National Institute for Health and Care Excellence

1

Draft for consultation

Type 2 diabetes in adults: management

[F8.2] Evidence reviews for subsequent pharmacological management of type 2 diabetes: appendix R

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.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN:

Appendix R Risk of bias and directness table

Table 1: Risk of bias and directness information for studies included in the review for subsequent therapy, model 1 (people with chronic heart failure)

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Arturi 2017	Liraglutide v Insulin	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Arturi 2017	Liraglutide v Insulin	Hospitalisation for heart failure	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Arturi 2017	Liraglutide v Insulin	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Arturi 2017	Sitagliptin v Insulin	HbA1c change	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Arturi 2017	Sitagliptin v Insulin	Hospitalisation for heart failure	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Arturi 2017	Sitagliptin v Insulin	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Arturi 2017	Liraglutide v Sitagliptin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Arturi 2017	Liraglutide v Sitagliptin	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Arturi 2017	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Cannon 2020 HF	Ertugliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Cannon 2020 HF	Ertugliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Chen 2017	Exenatide v Insulin	All-cause mortality	High	Concerns with allocation, blinding, method of analysis and attrition	Directly applicable	None specified
Chen 2017	Exenatide v Insulin	BMI change	High	Concerns with allocation, blinding, method of analysis and attrition	Directly applicable	None specified
Chen 2017	Exenatide v Insulin	HbA1c change	High	Concerns with allocation, blinding, method of analysis and attrition	Directly applicable	None specified
Green 2015 HF	Sitagliptin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified
Green 2015 HF	Sitagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Holman 2017 HF	Exenatide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Mahaffey 2018 HF	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Mahaffey 2018 HF	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mahaffey 2018 HF	Canagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 HF	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Marso 2016A HF	Liraglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Marso 2016B HF	Semaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
McMurray 2018	Vildagliptin v Placebo	All-cause mortality	Low	No concerns	Directly applicable	None specified
McMurray 2018	Vildagliptin v Placebo	Cardiac arrhythmia	Low	No concerns	Directly applicable	None specified
McMurray 2018	Vildagliptin v Placebo	Cardiovascular mortality	Low	No concerns	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
McMurray 2018	Vildagliptin v Placebo	Hospitalisation for heart failure	Low	No concerns	Directly applicable	None specified
McMurray 2018	Vildagliptin v Placebo	Hypoglycaemia episodes	Low	No concerns	Directly applicable	None specified
McMurray 2018	Vildagliptin v Placebo	Non-fatal stroke	Low	No concerns	Directly applicable	None specified
McMurray 2018	Vildagliptin v Placebo	HbA1c change	High	The publication did not report the type of analysis that was undertaken for the outcome data. Data were were rescue-censored, and the number of participants included in the analysis was not reported.	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Pfeffer 2015 HF	Lixisenatide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Rosenstock 2019A HF	Linagliptin v Placebo	Cardiovascular mortality	Low	Study described as multicentre,	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified		

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A HF	Linagliptin v Placebo	Hospitalisation for heart failure	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9%	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				(6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
White 2013 HF	Alogliptin v Placebo	3-point MACE	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	4-point MACE	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Hospitalisation for heart failure	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
White 2013 HF	Alogliptin v Placebo	Non-fatal stroke	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Unstable angina	High	None specified	Partially applicable	Reports revascularisation for unstable angina
Wiviott 2019 HF	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 HF	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 HF	Dapagliflozin v Placebo	Cardiac arrhythmia	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 HF	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 HF	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 HF	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 HF	Dapagliflozin v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Zinman 2015 HF	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified

Table 2: Risk of bias and directness information for studies included in the review for subsequent therapy, model 2 (people with atherosclerotic cardiovascular disease)

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Adel 2022	Empagliflozin v Placebo	Cardiovascular mortality	High	Concerns due to allocation concealment and effect of assignment of to the intervention	Partially applicable	Intervention indirectness - unclear if all people continued to receive insulin throughout the trial
Adel 2022	Empagliflozin v Placebo	HbA1c change	High	Concerns due to allocation concealment and effect of assignment of to the intervention	Partially applicable	Intervention indirectness - unclear if all people continued to receive insulin throughout the trial
Adel 2022	Empagliflozin v Placebo	Unstable angina	High	Concerns due to allocation concealment and effect of assignment of to the intervention	Partially applicable	Intervention indirectness - unclear if all people continued to receive insulin throughout the trial
Adel 2022	Empagliflozin v Placebo	Weight change	High	Concerns due to allocation concealment and effect of assignment of to the intervention	Partially applicable	Intervention indirectness - unclear if all people continued to receive insulin throughout the trial
Arturi 2017	Liraglutide v Insulin	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Arturi 2017	Liraglutide v Insulin	Hospitalisation for heart failure	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Arturi 2017	Liraglutide v Insulin	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Arturi 2017	Sitagliptin v Insulin	HbA1c change	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Arturi 2017	Sitagliptin v Insulin	Hospitalisation for heart failure	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Arturi 2017	Sitagliptin v Insulin	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Arturi 2017	Liraglutide v Sitagliptin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Arturi 2017	Liraglutide v Sitagliptin	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Arturi 2017	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Death from renal causes	High	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Development of end stage kidney disease	High	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Diabetic ketoacidosis	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Cannon 2020	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Cannon 2020	Ertugliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Cannon 2020	Ertugliflozin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Cannon 2020 CKD	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD high	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD high	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD mod	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD mod	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020 HF	Ertugliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Cannon 2020 HF	Ertugliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Cannon 2020 no CKD	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 no CKD	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020 no HF	Ertugliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Cannon 2020 no HF	Ertugliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Acute kidney injury	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	All-cause mortality	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Cardiovascular mortality	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Development of end stage kidney disease	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	HbA1c change	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Hospitalisation for heart failure	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Hypoglycaemia episodes	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Non-fatal myocardial infarction	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Cefalu 2015	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Unstable angina	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Cefalu 2015	Dapagliflozin v Placebo	Weight change	High	Concerns regarding method of analysis and attrition	Directly applicable	None specified
Chen 2017	Exenatide v Insulin	All-cause mortality	High	Concerns with allocation, blinding, method of analysis and attrition	Directly applicable	None specified
Chen 2017	Exenatide v Insulin	BMI change	High	Concerns with allocation, blinding, method of analysis and attrition	Directly applicable	None specified
Chen 2017	Exenatide v Insulin	HbA1c change	High	Concerns with allocation, blinding, method of analysis and attrition	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	4-point MACE	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Del Prato 2021	Tirzepatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Unstable angina	Low	None specified	Directly applicable	None specified
Del Prato 2021	Tirzepatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Gerstein 2019A CVD	Dulaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Gohari 2022	Empagliflozin v Placebo	HbA1c change	Some concerns	Some baseline differences	Directly applicable	NA
Gohari 2022	Empagliflozin v Placebo	All-cause mortality	Some concerns	Some baseline differences	Directly applicable	None specified
Gohari 2022	Empagliflozin v Placebo	Cardiovascular mortality	Some concerns	Some baseline differences	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Green 2015	Sitagliptin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Green 2015	Sitagliptin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Green 2015 HF	Sitagliptin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified
Green 2015 HF	Sitagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Green 2015 no HF	Sitagliptin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified
Green 2015 no HF	Sitagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Holman 2017 CVD	Exenatide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Lee 2013B	Pioglitazone v Placebo	All-cause mortality	High	1) no mention of precpecified plan/protocol 2) lack of info on method of analysis 3) unclear on blinding	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Lee 2013B	Pioglitazone v Placebo	HbA1c change	High	1) no mention of precpecified plan/protocol 2) lack of info on method of analysis 3) unclear on blinding	Directly applicable	None specified
Lee 2013B	Pioglitazone v Placebo	Non-fatal myocardial infarction	High	1) no mention of precpecified plan/protocol 2) lack of info on method of analysis 3) unclear on blinding	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	Acute kidney injury	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	All-cause mortality	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	HbA1c change	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	Higher attrition, not clear on the analysis	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				used to account for this.		
Leiter 2014	Dapagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	Some concerns	Higher attrition, not clear on the analysis used to account for this.	Directly applicable	None specified
Leiter 2014	Dapagliflozin v Placebo	Weight change	Some concerns	Higher attrition, not clear on the analysis used to account for this. LOCF used	Directly applicable	None specified
Li 2014C	Glimepiride v Insulin	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation concealment.	Directly applicable	None specified
Li 2014C	Glimepiride v Insulin	Hypoglycaemia episodes	Some concerns	Lack of information around method of randomisation and allocation concealment.	Directly applicable	None specified
Li 2014C	Glimepiride v Insulin	Weight change	Some concerns	Lack of information around method of	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomisation and allocation concealment.		
Mahaffey 2018 CVD	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Mahaffey 2018 CVD	Canagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	3-point MACE	Some concerns	Problems with attrition.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nissen 2008	Glimepiride v Pioglitazone	5-point MACE	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	All-cause mortality	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Cardiovascular mortality	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	HbA1c change	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Hospitalisation for heart failure	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Hypoglycaemia episodes	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Non-fatal myocardial infarction	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Non-fatal stroke	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Unstable angina	Some concerns	Problems with attrition.	Directly applicable	None specified
Nissen 2008	Glimepiride v Pioglitazone	Weight change	Some concerns	Problems with attrition.	Directly applicable	None specified
Oh 2021	Empagliflozin v Sitagliptin	HbA1c change	High	Open-label study ; main focus of the study was to assess myocardial perfusion reserve using SPECT examinations - this outcome was part of	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				laboratory findings but not prespecified in the study plan; lack of info on allocation concealment		
Oh 2021	Empagliflozin v Sitagliptin	Weight change	High	Open-label study ; main focus of the study was to assess myocardial perfusion reserve using SPECT examinations - this outcome was part of laboratory findings but not prespecified in the study plan; lack of info on allocation concealment	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	5-point MACE	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pfeffer 2015	Lixisenatide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Pfeffer 2015	Lixisenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Pfeffer 2015 HF	Lixisenatide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Pfeffer 2015 no HF	Lixisenatide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	HbA1c change	High	1) small sample size (N=49) 2) Limitation in the use of per-protocol analysis for the primary outcomes	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	BMI change	High	1) small sample size (N=49)2) Limitation in the use of per-	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				protocol analysis for the primary outcomes		
Phrommintikul 2019	Dapagliflozin v Vildagliptin	Weight change	High	1) small sample size (N=49)2) Limitation in the use of per-protocol analysis for the primary outcomes	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	All-cause mortality	Some concerns	small sample size (N=49); lack of information on allocation concealment	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	Cardiovascular mortality	Some concerns	small sample size (N=49); lack of information on allocation concealment	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	Hospitalisation for heart failure	Some concerns	small sample size (N=49); lack of information on allocation concealment	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	Hypoglycaemia episodes	Some concerns	small sample size (N=49); lack of information on allocation concealment	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Phrommintikul 2019	Dapagliflozin v Vildagliptin	Non-fatal myocardial infarction	Some concerns	small sample size (N=49); lack of information on allocation concealment	Directly applicable	None specified
Phrommintikul 2019	Dapagliflozin v Vildagliptin	Non-fatal stroke	Some concerns	small sample size (N=49); lack of information on allocation concealment	Directly applicable	None specified
Rosenstock 2019B CVD	Glimepiride v Linagliptin	3-point MACE	Low	None specified	Directly applicable	None specified
Scirica 2013 CVD	Saxagliptin v Placebo	3-point MACE	High	Problems with adherence to outcome	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Verma 2019	Empagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Verma 2019	Empagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	3-point MACE	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	4-point MACE	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Development of end stage kidney disease	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Hospitalisation for heart failure	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
White 2013	Alogliptin v Placebo	Non-fatal stroke	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Weight change	High	None specified	Directly applicable	None specified
White 2013	Alogliptin v Placebo	Unstable angina	High	None specified	Partially applicable	Reports revascularisation for unstable angina
White 2013 HF	Alogliptin v Placebo	3-point MACE	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	4-point MACE	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Hospitalisation for heart failure	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Non-fatal stroke	High	None specified	Directly applicable	None specified
White 2013 HF	Alogliptin v Placebo	Unstable angina	High	None specified	Partially applicable	Reports revascularisation for unstable angina
White 2013 no HF	Alogliptin v Placebo	3-point MACE	High	None specified	Directly applicable	None specified
White 2013 no HF	Alogliptin v Placebo	4-point MACE	High	None specified	Directly applicable	None specified
White 2013 no HF	Alogliptin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
White 2013 no HF	Alogliptin v Placebo	Hospitalisation for heart failure	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
White 2013 no HF	Alogliptin v Placebo	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
White 2013 no HF	Alogliptin v Placebo	Non-fatal stroke	High	None specified	Directly applicable	None specified
White 2013 no HF	Alogliptin v Placebo	Unstable angina	High	None specified	Partially applicable	Reports revascularisation for unstable angina
Wilcox 2008	Pioglitazone v Placebo	3-point MACE	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wilcox 2008	Pioglitazone v Placebo	All-cause mortality	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wilcox 2008	Pioglitazone v Placebo	Cardiac arrhythmia	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wilcox 2008	Pioglitazone v Placebo	Cardiovascular mortality	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wilcox 2008	Pioglitazone v Placebo	Hospitalisation for heart failure	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wilcox 2008	Pioglitazone v Placebo	Hypoglycaemia episodes	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wilcox 2008	Pioglitazone v Placebo	Non-fatal myocardial infarction	High	Concerns regarding allocation and attrition	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wilcox 2008	Pioglitazone v Placebo	Non-fatal stroke	High	Concerns regarding allocation and attrition	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	Cardiac arrhythmia	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CVD	Dapagliflozin v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	Intervention indirectness - >20% of the population were not receiving glucose lowering therapy before the study.
Zinman 2015	Empagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Zinman 2015	Empagliflozin v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Zinman 2015	Empagliflozin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Zinman 2015 CKD	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Zinman 2015 CKD	Empagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Zinman 2015 CKD	Empagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Zinman 2015 HF	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Zinman 2015 no CKD	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Zinman 2015 no CKD	Empagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Zinman 2015 no CKD	Empagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Zinman 2015 no HF	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified

