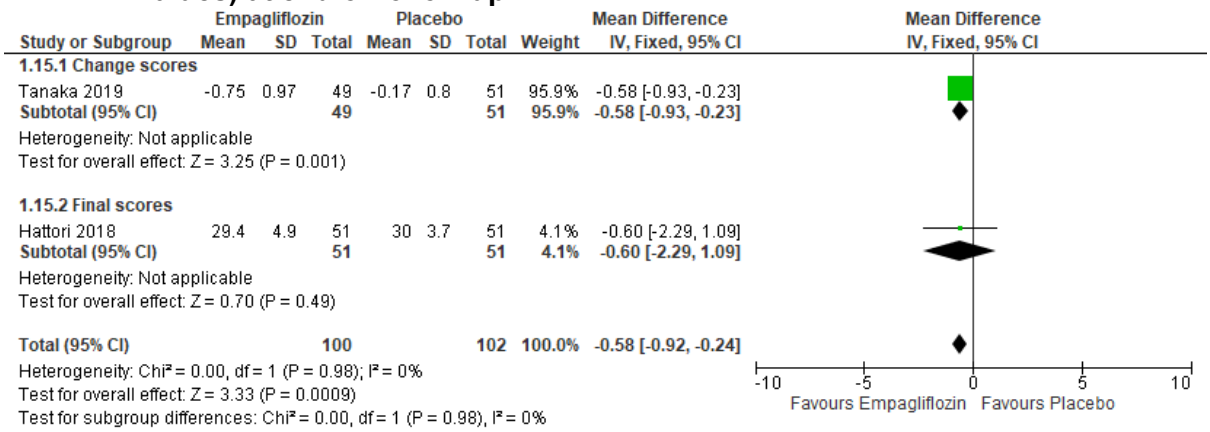
Figure 279: Weight change (kg, lower values are better, change scores) at end of follow up



Footnotes
(1) 10 mg Empagliflozin v Placebo
(2) 25 mg Empagliflozin v Placebo

Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR and obesity subgroups.

Figure 280: BMI change (kg/m², lower values are better, change scores and final values) at end of follow up



K.1.5.10 Adding empagliflozin compared to adding insulin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.11 Adding empagliflozin compared to adding linagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.12 Adding empagliflozin compared to adding liraglutide

Figure 281: HbA1c change (%, lower scores are better, change scores and final values) at end of follow up

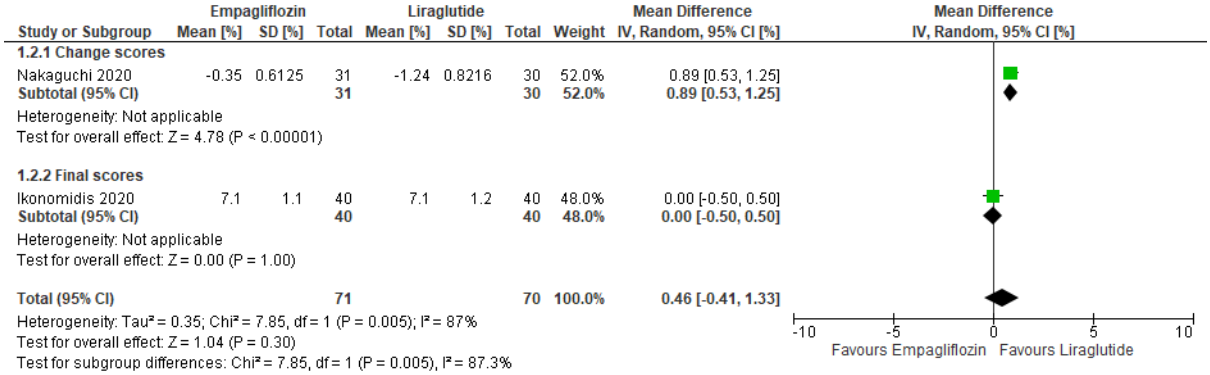


Figure 282: Weight change (kg, lower scores are better, change scores and final values) at end of follow up

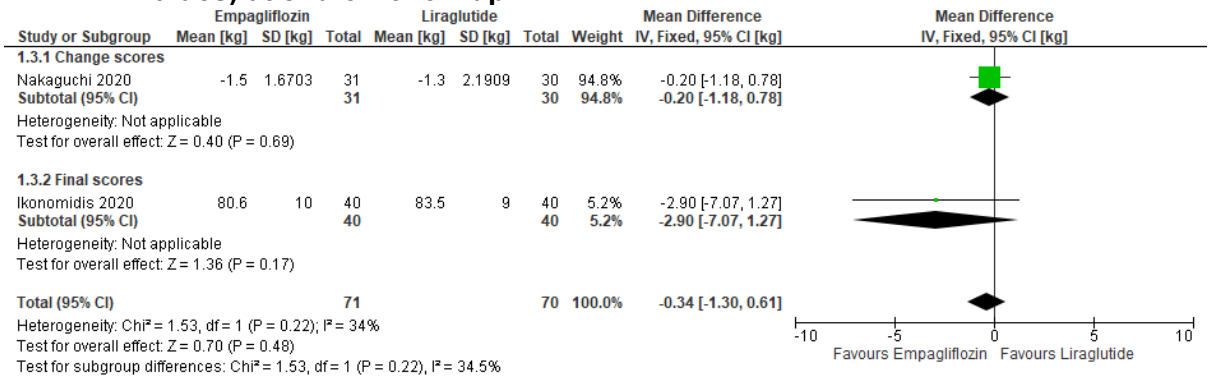
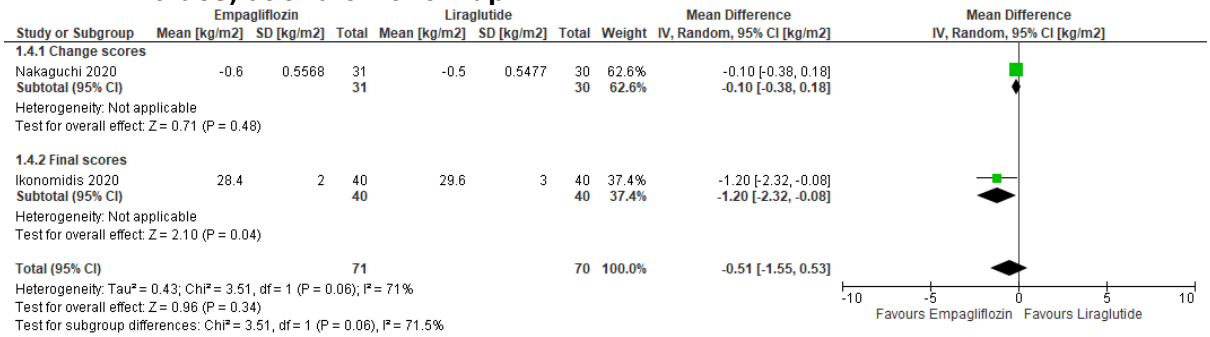


Figure 283: BMI change (kg/m^2, lower scores are better, change scores and final values) at end of follow up



K.1.5.13 Adding empagliflozin compared to adding semaglutide

There are no forest plots for this comparison (all outcomes include a single study)

K.1.5.14 Adding empagliflozin compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.15 Adding empagliflozin compared to adding vildagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.5.16 Adding ertugliflozin compared to adding placebo

Figure 284: All-cause mortality at end of follow up

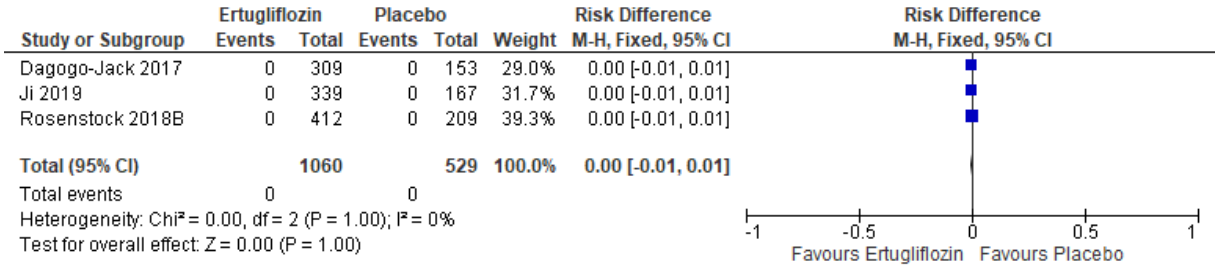


Figure 285: Cardiovascular mortality at end of follow up

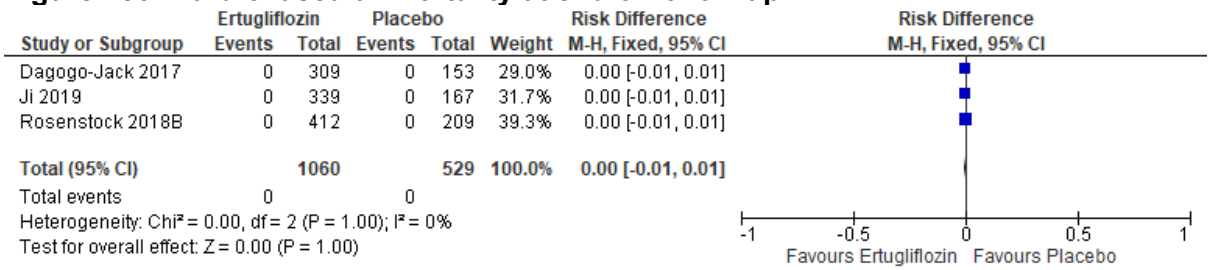


Figure 286: Hypoglycaemia episodes at end of follow up

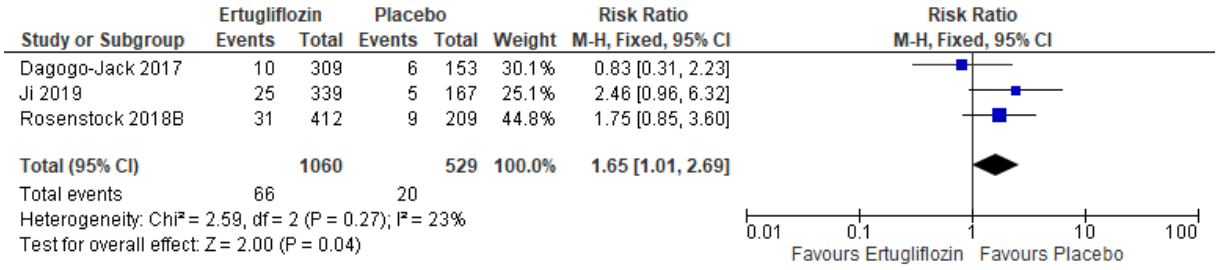


Figure 287: HbA1c change (%, lower scores are better, change scores) at end of follow up

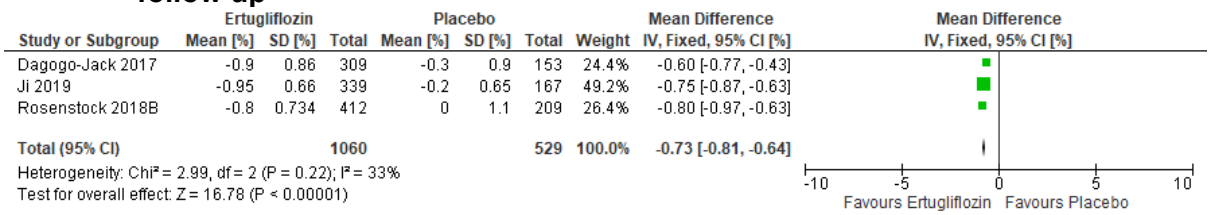
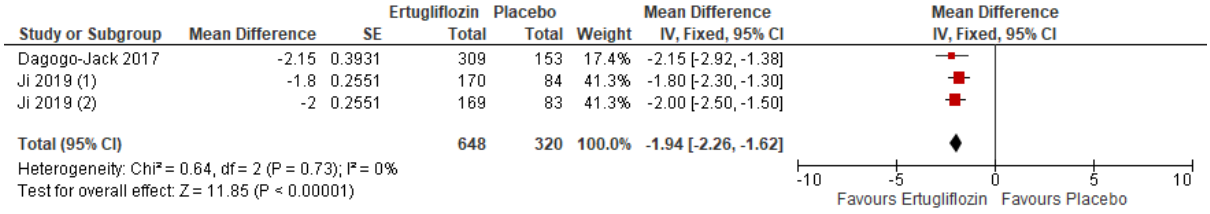


Figure 288: Weight change (kg, lower scores are better, change scores) at end of follow up



Footnotes
(1) 5mg ertugliflozin daily. Number of participants for placebo arm has been halved.
(2) 15mg ertugliflozin daily. Number of participants for placebo arm has been halved

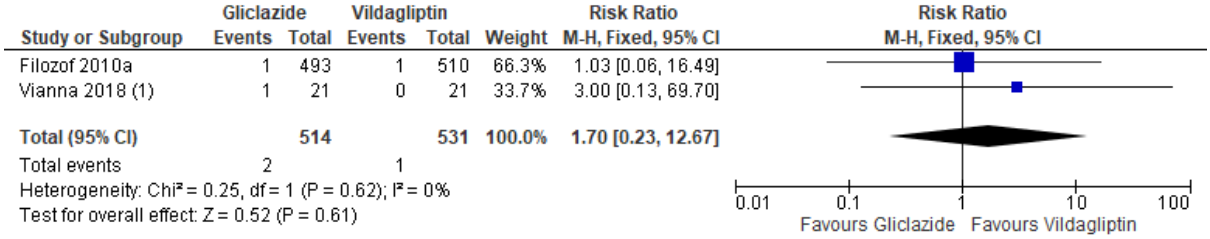
K.1.5.17 Adding ertugliflozin compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.6 Sulfonylureas

K.1.6.1 Adding gliclazide compared to adding vildagliptin

Figure 289: All-cause mortality at end of follow up



Footnotes
(1) Modified release formulation

Figure 290: HbA1c change (%, lower values are better, change scores) at end of follow up

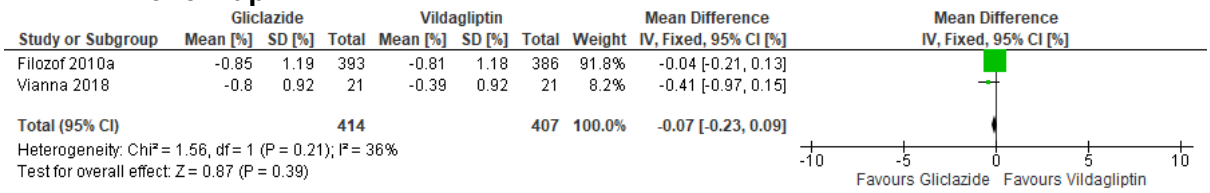
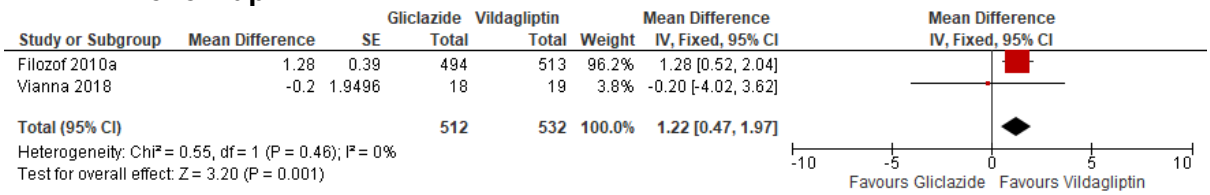


Figure 291: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.6.2 Adding glimepiride compared to adding placebo

Figure 292: All-cause mortality

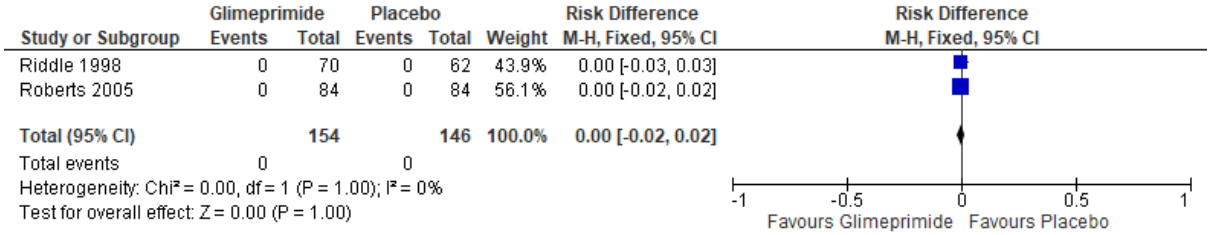


Figure 293: Cardiovascular mortality

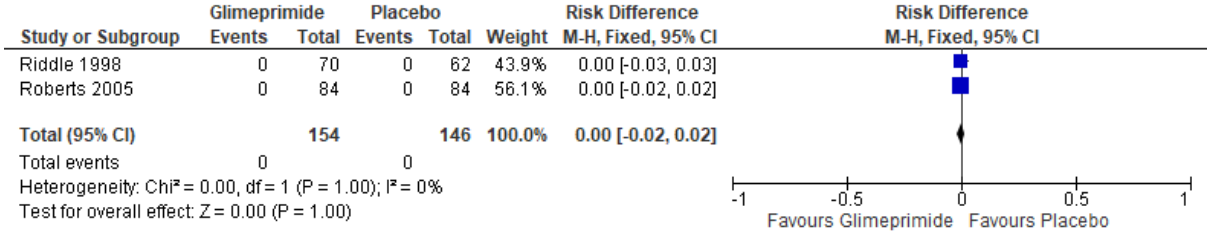
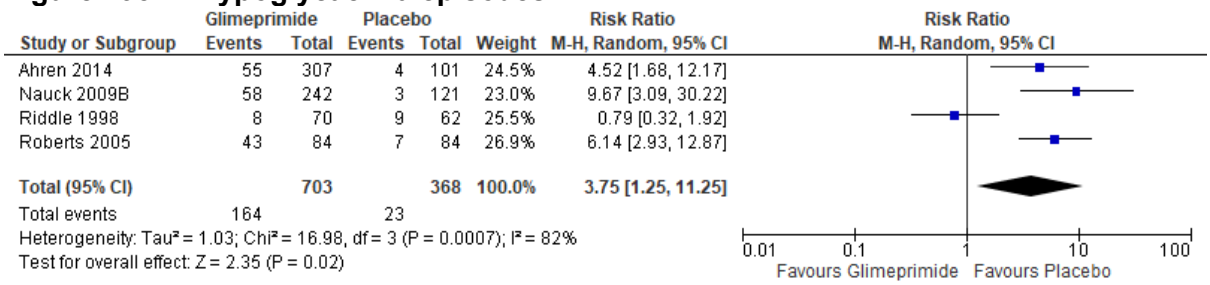


Figure 294: Non-fatal myocardial infarction

Figure 295: Hypoglycaemia episodes



Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen.