Table 3: Risk of bias and directness information for studies included in the review for subsequent therapy, model 3 (people with chronic kidney disease)

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Barnett 2014	Empagliflozin v Placebo	HbA1c change	Low	Concerns around attrition, however, the number of participants who	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				dropped out and the associated reasons appeared to be balanced across arms.		
Barnett 2014	Empagliflozin v Placebo	Weight change	Low	Concerns around attrition, however, the number of particpants who dropped out and the associated reasons appeared to be balanced across arms.	Directly applicable	None specified
Barnett 2014	Empagliflozin v Placebo	All-cause mortality	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				on the treated dataset.		
Barnett 2014	Empagliflozin v Placebo	Cardiac arrhythmia	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Barnett 2014	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	HbA1c change	Low	Concerns around attrition, however, the number of particpants who dropped out and the	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				associated reasons appeared to be balanced across arms.		
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	Weight change	Low	Concerns around attrition, however, the number of particpants who dropped out and the associated reasons appeared to be balanced across arms.	Directly applicable	None specified
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	All-cause mortality	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	Cardiac arrhythmia	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	Cardiovascular mortality	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 2 CKD	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Barnett 2014 stage 3 CKD	Empagliflozin v Placebo	HbA1c change	Low	Concerns around attrition, however, the number of particpants who dropped out and the associated reasons appeared to be balanced across arms.	Directly applicable	None specified
Barnett 2014 stage 3 CKD	Empagliflozin v Placebo	Weight change	Low	Concerns around attrition, however, the number of particpants who dropped out and the associated reasons appeared to be balanced across arms.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Barnett 2014 stage 3 CKD	Empagliflozin v Placebo	All-cause mortality	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 3 CKD	Empagliflozin v Placebo	Cardiac arrhythmia	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Barnett 2014 stage 3 CKD	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 3 CKD	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Barnett 2014 stage 4 CKD	Empagliflozin v Placebo	HbA1c change	Low	Concerns around attrition, however, the number of particpants who dropped out and the associated reasons appeared to be balanced across arms.	Directly applicable	None specified
Barnett 2014 stage 4 CKD	Empagliflozin v Placebo	Weight change	Low	Concerns around attrition, however, the number of particpants who dropped out and the associated reasons appeared to be balanced across arms.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Barnett 2014 stage 4 CKD	Empagliflozin v Placebo	All-cause mortality	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 4 CKD	Empagliflozin v Placebo	Cardiac arrhythmia	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Barnett 2014 stage 4 CKD	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.	Directly applicable	None specified
Barnett 2014 stage 4 CKD	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomisation and allocation conealment appear to be adequate. The study was double-blinded. Although there is little	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				information about what consitutes a protocol violation, only a very small number of participants were excluded due to protocol non-compliance. Outcome was based on the treated dataset.		
Cannon 2020 CKD	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD high	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD high	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD mod	Ertugliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Cannon 2020 CKD mod	Ertugliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	BMI change	Some concerns	Double-blind trial with mITT analysis, assuming missing data similar to those in same group	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Davies 2016	Liraglutide v Placebo	HbA1c change	Some concerns	Double-blind trial with mITT analysis, assuming missing data similar to those in same group	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	Weight change	Some concerns	Double-blind trial with mITT analysis, assuming missing data similar to those in same group	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Davies 2016	Liraglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	HbA1c change	Some concerns	mITT analysis with missing data assumed to be at random	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Weight change	Some concerns	mITT analysis with missing data	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				assumed to be at random		
Fioretto 2018	Dapagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Fioretto 2018	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Galle 2012	Pioglitazone v Placebo	HbA1c change	High	No information about randomisation/allocation concealment; ITT but includes missing data, trial not registered; 27% exclusions, no info about missing data strategy	Directly applicable	None specified
Galle 2012	Pioglitazone v Placebo	Hypoglycaemia episodes	High	No information about	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomisation/allocation concealment; trial not registered		
Galle 2012	Pioglitazone v Placebo	Severe hypoglycaemic episodes	High	No information about randomisation/allocation concealment; trial not registered	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Groop 2017	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Groop 2017 UACR<300	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Groop 2017 UACR≥300	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Grunberger 2018	Ertugliflozin v Placebo	All-cause mortality	High	~17% of participants in each group used off-protocol metformin. ITT analysis conducted for this outcome.	Directly applicable	None specified
Grunberger 2018	Ertugliflozin v Placebo	Cardiovascular mortality	High	~17% of participants in each group used off-protocol metformin. ITT analysis conducted for this outcome.	Directly applicable	None specified
Grunberger 2018	Ertugliflozin v Placebo	Hospitalisation for heart failure	High	~17% of participants in each group used off-protocol metformin. ITT analysis conducted for this outcome.	Directly applicable	None specified
Grunberger 2018	Ertugliflozin v Placebo	Persistent signs of worsening kidney disease	High	~17% of participants in each group used off-protocol metformin. ITT analysis conducted for this outcome.	Directly applicable	None specified
Grunberger 2018	Ertugliflozin v Placebo	HbA1c change	High	~17% of participants in each group used	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				off-protocol metformin. mITT analysis conducted for this outcome.		
Grunberger 2018	Ertugliflozin v Placebo	Hypoglycaemia episodes	High	~17% of participants in each group used off-protocol metformin. mITT analysis conducted for this outcome.	Directly applicable	None specified
Grunberger 2018	Ertugliflozin v Placebo	Weight change	High	~17% of participants in each group used off-protocol metformin. mITT analysis conducted for this outcome.	Directly applicable	None specified
Hiramatsu 2018	Liraglutide v Sitagliptin	All-cause mortality	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	All-cause mortality	High	No information about blinding; 30% randomised participants excluded due to death or end stage	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				kidney disease; trial not registered		
Hiramatsu 2018	Liraglutide v Sitagliptin	BMI change	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	BMI change	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Liraglutide v Sitagliptin	Cardiac arrhythmia	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	Cardiac arrhythmia	High	No information about blinding; 30% randomised participants excluded due to	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				death or end stage kidney disease; trial not registered		
Hiramatsu 2018	Liraglutide v Sitagliptin	Development of end stage kidney disease	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	Development of end stage kidney disease	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Liraglutide v Sitagliptin	HbA1c change	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	HbA1c change	High	No information about blinding; 30% randomised participants	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				excluded due to death or end stage kidney disease; trial not registered		
Hiramatsu 2018	Liraglutide v Sitagliptin	Hospitalisation for heart failure	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	Hospitalisation for heart failure	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Liraglutide v Sitagliptin	Non-fatal myocardial infarction	High	No information about blinding; 30% randomised participants excluded due to death or end stage kidney disease; trial not registered	Directly applicable	None specified
Hiramatsu 2018	Sitagliptin v Linagliptin	Non-fatal myocardial infarction	High	No information about blinding; 30% randomised	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				participants excluded due to death or end stage kidney disease; trial not registered		
Hiramatsu 2018	Linagliptin v Liraglutide	All-cause mortality	High	None specified	Directly applicable	None specified
Hiramatsu 2018	Linagliptin v Liraglutide	BMI change	High	None specified	Directly applicable	None specified
Hiramatsu 2018	Linagliptin v Liraglutide	Cardiac arrhythmia	High	None specified	Directly applicable	None specified
Hiramatsu 2018	Linagliptin v Liraglutide	Development of end stage kidney disease	High	None specified	Directly applicable	None specified
Hiramatsu 2018	Linagliptin v Liraglutide	HbA1c change	High	None specified	Directly applicable	None specified
Hiramatsu 2018	Linagliptin v Liraglutide	Hospitalisation for heart failure	High	None specified	Directly applicable	None specified
Hiramatsu 2018	Linagliptin v Liraglutide	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Kimura 2023	Semaglutide v Dulaglutide	BMI change	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kimura 2023	Semaglutide v Dulaglutide	Diabetic ketoacidosis	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kimura 2023	Semaglutide v Dulaglutide	HbA1c change	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kimura 2023	Semaglutide v Dulaglutide	Hospitalisation for heart failure	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kimura 2023	Semaglutide v Dulaglutide	Severe hypoglycaemic episodes	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kimura 2023	Semaglutide v Dulaglutide	Weight change	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kimura 2023	Semaglutide v Dulaglutide	Health-related quality of life - overall	High	Concerns due to appropriateness of the method of analysis and outcome measurement	Directly applicable	None specified
Kimura 2023 NAFLD	Semaglutide v Dulaglutide	BMI change	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kimura 2023 NAFLD	Semaglutide v Dulaglutide	HbA1c change	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kimura 2023 NAFLD	Semaglutide v Dulaglutide	Weight change	Some concerns	Concerns due to appropriateness of the method of analysis	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Acute kidney injury	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Development of end stage kidney disease	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Kohan 2014	Dapagliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Kothny 2015	Vildagliptin v Sitagliptin	Cardiovascular mortality	High	77.1% participants in the vildagliptin and 81.5% participants in the	Directly applicable	The population did include participants who were treatment naïve. However, the

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				sitagliptin group completed. As this was a rare outcome, it was deemed that this could have an effect		baseline characteristics table shows that only 3 participants in the vildagliptin group (3.6%), and 1 participant in the sitagliptin group (1.5%), and therefore, this is deemed unlikely to affect the overall results.
Kothny 2015	Vildagliptin v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	The population did include participants who were treatment naïve. However, the baseline characteristics table shows that only 3 participants in the vildagliptin group (3.6%), and 1 participant in the sitagliptin group (1.5%), and therefore, this is deemed unlikely to affect the overall results.
Kothny 2015	Vildagliptin v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	The population did include participants

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						who were treatment naïve. However, the baseline characteristics table shows that only 3 participants in the vildagliptin group (3.6%), and 1 participant in the sitagliptin group (1.5%), and therefore, this is deemed unlikely to affect the overall results.
Kothny 2015	Vildagliptin v Sitagliptin	HbA1c change	Some concerns	There were some concerns around the lack of information on whether the results were taken from multiple analyses of the data.	Directly applicable	The population did include participants who were treatment naïve. However, the baseline characteristics table shows that only 3 participants in the vildagliptin group (3.6%), and 1 participant in the sitagliptin group (1.5%), and therefore, this is deemed unlikely to affect the overall results.

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Li 2014C	Glimepiride v Insulin	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation concealment.	Directly applicable	None specified
Li 2014C	Glimepiride v Insulin	Hypoglycaemia episodes	Some concerns	Lack of information around method of randomisation and allocation concealment.	Directly applicable	None specified
Li 2014C	Glimepiride v Insulin	Weight change	Some concerns	Lack of information around method of randomisation and allocation concealment.	Directly applicable	None specified
Lukashevich 2011 severe renal impairment	Vildagliptin v Placebo	All-cause mortality	High	Poorly described analysis, no detail on randomisation, concealment or statistical analysis	Directly applicable	None specified
Lukashevich 2011 severe renal impairment	Vildagliptin v Placebo	Hypoglycaemia episodes	High	Poorly described analysis, no detail on randomisation, concealment or statistical analysis. High attrition rates	Directly applicable	None specified
Lukashevich 2011 severe renal impairment	Vildagliptin v Placebo	Severe hypoglycaemic episodes	High	Poorly described analysis, no detail on randomisation, concealment or	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				statistical analysis. High attrition rates		
McGill 2013	Linagliptin v Placebo	HbA1c change	High	There was a lack of information around allocation concealment and adherence. High proportion of participants did not complete treatment. Missing outcome data were high, and data were censored for rescue-therapy use, meaning that is is likely that data were missing from participants who had poorly controlled diabetes. There	Directly applicable	None specified
McGill 2013	Linagliptin v Placebo	Acute kidney injury	High	There was a lack of information around allocation concealment and adherence. There was a high level of discontinuation, and most participants were still analysed in the safety set.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
McGill 2013	Linagliptin v Placebo	Hypoglycaemia episodes	High	There was a lack of information around allocation concealment and adherence. There was a high level of discontinuation, and most participants were still analysed in the safety set.	Directly applicable	None specified
McGill 2013	Linagliptin v Placebo	Non-fatal myocardial infarction	High	There was a lack of information around allocation concealment and adherence. There was a high level of discontinuation, and most participants were still analysed in the safety set.	Directly applicable	None specified
McGill 2013	Linagliptin v Placebo	Non-fatal stroke	High	There was a lack of information around allocation concealment and adherence. There was a high level of discontinuation, and most participants were still analysed in the safety set.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
McGill 2013	Linagliptin v Placebo	Severe hypoglycaemic episodes	High	There was a lack of information around allocation concealment and adherence. There was a high level of discontinuation, and most participants were still analysed in the safety set.	Directly applicable	None specified
McGill 2013	Linagliptin v Placebo	Weight change	High	There was a lack of information around allocation concealment. A high proportion of participants did not complete treatment. There was a lack of clarity around the type of analysis used to evaluate weight change, and the nmber of participants included in the analysis was unclear.	Directly applicable	None specified
McGill 2013	Linagliptin v Placebo	All-cause mortality	High	There was a lack of information around allocation concealment. There was a high level of	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation, and most participants were still analysed in the safety set.		
Moeinzadeh 2021	Linagliptin v Placebo	HbA1c change	High	Lack of information around allocation conceallment and differences in baseline characteristics indicated that the results may be biased.	Directly applicable	None specified
Moeinzadeh 2021	Linagliptin v Placebo	Weight change	High	Lack of information around allocation conceallment and differences in baseline characteristics indicated that the results may be biased.	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mosenzon 2019	Semaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Health-related quality of life - subscale mental component	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Health-related quality of life - subscale physical component	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Mosenzon 2019	Semaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Nowicki 2011A	Saxagliptin v Placebo	HbA1c change	High	Serious risk of bias due to high attrition. This was partially due to pre-specified study discontinuation for patients who did not achieve glycaemic targets to provide best patient care. However, this could	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				also bias the results, as data were missing for patients would did not have controlled glycaemic levels.		
Nowicki 2011A	Saxagliptin v Placebo	All-cause mortality	High	Serious risk of bias due to high treatment discontinuation with no analysis to account for non-compliance.	Directly applicable	None specified
Nowicki 2011A	Saxagliptin v Placebo	Development of end stage kidney disease	High	Serious risk of bias due to high treatment discontinuation with no analysis to account for non-compliance.	Directly applicable	None specified
Nowicki 2011A	Saxagliptin v Placebo	Hypoglycaemia episodes	High	Serious risk of bias due to high treatment discontinuation with no analysis to account for non-compliance.	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	5-point MACE	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Perkovic 2019	Canagliflozin v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Death from renal causes	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Perkovic 2019	Canagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Perkovic 2019 HF	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Perkovic 2019 HF	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Perkovic 2019 no HF	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Perkovic 2019 no HF	Canagliflozin v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Perkovic 2019 no HF	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Perkovic 2019 no HF	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Diabetic ketoacidosis	High	Around 26% of participants did not complete treatment. As this was a rare outcome, it was judged that this may introduce bias.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Weight change	High	Data only available in extractable format for week 104 and not at longest follow-up	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	3-point MACE	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Perkovic 2024	Semaglutide v Placebo	Acute kidney injury	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	All-cause mortality	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Cardiac arrhythmia	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Cardiovascular mortality	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Death from renal causes	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Development of end stage kidney disease	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Perkovic 2024	Semaglutide v Placebo	HbA1c change	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Non-fatal myocardial infarction	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Non-fatal stroke	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Persistent signs of worsening kidney disease	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Severe hypoglycaemic episodes	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified
Perkovic 2024	Semaglutide v Placebo	Unstable angina	Low	Double blind ITT analysis randomised by central web-based system with low attrition.	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	All-cause mortality	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	Diabetic ketoacidosis	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	Diabetic ketoacidosis	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin v Placebo	Diabetic ketoacidosis	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	HbA1c change	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	Persistent signs of worsening kidney disease	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	Persistent signs of worsening kidney disease	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Dapagliflozin	Weight change	High	None specified	Directly applicable	None specified
Pollock 2019	Dapagliflozin + Saxagliptin v Placebo	Weight change	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pollock 2019	Dapagliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Raman 2022	Empagliflozin v Linagliptin	HbA1c change	High	None specified	Directly applicable	None specified
Raman 2022	Empagliflozin v Linagliptin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Rosenstock 2019A CKD	Linagliptin v Placebo	Hospitalisation for heart failure	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Takahashi 2023	Semaglutide v Liraglutide	BMI change	Some concerns	Baseline difference on duration of diabetes	Directly applicable	None specified
Takahashi 2023	Semaglutide v Liraglutide	HbA1c change	Some concerns	Baseline difference on duration of diabetes	Directly applicable	None specified
Takahashi 2023	Semaglutide v Liraglutide	Hypoglycaemia episodes	Some concerns	Baseline difference on duration of diabetes	Directly applicable	None specified
Takahashi 2023	Semaglutide v Liraglutide	Severe hypoglycaemic episodes	Some concerns	Baseline difference on duration of diabetes	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Takahashi 2023	Semaglutide v Liraglutide	Weight change	Some concerns	Baseline difference on duration of diabetes	Directly applicable	None specified
Takahashi 2023	Semaglutide v Dulaglutide	BMI change	Some concerns	Baseline difference on use of statins and SGLT2 inhibitors	Directly applicable	None specified
Takahashi 2023	Semaglutide v Dulaglutide	HbA1c change	Some concerns	Baseline difference on use of statins and SGLT2 inhibitors	Directly applicable	None specified
Takahashi 2023	Semaglutide v Dulaglutide	Hypoglycaemia episodes	Some concerns	Baseline difference on use of statins and SGLT2 inhibitors	Directly applicable	None specified
Takahashi 2023	Semaglutide v Dulaglutide	Severe hypoglycaemic episodes	Some concerns	Baseline difference on use of statins and SGLT2 inhibitors	Directly applicable	None specified
Takahashi 2023	Semaglutide v Dulaglutide	Weight change	Some concerns	Baseline difference on use of statins and SGLT2 inhibitors	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	All-cause mortality	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	At night hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	Cardiovascular mortality	High	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Tuttle 2018	Dulaglutide v Insulin	Death from renal causes	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	Development of end stage kidney disease	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	HbA1c change	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	Persistent signs of worsening kidney disease	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Tuttle 2018	Dulaglutide v Insulin	Weight change	High	None specified	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	All-cause mortality	High	Clear problems with reporting of this outcome	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	5-point MACE	Low	None specified	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wada 2022	Canagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	Cardiovascular mortality	Some concerns	Some concerns about selective reporting	Directly applicable	None specified
Wada 2022	Canagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	Some concerns about selective reporting	Directly applicable	None specified
Wang 2020B	Exenatide v Insulin	Hypoglycaemia episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Wang 2020B	Exenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Wang 2020B	Exenatide v Insulin	HbA1c change	High	No info about allocation concealment; mITT analysis missing data treated as similar to those in same group	Directly applicable	None specified
Wang 2020B	Exenatide v Insulin	Weight change	High	No info about allocation concealment; mITT analysis missing data treated as similar to those in same group	Directly applicable	None specified
Wiviott 2019 CKD	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wiviott 2019 CKD	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CKD	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CKD	Dapagliflozin v Placebo	Diabetic ketoacidosis	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CKD	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 CKD	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Yale 2013	Canagliflozin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Yale 2013	Canagliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Yale 2013	Canagliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Zinman 2015 CKD	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Zinman 2015 CKD	Empagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Zinman 2015 CKD	Empagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified

Table 4: Risk of bias and directness information for studies included in the review for subsequent therapy, model 5 (people with high risk of cardiovascular disease)