Figure 296: Severe hypoglycaemic episodes

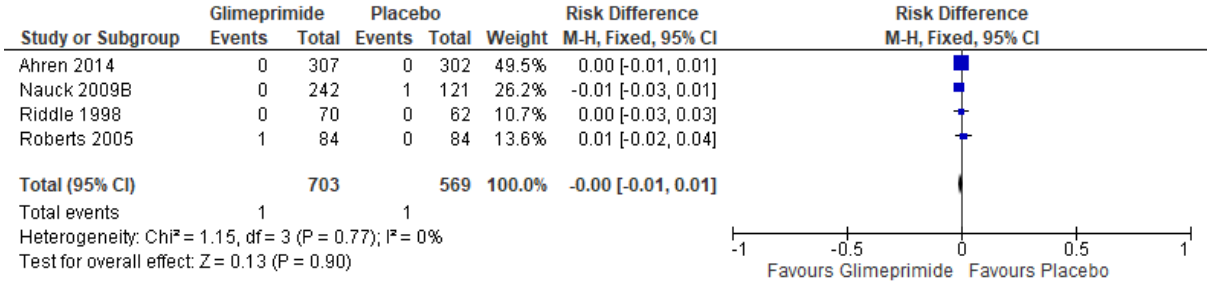
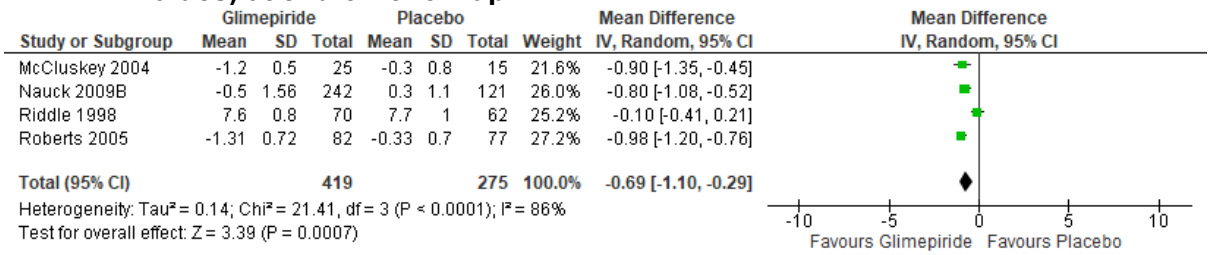
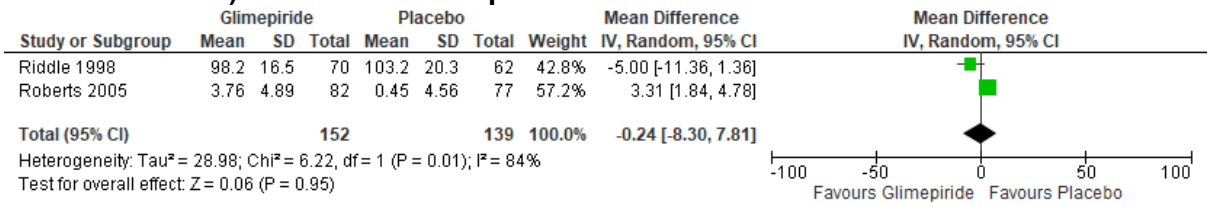


Figure 297: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so a random effects model has been chosen.

Figure 298: Weight change (kg, lower values are better, change scores and final values) at end of follow up



K.1.6.3 Adding glimepiride compared to adding metformin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.4 Adding glimepiride compared to adding insulin

Figure 299: Hypoglycaemia episodes at end of follow up

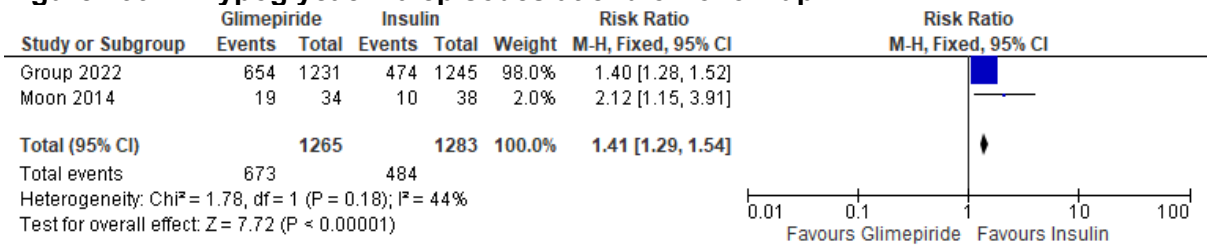


Figure 300: Severe hypoglycaemic episodes at end of follow up

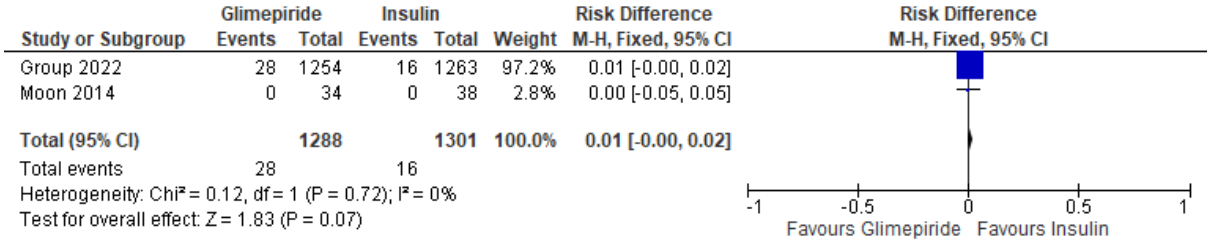
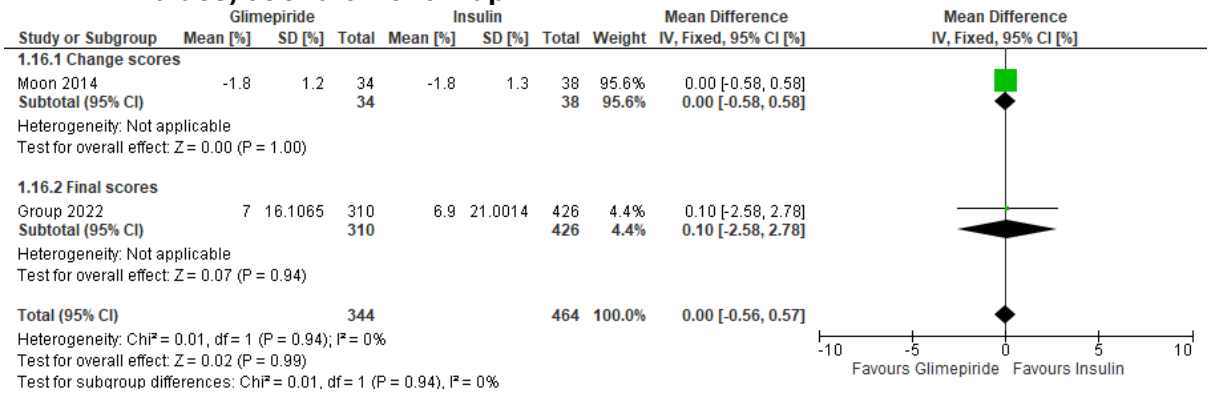


Figure 301: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



K.1.6.5 Adding glimepiride compared to adding canagliflozin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.6 Adding glimepiride compared to adding dapagliflozin

Figure 302: Hypoglycaemia episodes at end of follow up

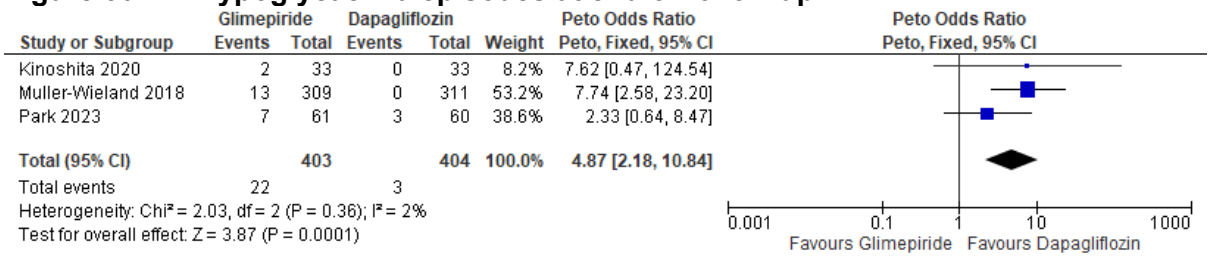


Figure 303: HbA1c change (%, lower values are better, change scores) at end of follow up

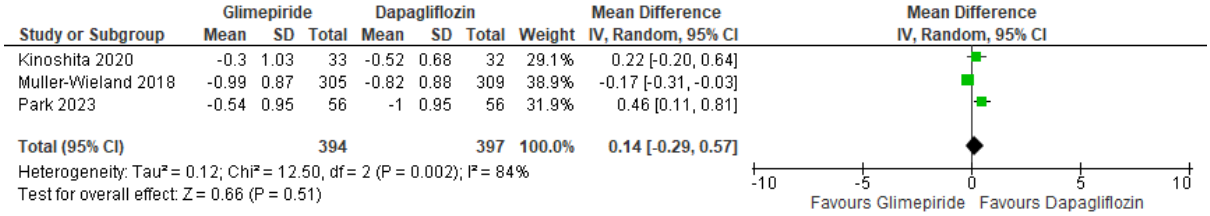
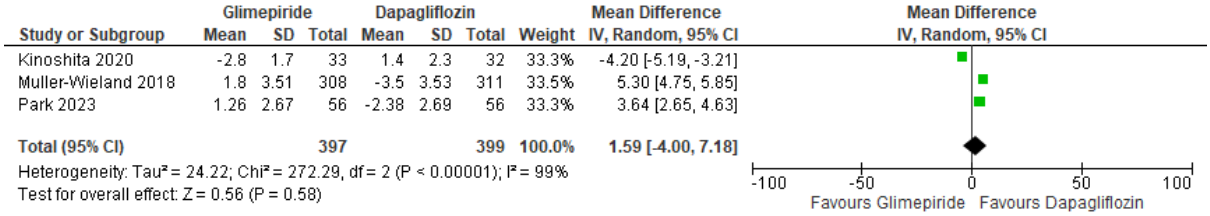


Figure 304: Weight change (kg, lower values are better, change score) at end of follow up



K.1.6.7 Adding glimepiride compared to adding empagliflozin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.8 Adding glimepiride compared to adding ertugliflozin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.9 Adding glimepiride compared to adding exenatide

Figure 305: Hypoglycaemia episodes at end of follow up

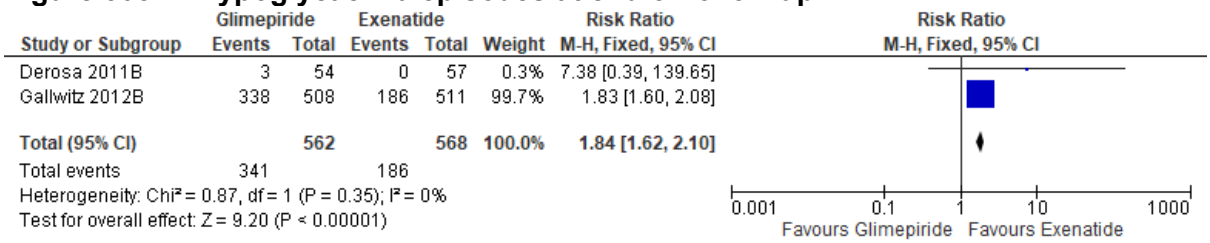


Figure 306: HbA1c change (%, lower values are better, change scores and final values) at end of follow up

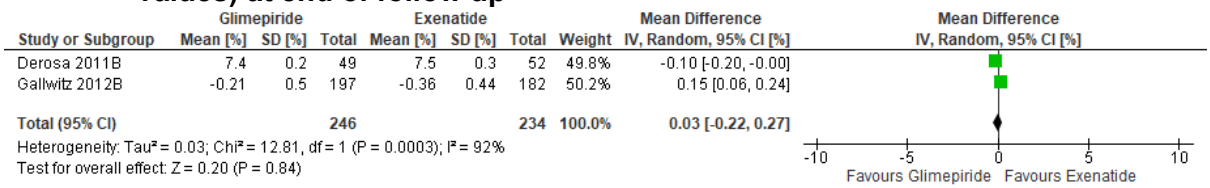


Figure 307: Weight change (kg, lower values are better, change scores and final values) at end of follow up

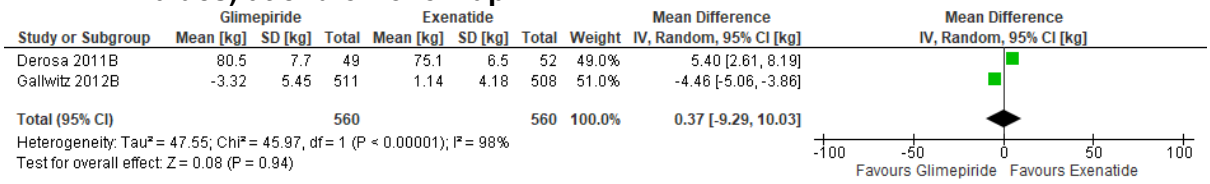
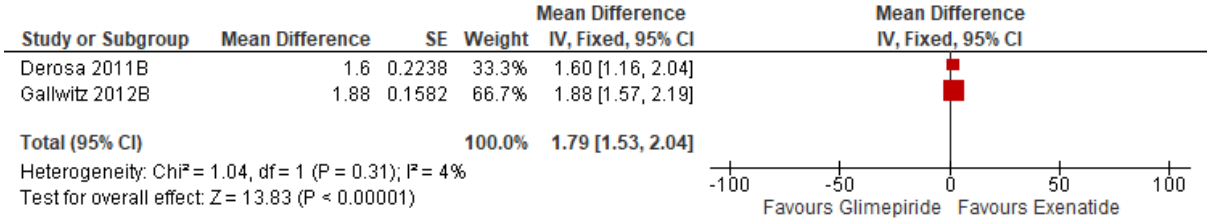


Figure 308: BMI change (kg/m^2, lower values are better, change scores and final values) at end of follow up



K.1.6.10 Adding glimepiride compared to adding gliclazide

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.11 Adding glimepiride compared to adding linagliptin

Figure 309: All-cause mortality at end of follow up

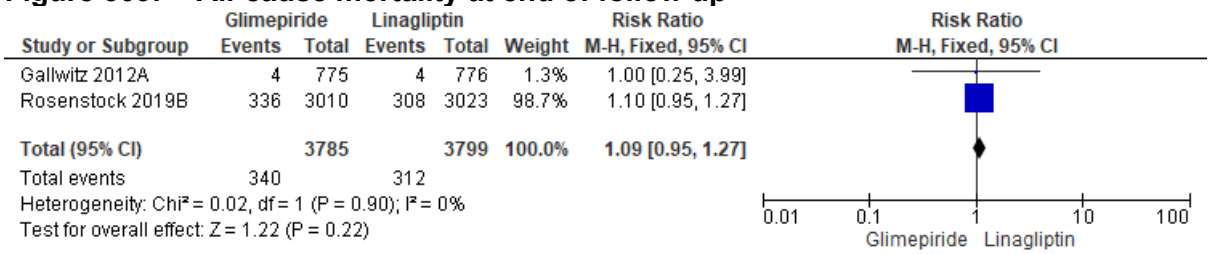


Figure 310: Cardiovascular mortality at end of follow up

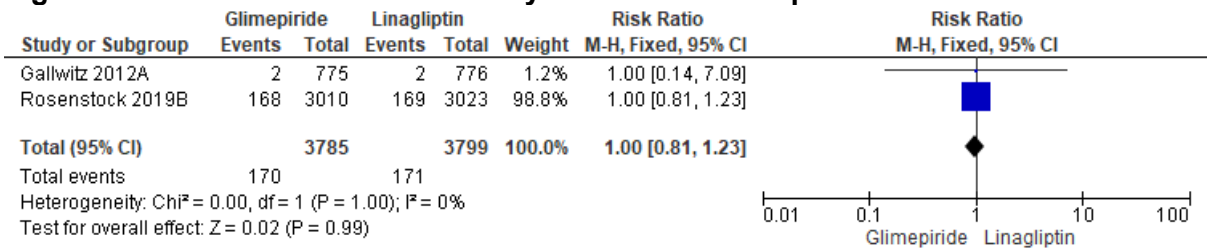


Figure 311: Non-fatal stroke at end of follow up

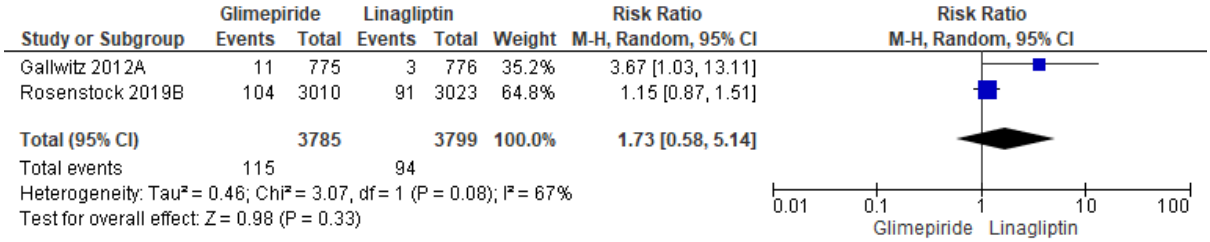


Figure 312: Unstable angina at end of follow up

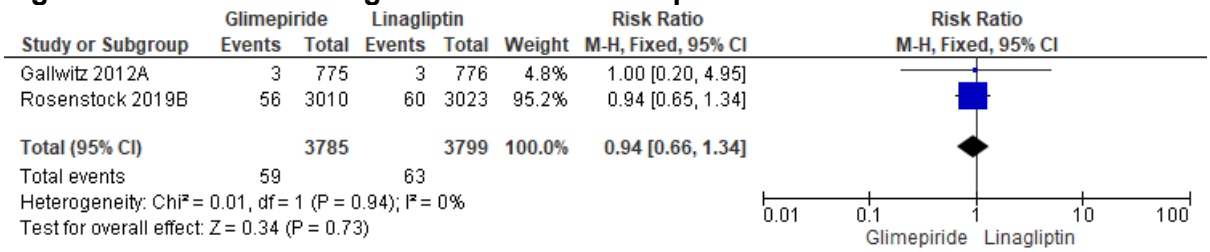


Figure 313: Hospitalisation for heart failure at follow up

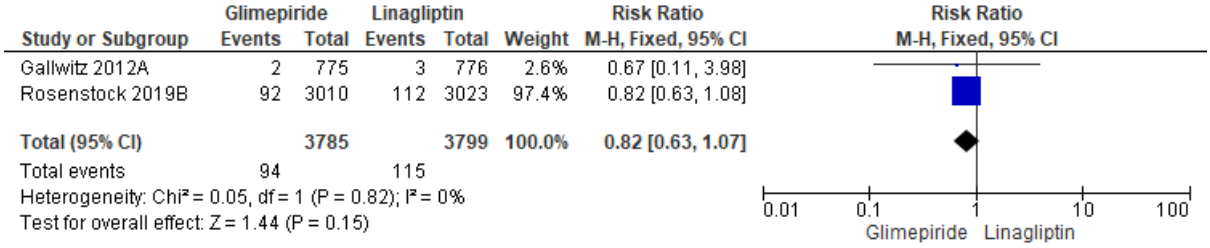


Figure 314: Hypoglycaemia episodes at end of follow up

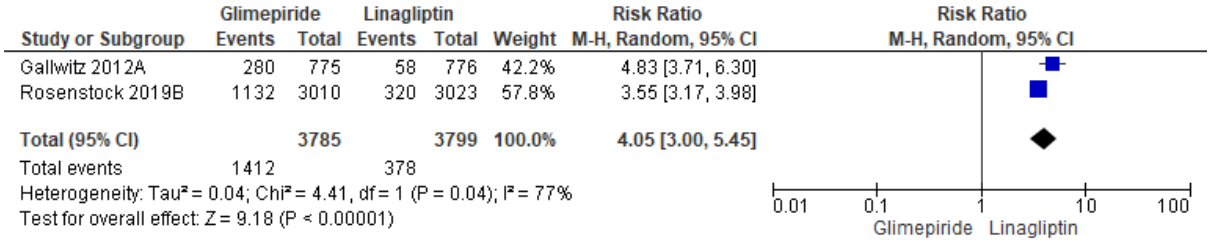


Figure 315: Severe hypoglycaemic episodes at end of follow up

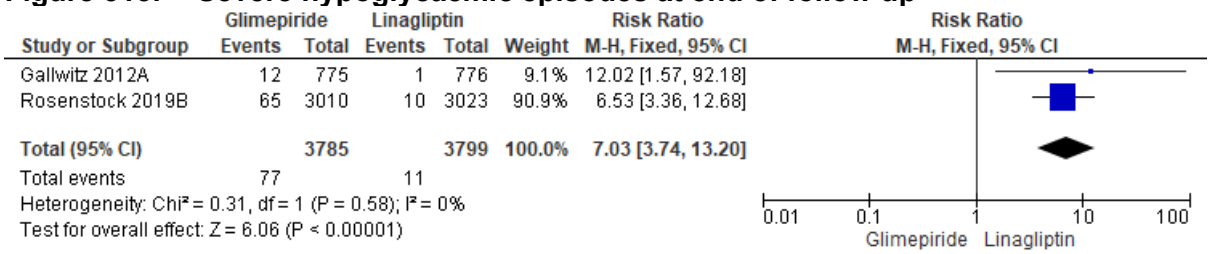


Figure 316: HbA1c change (%, lower values are better, change scores) at end of follow up