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Abdul-Ghani 2017	Pioglitazone + Exenatide v Insulin	All-cause mortality	Some concerns	Concerns for risk of selection bias	Directly applicable	None specified
Abdul-Ghani 2017	Pioglitazone + Exenatide v Insulin	Hospitalisation for heart failure	Some concerns	Concerns for risk of selection bias	Directly applicable	None specified
Abdul-Ghani 2017	Pioglitazone + Exenatide v Insulin	Hypoglycaemia episodes	Some concerns	Concerns for risk of selection bias	Directly applicable	None specified
Abdul-Ghani 2017	Pioglitazone + Exenatide v Insulin	Non-fatal stroke	Some concerns	Concerns for risk of selection bias	Directly applicable	None specified
Abdul-Ghani 2017	Pioglitazone + Exenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	Concerns for risk of selection bias	Directly applicable	None specified
Abdul-Ghani 2017	Pioglitazone + Exenatide v Insulin	Weight change	Some concerns	Concerns for risk of selection bias	Directly applicable	None specified
Abreu 2019	Liraglutide v Insulin	HbA1c change	High	Concerns with attrition and deviations from the intended interventions.	Directly applicable	None specified
Abreu 2019	Liraglutide v Insulin	Hypoglycaemia episodes	High	Concerns with attrition and deviations from the intended interventions.	Directly applicable	None specified
Abreu 2019	Liraglutide v Insulin	Severe hypoglycaemic episodes	High	Concerns with attrition and deviations from the	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				intended interventions.		
Abreu 2019	Liraglutide v Insulin	Weight change	High	Concerns with attrition and deviations from the intended interventions.	Directly applicable	None specified
Abreu 2019	Liraglutide v Insulin	Health-related quality of life - subscale mental component	High	Concerns with attrition, deviations from the intended interventions and outcome assessment.	Directly applicable	None specified
Abreu 2019	Liraglutide v Insulin	Health-related quality of life - subscale physical component	High	Concerns with attrition, deviations from the intended interventions and outcome assessment.	Directly applicable	None specified
Ahmann 2015	Liraglutide v Placebo	All-cause mortality	High	Concerns with selection bias and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2015	Liraglutide v Placebo	BMI change	High	Concerns with selection bias and deviations from the intended interventions.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ahmann 2015	Liraglutide v Placebo	HbA1c change	High	Concerns with selection bias and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2015	Liraglutide v Placebo	Hypoglycaemia episodes	High	Concerns with selection bias and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2015	Liraglutide v Placebo	Weight change	High	Concerns with selection bias and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2018	Semaglutide v Exenatide	All-cause mortality	High	Concerns with baseline values, attrition and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2018	Semaglutide v Exenatide	BMI change	High	Concerns with baseline values, attrition and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2018	Semaglutide v Exenatide	HbA1c change	High	Concerns with baseline values, attrition and	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				deviations from the intended interventions.		
Ahmann 2018	Semaglutide v Exenatide	Severe hypoglycaemic episodes	High	Concerns with baseline values, attrition and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2018	Semaglutide v Exenatide	Weight change	High	Concerns with baseline values, attrition and deviations from the intended interventions.	Directly applicable	None specified
Ahmann 2018	Semaglutide v Exenatide	Health-related quality of life - subscale mental component	High	Concerns with baseline values, attrition, deviations from the intended interventions and outcome assessment.	Directly applicable	None specified
Ahmann 2018	Semaglutide v Exenatide	Health-related quality of life - subscale physical component	High	Concerns with baseline values, attrition, deviations from the intended interventions and outcome assessment.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ahren 2004	Vildagliptin v Placebo	All-cause mortality	High	Concerns with selection and attrition bias	Directly applicable	None specified
Ahren 2004	Vildagliptin v Placebo	Cardiovascular mortality	High	Concerns with selection and attrition bias	Directly applicable	None specified
Ahren 2013	Lixisenatide v Placebo	All-cause mortality	Some concerns	Concerns with selection bias	Directly applicable	None specified
Ahren 2013	Lixisenatide v Placebo	Cardiovascular mortality	Some concerns	Concerns with selection bias	Directly applicable	None specified
Ahren 2013	Lixisenatide v Placebo	HbA1c change	Some concerns	Concerns with selection bias	Directly applicable	None specified
Ahren 2013	Lixisenatide v Placebo	Hypoglycaemia episodes	Some concerns	Concerns with selection bias	Directly applicable	None specified
Ahren 2013	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Some concerns	Concerns with selection bias	Directly applicable	None specified
Ahren 2013	Lixisenatide v Placebo	Weight change	Some concerns	Concerns with selection bias	Directly applicable	None specified
Ahren 2014	Glimepiride v Placebo	Hypoglycaemia episodes	High	Concerns with selection and attrition bias	Directly applicable	None specified
Ahren 2014	Glimepiride v Sitagliptin	Hypoglycaemia episodes	High	Concerns with selection and attrition bias	Directly applicable	None specified
Ahren 2014	Glimepiride v Placebo	Severe hypoglycaemic episodes	High	Concerns with selection and attrition bias	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ahren 2014	Glimepiride v Sitagliptin	Severe hypoglycaemic episodes	High	Concerns with selection and attrition bias	Directly applicable	None specified
Ahren 2014	Sitagliptin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Ahren 2014	Sitagliptin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	BMI change	Low	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Ahren 2017	Semaglutide v Sitagliptin	Weight change	Low	None specified	Directly applicable	None specified
Ando 2021	Canagliflozin v Liraglutide	BMI change	High	Concerns with blinding.	Directly applicable	None specified
Ando 2021	Canagliflozin v Liraglutide	HbA1c change	High	Concerns with blinding.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ando 2021	Canagliflozin v Liraglutide	Health-related quality of life - overall	High	Concerns with blinding.	Directly applicable	None specified
Ando 2021	Canagliflozin v Liraglutide	Severe hypoglycaemic episodes	High	Concerns with blinding.	Directly applicable	None specified
Ando 2021	Canagliflozin v Liraglutide	Weight change	High	Concerns with blinding.	Directly applicable	None specified
Araki 2015A	Empagliflozin v Metformin	All-cause mortality	Some concerns	Concerns with blinding	Directly applicable	None specified
Araki 2015A	Empagliflozin v Metformin	Cardiovascular mortality	Some concerns	Concerns with blinding	Directly applicable	None specified
Araki 2015A	Empagliflozin v Metformin	HbA1c change	Some concerns	Concerns with blinding	Directly applicable	None specified
Araki 2015A	Empagliflozin v Metformin	Hypoglycaemia episodes	Some concerns	Concerns with blinding	Directly applicable	None specified
Araki 2015A	Empagliflozin v Metformin	Severe hypoglycaemic episodes	Some concerns	Concerns with blinding	Directly applicable	None specified
Araki 2015A	Empagliflozin v Metformin	Weight change	Some concerns	Concerns with blinding	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	All-cause mortality	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	At night hypoglycaemic episodes	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	Cardiovascular mortality	Low	Open label trial clearly reported.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Araki 2015B	Dulaglutide v Insulin	HbA1c change	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	Hypoglycaemia episodes	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	Non-fatal myocardial infarction	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	Non-fatal stroke	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	Severe hypoglycaemic episodes	Low	Open label trial clearly reported.	Directly applicable	None specified
Araki 2015B	Dulaglutide v Insulin	Weight change	Low	Open label trial clearly reported.	Directly applicable	None specified
Arechavaleta 2011	Glimepiride v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Arechavaleta 2011	Glimepiride v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Arechavaleta 2011	Glimepiride v Sitagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Arechavaleta 2011	Glimepiride v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Arechavaleta 2011	Glimepiride v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Arechavaleta 2011	Glimepiride v Sitagliptin	Weight change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Aroda 2016B	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Low	Low attrition (4%), open label but necessary due to intervention administration. mITT used.	Directly applicable	None specified
Aroda 2016B	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Low	Low attrition (4%), open label but necessary due to intervention administration. mITT used.	Directly applicable	None specified
Aroda 2016B	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Low	Low attrition (4%), open label but necessary due to intervention administration. mITT used.	Directly applicable	None specified
Aroda 2016B	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Low	Low attrition (4%), open label but necessary due to intervention administration. mITT used.	Directly applicable	None specified
Aroda 2016B	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Low	Low attrition (4%), open label but necessary due to intervention administration. mITT used.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Aroda 2016B	Insulin glargine/Lixisenatide v Insulin	Weight change	Low	Low attrition (4%), open label but necessary due to intervention administration. mITT used.	Directly applicable	None specified
Aroda 2017	Semaglutide v Insulin	All-cause mortality	High	Concerns with blinding and analysis method	Directly applicable	None specified
Aroda 2017	Semaglutide v Insulin	At night hypoglycaemic episodes	High	Concerns with blinding and analysis method	Directly applicable	None specified
Aroda 2017	Semaglutide v Insulin	Cardiovascular mortality	High	Concerns with blinding and analysis method	Directly applicable	None specified
Aroda 2017	Semaglutide v Insulin	HbA1c change	High	Concerns with blinding and analysis method	Directly applicable	None specified
Aroda 2017	Semaglutide v Insulin	Severe hypoglycaemic episodes	High	Concerns with blinding and analysis method	Directly applicable	None specified
Aroda 2017	Semaglutide v Insulin	Weight change	High	Concerns with blinding and analysis method	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	All-cause mortality	High	Concerns with attrition.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Aroda 2019A	Insulin degludec/liraglutide v Insulin	At night hypoglycaemic episodes	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Cardiac arrhythmia	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Development of end stage kidney disease	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Hospitalisation for heart failure	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Non-fatal myocardial infarction	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Non-fatal stroke	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Unstable angina	High	Concerns with attrition.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Aroda 2019A	Insulin degludec/liraglutide v Insulin	Weight change	High	Concerns with attrition.	Directly applicable	None specified
Aroda 2019A	Insulin degludec/liraglutide v Insulin	HbA1c change	Some concerns	Concerns with outcome timepoint selection.	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	At night hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	HbA1c change	High	None specified	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	Unstable angina	High	None specified	Directly applicable	None specified
Aschner 2012	Sitagliptin v Insulin	Weight change	High	None specified	Directly applicable	None specified
Attaran 2023	Pioglitazone v Empagliflozin	BMI change	Some concerns	Trial registered but record no currently accessible	Directly applicable	None specified
Attaran 2023	Pioglitazone v Empagliflozin	HbA1c change	Some concerns	Trial registered but record no currently accessible	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Attaran 2023	Pioglitazone v Empagliflozin	Hypoglycaemia episodes	Some concerns	Trial registered but record no currently accessible	Directly applicable	None specified
Attaran 2023	Pioglitazone v Empagliflozin	Non-fatal stroke	Some concerns	Trial registered but record no currently accessible	Directly applicable	None specified
Attaran 2023	Pioglitazone v Empagliflozin	Severe hypoglycaemic episodes	Some concerns	Trial registered but record no currently accessible	Directly applicable	None specified
Avilés-Santa 1999	Metformin v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Avilés-Santa 1999	Metformin v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Avilés-Santa 1999	Metformin v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Ba 2017	Sitagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Babar 2021	Empagliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Babar 2021	Empagliflozin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Babar 2021	Empagliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Bae 2021	Pioglitazone v Empagliflozin	BMI change	Some concerns	None specified	Directly applicable	None specified
Bae 2021	Pioglitazone v Empagliflozin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bae 2021	Pioglitazone v Empagliflozin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Bae 2021	Pioglitazone v Empagliflozin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Bailey 2010	Dapagliflozin v Placebo	All-cause mortality	Some concerns	Some concerns regarding high attrition rate which was imbalanced between intervention and comprator	Directly applicable	None specified
Bailey 2010	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	Some concerns regarding high attrition rate which was imbalanced between intervention and comprator	Directly applicable	None specified
Bailey 2010	Dapagliflozin v Placebo	HbA1c change	Some concerns	Some concerns regarding high attrition rate which	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				was imbalanced between intervention and comprator		
Bailey 2010	Dapagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	Some concerns regarding high attrition rate which was imbalanced between intervention and comprator	Directly applicable	None specified
Bailey 2010	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	Some concerns	Some concerns regarding high attrition rate which was imbalanced between intervention and comprator	Directly applicable	None specified
Bailey 2010	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	Some concerns regarding high attrition rate which was imbalanced between intervention and comprator	Directly applicable	None specified
Bailey 2010	Dapagliflozin v Placebo	Weight change	Some concerns	Some concerns regarding high attrition rate which was imbalanced between	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				intervention and comprator		
Bailey 2016	Liraglutide v Sitagliptin	All-cause mortality	Some concerns	Concerns with attrition.	Directly applicable	None specified
Bailey 2016	Liraglutide v Sitagliptin	HbA1c change	Some concerns	Concerns with attrition.	Directly applicable	None specified
Bailey 2016	Liraglutide v Sitagliptin	Hypoglycaemia episodes	Some concerns	Concerns with attrition.	Directly applicable	None specified
Bailey 2016	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	Concerns with attrition.	Directly applicable	None specified
Bailey 2016	Liraglutide v Sitagliptin	Weight change	Some concerns	Concerns with attrition.	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bajaj 2014	Linagliptin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Bajaj 2014	Linagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Barnett 2012	Saxagliptin v Placebo	All-cause mortality	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of saxagliptin. However no disproportional increase in the mean total daily does of insulin between groups was reported	Directly applicable	None specified
Barnett 2012	Saxagliptin v Placebo	BMI change	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of saxagliptin. However no disproportional increase in the mean total daily does of insulin between groups was reported	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Barnett 2012	Saxagliptin v Placebo	Cardiovascular mortality	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of saxagliptin. However no disproportional increase in the mean total daily does of insulin between groups was reported	Directly applicable	None specified
Barnett 2012	Saxagliptin v Placebo	HbA1c change	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of saxagliptin. However no disproportional increase in the mean total daily does of insulin between groups was reported	Directly applicable	None specified
Barnett 2012	Saxagliptin v Placebo	Hypoglycaemia episodes	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				saxagliptin. However no disproportional increase in the mean total daily does of insulin between groups was reported		
Barnett 2012	Saxagliptin v Placebo	Severe hypoglycaemic episodes	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of saxagliptin. However no disproportional increase in the mean total daily does of insulin between groups was reported	Directly applicable	None specified
Barnett 2012	Saxagliptin v Placebo	Weight change	High	Randomised double blind study however the flexible dosing of insulin limits scrutiny of efect of saxagliptin. However no disproportional increase in the mean total daily does of insulin	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				between groups was reported		
Barnett 2013	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Barnett 2013	Linagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Bergenstal 2009	Exenatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Bergenstal 2009	Exenatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Bergenstal 2009	Exenatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bergenstal 2009	Exenatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Bergenstal 2009	Exenatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Bergenstal 2009	Exenatide v Insulin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Acute kidney injury	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	Acute kidney injury	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	All-cause mortality	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	All-cause mortality	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	Health-related quality of life - overall	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Health-related quality of life - overall	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	Health-related quality of life - overall	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bergenstal 2010	Pioglitazone v Sitagliptin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Unstable angina	High	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	Unstable angina	High	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	Acute kidney injury	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bergenstal 2010	Exenatide v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	Unstable angina	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Exenatide v Sitagliptin	Weight change	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Exenatide	Weight change	Some concerns	None specified	Directly applicable	None specified
Bergenstal 2010	Pioglitazone v Sitagliptin	Weight change	Some concerns	None specified	Directly applicable	None specified
Berndt-Zipfel 2013	Glimepiride v Vildagliptin	HbA1c change	High	None specified	Directly applicable	None specified
Berndt-Zipfel 2013	Glimepiride v Vildagliptin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Berndt-Zipfel 2013	Glimepiride v Vildagliptin	Weight change	High	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Health-related quality of life - subscale mental component	High	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Health-related quality of life - subscale physical component	High	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Billings 2018	Insulin degludec/liraglutide v Insulin	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Unstable angina	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Billings 2018	Insulin degludec/liraglutide v Insulin	At night hypoglycaemic episodes	Low	None specified	Partially applicable	None specified
Bizino 2019	Liraglutide v Placebo	HbA1c change	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bizino 2019	Liraglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Blonde 2015	Dulaglutide v Insulin	Hypoglycaemia episodes	Some concerns	high attrition but fairly uniform across arms	Directly applicable	None specified
Blonde 2015	Dulaglutide v Insulin	All-cause mortality	High	The study authors state that BMI change and EuroQoL-5 would be included as outcomes but the results for those outcomes were not reported.	Directly applicable	None specified
Blonde 2015	Dulaglutide v Insulin	HbA1c change	Some concerns	The study authors state that BMI change and EuroQoL-5 would be included as outcomes but the results for those outcomes were not reported.	Directly applicable	None specified
Blonde 2015	Dulaglutide v Insulin	Severe hypoglycaemic episodes	Some concerns	The study authors state that BMI change and EuroQoL-5 would be included as outcomes but the results for those	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				outcomes were not reported.		
Blonde 2015	Dulaglutide v Insulin	Weight change	Some concerns	The study authors state that BMI change and EuroQoL-5 would be included as outcomes but the results for those outcomes were not reported.	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Blonde 2020	Liraglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bode 2013	Canagliflozin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Bode 2013	Canagliflozin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Bode 2013	Canagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Bode 2013	Canagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Bode 2013	Canagliflozin v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified
Bode 2013	Canagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Partially applicable	None specified
Bolinder 2012	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Bolinder 2012	Dapagliflozin v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bolinder 2012	Dapagliflozin v Placebo	Health-related quality of life - overall	Some concerns	None specified	Directly applicable	None specified
Bolinder 2012	Dapagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Bolinder 2012	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Bolinder 2012	Dapagliflozin v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bolli 2008	Pioglitazone v Vildagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Bolli 2008	Pioglitazone v Vildagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Bolli 2008	Pioglitazone v Vildagliptin	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Bolli 2008	Pioglitazone v Vildagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Bolli 2008	Pioglitazone v Vildagliptin	Weight change	Low	None specified	Directly applicable	None specified
Bolli 2014	Lixisenatide v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Bolli 2014	Lixisenatide v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Bolli 2014	Lixisenatide v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Bolli 2014	Lixisenatide v Placebo	Weight change	High	None specified	Directly applicable	None specified
Bolli 2014	Lixisenatide v Placebo	HbA1c change	High	Study lacks information about the randomaisation process and allocation concealment. Overall attrition rate is >20 %. Reasons	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				for attrition are not reported		
Bosi 2007	Vildagliptin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Bosi 2007	Vildagliptin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Bosi 2007	Vildagliptin v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Bosi 2007	Vildagliptin v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Bosi 2007	Vildagliptin v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Bosi 2007	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Bosi 2007	Vildagliptin v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified
Brown 2020	Dapagliflozin v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Brown 2020	Dapagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Brown 2020	Dapagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Brown 2020	Dapagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Brown 2020	Dapagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Bunck 2009	Exenatide v Insulin	HbA1c change	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Bunck 2009	Exenatide v Insulin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Bunck 2009	Exenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Bunck 2009	Exenatide v Insulin	Weight change	Some concerns	None specified	Directly applicable	None specified
Buse 2004	Exenatide v Placebo	HbA1c change	High	mITT LOCF analysis; high proportion of missing data; No information about randomisation and no protocol available	Directly applicable	None specified
Buse 2004	Exenatide v Placebo	Weight change	High	mITT LOCF analysis; high proportion of missing data; No information about randomisation and no protocol available	Directly applicable	None specified
Buse 2004	Exenatide v Placebo	Hypoglycaemia episodes	High	No information about randomisation and no protocol available	Directly applicable	None specified
Buse 2004	Exenatide v Placebo	Non-fatal myocardial infarction	High	No information about randomisation and no protocol available	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Buse 2004	Exenatide v Placebo	Severe hypoglycaemic episodes	High	No information about randomisation and no protocol available	Directly applicable	None specified
Buse 2009	Exenatide v Liraglutide	HbA1c change	Low	None specified	Directly applicable	None specified
Buse 2009	Exenatide v Liraglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Buse 2009	Exenatide v Liraglutide	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Buse 2009	Exenatide v Liraglutide	Weight change	Low	None specified	Directly applicable	None specified
Buse 2011	Exenatide v Placebo	All-cause mortality	Some concerns	Some baseline differences between groups suggesting problem with randomisation process	Directly applicable	None specified
Buse 2011	Exenatide v Placebo	At night hypoglycaemic episodes	Some concerns	Some baseline differences between groups suggesting problem with randomisation process	Directly applicable	None specified
Buse 2011	Exenatide v Placebo	Cardiovascular mortality	Some concerns	Some baseline differences between groups suggesting problem with	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomisation process		
Buse 2011	Exenatide v Placebo	Hypoglycaemia episodes	Some concerns	Some baseline differences between groups suggesting problem with randomisation process	Directly applicable	None specified
Buse 2011	Exenatide v Placebo	Severe hypoglycaemic episodes	Some concerns	Some baseline differences between groups suggesting problem with randomisation process	Directly applicable	None specified
Buse 2011	Exenatide v Placebo	HbA1c change	High	Some baseline differences between groups suggesting problem with randomisation process; mITT analysis, unclear whether LOCF	Directly applicable	None specified
Buse 2011	Exenatide v Placebo	Weight change	High	Some baseline differences between groups suggesting problem with randomisation process; mITT analysis, unclear whether LOCF	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Buse 2013	Exenatide v Liraglutide	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Buse 2013	Exenatide v Liraglutide	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Buse 2013	Exenatide v Liraglutide	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Buse 2013	Exenatide v Liraglutide	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Buse 2013	Exenatide v Liraglutide	Weight change	Some concerns	None specified	Directly applicable	None specified
Buse 2013 non-obese	Exenatide v Liraglutide	Weight change	Some concerns	None specified	Directly applicable	None specified
Buse 2013 obese	Exenatide v Liraglutide	Weight change	Some concerns	None specified	Directly applicable	None specified
Buse 2014	Insulin degludec/liraglutide v Insulin	HbA1c change	Low	No concerns	Directly applicable	None specified
Buse 2014	Insulin degludec/liraglutide v Insulin	Hypoglycaemia episodes	Low	No concerns	Directly applicable	None specified
Buse 2014	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	Low	No concerns	Directly applicable	None specified
Buse 2014	Insulin degludec/liraglutide v Insulin	Weight change	Low	No concerns	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Buse 2020	Semaglutide v Sitagliptin	BMI change	Some concerns	ITT analysis with multiple imputation	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	HbA1c change	Some concerns	ITT analysis with multiple imputation	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	Weight change	Some concerns	ITT analysis with multiple imputation	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	Acute kidney injury	Low	None specified	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Buse 2020	Semaglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Camerini-Davalos 1994	Glipizide v Placebo	HbA1c change	High	Some baseline differences between groups suggesting problem with randomisation process; compliance	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				with background diet only fair or poor; no protocol available		
Capehorn 2020	Semaglutide v Liraglutide	All-cause mortality	High	Open-label trial, no info about randomisation/allocation concealment	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	Cardiovascular mortality	High	Open-label trial, no info about randomisation/allocation concealment	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	Hypoglycaemia episodes	High	Open-label trial, no info about randomisation/allocation concealment	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	Severe hypoglycaemic episodes	High	Open-label trial, no info about randomisation/allocation concealment	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	BMI change	High	Open-label trial, no info about randomisation/allocation concealment; ITT analysis with multiple imputation	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	HbA1c change	High	Open-label trial, no info about randomisation/allocation concealment;	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				ITT analysis with multiple imputation		
Capehorn 2020	Semaglutide v Liraglutide	Health-related quality of life - subscale mental component	High	Open-label trial, no info about randomisation/allocation concealment; ITT analysis with multiple imputation	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	Health-related quality of life - subscale physical component	High	Open-label trial, no info about randomisation/allocation concealment; ITT analysis with multiple imputation	Directly applicable	None specified
Capehorn 2020	Semaglutide v Liraglutide	Weight change	High	Open-label trial, no info about randomisation/allocation concealment; ITT analysis with multiple imputation	Directly applicable	None specified
Cefalu 2013	Glimepiride v Canagliflozin	HbA1c change	High	mITT LOCf analysis; ~33% missing data	Directly applicable	None specified
Cefalu 2013	Glimepiride v Canagliflozin	Weight change	High	mITT LOCf analysis; ~33% missing data	Directly applicable	None specified
Cefalu 2013	Glimepiride v Canagliflozin	All-cause mortality	Low	None specified	Directly applicable	None specified
Cefalu 2013	Glimepiride v Canagliflozin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Cefalu 2013	Glimepiride v Canagliflozin	Death from renal causes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Cefalu 2013	Glimepiride v Canagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Cefalu 2013	Glimepiride v Canagliflozin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Charbonnel 2006	Sitagliptin v Placebo	HbA1c change	High	No information about randomisation/allocation concealment, mITT analysis with LOCF; trial protocol not available	Directly applicable	None specified
Charbonnel 2006	Sitagliptin v Placebo	Hypoglycaemia episodes	High	No information about randomisation/allocation concealment, trial protocol not available	Directly applicable	None specified
Charbonnel 2013	Liraglutide v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Charbonnel 2013	Liraglutide v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Charbonnel 2013	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Charbonnel 2013	Liraglutide v Sitagliptin	HbA1c change	High	Per protocol analysis for this outcome, high proportion missing data	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Charbonnel 2013	Liraglutide v Sitagliptin	Weight change	High	Per protocol analysis for this outcome, high proportion missing data	Directly applicable	None specified
Charpentier 2009	Pioglitazone v Placebo	All-cause mortality	High	No information about randomisation/allocation concealment, baseline difference on insulin resistance, trial protocol not available	Directly applicable	None specified
Charpentier 2009	Pioglitazone v Placebo	Cardiovascular mortality	High	No information about randomisation/allocation concealment, baseline difference on insulin resistance, trial protocol not available	Directly applicable	None specified
Charpentier 2009	Pioglitazone v Placebo	HbA1c change	High	No information about randomisation/allocation concealment, baseline difference on insulin resistance, trial	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				protocol not available		
Charpentier 2009	Pioglitazone v Placebo	Hospitalisation for heart failure	High	No information about randomisation/allocation concealment, baseline difference on insulin resistance, trial protocol not available	Directly applicable	None specified
Charpentier 2009	Pioglitazone v Placebo	Hypoglycaemia episodes	High	No information about randomisation/allocation concealment, baseline difference on insulin resistance, trial protocol not available	Directly applicable	None specified
Chen 2016	Vildagliptin v Saxagliptin	All-cause mortality	High	Open-label trial, lack of information available about trial in paper/protocol	Directly applicable	None
Chen 2016	Vildagliptin v Saxagliptin	At night hypoglycaemic episodes	High	Open-label trial, lack of information available about trial in paper/protocol	Directly applicable	None
Chen 2016	Vildagliptin v Saxagliptin	BMI change	High	Open-label trial, lack of information	Directly applicable	None