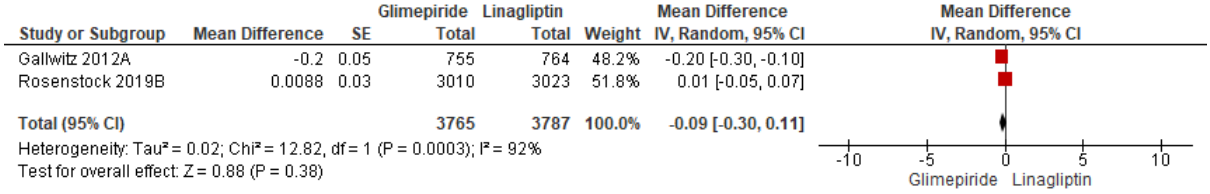
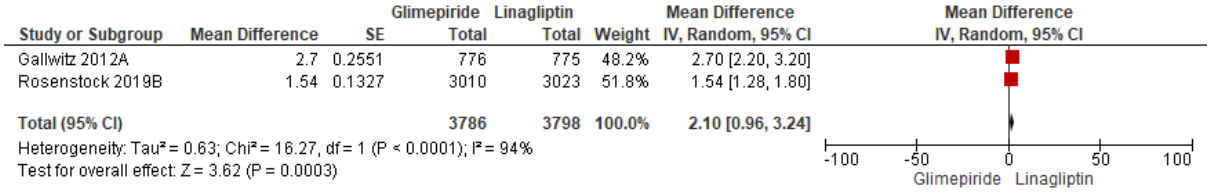


Figure 317: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.6.12 Adding glimepiride compared to adding liraglutide

Figure 318: Hypoglycaemia episodes at end of follow up

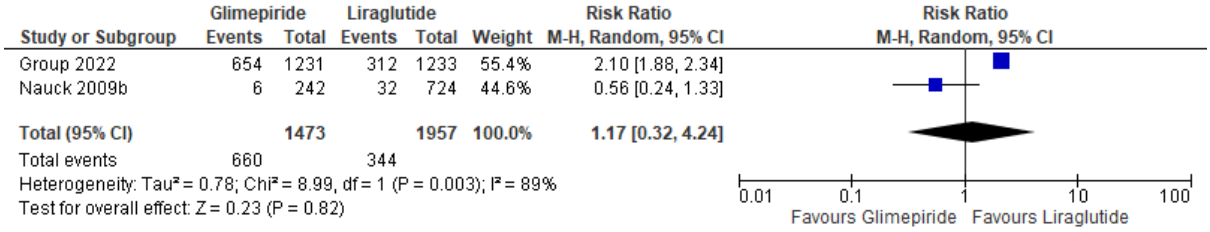
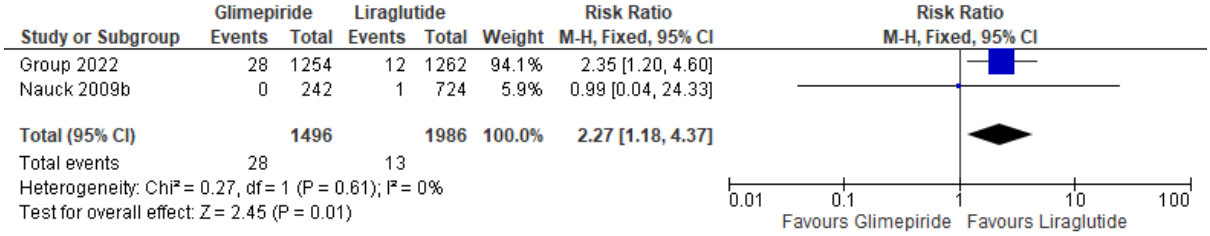


Figure 319: Severe hypoglycaemic episodes at end of follow up



K.1.6.13 Adding glimepiride compared to adding saxagliptin

Figure 320: Hypoglycaemia episodes at end of follow up

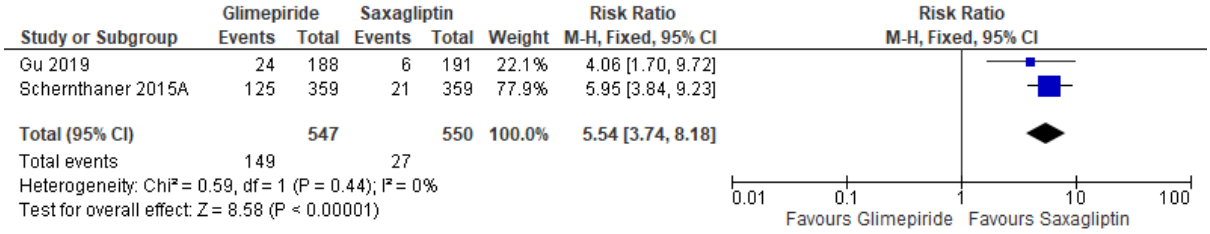
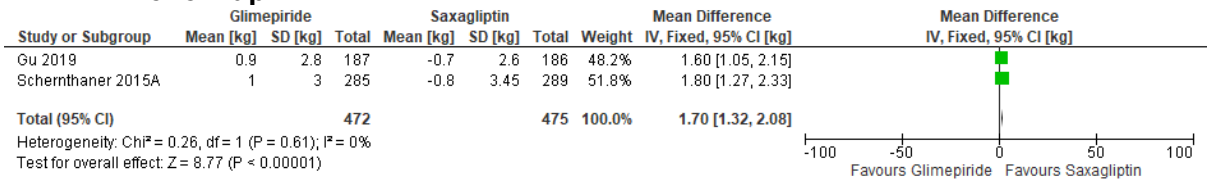


Figure 321: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.6.14 Adding glimepiride compared to adding sitagliptin

Figure 322: All-cause mortality at end of follow up

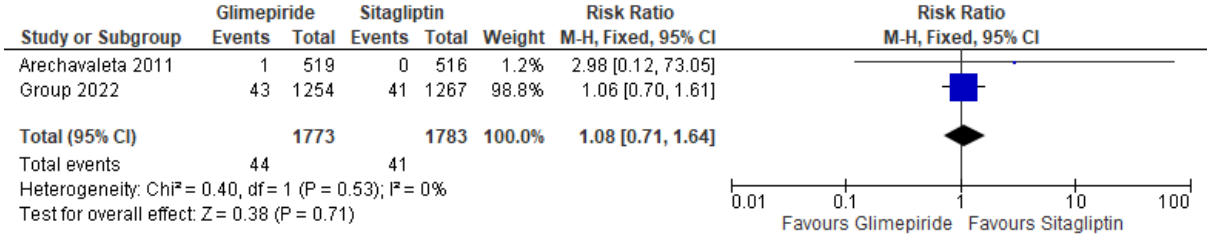


Figure 323: Cardiovascular mortality at end of follow up

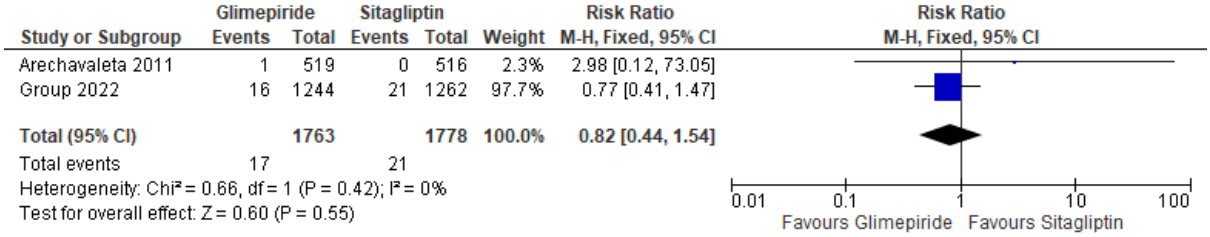


Figure 324: Hospitalisation for heart failure at end of follow up

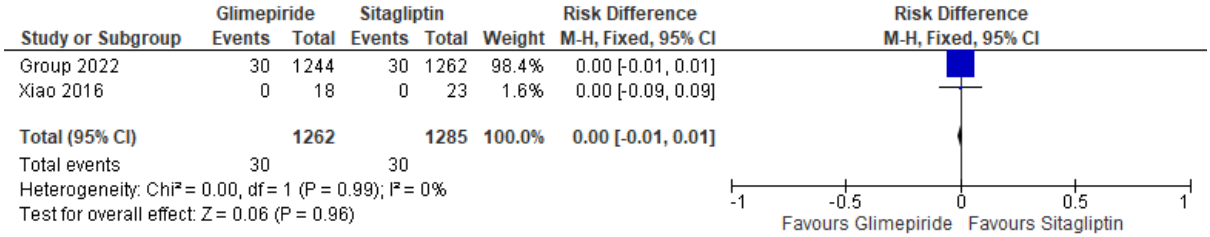
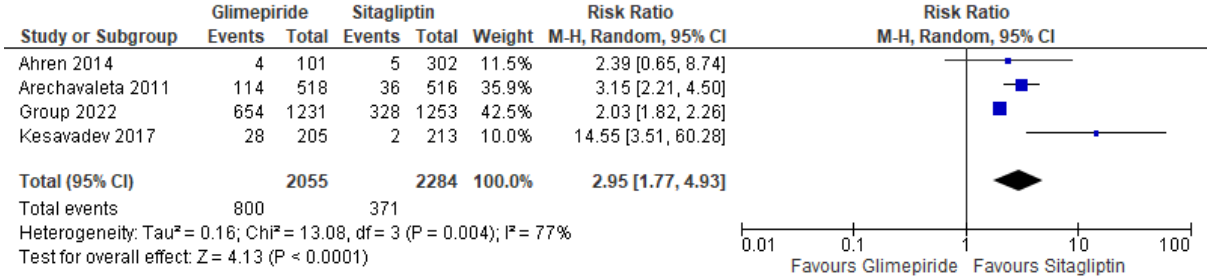
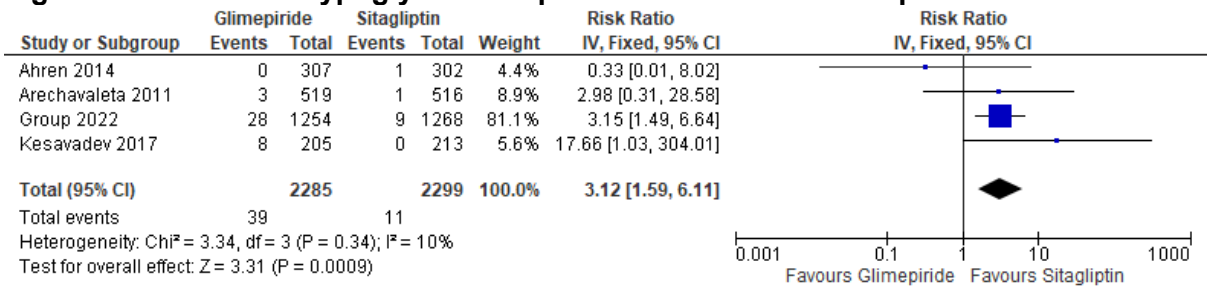


Figure 325: Hypoglycaemia episodes at end of follow up



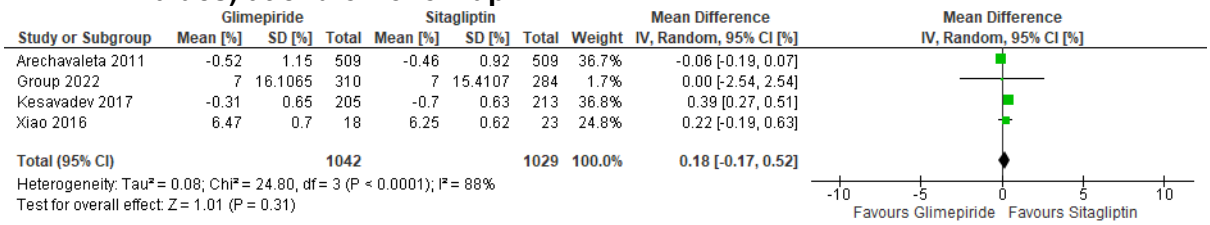
Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen.

Figure 326: Severe hypoglycaemic episodes at end of follow up



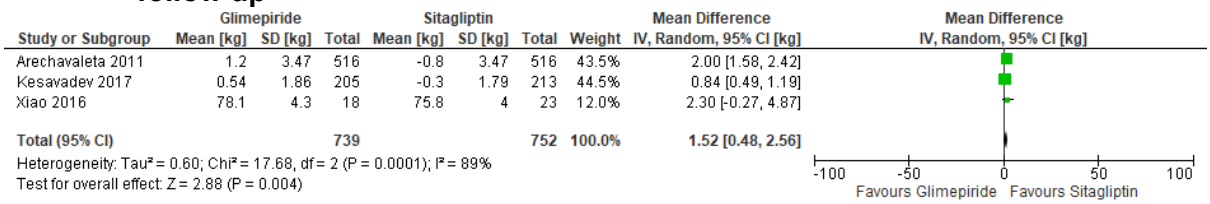
Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen.

Figure 327: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen.

Figure 328: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.6.15 Adding glimepiride compared to adding vildagliptin

Figure 329: All-cause mortality at end of follow up

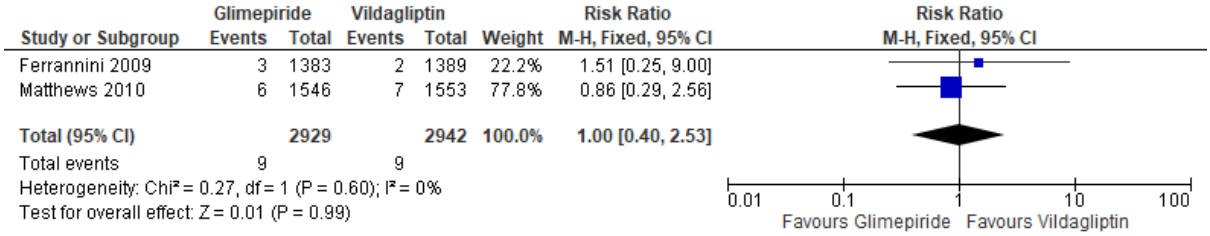


Figure 330: Hypoglycaemia episodes at end of follow up

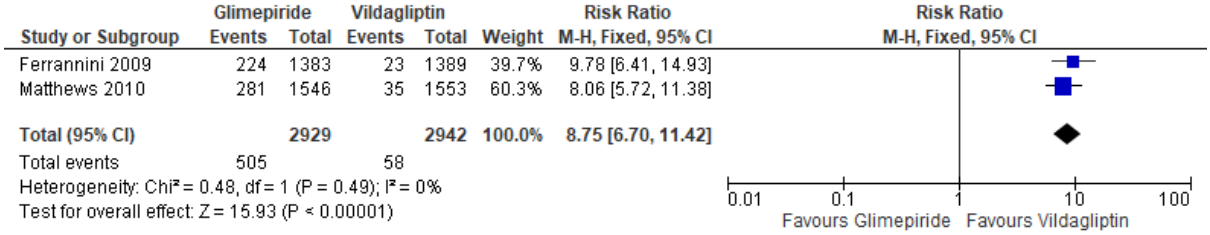


Figure 331: Severe hypoglycaemic episodes at end of follow up

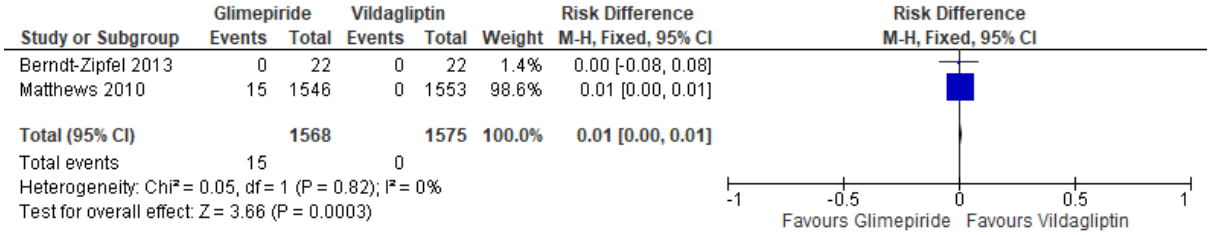


Figure 332: HbA1c change (%, lower values are better, change scores and final values) at end of follow up

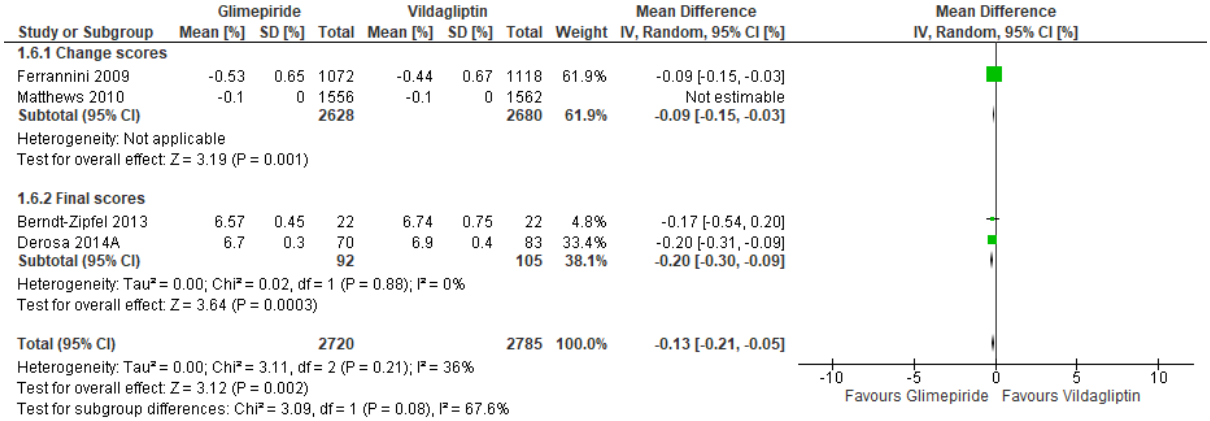
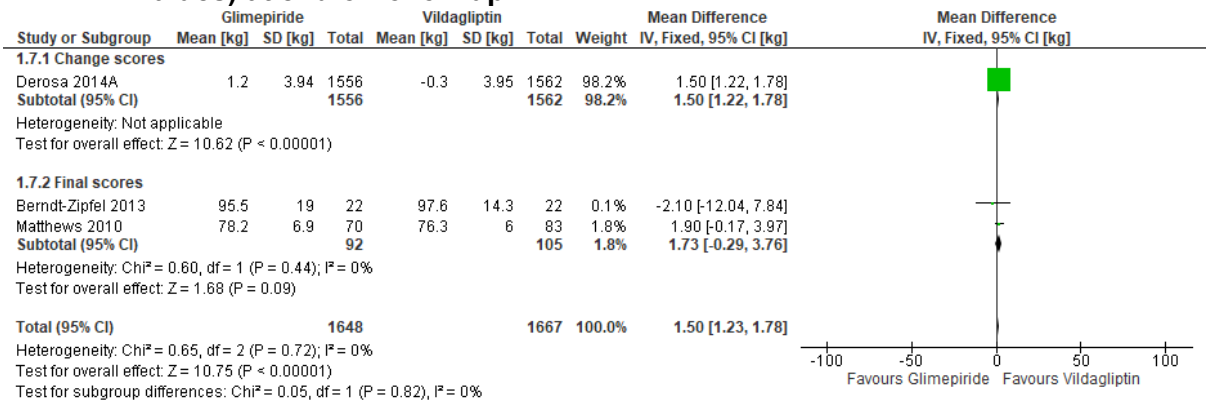