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				available about trial in paper/protocol		
Chen 2016	Vildagliptin v Saxagliptin	HbA1c change	High	Open-label trial, lack of information available about trial in paper/protocol	Directly applicable	None
Chen 2016	Vildagliptin v Saxagliptin	Hospitalisation for heart failure	High	Open-label trial, lack of information available about trial in paper/protocol	Directly applicable	None
Chen 2016	Vildagliptin v Saxagliptin	Hypoglycaemia episodes	High	Open-label trial, lack of information available about trial in paper/protocol	Directly applicable	None
Chen 2016	Vildagliptin v Saxagliptin	Severe hypoglycaemic episodes	High	Open-label trial, lack of information available about trial in paper/protocol	Directly applicable	None
Chen 2018A	Saxagliptin v Placebo	Hypoglycaemia episodes	Some concerns	lack of information around allocation concealment and methods of randomisation	Directly applicable	None specified
Chen 2018A	Saxagliptin v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment and randomisation	Directly applicable	None specified
Chen 2018A	Saxagliptin v Placebo	Non-fatal myocardial infarction	Some concerns	Lack of information around allocation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concealment and randomisation		
Chen 2018A	Saxagliptin v Placebo	BMI change	Some concerns	lack of information around allocation concealment and randomisation methods	Directly applicable	None specified
Chen 2018A	Saxagliptin v Placebo	Weight change	Some concerns	lack of information around allocation concelament and randomisation	Directly applicable	None specified
Chen 2018A	Saxagliptin v Placebo	Cardiovascular mortality	Some concerns	Method of randomisation not stated	Directly applicable	None specified
Chen 2018A	Saxagliptin v Placebo	All-cause mortality	Some concerns	no information about methods of randomisation	Directly applicable	None specified
Chen 2018A	Saxagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	no information about methods of randomisation	Directly applicable	None specified
Cho 2019	Pioglitazone v Dapagliflozin	HbA1c change	Some concerns	Open label study; lack of info on randomisation	Directly applicable	None specified
Cho 2019	Pioglitazone v Dapagliflozin	Hypoglycaemia	Some concerns	Open label study; lack of info on randomisation	Directly applicable	None specified
Cho 2019	Pioglitazone v Dapagliflozin	Severe hypoglycaemic episodes	Some concerns	Open label study; lack of info on randomisation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Cho 2019	Pioglitazone v Dapagliflozin	Weight change	Some concerns	Open label study; lack of info on randomisation	Directly applicable	None specified
Civera 2008	Metformin v Insulin	Cardiovascular mortality	Some concerns	Lack of information on methods for allocation/randomisation.	Directly applicable	None specified
Civera 2008	Metformin v Insulin	All-cause mortality	Some concerns	Lack of information on methods for allocation/randomisation.	Directly applicable	None specified
Civera 2008	Metformin v Insulin	HbA1c change	Some concerns	Lack of information on methods for allocation/randomisation.	Directly applicable	None specified
Civera 2008	Metformin v Insulin	Weight change	Some concerns	Lack of information on methods for allocation/randomisation.	Directly applicable	None specified
Cusi 2019	Canagliflozin v Placebo	HbA1c change	High	Per-protocol analysis was used, some statisitcally significant differences in baseline	Directly applicable	None specified
Cusi 2019	Canagliflozin v Placebo	Weight change	High	Per-protocol analysis was used, some statisitcally significant	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				differences in baseline		
da Silva 2016	Sitagliptin v Insulin	BMI change	High	Lack of information on randomisaion/allocation methods and analysis	Directly applicable	None specified
da Silva 2016	Sitagliptin v Insulin	HbA1c change	High	Lack of information on randomisaion/allocation methods and analysis	Directly applicable	None specified
da Silva 2016	Sitagliptin v Insulin	Weight change	High	Lack of information on randomisaion/allocation methods and analysis	Directly applicable	None specified
Dagogo-Jack 2017	Ertugliflozin v Placebo	All-cause mortality	Low	Attrition <20%; doesn't seem to be a problem with compliance/adherence; ITT analysis seems to have been done as all randomised patients were included in the analysis.	Directly applicable	None specified
Dagogo-Jack 2017	Ertugliflozin v Placebo	Cardiovascular mortality	Low	Attrition <20%; doesn't seem to be a problem with compliance/adheren	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				ce; ITT analysis seems to have been done as all randomised patients were included in the analysis.		
Dagogo-Jack 2017	Ertugliflozin v Placebo	Diabetic ketoacidosis	Low	Attrition <20%; doesn't seem to be a problem with compliance/adherence; ITT analysis seems to have been done as all randomised patients were included in the analysis.	Directly applicable	None specified
Dagogo-Jack 2017	Ertugliflozin v Placebo	Hypoglycaemia episodes	Low	Attrition <20%; doesn't seem to be a problem with compliance/adherence; ITT analysis seems to have been done as all randomised patients were included in the analysis.	Directly applicable	None specified
Dagogo-Jack 2017	Ertugliflozin v Placebo	Severe hypoglycaemic episodes	Low	Attrition <20%; doesn't seem to be a problem with compliance/adherence; ITT analysis	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				seems to have been done as all randomised patients were included in the analysis.		
Dagogo-Jack 2017	Ertugliflozin v Placebo	HbA1c change	Low	Attrition <20%; doesn't seem to be a problem with compliance/adherence; mITT analysis seems to have been done	Directly applicable	None specified
Dagogo-Jack 2017	Ertugliflozin v Placebo	Weight change	Low	Attrition <20%; doesn't seem to be a problem with compliance/adherence; mITT analysis seems to have been done	Directly applicable	None specified
Dahl 2022	Tirzepatide v Placebo	4-point MACE	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some form of ITT seems to have been used	Directly applicable	None specified
Dahl 2022	Tirzepatide v Placebo	All-cause mortality	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				form of ITT seems to have been used		
Dahl 2022	Tirzepatide v Placebo	Cardiovascular mortality	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some form of ITT seems to have been used	Directly applicable	None specified
Dahl 2022	Tirzepatide v Placebo	HbA1c change	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some form of ITT seems to have been used	Directly applicable	None specified
Dahl 2022	Tirzepatide v Placebo	Hypoglycaemia episodes	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some form of ITT seems to have been used	Directly applicable	None specified
Dahl 2022	Tirzepatide v Placebo	Severe hypoglycaemic episodes	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some form of ITT seems to have been used	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Dahl 2022	Tirzepatide v Placebo	Weight change	Low	Attrition is <20% (5%), there doesn't seem to be a problem with compliance. Some form of ITT seems to have been used	Directly applicable	None specified
D'Alessio 2015	Liraglutide v Insulin	At night hypoglycaemic episodes	Low	Open-label RCT, low attrition (<20%)	Directly applicable	None specified
D'Alessio 2015	Liraglutide v Insulin	HbA1c change	Low	Open-label RCT, low attrition (<20%)	Directly applicable	None specified
D'Alessio 2015	Liraglutide v Insulin	Hypoglycaemia episodes	Low	Open-label RCT, low attrition (<20%)	Directly applicable	None specified
D'Alessio 2015	Liraglutide v Insulin	Non-fatal stroke	Low	Open-label RCT, low attrition (<20%)	Directly applicable	None specified
D'Alessio 2015	Liraglutide v Insulin	Severe hypoglycaemic episodes	Low	Open-label RCT, low attrition (<20%)	Directly applicable	None specified
D'Alessio 2015	Liraglutide v Insulin	Weight change	Low	Open-label RCT, low attrition (<20%)	Directly applicable	None specified
Davies 2009	Exenatide v Insulin	At night hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Davies 2009	Exenatide v Insulin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Davies 2009	Exenatide v Insulin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Davies 2009	Exenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Davies 2009	Exenatide v Insulin	Weight change	Some concerns	None specified	Directly applicable	None specified
Davies 2013	Exenatide v Insulin	All-cause mortality	Some concerns	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm	Directly applicable	None specified
Davies 2013	Exenatide v Insulin	At night hypoglycaemic episodes	Some concerns	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm	Directly applicable	None specified
Davies 2013	Exenatide v Insulin	BMI change	Some concerns	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm	Directly applicable	None specified
Davies 2013	Exenatide v Insulin	Cardiovascular mortality	Some concerns	Overall 12% attrition (25/216); there was	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				>10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm		
Davies 2013	Exenatide v Insulin	HbA1c change	Some concerns	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm	Directly applicable	None specified
Davies 2013	Exenatide v Insulin	Hypoglycaemia episodes	Some concerns	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm	Directly applicable	None specified
Davies 2013	Exenatide v Insulin	Weight change	Some concerns	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Davies 2013	Exenatide v Insulin	Health-related quality of life - overall	High	Overall 12% attrition (25/216); there was >10% differential attrition between the arms: 17% in exenatide arm and 6% in the insulin arm . Some additional risk with patient reported outcomes from patients who discontinued early.	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	All-cause mortality	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	BMI change	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	Cardiovascular mortality	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				are listed. Some issues with adherence		
Davies 2015	Liraglutide v Placebo	Development of end stage kidney disease	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	HbA1c change	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	Health-related quality of life - overall	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	Hypoglycaemia episodes	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Davies 2015	Liraglutide v Placebo	Severe hypoglycaemic episodes	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2015	Liraglutide v Placebo	Weight change	High	Attrition >20%. Differential attrition around 10%. But reasons for drop out are listed. Some issues with adherence	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	All-cause mortality	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	HbA1c change	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Health-related quality of life -	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale mental component				
Davies 2017	Semaglutide v Placebo	Health-related quality of life - subscale mental component	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Health-related quality of life - subscale physical component	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Health-related quality of life - subscale physical component	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Non-fatal stroke	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Non-fatal stroke	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Davies 2017	SC Semaglutide v Oral Semaglutide	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Davies 2017	SC Semaglutide v Oral Semaglutide	Weight change	High	None specified	Directly applicable	None specified
Davies 2017	Semaglutide v Placebo	Weight change	High	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	Health-related quality of life - subscale mental component	Low	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	Health-related quality of life - subscale physical component	Low	None specified	Directly applicable	None specified
Davies 2021	Semaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Davies 2021	Semaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
DeFronzo 2005	Exenatide v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
DeFronzo 2005	Exenatide v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
DeFronzo 2005	Exenatide v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
DeFronzo 2005	Exenatide v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified
DeFronzo 2009	Saxagliptin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
DeFronzo 2009	Saxagliptin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
DeFronzo 2009	Saxagliptin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
DeFronzo 2009	Saxagliptin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
DeFronzo 2009	Saxagliptin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
DeFronzo 2012	Pioglitazone + Alogliptin v Pioglitazone	All-cause mortality	High	None specified	Directly applicable	None specified
DeFronzo 2012	Pioglitazone + Alogliptin v Pioglitazone	Cardiovascular mortality	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
DeFronzo 2012	Pioglitazone + Alogliptin v Pioglitazone	HbA1c change	High	None specified	Directly applicable	None specified
DeFronzo 2012	Pioglitazone + Alogliptin v Pioglitazone	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
DeFronzo 2012	Pioglitazone + Alogliptin v Pioglitazone	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Linagliptin	All-cause mortality	Low	Low	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Linagliptin	Cardiovascular mortality	Low	Low	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Linagliptin	HbA1c change	Low	Low	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Linagliptin	Hospitalisation for heart failure	Low	Low	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Linagliptin	Hypoglycaemia episodes	Low	Low	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Empagliflozin	All-cause mortality	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin v Linagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
DeFronzo 2015	Empagliflozin + Linagliptin v Empagliflozin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin v Linagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Empagliflozin	HbA1c change	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin v Linagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Empagliflozin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin v Linagliptin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin + Linagliptin v Empagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
DeFronzo 2015	Empagliflozin v Linagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	3-point MACE	High	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	All-cause mortality	High	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	HbA1c change	High	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Del Prato 2014	Glipizide v Alogliptin	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	Non-fatal stroke	High	None specified	Directly applicable	None specified
Del Prato 2014	Glipizide v Alogliptin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
DePaoli 2014	Pioglitazone v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
DePaoli 2014	Pioglitazone v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
DePaoli 2014	Pioglitazone v Placebo	Weight change	High	None specified	Directly applicable	None specified
Derosa 2010A	Pioglitazone v Glimepiride	BMI change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this ws monitored.	Directly applicable	None specified
Derosa 2010A	Pioglitazone v Glimepiride	HbA1c change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this ws monitored.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Derosa 2010A	Pioglitazone v Glimepiride	Hypoglycaemia episodes	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this ws monitored.	Directly applicable	None specified
Derosa 2010A	Pioglitazone v Glimepiride	Weight change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this ws monitored.	Directly applicable	None specified
Derosa 2010B	Sitagliptin v Metformin	BMI change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Directly applicable	None specified
Derosa 2010B	Sitagliptin v Metformin	HbA1c change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				section stating that this was monitored.		
Derosa 2010B	Sitagliptin v Metformin	Hypoglycaemia episodes	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Directly applicable	None specified
Derosa 2010B	Sitagliptin v Metformin	Weight change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Directly applicable	None specified
Derosa 2011B	Glimepiride v Exenatide	BMI change	High	There was a lack of information around allocation conceallment. The report states that the trial was single-blind, however, it is not clear whether this is possible as one drug is injectable, and the other is taken orally. Altough the report	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				states that medication compliance was monitored, the publication does not report adherence. It is likely that assessors were aware of the treatment received by participants, however the measures are objective and unlikely to be influenced by knowledge of the intervention.		
Derosa 2011B	Glimepiride v Exenatide	HbA1c change	High	There was a lack of information around allocation conceallment. The report states that the trial was single-blind, however, it is not clear whether this is possible as one drug is injectable, and the other is taken orally. Altough the report states that	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				medication compliance was monitored, the publication does not report adherence. It is likely that assessors were aware of the treatment received by participants, however the measures are objective and unlikely to be influenced by knowledge of the intervention.		
Derosa 2011B	Glimepiride v Exenatide	Hypoglycaemia episodes	High	There was a lack of information around allocation conceallment. The report states that the trial was single-blind, however, it is not clear whether this is possible as one drug is injectable, and the other is taken orally. Altough the report states that medication	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				compliance was monitored, the publication does not report adherence. It is likely that assessors were aware of the treatment received by participants, however the measures are objective and unlikely to be influenced by knowledge of the intervention.		
Derosa 2011B	Glimepiride v Exenatide	Weight change	High	There was a lack of information around allocation conceallment. The report states that the trial was single-blind, however, it is not clear whether this is possible as one drug is injectable, and the other is taken orally. Altough the report states that medication compliance was	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				monitored, the publication does not report adherence. It is likely that assessors were aware of the treatment received by participants, however the measures are objective and unlikely to be influenced by knowledge of the intervention.		
Derosa 2012A	Sitagliptin v Placebo	BMI change	High	Lack of information around allocation conceallment. The report states that medication compliance was monitored, however, there were no details about adherence.	Partially applicable	The study recruited participants who were treatment naïve, and participants may have responded sufficiently to metformin alone prior to randomisation to either sitagliptin or placebo
Derosa 2012A	Sitagliptin v Placebo	HbA1c change	High	Lack of information around allocation conceallment. The report states that medication	Partially applicable	The study recruited participants who were treatment naïve, and participants may