Figure 333: Weight change (kg, lower values are better, change scores and final values) at end of follow up



K.1.6.16 Adding glipizide compared to adding placebo

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.17 Adding glipizide compared to adding metformin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.18 Adding glipizide compared to adding alogliptin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.19 Adding glipizide compared to adding dapagliflozin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.20 Adding glipizide compared to adding saxagliptin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.6.21 Adding glipizide compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study)

K.1.7 Thiazolidinediones

K.1.7.1 Adding pioglitazone compared to adding placebo

Figure 334: All-cause mortality at end of follow up

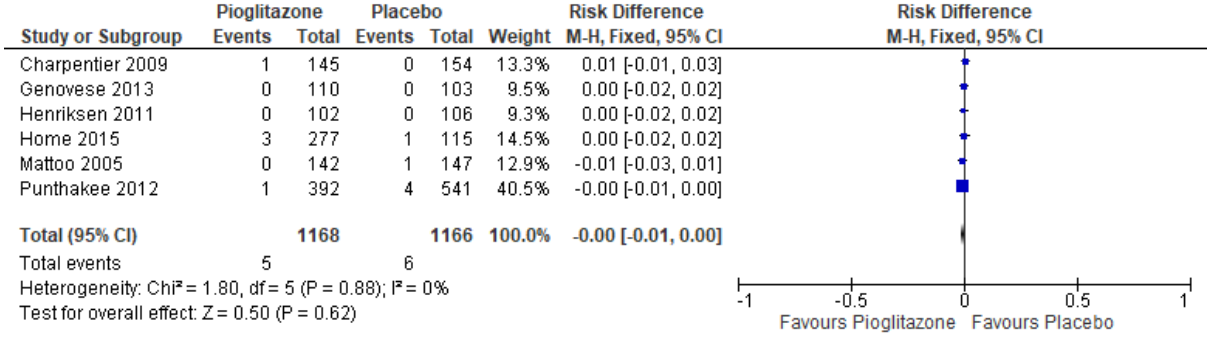


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Figure 335: Cardiovascular mortality at end of follow up

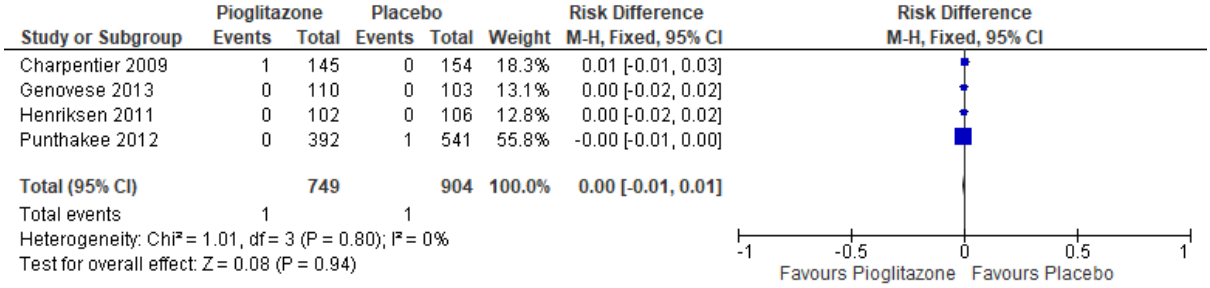


Figure 336: 3-point MACE at end of follow up

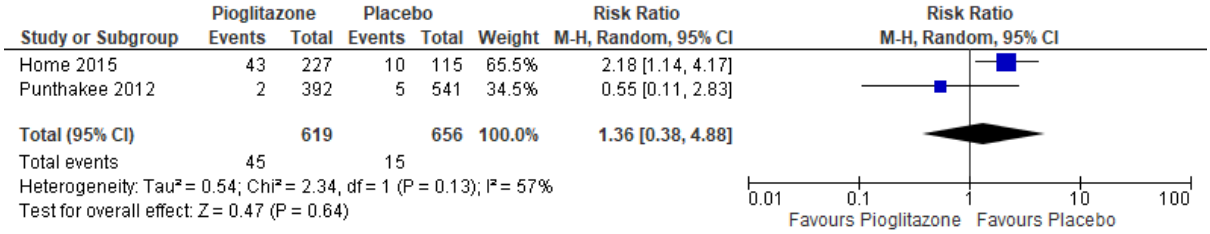


Figure 337: Non-fatal myocardial infarction at follow up

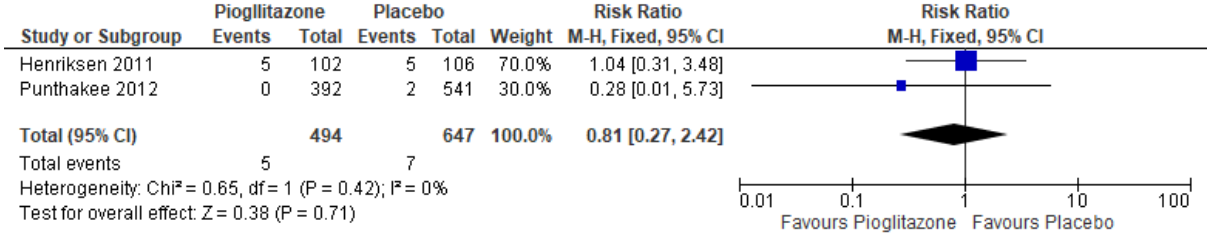


Figure 338: Hospitalisation for heart failure at end of follow up

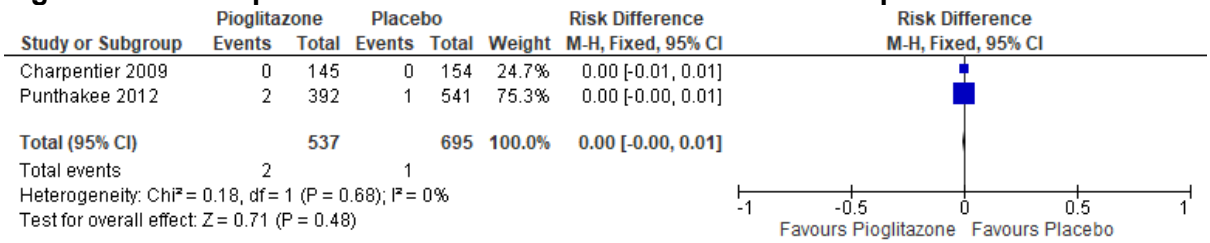
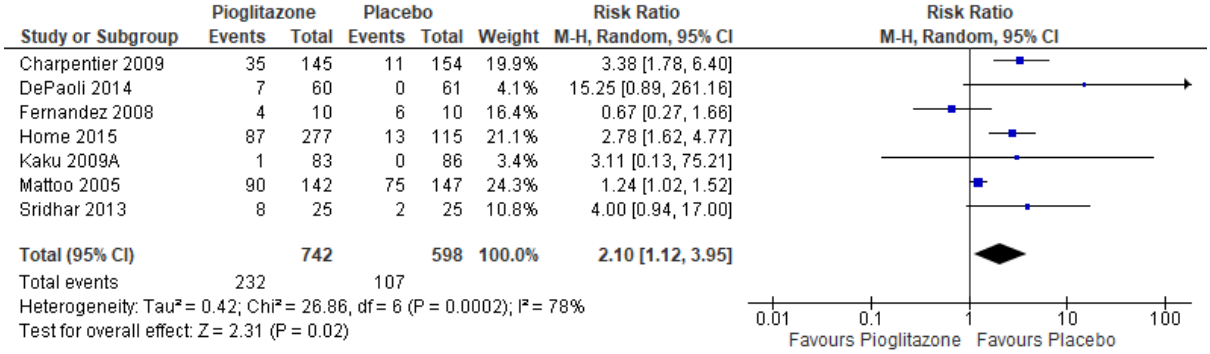


Figure 339: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen

Figure 340: Severe hypoglycaemic episodes at end of follow up

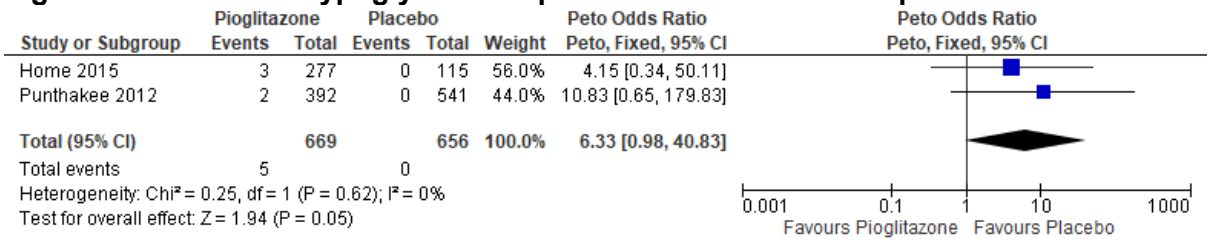
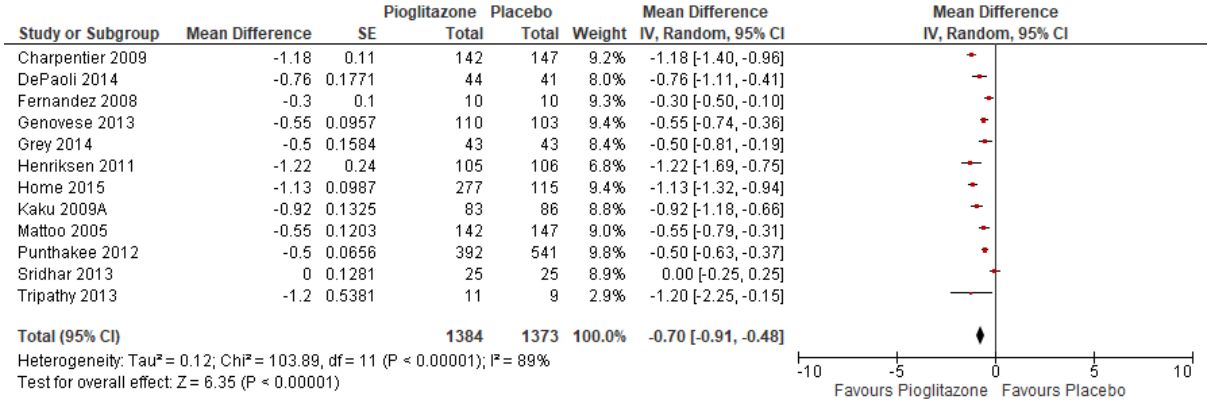
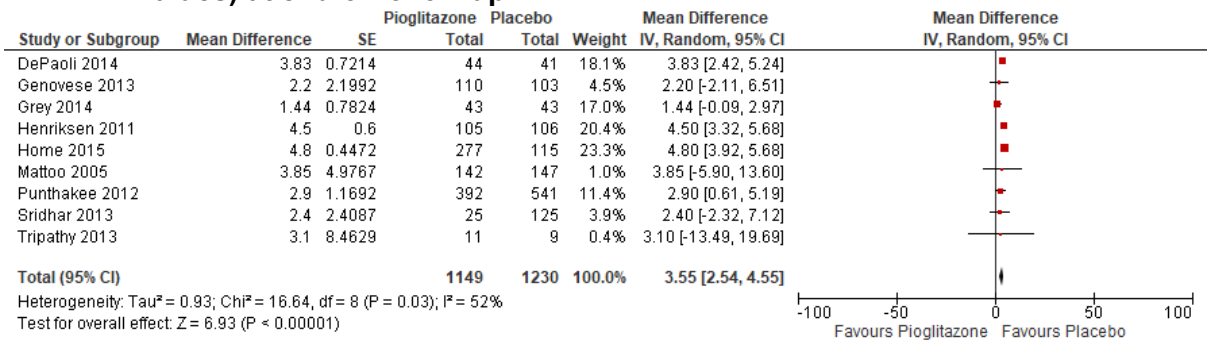


Figure 341: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



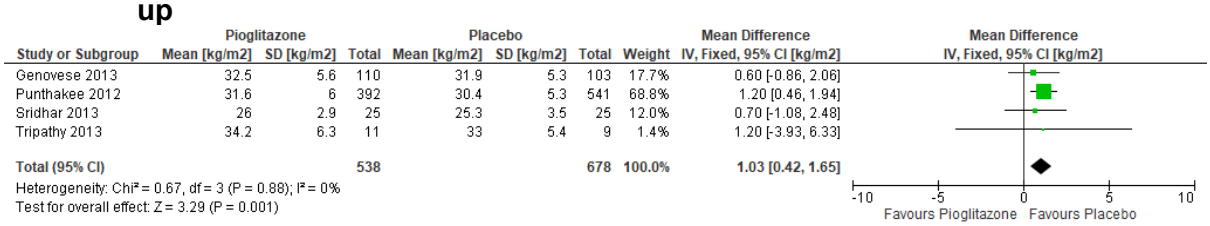
Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis.

Figure 342: Weight change (kg, lower values are better, change scores and final values) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis.

Figure 343: BMI change (kg/m^2, lower values are better, final values) at end of follow up



K.1.7.2 Adding pioglitazone compared to adding metformin

Figure 344: All-cause mortality at end of follow up

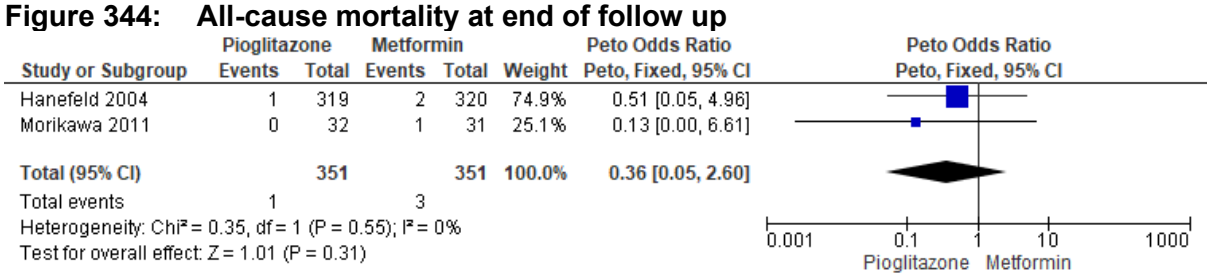


Figure 345: Hypoglycaemia episodes at end of follow up

Figure 346: HbA1c change (%, lower values are better, change scores and final values) at end of follow up

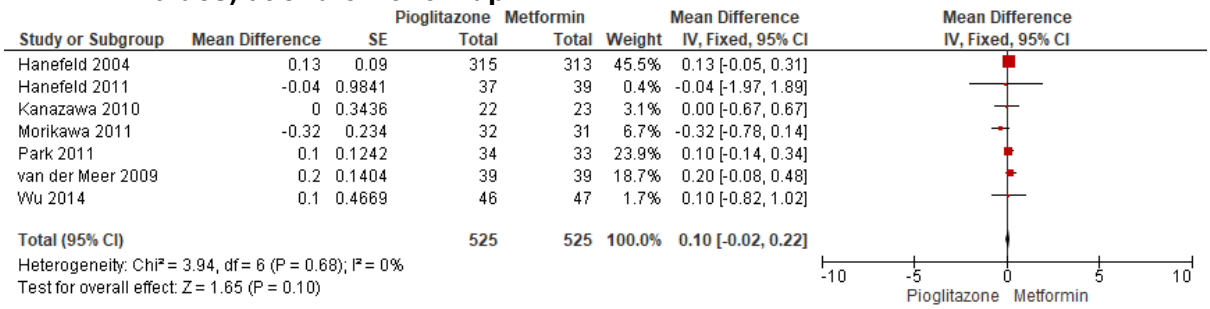


Figure 347: Weight change (kg, lower values are better, change scores and final values) at end of follow up

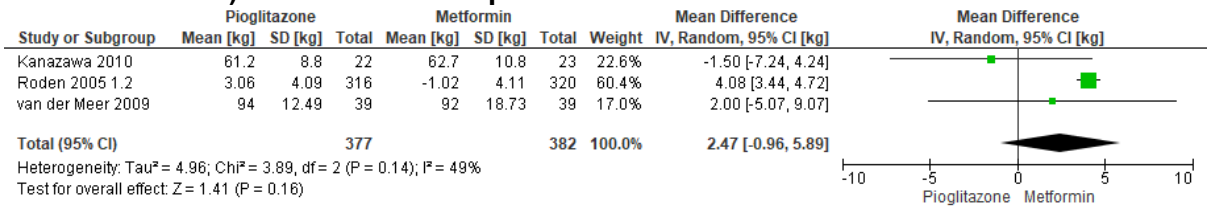
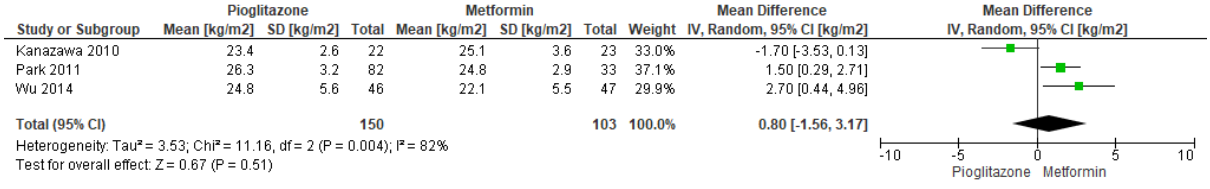


Figure 348: BMI change (kg/m^2, lower values are better, final values) at end of follow up