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				compliance was monitored, however, there were no details about adherence.		have responded sufficiently to metformin alone prior to randomisation to either sitagliptin or placebo
Derosa 2012A	Sitagliptin v Placebo	Hypoglycaemia episodes	High	Lack of information around allocation conceallment. The report states that medication compliance was monitored, however, there were no details about adherence.	Partially applicable	The study recruited participants who were treatment naïve, and participants may have responded sufficiently to metformin alone prior to randomisation to either sitagliptin or placebo
Derosa 2012A	Sitagliptin v Placebo	Weight change	High	Lack of information around allocation conceallment. The report states that medication compliance was monitored, however, there were no details about adherence.	Partially applicable	The study recruited participants who were treatment naïve, and participants may have responded sufficiently to metformin alone prior to randomisation to either sitagliptin or placebo

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Derosa 2012B	Vildagliptin v Placebo	BMI change	High	Lack of clarity around allocation concealment. The methods section stated that medication compliance was measured, however, the results were not reported, meaning that the effect of non-adherence is unclear.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded adequately to metformin alone.
Derosa 2012B	Vildagliptin v Placebo	HbA1c change	High	Lack of clarity around allocation concealment. The methods section stated that medication compliance was measured, however, the results were not reported, meaning that the effect of non-adherence is unclear.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded adequately to metformin alone.
Derosa 2012B	Vildagliptin v Placebo	Hypoglycaemia episodes	High	Lack of clarity around allocation concealment. The methods section stated that	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				medication compliance was measured, however, the results were not reported, meaning that the effect of non-adherence is unclear.		population included participants that may have responded adequately to metformin alone.
Derosa 2012B	Vildagliptin v Placebo	Weight change	High	Lack of clarity around allocation concealment. The methods section stated that medication compliance was measured, however, the results were not reported, meaning that the effect of non-adherence is unclear.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded adequately to metformin alone.
Derosa 2012C	Exenatide v Placebo	BMI change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded adequately to metformin alone.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Derosa 2012C	Exenatide v Placebo	HbA1c change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded adequately to metformin alone.
Derosa 2012C	Exenatide v Placebo	Hypoglycaemia episodes	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded adequately to metformin alone.
Derosa 2012C	Exenatide v Placebo	Weight change	High	Lack of information around allocation conceallment. Lack of information around adherence despite the methods section stating that this was monitored.	Partially applicable	Participants were treatment naive prior to initiation of the metformin run-in period, and the population included participants that may have responded