K.1.7.3 Adding pioglitazone compared to adding insulin

Figure 349: Hypoglycaemia episodes at end of follow up

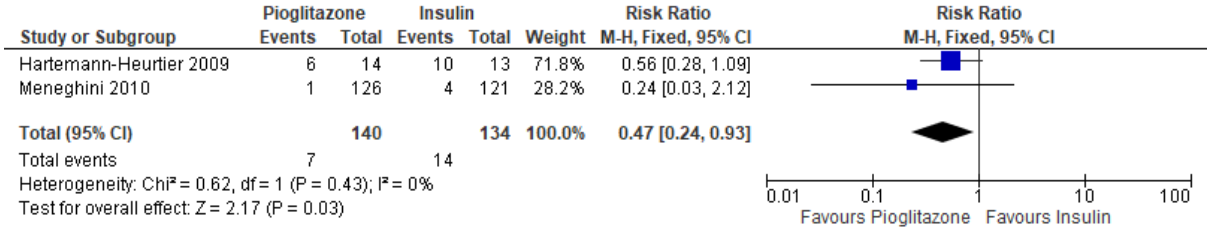


Figure 350: Severe hypoglycaemic episodes at end of follow up

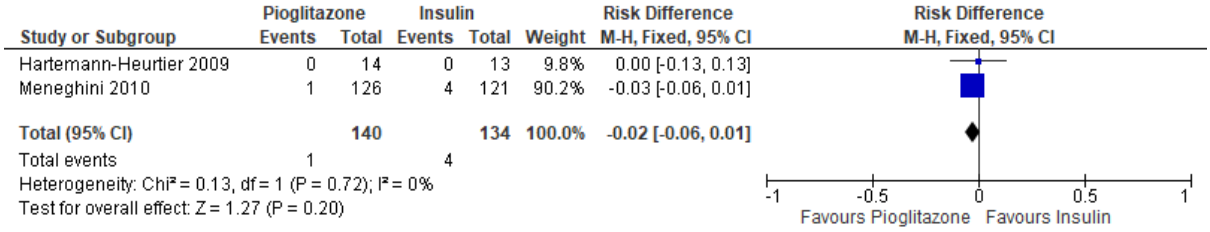
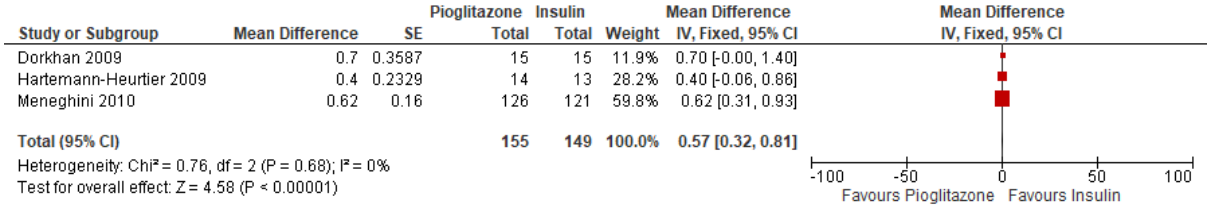


Figure 351: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



K.1.7.4 Adding pioglitazone compared to adding dapagliflozin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.7.5 Adding pioglitazone compared to adding empagliflozin

Figure 352: Hypoglycaemia episodes at end of follow up

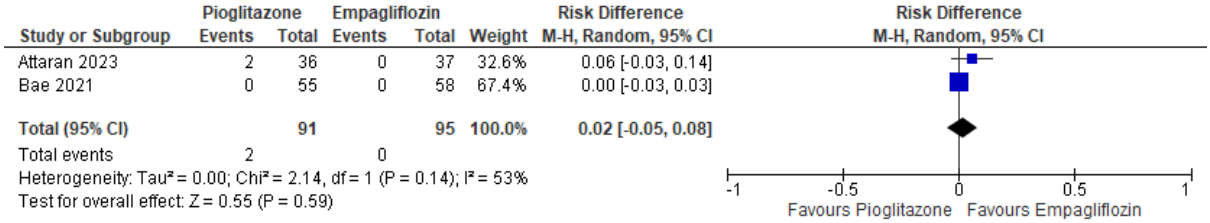


Figure 353: Severe hypoglycaemic episodes at end of follow up

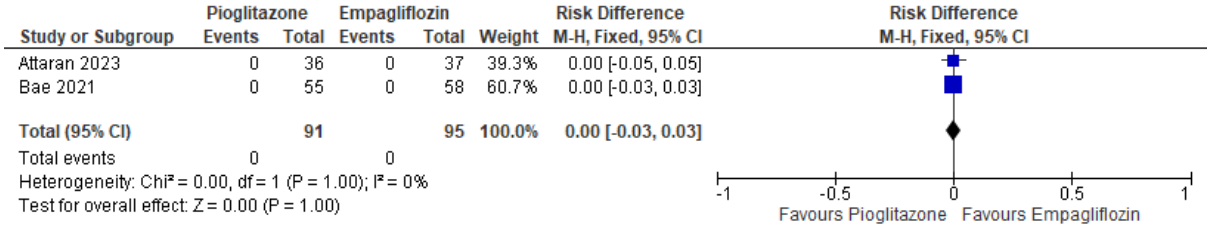


Figure 354: HbA1c change (%, lower values are better, change scores and final values) at end of follow up

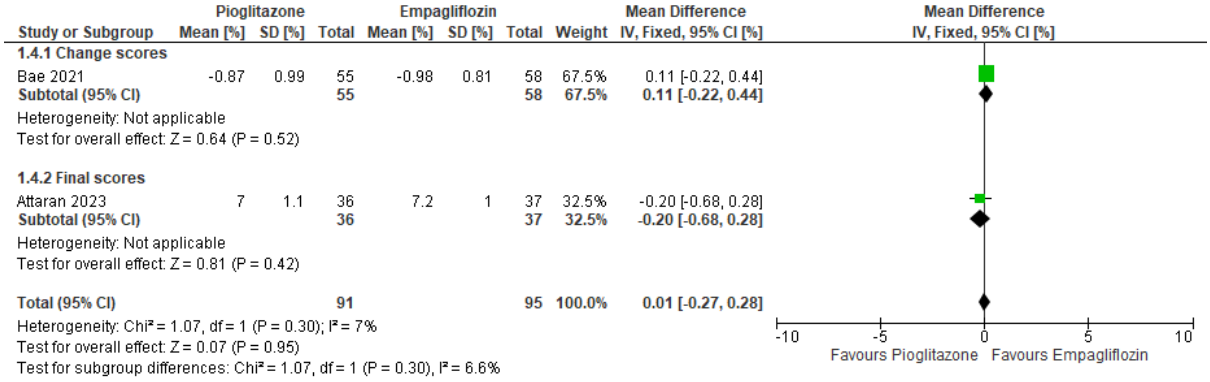
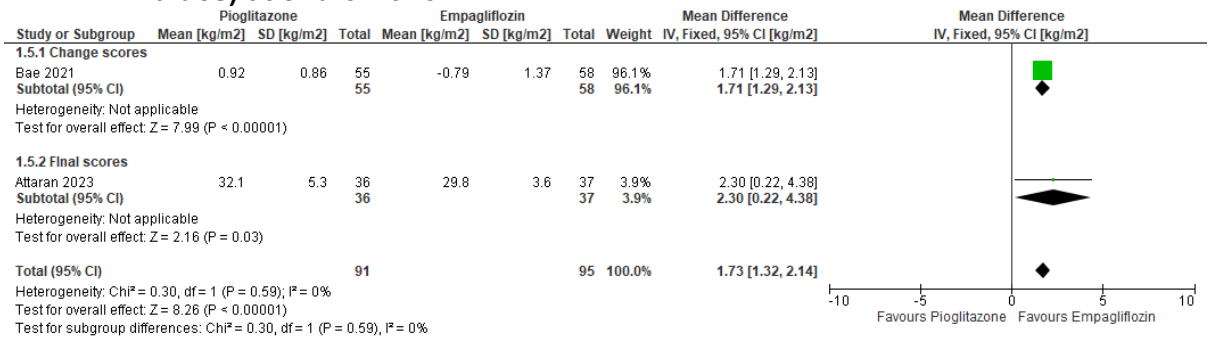


Figure 355: BMI change (kg/m^2, lower values are better, change scores and final values) at end of follow



K.1.7.6 Adding pioglitazone compared to adding exenatide

There are no forest plots for this comparison (all outcomes include a single study)

K.1.7.7 Adding pioglitazone compared to adding gliclazide

There are no forest plots for this comparison (all outcomes include a single study)

K.1.7.8 Adding pioglitazone compared to adding glimepiride

Figure 356: Non-fatal stroke at end of follow up

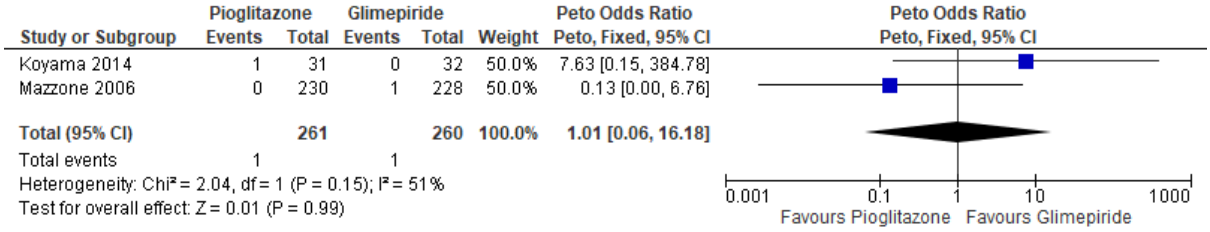


Figure 357: Non-fatal myocardial infarction at end of follow up

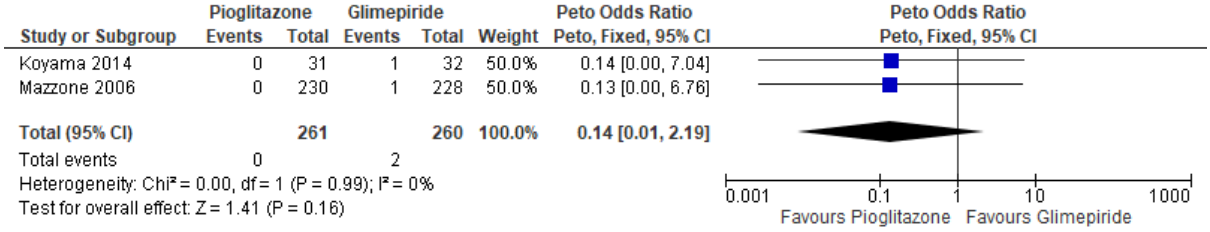


Figure 358: Hospitalisation for heart failure at end of follow up

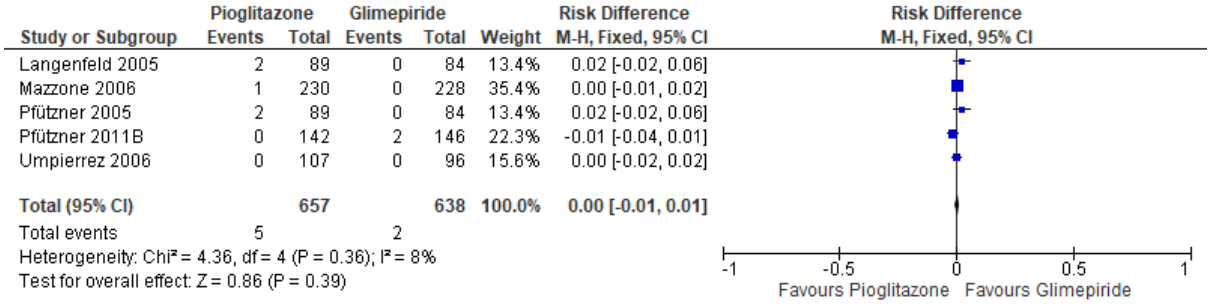
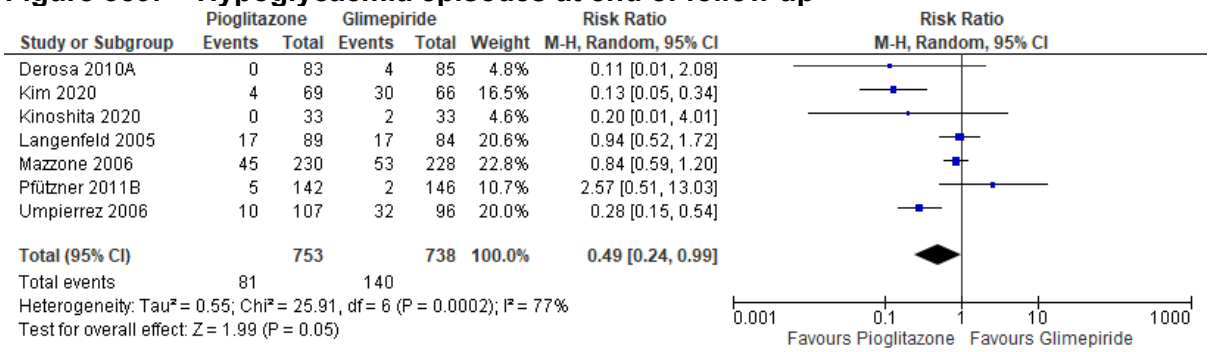


Figure 359: Hypoglycaemia episodes at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis.

Figure 360: Severe hypoglycaemic episodes at end of follow up

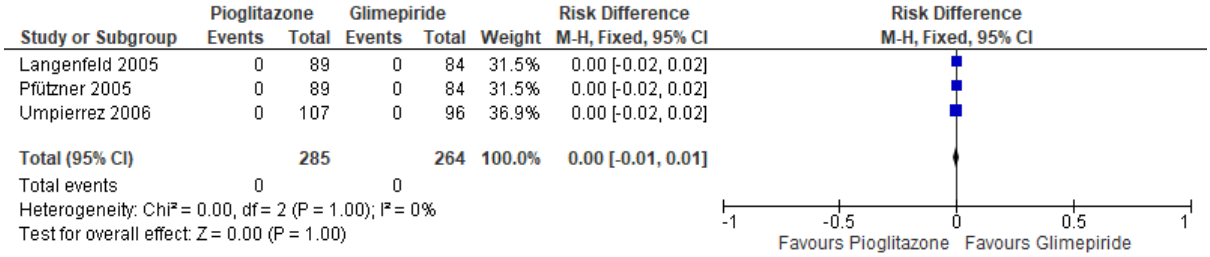
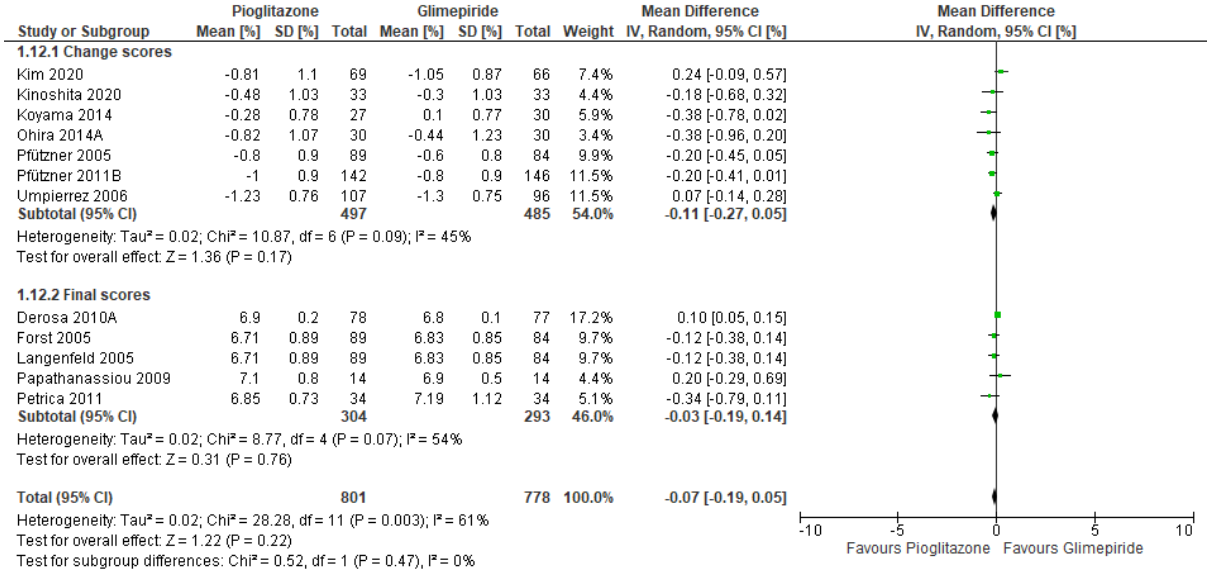
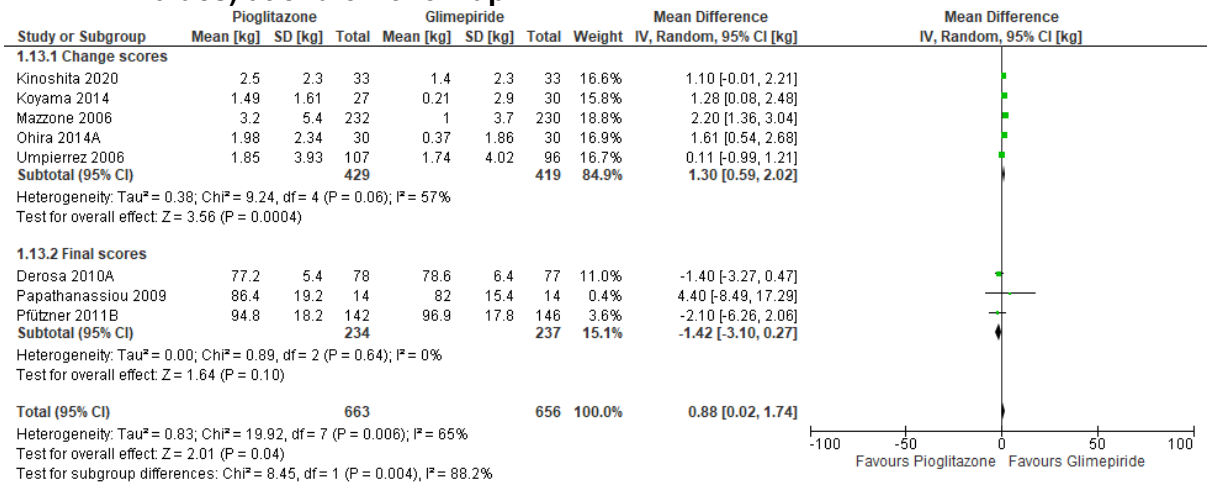


Figure 361: HbA1c change (%, lower values are better, change scores and final values) at end of follow up



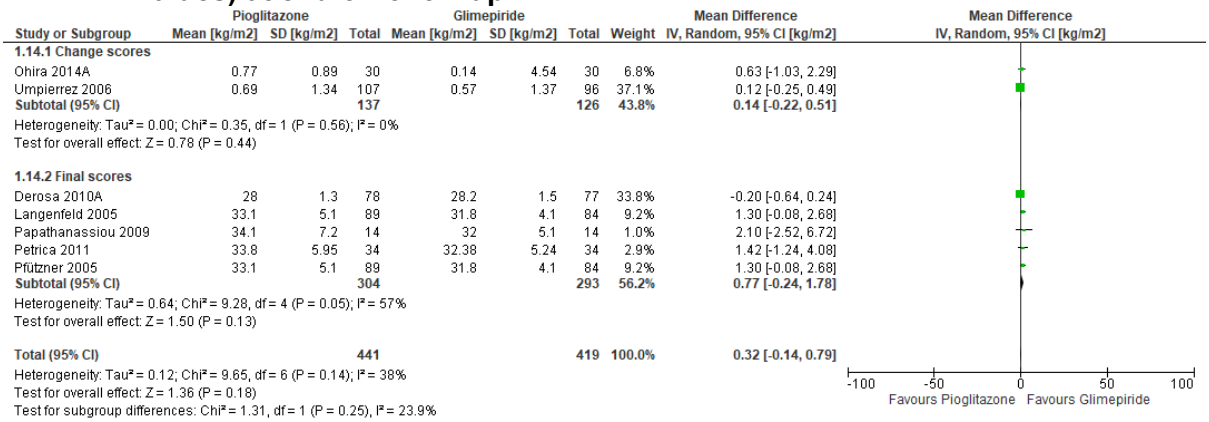
Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis.

Figure 362: Weight change (kg, lower values are better, change scores and final values) at end of follow up



Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen

Figure 363: BMI change (kg/m^2, lower values are better, change scores and final values) at end of follow up



Note: Heterogeneity for this outcome could not be explored due to low number of studies for each subgroup so random effects model has been chosen

K.1.7.9 Adding pioglitazone compared to adding glipizide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.7.10 Adding pioglitazone compared to adding sitagliptin

Figure 364: Hypoglycaemia episodes at end of follow up

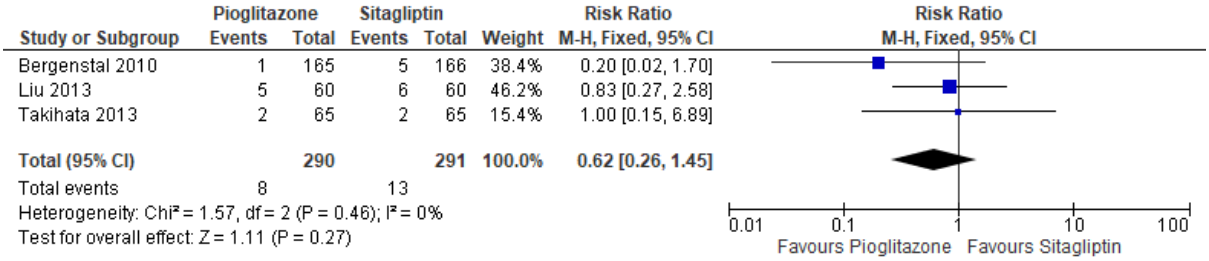


Figure 365: Severe hypoglycaemic episodes at end of follow up

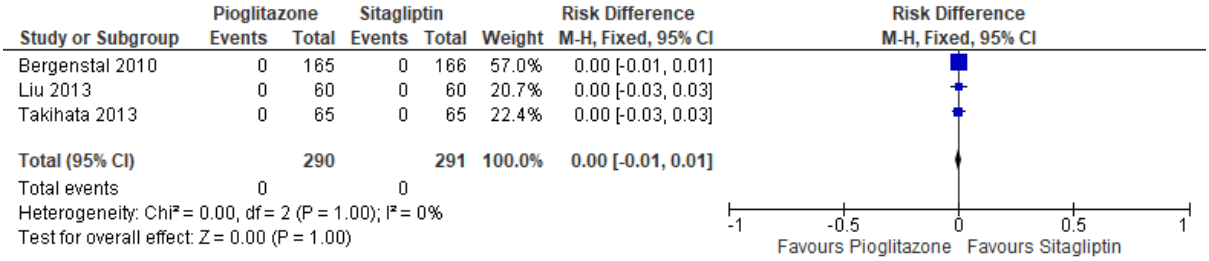
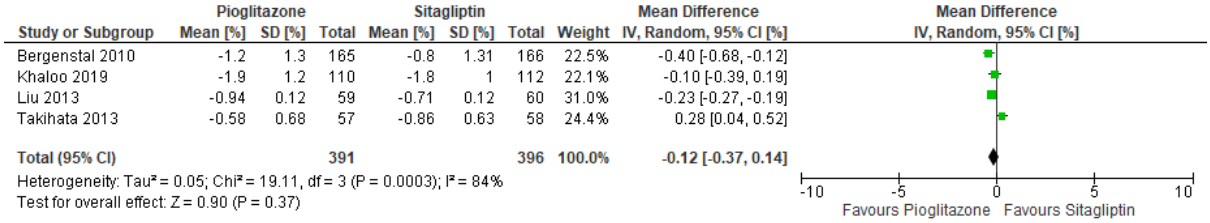
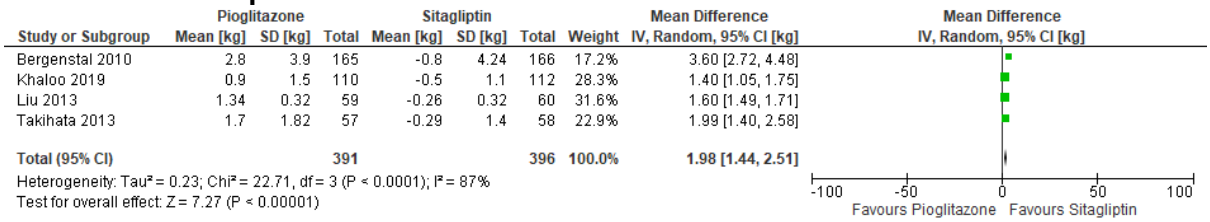


Figure 366: HbA1c change (%, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR subgroup.

Figure 367: Weight change (kg, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis nor subgroup analysis by eGFR subgroup.

K.1.7.11 Adding pioglitazone compared to adding vildagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.8 Insulin combinations

K.1.8.1 Adding insulin degludec/Liraglutide compared to adding placebo

There are no forest plots for this comparison (all outcomes include a single study).

K.1.8.2 Adding insulin degludec/Liraglutide compared to adding insulin

Figure 368: Health-related quality of life - subscale mental component (SF-36 v2, 0-100, higher scores are better, change scores and final values) at end of follow up

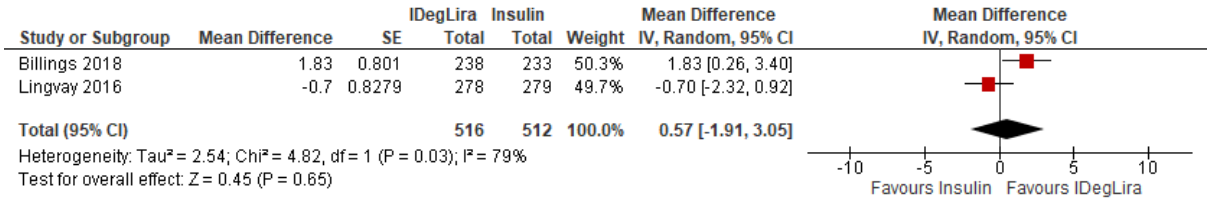


Figure 369: Health-related quality of life - subscale physical component (SF-36 v2, 0-100, higher scores are better, change scores and final values) at end of follow up