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						adequately to metformin alone.
Derosa 2014A	Glimepiride v Vildagliptin	BMI change	High	Lack of information around allocation concealment and whether there was a prespecified analysis plan. Although the methods state that medication compliance was monitored, there was a lack of information around adherence.	Directly applicable	None specified
Derosa 2014A	Glimepiride v Vildagliptin	HbA1c change	High	Lack of information around allocation concealment and whether there was a prespecified analysis plan. Although the methods state that medication compliance was monitored, there was a lack of information around adherence.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Derosa 2014A	Glimepiride v Vildagliptin	Weight change	High	Lack of information around allocation concealment and whether there was a prespecified analysis plan. Although the methods state that medication compliance was monitored, there was a lack of information around adherence.	Directly applicable	None specified
Derosa 2014B	Sitagliptin v Placebo	BMI change	High	Lack of clarity around allocation concealment and whether there was a pre-specified analysis plan. The methods suggest that compliance was monitored, however medication adherence was not reported.	Directly applicable	None specified
Derosa 2014B	Sitagliptin v Placebo	HbA1c change	High	Lack of clarity around allocation concealment and whether there was a pre-specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				analysis plan. The methods suggest that compliance was monitored, however medication adherence was not reported.		
Derosa 2014B	Sitagliptin v Placebo	Weight change	High	Lack of clarity around allocation concealment and whether there was a pre-specified analysis plan. The methods suggest that compliance was monitored, however medication adherence was not reported.	Directly applicable	None specified
Diamant 2010	Exenatide v Insulin	All-cause mortality	High	High attiritioon rate overall however low attrition between interventions. Patients and investigators were not masked to treatment regimen	Directly applicable	None specified
Diamant 2010	Exenatide v Insulin	HbA1c change	High	High attiritioon rate overall however low attrition between interventions.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Patients and investigators were not masked to treatment regimen		
Diamant 2010	Exenatide v Insulin	Health-related quality of life - overall	High	High attiritioon rate overall however low attrition between interventions. Patients and investigators were not masked to treatment regimen	Directly applicable	None specified
Diamant 2010	Exenatide v Insulin	Severe hypoglycaemic episodes	High	High attiritioon rate overall however low attrition between interventions. Patients and investigators were not masked to treatment regimen	Directly applicable	None specified
Diamant 2010	Exenatide v Insulin	Weight change	High	High attiritioon rate overall however low attrition between interventions. Patients and investigators were not masked to treatment regimen	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	Acute kidney injury	Some concerns	Concerns around treatment compliance	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Diamant 2014	Exenatide v Insulin	All-cause mortality	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	At night hypoglycaemic episodes	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	BMI change	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	Cardiovascular mortality	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	HbA1c change	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	Health-related quality of life - overall	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	Hypoglycaemia episodes	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	Non-fatal myocardial infarction	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Diamant 2014	Exenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	Concerns around treatment compliance	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Diamant 2014	Exenatide v Insulin	Weight change	Some concerns	Concerns around treatment compliance	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Dobs 2013	Sitagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Dorkhan 2009	Pioglitazone v Insulin	BMI change	High	No information regarding randomisation or adherance. Outcomes unlikley to be affected by open label study design	Directly applicable	None specified
Dorkhan 2009	Pioglitazone v Insulin	HbA1c change	High	No information regarding randomisation or adherance.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Outcomes unlikley to be affected by open label study design		
Douek 2005	Metformin v Placebo	Hypoglycaemia episodes	High	Missing data may affect rare outcomes. No detail on concealment	Directly applicable	None specified
Douek 2005	Metformin v Placebo	Severe hypoglycaemic episodes	High	Missing data may affect rare outcomes. No detail on concealment	Directly applicable	None specified
Douek 2005	Metformin v Placebo	HbA1c change	Some concerns	No detail on concealment	Directly applicable	None specified
Douek 2005	Metformin v Placebo	Weight change	Some concerns	No detail on concealment	Directly applicable	None specified
Dungan 2014	Liraglutide v Dulaglutide	All-cause mortality	Low	None specified	Directly applicable	None specified
Dungan 2014	Liraglutide v Dulaglutide	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Dungan 2014	Liraglutide v Dulaglutide	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Dungan 2014	Liraglutide v Dulaglutide	HbA1c change	Low	None specified	Directly applicable	None specified
Dungan 2014	Liraglutide v Dulaglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Dungan 2014	Liraglutide v Dulaglutide	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Dungan 2014	Liraglutide v Dulaglutide	Weight change	Low	None specified	Directly applicable	None specified
Dungan 2016	Dulaglutide v Placebo	All-cause mortality	Low	Study is a a randomised, double-blind, placebo controlled clinical trial but specific randomisation and concealment methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight); Data provided for all primary and secondary outcomes. Evidence of prespecified analytical plan, and the data presented, and methods of analysis outlined aligns with prespecified plans	Directly applicable	None specified
Dungan 2016	Dulaglutide v Placebo	At night hypoglycaemic episodes	Low	Study is a a randomised, double-blind, placebo	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				controlled clinical trial but specific randomisation and concealment methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight); Data provided for all primary and secondary outcomes. Evidence of prespecified analytical plan, and the data presented, and methods of analysis outlined aligns with prespecified plans		
Dungan 2016	Dulaglutide v Placebo	HbA1c change	Low	Study is a a randomised, double-blind, placebo controlled clinical trial but specific randomisation and concealment methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight);	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Data provided for all primary and secondary outcomes. Evidence of prespecified analytical plan, and the data presented, and methods of analysis outlined aligns with prespecified plans		
Dungan 2016	Dulaglutide v Placebo	Hypoglycaemia episodes	Low	Study is a a randomised, double-blind, placebo controlled clinical trial but specific randomisation and concealment methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight); Data provided for all primary and secondary outcomes. Evidence of prespecified analytical plan, and the data presented, and methods of analysis outlined	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				aligns with prespecified plans		
Dungan 2016	Dulaglutide v Placebo	Non-fatal stroke	Low	Study is a a randomised, double-blind, placebo controlled clinical trial but specific randomisation and concealment methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight); Data provided for all primary and secondary outcomes. Evidence of prespecified analytical plan, and the data presented, and methods of analysis outlined aligns with prespecified plans	Directly applicable	None specified
Dungan 2016	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	Study is a a randomised, double-blind, placebo controlled clinical trial but specific randomisation and concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight); Data provided for all primary and secondary outcomes. Evidence of prespecified analytical plan, and the data presented, and methods of analysis outlined aligns with prespecified plans		
Dungan 2016	Dulaglutide v Placebo	Weight change	Low	Study is a a randomised, double-blind, placebo controlled clinical trial but specific randomisation and concealment methods not outlined. ITT undertaken for efficacy data (Hb1Ac, weight); Data provided for all primary and secondary outcomes. Evidence	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				of prespecified analytical plan, and the data presented, and methods of analysis outlined aligns with prespecified plans		
Ferdinand 2019	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Ferdinand 2019	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Ferdinand 2019	Empagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Ferdinand 2019	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Ferdinand 2019	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Ferdinand 2019	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Ferdinand 2019	Empagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Fernandez 2008	Pioglitazone v Placebo	HbA1c change	High	Concerns about small sample with significant drop out	Partially applicable	also switch insulin at the start of the trial
Fernandez 2008	Pioglitazone v Placebo	Hypoglycaemia episodes	High	Concerns about small sample with significant drop out	Partially applicable	also switch insulin at the start of the trial