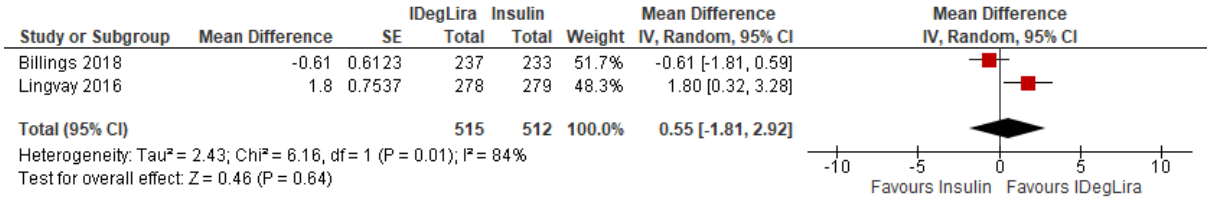


Figure 370: All-cause mortality at end of follow up

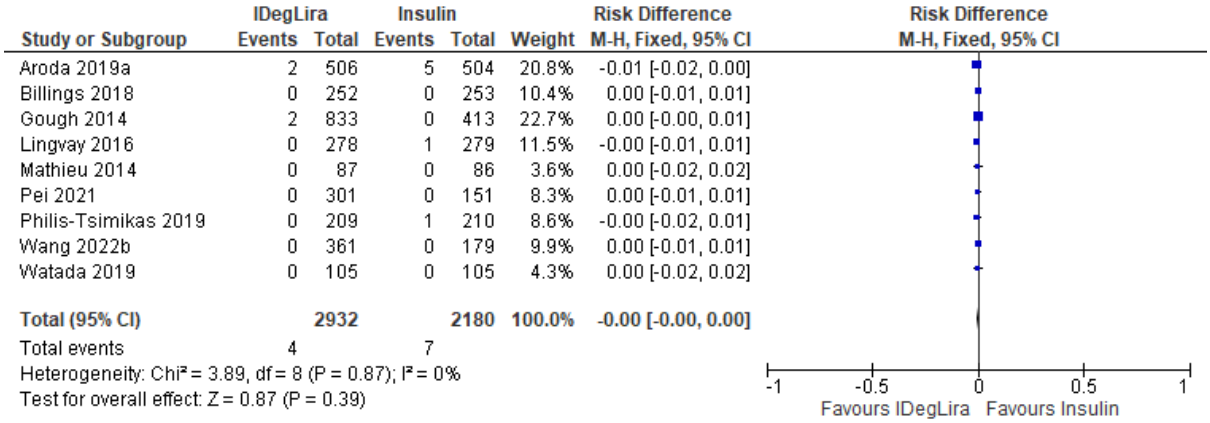


Figure 371: Cardiovascular mortality at end of follow up

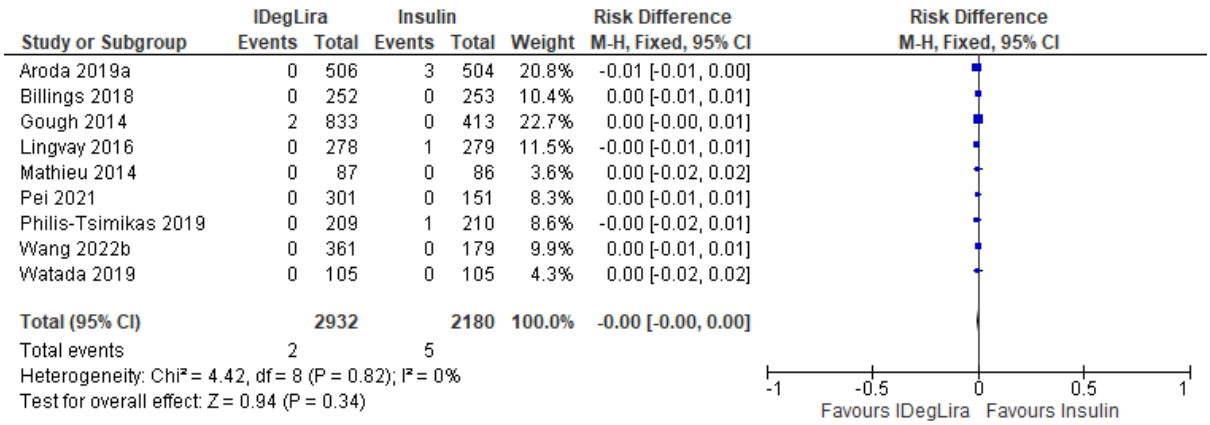


Figure 372: 3-point MACE at end of follow up

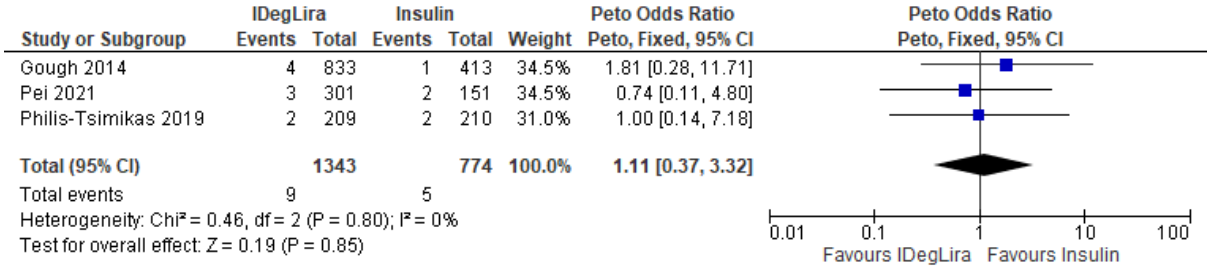


Figure 373: Non-fatal stroke at end of follow up

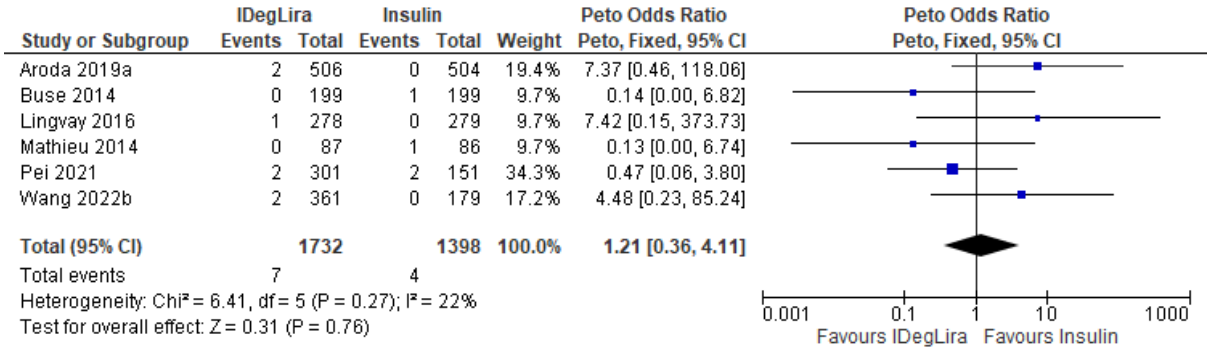


Figure 374: Non-fatal myocardial infarction at end of follow up

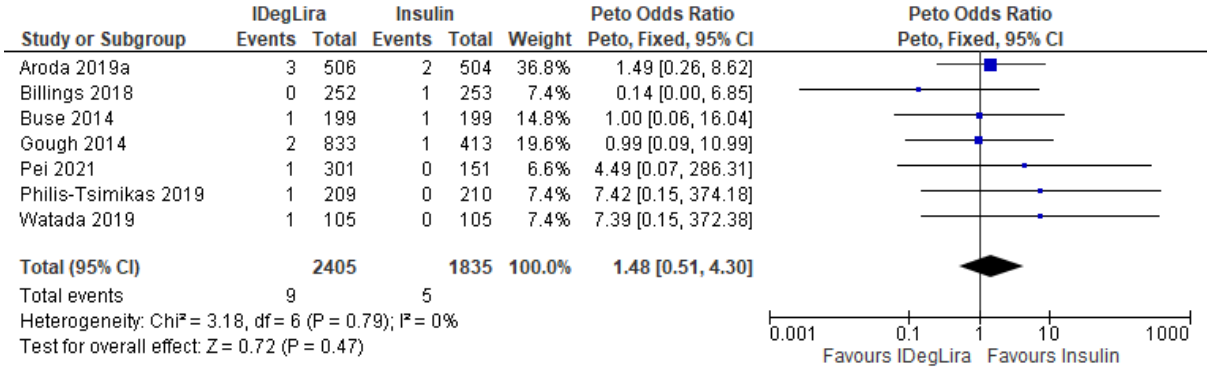


Figure 375: Unstable angina at end of follow up

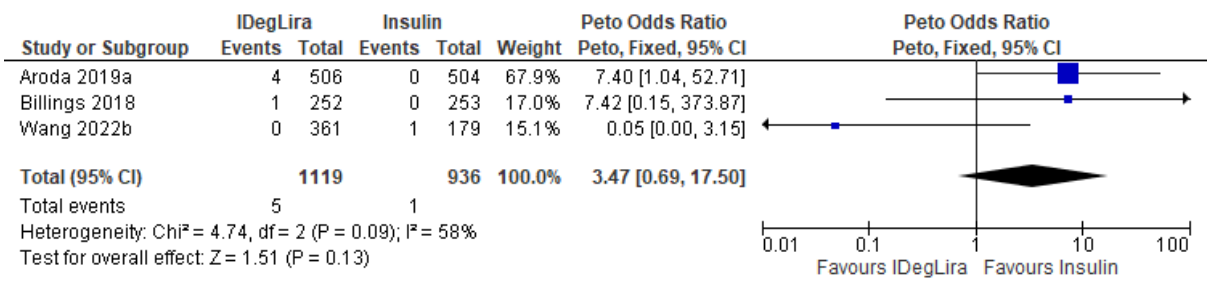


Figure 376: Hospitalisation for heart failure at end of follow up

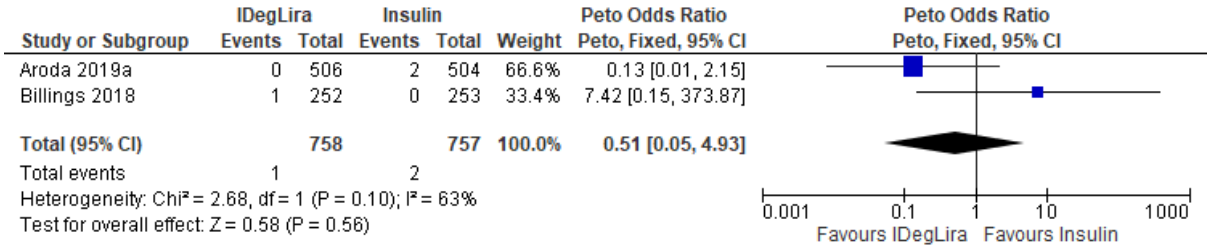


Figure 377: Cardiac arrhythmia at end of follow up

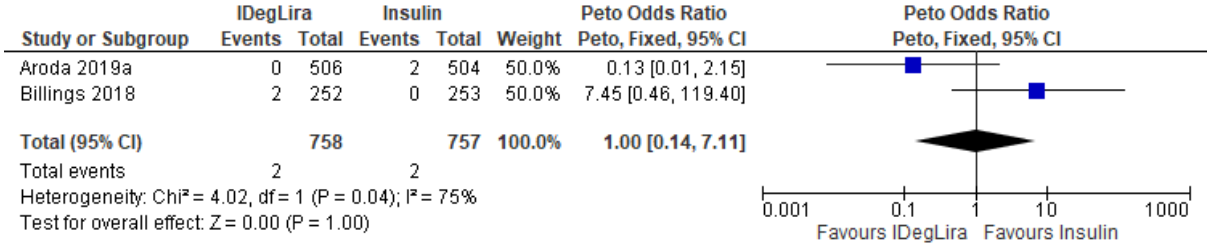


Figure 378: Hypoglycaemia episodes at end of follow up

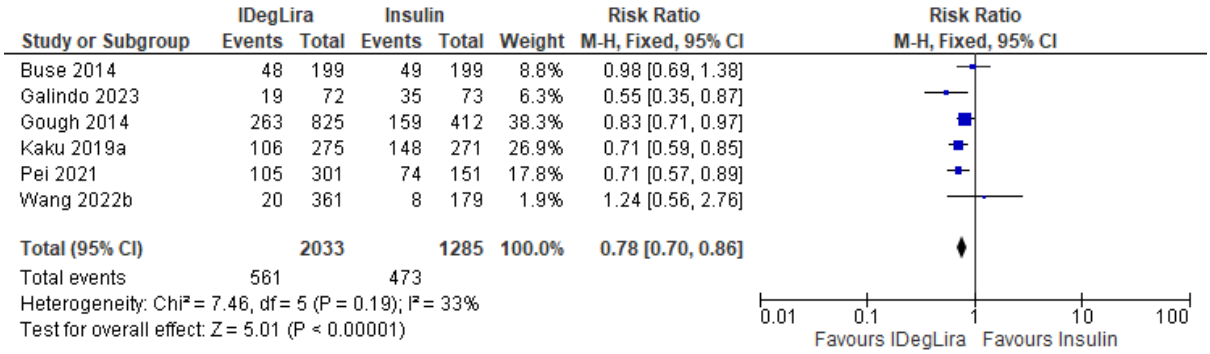


Figure 379: At night hypoglycaemic episodes

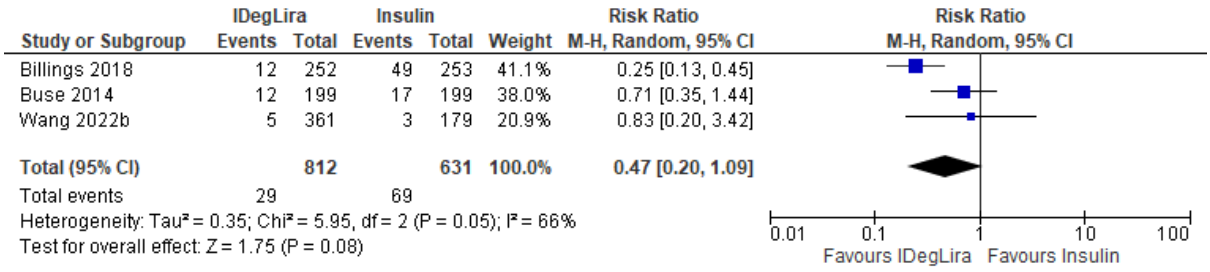


Figure 380: Severe hypoglycaemic episodes

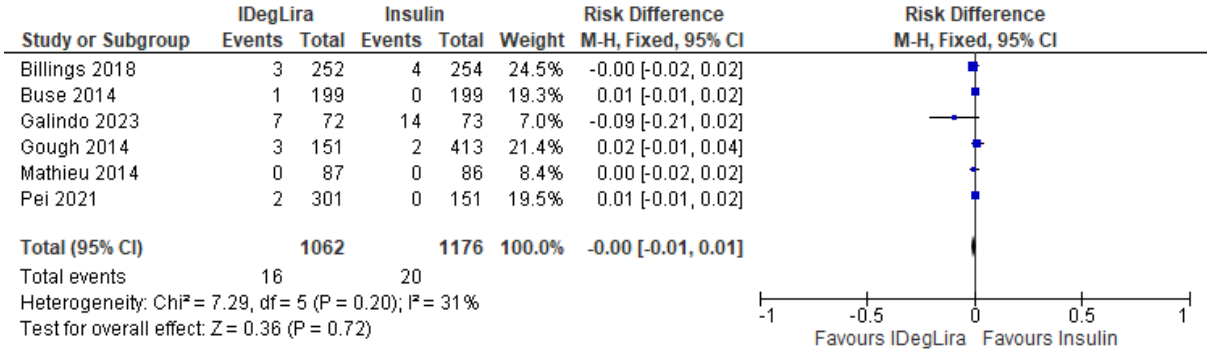
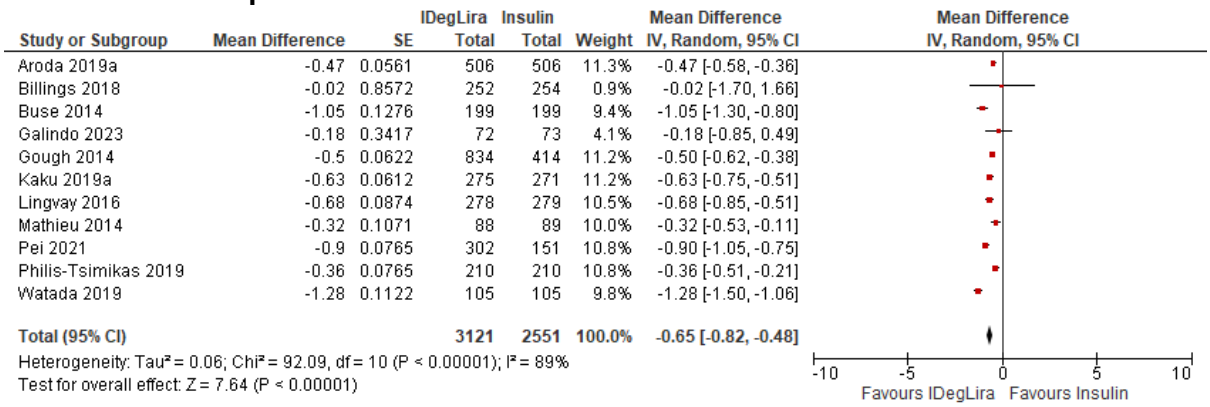
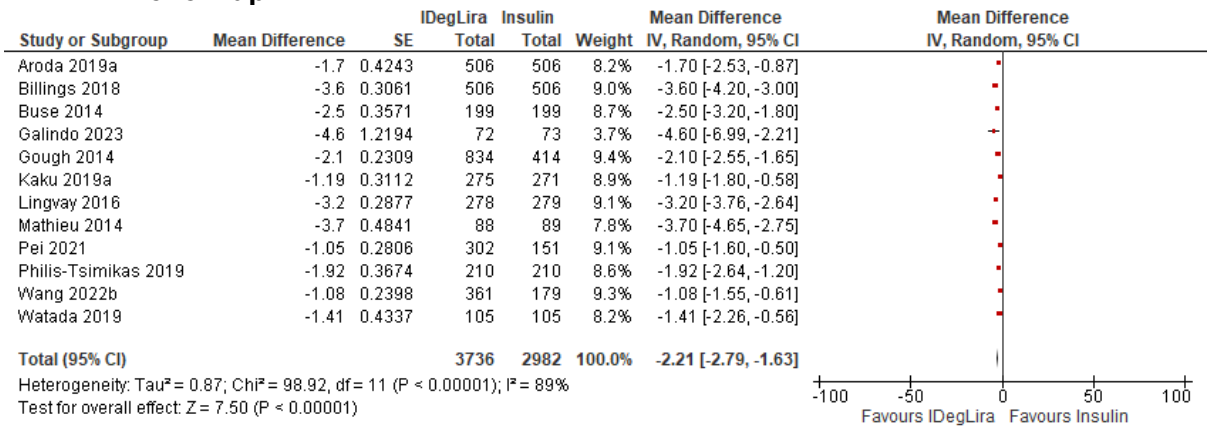


Figure 381: HbA1c change (%, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR and NAFLD subgroups.

Figure 382: Weight change (kg, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by eGFR and NAFLD subgroups.

K.1.8.3 Adding insulin degludec/Liraglutide compared to adding liraglutide

Figure 383: All-cause mortality at end of follow up

Study or Subgroup	IDegLira Events	IDegLira Total	Liraglutide Events	Liraglutide Total	Weight	Risk Difference M-H, Fixed, 95% CI
Gough 2014	2	833	0	414	69.7%	0.00 [-0.00, 0.01]
Wang 2022B	0	361	0	180	30.3%	0.00 [-0.01, 0.01]
Total (95% CI)		**1194**		**594**	**100.0%**	**0.00 [-0.00, 0.01]**
Total events	2		0			

Heterogeneity: Chi² = 0.23, df = 1 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.75 (P = 0.45)

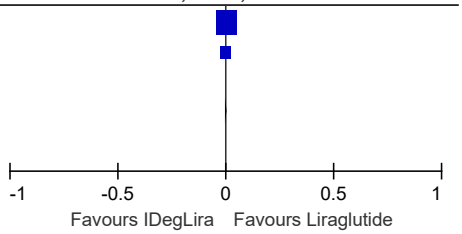


Figure 384: Hypoglycaemia episodes at end of follow up

Study or Subgroup	IDegLira Events	IDegLira Total	Liraglutide Events	Liraglutide Total	Weight	Risk Ratio M-H, Random, 95% CI
Gough 2014	263	825	28	412	44.9%	4.69 [3.24, 6.80]
Kaku 2019A	106	275	6	273	37.4%	17.54 [7.84, 39.24]
Wang 2022B	20	361	1	180	17.7%	9.97 [1.35, 73.71]
Total (95% CI)		**1461**		**865**	**100.0%**	**8.77 [3.03, 25.43]**
Total events	389		35			

Heterogeneity: Tau² = 0.62; Chi² = 9.05, df = 2 (P = 0.01); I² = 78%
Test for overall effect: Z = 4.00 (P < 0.0001)

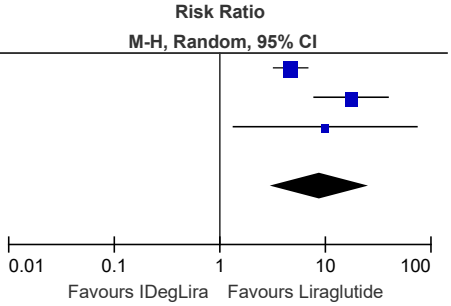


Figure 385: HbA1c change (%, lower values are better, mean difference) at end of follow up

Study or Subgroup	Mean Difference	SE	IDegLira Total	Liraglutide Total	Weight	Mean Difference IV, Fixed, 95% CI
Gough 2014	-0.6	0.0661	834	415	46.2%	-0.60 [-0.73, -0.47]
Kaku 2019A	-0.48	0.0612	361	273	53.8%	-0.48 [-0.60, -0.36]
Total (95% CI)			**1195**	**688**	**100.0%**	**-0.54 [-0.62, -0.45]**

Heterogeneity: Chi² = 1.77, df = 1 (P = 0.18); I² = 44%
Test for overall effect: Z = 11.92 (P < 0.00001)

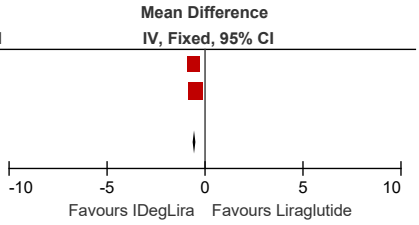
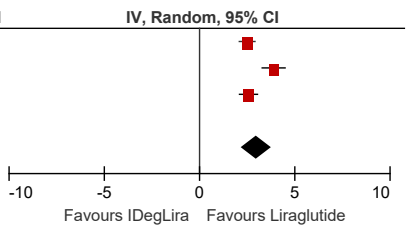


Figure 386: Weight change (kg, lower values are better, mean difference) at end of follow up

Study or Subgroup	Mean Difference	SE	IDegLira Total	Liraglutide Total	Weight	Mean Difference IV, Random, 95% CI
Gough 2014	2.5	0.2104	834	414	34.8%	2.50 [2.09, 2.91]
Kaku 2019A	3.89	0.3061	275	273	31.4%	3.89 [3.29, 4.49]
Wang 2022B	2.57	0.2398	361	180	33.8%	2.57 [2.10, 3.04]
Total (95% CI)			**1470**	**867**	**100.0%**	**2.96 [2.17, 3.75]**

Heterogeneity: Tau² = 0.42; Chi² = 15.62, df = 2 (P = 0.0004); I² = 87%
Test for overall effect: Z = 7.36 (P < 0.00001)



K.1.8.4 Adding insulin glargine/Lixisenatide compared to adding insulin

Figure 387: All-cause mortality at end of follow up

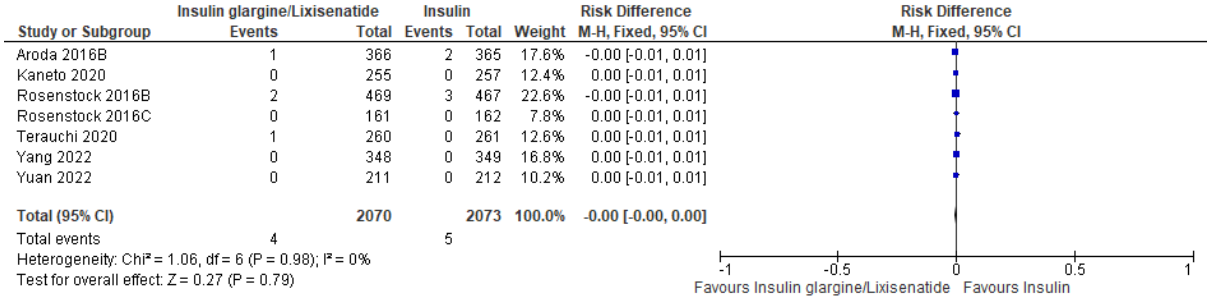


Figure 388: Cardiovascular mortality at end of follow up

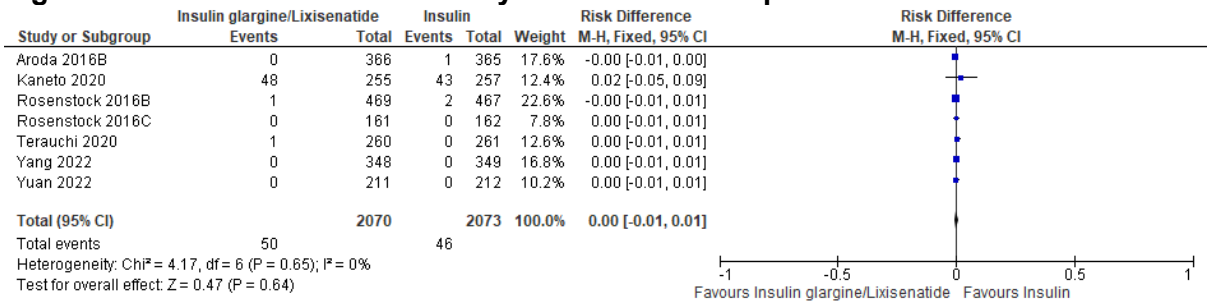


Figure 389: Hypoglycaemia episodes at end of follow up

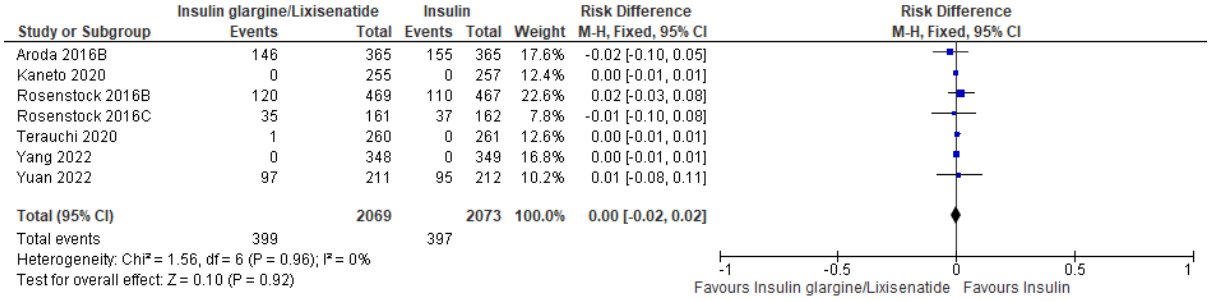


Figure 390: Severe hypoglycaemic episodes at end of follow up

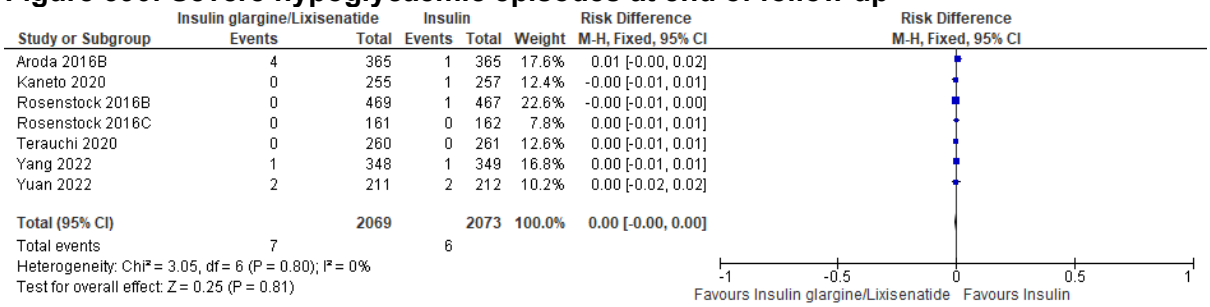
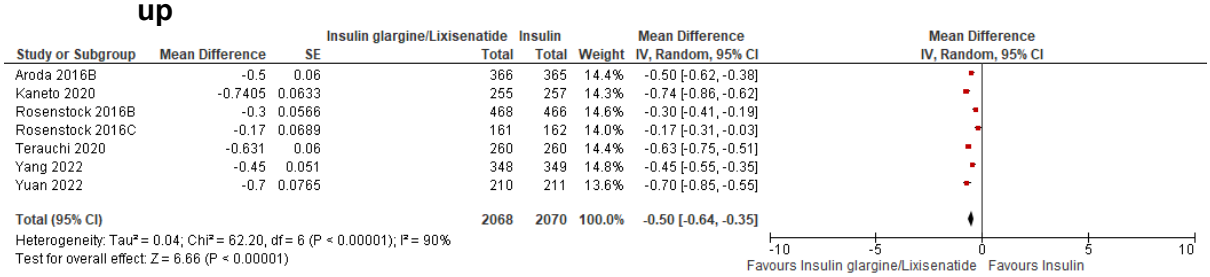
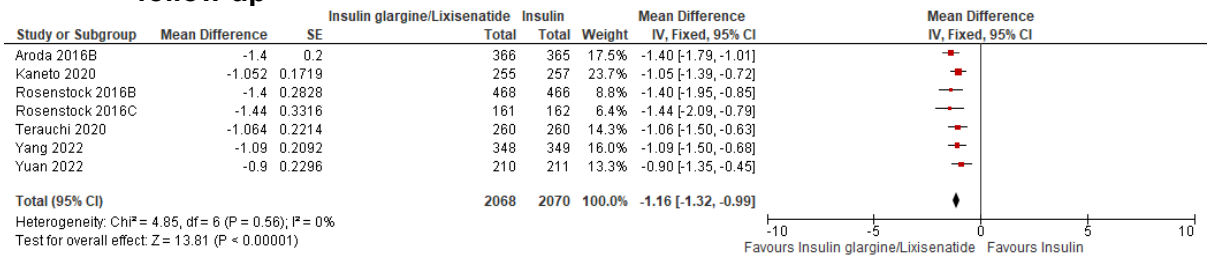


Figure 391: HbA1c change (%, lower values are better, change scores) at end of follow up



Note: Heterogeneity was not explained by sensitivity analysis, nor subgroup analysis by obesity subgroup.

Figure 392: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.8.5 Adding insulin glargine/Lixisenatide compared to adding lixisenatide

Figure 393: All-cause mortality at end of follow up

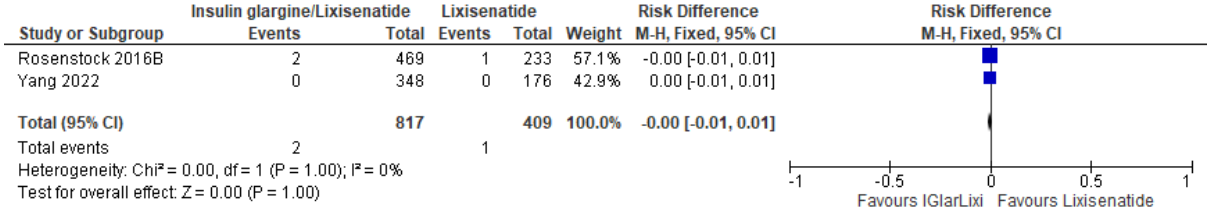


Figure 394: Cardiovascular mortality at end of follow up

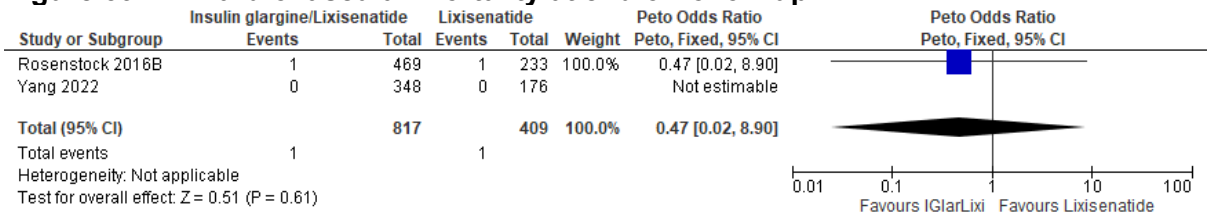


Figure 395: Hypoglycaemia episodes at end of follow up

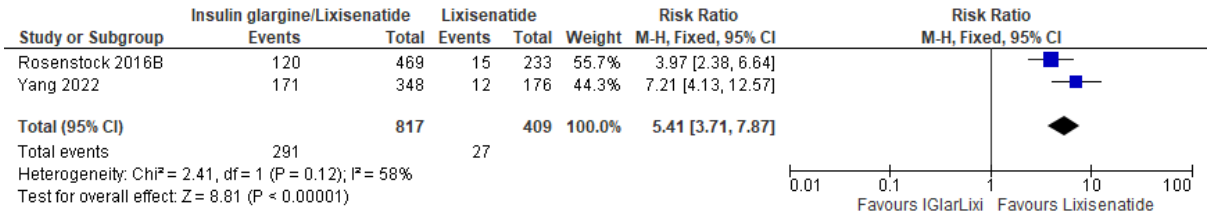


Figure 396: Severe hypoglycaemic episodes at end of follow up

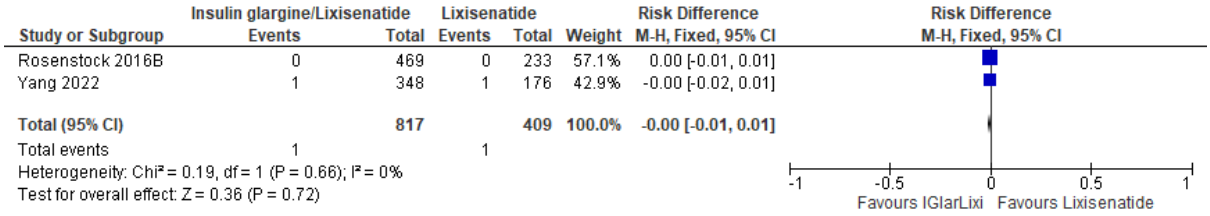


Figure 397: HbA1c change (%, lower values are better, change scores) at end of follow up

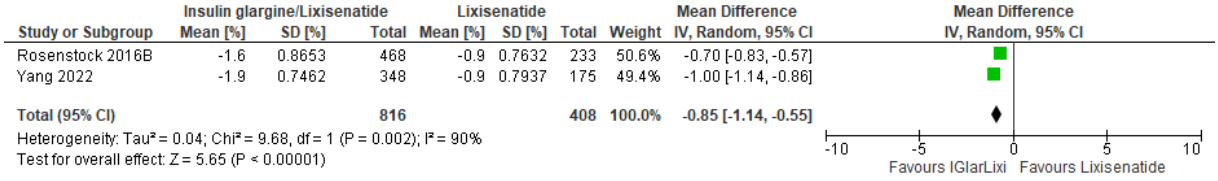
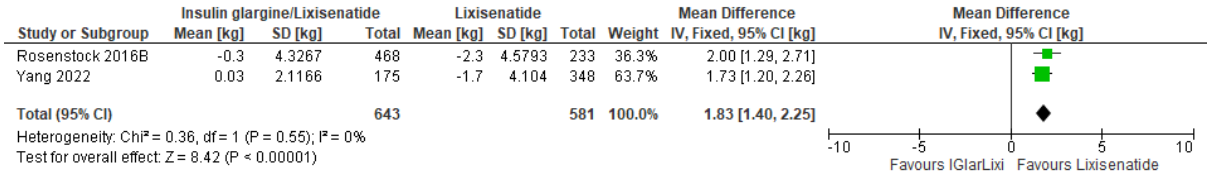


Figure 398: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.9 Combinations

K.1.9.1 Adding dapagliflozin + exenatide compared to adding dapagliflozin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.2 Adding dapagliflozin + exenatide compared to adding exenatide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.3 Adding dapagliflozin + saxagliptin compared to adding dapagliflozin

Figure 399: All-cause mortality at end of follow up

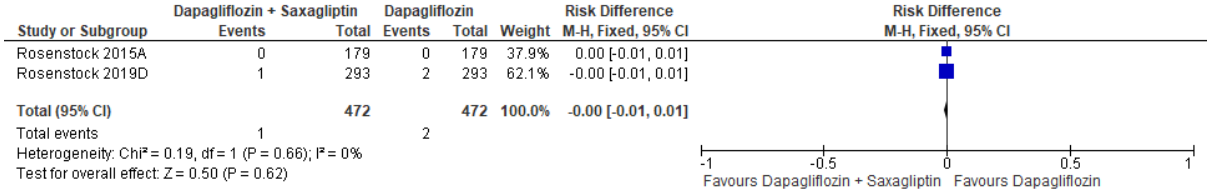


Figure 400: Cardiovascular mortality at end of follow up

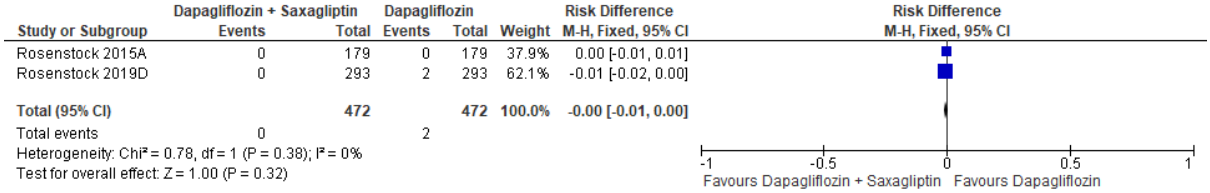


Figure 401: Hypoglycaemia episodes at end of follow up

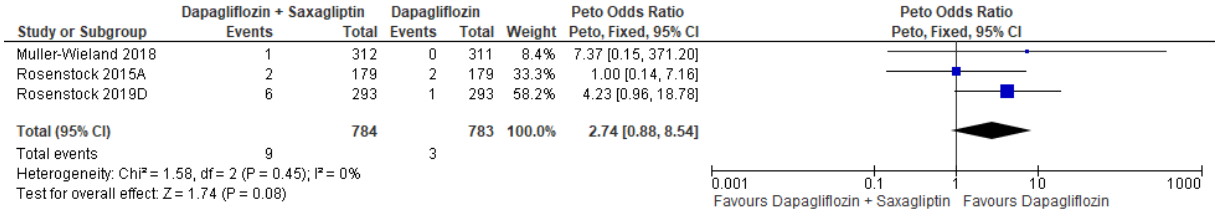


Figure 402: Severe hypoglycaemic episodes at end of follow up

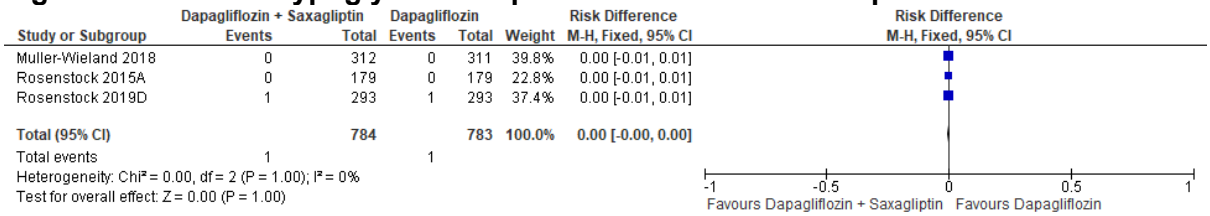


Figure 403: HbA1c change (%, lower values are better, change scores) at end of follow up

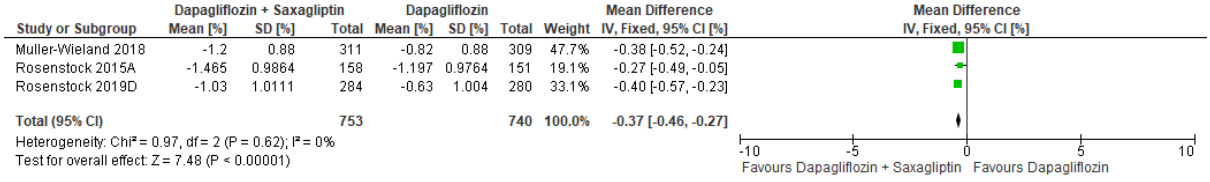
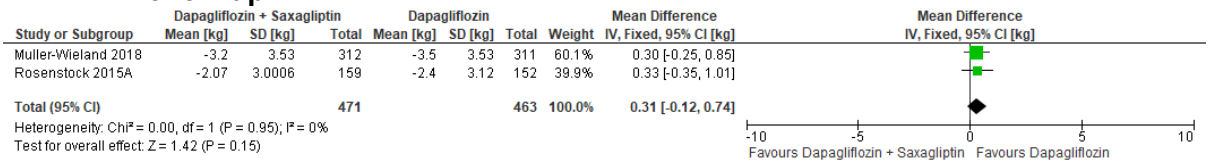


Figure 404: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.9.4 Adding dapagliflozin + saxagliptin compared to adding glimepiride

Figure 405: Hospitalisation for heart failure at end of follow up

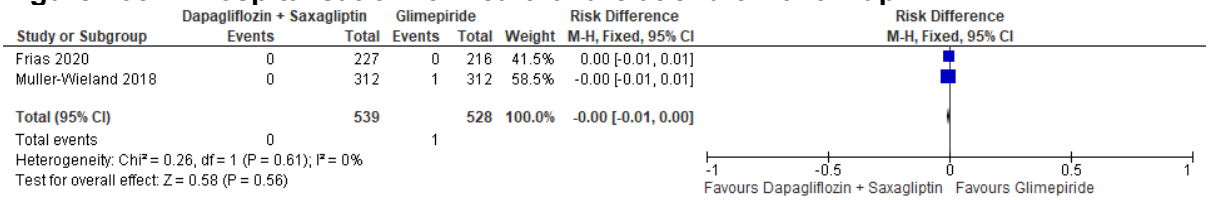


Figure 406: Hypoglycaemia episodes at end of follow up

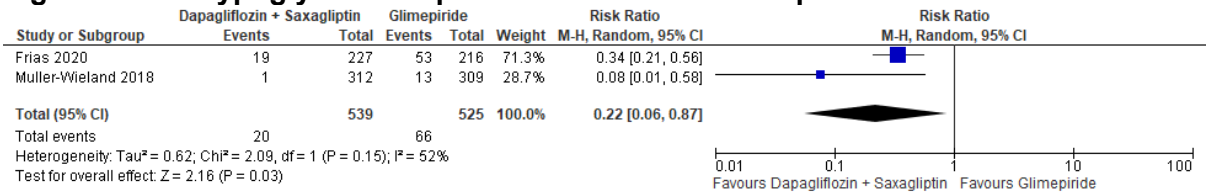


Figure 407: Severe hypoglycaemic episodes at end of follow up

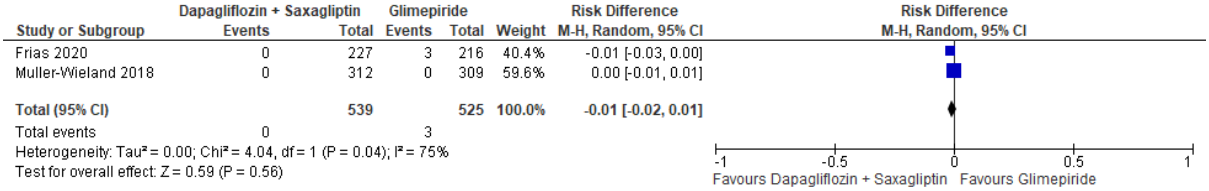


Figure 408: HbA1c change (%, lower values are better, change scores) at end of follow up

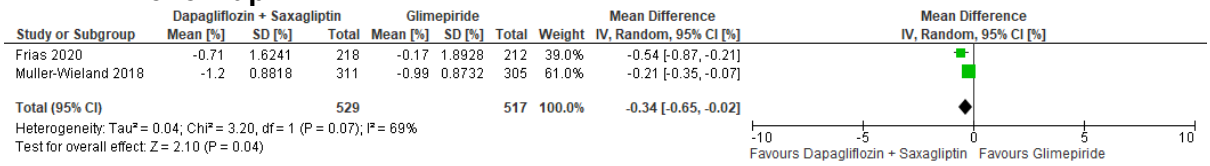
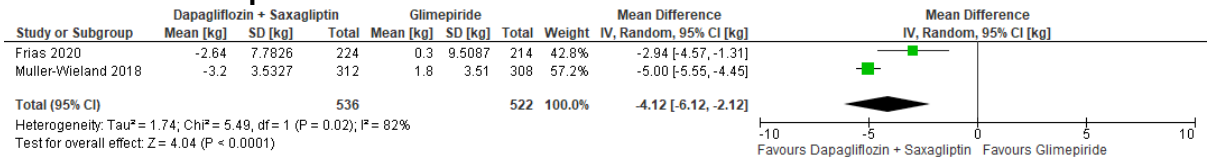


Figure 409: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.9.5 Adding dapagliflozin + saxagliptin compared to adding insulin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.6 Adding dapagliflozin + saxagliptin compared to adding saxagliptin

Figure 410: All-cause mortality at end of follow up

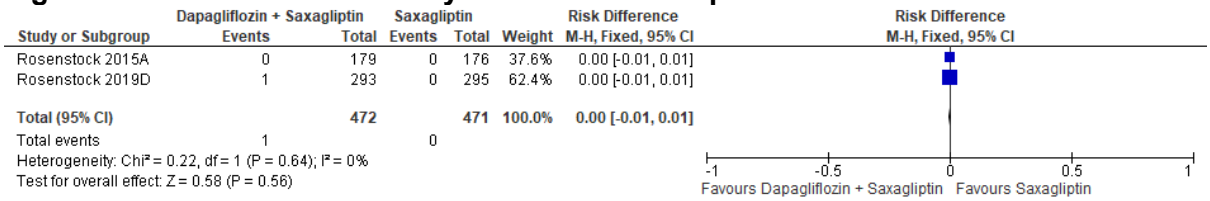


Figure 411: Cardiovascular mortality at end of follow up

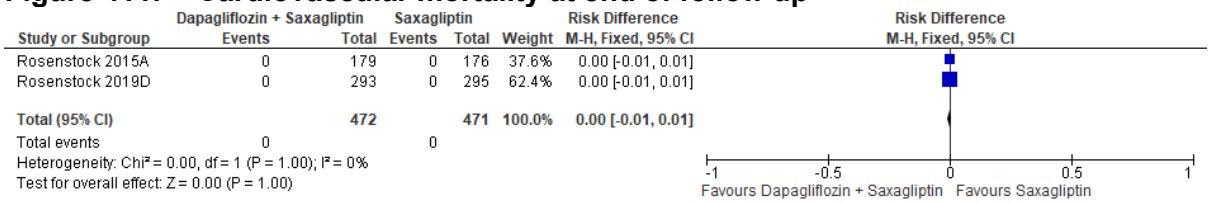


Figure 412: Hypoglycaemia episodes at end of follow up

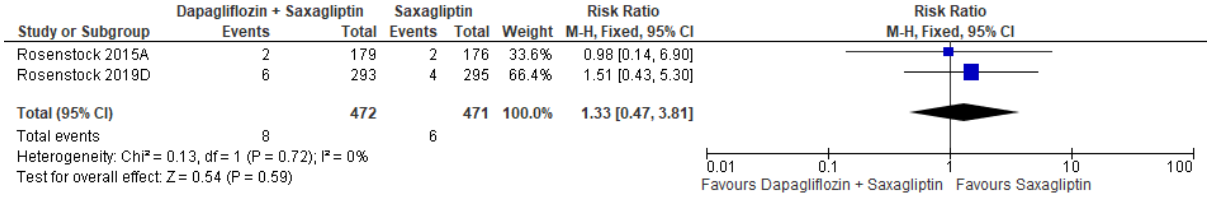


Figure 413: Severe hypoglycaemic episodes at end of follow up

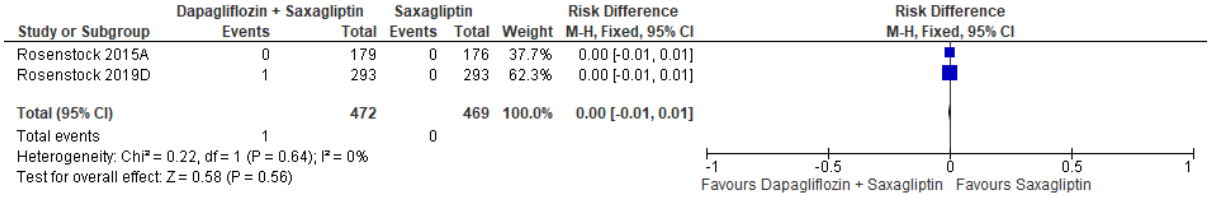


Figure 414: HbA1c change (%, lower values are better, change scores) at end of follow up

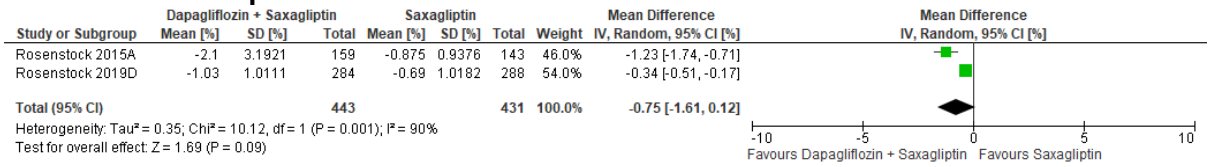
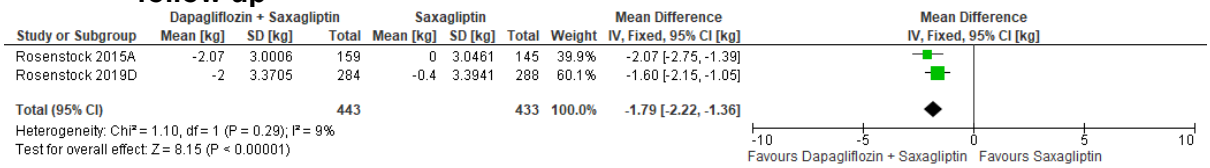


Figure 415: Weight change (kg, lower values are better, change scores) at end of follow up



K.1.9.7 Adding dapagliflozin + saxagliptin compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.8 Adding empagliflozin + liraglutide compared to adding empagliflozin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.9 Adding empagliflozin + liraglutide compared to adding insulin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.10 Adding empagliflozin + liraglutide compared to adding liraglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.11 Adding ertugliflozin + sitagliptin compared to adding ertugliflozin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.12 Adding ertugliflozin + sitagliptin compared to adding sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.13 Adding glimepiride + metformin compared to adding glimepiride

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.14 Adding glimepiride + metformin compared to adding metformin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.15 Adding glimepiride + metformin slow release compared to adding glimepiride + metformin standard release

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.16 Adding liraglutide + metformin compared to adding metformin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.17 Adding pioglitazone + alogliptin compared to adding pioglitazone

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.18 Adding pioglitazone + exenatide compared to adding insulin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.19 Adding pioglitazone + exenatide compared to adding pioglitazone

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.20 Adding pioglitazone + metformin compared to adding metformin

There are no forest plots for this comparison (all outcomes include a single study).

K.1.9.21 Adding pioglitazone + metformin compared to adding pioglitazone

There are no forest plots for this comparison (all outcomes include a single study).

K.2 Switching

K.2.1 Metformin

K.2.1.1 Switching to metformin slow release compared to staying on metformin standard release

There are no forest plots for this comparison (all outcomes include a single study).

K.2.2 DPP-4 inhibitors

K.2.2.1 Switching to sitagliptin compared to switching to placebo

There are no forest plots for this comparison (all outcomes include a single study).

K.2.2.2 Switching to vildagliptin compared to switching to alogliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.2.3 GLP-1 receptor agonist

K.2.3.1 Switching to liraglutide compared to staying on sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.2.3.2 Switching to semaglutide compared to switching to dulaglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.2.3.3 Switching to semaglutide compared to staying on sitagliptin

There are no forest plots for this comparison (all outcomes include a single study).

K.2.4 SGLT2 inhibitors

K.2.4.1 Switching to glimepiride compared to switching to liraglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.2.4.2 Switching to canagliflozin compared to switching to liraglutide

There are no forest plots for this comparison (all outcomes include a single study).

K.2.1 Thiazolidinediones

K.2.1.1 Staying on pioglitazone compared to switching to dapagliflozin

There are no forest plots for this comparison (all outcomes include a single study).

K.2.1.2 Switching to pioglitazone compared to switching to glimepiride

There are no forest plots for this comparison (all outcomes include a single study).

K.2.2 Combinations

K.2.2.1 Switching to fixed-dose combination glimepiride/metformin slow release compared to staying on fixed-dose combination glimepiride/metformin standard release

There are no forest plots for this comparison (all outcomes include a single study).