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ferrannini 2009	Glimepiride v Vildagliptin	All-cause mortality	High	High concerns resulting from the disporportionate drop out being due to hypoglycaemia, which is likely to impact this outcome	Directly applicable	None specified
Ferrannini 2009	Glimepiride v Vildagliptin	Cardiac arrhythmia	High	High concerns resulting from the disporportionate drop out being due to hypoglycaemia, which is likely to impact this outcome	Directly applicable	None specified
Ferrannini 2009	Glimepiride v Vildagliptin	Cardiovascular mortality	High	High concerns resulting from the disporportionate drop out being due to hypoglycaemia, which is likely to impact this outcome	Directly applicable	None specified
Ferrannini 2009	Glimepiride v Vildagliptin	HbA1c change	High	High concerns resulting from the disporportionate drop out being due to hypoglycaemia, which is likely to impact this outcome	Directly applicable	None specified
Ferrannini 2009	Glimepiride v Vildagliptin	Hypoglycaemia episodes	High	High concerns resulting from the disporportionate	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				drop out being due to hypoglycaemia, which is likely to impact this outcome		
Ferrannini 2009	Glimepiride v Vildagliptin	Severe hypoglycaemic episodes	High	High concerns resulting from the disporportionate drop out being due to hypoglycaemia, which is likely to impact this outcome	Directly applicable	None specified
Filozof 2010a	Gliclazide v Vildagliptin	HbA1c change	High	None specified	Directly applicable	None specified
Filozof 2010a	Gliclazide v Vildagliptin	Weight change	High	None specified	Directly applicable	None specified
Filozof 2010a	Gliclazide v Vildagliptin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Filozof 2010b	Vildagliptin v Metformin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Filozof 2010b	Vildagliptin v Metformin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Filozof 2010b	Vildagliptin v Metformin	Acute kidney injury	Low	None specified	Partially applicable	only reported as renal failure and unclear if acute
Fonseca 2007	Vildagliptin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Fonseca 2007	Vildagliptin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Fonseca 2007	Vildagliptin v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Fonseca 2007	Vildagliptin v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Fonseca 2007	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Fonseca 2007	Vildagliptin v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified
Fonseca 2013	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Fonseca 2013	Sitagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Fonseca 2013	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Fonseca 2013	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Fonseca 2013	Sitagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Forst 2005	Pioglitazone v Glimepiride	HbA1c change	Some concerns	Due to concerns about randomisation method and analysis	Directly applicable	None specified
Forst 2014	Canagliflozin v Placebo	All-cause mortality	High	Due to concerns about the integrity of the placebo group and the high level of attrition from it and rescue therapy required.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Forst 2014	Canagliflozin v Placebo	Cardiovascular mortality	High	Due to concerns about the integrity of the placebo group and the high level of attrition from it and rescue therapy required.	Directly applicable	None specified
Forst 2014	Canagliflozin v Placebo	HbA1c change	High	Due to concerns about the integrity of the placebo group and the high level of attrition from it and rescue therapy required.	Directly applicable	None specified
Forst 2014	Canagliflozin v Placebo	Weight change	High	Due to concerns about the integrity of the placebo group and the high level of attrition from it and rescue therapy required.	Directly applicable	None specified
Forst 2015	Vildagliptin v Insulin	All-cause mortality	High	Open-label study. Participants were excluded due to unsatisfactory therapeutic effect, and this proportion was higher in the vildagliptin group. There was protocol deviation in the	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				vildagliptin group, and adherance was not reported. There was also a lack of information around randomisation and allocation concealment.		
Forst 2015	Vildagliptin v Insulin	HbA1c change	High	Open-label study. Participants were excluded due to unsatisfactory therapeutic effect, and this proportion was higher in the vildagliptin group. There was protocol deviation in the vildagliptin group, and adherance was not reported. There was also a lack of information around randomisation and allocation concealment.	Directly applicable	None specified
Forst 2015	Vildagliptin v Insulin	Hypoglycaemia episodes	High	Open-label study. Participants were excluded due to unsatisfactory therapeutic effect, and this proportion	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				was higher in the vildagliptin group. There was protocol deviation in the vildagliptin group, and adherance was not reported. There was also a lack of information around randomisation and allocation concealment.		
Forst 2015	Vildagliptin v Insulin	Severe hypoglycaemic episodes	High	Open-label study. Participants were excluded due to unsatisfactory therapeutic effect, and this proportion was higher in the vildagliptin group. There was protocol deviation in the vildagliptin group, and adherance was not reported. There was also a lack of information around randomisation and allocation concealment.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Frias 2016	Dapagliflozin + Exenatide v Exenatide	HbA1c change	High	High attrition and missing outcome data were higher in the Dapagliflozin compared with the Exenatide + dapagliflozin arm	Directly applicable	None specified
Frias 2016	Dapagliflozin + Exenatide v Exenatide	Weight change	High	High attrition, and missing data were higher in the Dapagliflozin compared with the Exenatide + Dapagliflozin arm	Directly applicable	None specified
Frias 2016	Dapagliflozin + Exenatide v Exenatide	Acute kidney injury	High	High proportion of participants did not complete treatment	Directly applicable	None specified
Frias 2016	Dapagliflozin + Exenatide v Exenatide	All-cause mortality	High	High proportion of participants did not complete treatment	Directly applicable	None specified
Frias 2016	Dapagliflozin + Exenatide v Exenatide	Cardiovascular mortality	High	High proportion of participants did not complete treatment	Directly applicable	None specified
Frias 2016	Dapagliflozin + Exenatide v Exenatide	Hypoglycaemia episodes	High	High proportion of participants did not complete treatment	Directly applicable	None specified
Frias 2016	Dapagliflozin + Exenatide v Exenatide	Severe hypoglycaemic episodes	High	High proportion of participants did not complete treatment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	Acute kidney injury	High	High proportion of participants did not complete treatment	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	All-cause mortality	High	High proportion of participants did not complete treatment	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	Cardiovascular mortality	High	High proportion of participants did not complete treatment	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	Hypoglycaemia episodes	High	High proportion of participants did not complete treatment	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	Severe hypoglycaemic episodes	High	High proportion of participants did not complete treatment	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	HbA1c change	High	High proportion of participants did not complete treatment. Missing data were higher in the	Directly applicable	Population, intervention, comparator, and outcome match protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Exenatide compared with the Exenatide + Dapagliflozin arm		
Frias 2016	Dapagliflozin + Exenatide v Dapagliflozin	Weight change	High	High proportion of participants did not complete treatment. Missing data were higher in the Exenatide compared with the Exenatide + Dapagliflozin arm	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	Acute kidney injury	High	None specified	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	All-cause mortality	High	None specified	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	Cardiovascular mortality	High	None specified	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	HbA1c change	High	None specified	Directly applicable	Population, intervention, comparator, and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	Hypoglycaemia episodes	High	None specified	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	Severe hypoglycaemic episodes	High	None specified	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2016	Dapagliflozin v Exenatide	Weight change	High	None specified	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Frias 2018	Dulaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Frias 2018	Dulaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Frias 2018	Dulaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Frias 2018	Dulaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Frias 2018	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Frias 2018	Dulaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Dulaglutide	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Dulaglutide	BMI change	Some concerns	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Dulaglutide	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Dulaglutide	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Dulaglutide	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Dulaglutide	Weight change	Some concerns	None specified	Directly applicable	None specified
Frias 2018	Tirzepatide v Placebo	All-cause mortality	Some concerns	There was no information around adherence. Treatment discontinuation was higher in the 15 mg tirzepatide arm, however,discontinuations were comparable to the placebo arm overall	Directly applicable	None specified
Frias 2018	Tirzepatide v Placebo	BMI change	Some concerns	There was no information around adherence. Treatment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation was higher in the 15 mg tirzepatide arm, however,discontinuations were comparable to the placebo arm overall		
Frias 2018	Tirzepatide v Placebo	HbA1c change	Some concerns	There was no information around adherence. Treatment discontinuation was higher in the 15 mg tirzepatide arm, however,discontinuations were comparable to the placebo arm overall	Directly applicable	None specified
Frias 2018	Tirzepatide v Placebo	Hypoglycaemia episodes	Some concerns	There was no information around adherence. Treatment discontinuation was higher in the 15 mg tirzepatide arm, however,discontinuations were comparable to the placebo arm overall	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Frias 2018	Tirzepatide v Placebo	Severe hypoglycaemic episodes	Some concerns	There was no information around adherence. Treatment discontinuation was higher in the 15 mg tirzepatide arm, however,discontinuations were comparable to the placebo arm overall	Directly applicable	None specified
Frias 2018	Tirzepatide v Placebo	Weight change	Some concerns	There was no information around adherence. Treatment discontinuation was higher in the 15 mg tirzepatide arm, however,discontinuations were comparable to the placebo arm overall	Directly applicable	None specified
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	All-cause mortality	High	Around 76% of participants did not complete treatment, and as it was a rare outcome it was deemed that this could have an effect.	Directly applicable	Population, intervention, comparator and outcome matched the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	Diabetic ketoacidosis	High	Around 76% of participants did not complete treatment, and as it was a rare outcome it was deemed that this could have an effect.	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	Hospitalisation for heart failure	High	Around 76% of participants did not complete treatment, and as it was a rare outcome it was deemed that this could have an effect.	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	Hypoglycaemia episodes	High	Around 76% of participants did not complete treatment, and as it was a rare outcome it was deemed that this could have an effect.	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	Severe hypoglycaemic episodes	High	Around 76% of participants did not complete treatment, and as it was a rare outcome it was deemed that this	Directly applicable	Population, intervention, comparator and outcome matched the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				could have an effect.		
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	HbA1c change	High	Attrition was high, presumably mainly due to rescue and treatment discontinuation. Attrition was also higher in the glimepiride arm.	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Frias 2020	Dapagliflozin + Saxagliptin v Glimepiride	Weight change	High	Attrition was high, presumably mainly due to rescue and treatment discontinuation. Attrition was also higher in the glimepiride arm.	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Frias 2023	Dulaglutide v Placebo	HbA1c change	Some concerns	Missing data were higher in the placebo group as 7 participants in the placebo group required rescue therapy. No participants in the dulaglutide group required rescue therapy.	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Frias 2023	Dulaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Frias 2023	Dulaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Frias 2023 non-obese	Dulaglutide v Placebo	HbA1c change	High	For the main analysis, missing data were higher in the placebo group as 7 participants in the placebo group required rescue therapy and no participants in the dulaglutide group required rescue therapy. However, the report does not state how many participants did not	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				have obesity at baseline, so it is unclear how many participant were missing.		
Frias 2023 obese	Dulaglutide v Placebo	HbA1c change	High	For the main analysis, missing data were higher in the placebo group as 7 participants in the placebo group required rescue therapy and no participants in the dulaglutide group required rescue therapy. However, the report does not state how many participants did not have obesity at baseline, so it is unclear how many participant were missing.	Directly applicable	None specified
Fujioka 2003	Metformin slow release v Metformin standard release	All-cause mortality	High	Does not detail randomisation, concelament or attrition per arm. Authors state study is under-powered to detect difference in	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				adverse events. Trial is not registered		
Fujioka 2003	Metformin slow release v Metformin standard release	Hypoglycaemia episodes	High	Does not detail randomisation, concelament or attrition per arm. Authors state study is under-powered to detect difference in adverse events. Trial is not registered	Directly applicable	None specified
Fujioka 2003	Metformin slow release v Metformin standard release	Severe hypoglycaemic episodes	High	Does not detail randomisation, concelament or attrition per arm. Authors state study is under-powered to detect difference in adverse events. Trial is not registered	Directly applicable	None specified
Gadde 2017	Exenatide v Placebo	HbA1c change	High	Imbalance in randomisation plus the high dropout rate in placebo arm compared to other arms	Directly applicable	None specified
Gadde 2017	Exenatide v Placebo	Hypoglycaemia episodes	High	Imbalance in randomisation plus	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				the high dropout rate in placebo arm compared to other arms		
Gadde 2017	Exenatide v Placebo	Non-fatal myocardial infarction	High	Imbalance in randomisation plus the high dropout rate in placebo arm compared to other arms	Directly applicable	None specified
Gadde 2017	Exenatide v Placebo	Severe hypoglycaemic episodes	High	Imbalance in randomisation plus the high dropout rate in placebo arm compared to other arms	Directly applicable	None specified
Gadde 2017	Exenatide v Placebo	Weight change	High	Imbalance in randomisation plus the high dropout rate in placebo arm compared to other arms	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	Health-related quality of life - overall	Some concerns	Lack of blinding particularly affects PROs as stated by the authors	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	Health-related quality of life - subscale well being	Some concerns	Lack of blinding particularly affects PROs as stated by the authors	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gadde 2017	Exenatide v Placebo	Health-related quality of life - overall	High	Lack of blinding particularly affects PROs, imbalance in randomisation plus concerns about the high dropout rate in placebo group	Directly applicable	None specified
Gadde 2017	Exenatide v Placebo	Health-related quality of life - subscale well being	High	Lack of blinding particularly affects PROs, imbalance in randomisation plus concerns about the high dropout rate in placebo group	Directly applicable	None specified
Gadde 2017	Sitagliptin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Gadde 2017	Sitagliptin v Placebo	Health-related quality of life - overall	High	None specified	Directly applicable	None specified
Gadde 2017	Sitagliptin v Placebo	Health-related quality of life - subscale well being	High	None specified	Directly applicable	None specified
Gadde 2017	Sitagliptin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Gadde 2017	Sitagliptin v Placebo	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Gadde 2017	Sitagliptin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gadde 2017	Sitagliptin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Gadde 2017	Exenatide v Sitagliptin	Weight change	Low	None specified	Directly applicable	None specified
Galindo 2023	Insulin degludec/liraglutide v Insulin	HbA1c change	High	High attrition; lack of info on allocation concealment	Directly applicable	None specified
Galindo 2023	Insulin degludec/liraglutide v Insulin	Hypoglycaemia episodes	High	High attrition; lack of info on allocation concealment	Directly applicable	None specified
Galindo 2023	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	High	High attrition; lack of info on allocation concealment	Directly applicable	None specified
Galindo 2023	Insulin degludec/liraglutide v Insulin	Weight change	High	High attrition; lack of info on allocation concealment	Directly applicable	None specified
Gallwitz 2011	Exenatide v Insulin	At night hypoglycaemic episodes	High	No information regarding randomisation, few baseline	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				charactersitics reported.		
Gallwitz 2011	Exenatide v Insulin	HbA1c change	High	No information regarding randomisation, few baseline charactersitics reported.	Directly applicable	None specified
Gallwitz 2011	Exenatide v Insulin	Hypoglycaemia episodes	High	No information regarding randomisation, few baseline charactersitics reported.	Directly applicable	None specified
Gallwitz 2011	Exenatide v Insulin	Severe hypoglycaemic episodes	High	No information regarding randomisation, few baseline charactersitics reported.	Directly applicable	None specified
Gallwitz 2011	Exenatide v Insulin	Weight change	High	No information regarding randomisation, few baseline charactersitics reported.	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	All-cause mortality	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				and high adherance rate		
Gallwitz 2012A	Glimepiride v Linagliptin	Cardiovascular mortality	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	HbA1c change	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	Hospitalisation for heart failure	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	Hypoglycaemia episodes	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gallwitz 2012A	Glimepiride v Linagliptin	Non-fatal myocardial infarction	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	Non-fatal stroke	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	Severe hypoglycaemic episodes	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	Unstable angina	Low	High overall attrition rate over 24 months however study was double blinded with a large sample size and high adherance rate	Directly applicable	None specified
Gallwitz 2012A	Glimepiride v Linagliptin	Weight change	Low	High overall attrition rate over 24 months however study was	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				double blinded with a large sample size and high adherance rate		
Gallwitz 2012B	Glimepiride v Exenatide	All-cause mortality	Low	High attrition rate overall however the study was conducted over 36 months and authors conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with high numbers of attrition	Directly applicable	None specified
Gallwitz 2012B	Glimepiride v Exenatide	At night hypoglycaemic episodes	Low	High attrition rate overall however the study was conducted over 36 months and authors conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with high numbers of attrition	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gallwitz 2012B	Glimepiride v Exenatide	BMI change	Low	High attrition rate overall however the study was conducted over 36 months and authors conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with high numbers of attrition	Directly applicable	None specified
Gallwitz 2012B	Glimepiride v Exenatide	HbA1c change	Low	High attrition rate overall however the study was conducted over 36 months and authors conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with high numbers of attrition	Directly applicable	None specified
Gallwitz 2012B	Glimepiride v Exenatide	Hypoglycaemia episodes	Low	High attrition rate overall however the study was conducted over 36 months and authors	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with high numbers of attrition		
Gallwitz 2012B	Glimepiride v Exenatide	Severe hypoglycaemic episodes	Low	High attrition rate overall however the study was conducted over 36 months and authors conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with high numbers of attrition	Directly applicable	None specified
Gallwitz 2012B	Glimepiride v Exenatide	Weight change	Low	High attrition rate overall however the study was conducted over 36 months and authors conducted a power calculation showing that sample size was appropriately powered to detect treatment effect with	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				high numbers of attrition		
Gao 2023	Tirzepatide v Insulin	4-point MACE	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	All-cause mortality	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Cardiac arrhythmia	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Cardiovascular mortality	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	HbA1c change	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Hospitalisation for heart failure	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Hypoglycaemia episodes	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Non-fatal myocardial infarction	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Non-fatal stroke	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gao 2023	Tirzepatide v Insulin	Severe hypoglycaemic episodes	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Gao 2023	Tirzepatide v Insulin	Weight change	Some concerns	Concerns with blinding and analysis method.	Directly applicable	None specified
Garber 2007	Vildagliptin v Placebo	HbA1c change	Some concerns	Lack of data on reandomisation and concealment	Directly applicable	None specified
Garber 2007	Vildagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of data on reandomisation and concealment	Directly applicable	None specified
Garber 2007	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of data on reandomisation and concealment	Directly applicable	None specified
Garber 2008	Vildagliptin v Placebo	All-cause mortality	High	Higher discontinuation in the placebo arm than the vildagliptin arms and lack of information around allocation concealment.	Directly applicable	None specified
Garber 2008	Vildagliptin v Placebo	HbA1c change	High	Higher discontinuation in the placebo arm than the vildagliptin arms and lack of information around	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				allocation concealment.		
Garber 2008	Vildagliptin v Placebo	Hypoglycaemia episodes	High	Higher discontinuation in the placebo arm than the vildagliptin arms and lack of information around allocation concealment.	Directly applicable	None specified
Garber 2008	Vildagliptin v Placebo	Severe hypoglycaemic episodes	High	Higher discontinuation in the placebo arm than the vildagliptin arms and lack of information around allocation concealment.	Directly applicable	None specified
Garber 2008	Vildagliptin v Placebo	Weight change	High	Higher discontinuation in the placebo arm than the vildagliptin arms and lack of information around allocation concealment.	Directly applicable	None specified
Garvey 2020	Liraglutide v Placebo	HbA1c change	Low	Double blind RCT with power calculations to show number of participants enrolled	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				was adqequate to evaulate end points		
Garvey 2020	Liraglutide v Placebo	Health-related quality of life - subscale physical functioning	Low	Double blind RCT with power calculations to show number of participants enrolled was adqequate to evaulate end points	Directly applicable	None specified
Garvey 2020	Liraglutide v Placebo	Hypoglycaemia episodes	Low	Double blind RCT with power calculations to show number of participants enrolled was adqequate to evaulate end points	Directly applicable	None specified
Garvey 2020	Liraglutide v Placebo	Severe hypoglycaemic episodes	Low	Double blind RCT with power calculations to show number of participants enrolled was adqequate to evaulate end points	Directly applicable	None specified
Garvey 2020	Liraglutide v Placebo	Weight change	Low	Double blind RCT with power calculations to show number of participants enrolled was adqequate to evaulate end points	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Garvey 2023	Tirzepatide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	Health-related quality of life - subscale physical functioning	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Garvey 2023	Tirzepatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Genovese 2013	Pioglitazone v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Genovese 2013	Pioglitazone v Placebo	BMI change	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome match protocol
Genovese 2013	Pioglitazone v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome match protocol
Genovese 2013	Pioglitazone v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome match protocol
Genovese 2013	Pioglitazone v Placebo	Weight change	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome match protocol
Gerstein 2019A	Dulaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gerstein 2019A	Dulaglutide v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Gerstein 2019A	Dulaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Gerstein 2019A no CVD	Dulaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Giorgino 2015	Dulaglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol
Giorgino 2015	Dulaglutide v Insulin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol
Giorgino 2015	Dulaglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol
Giorgino 2015	Dulaglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol
Giorgino 2015	Dulaglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol
Giorgino 2015	Dulaglutide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Giorgino 2015	Dulaglutide v Insulin	Weight change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched protocol
Giugliano 1993	Metformin v Placebo	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	Population, intervention, comparator and outcomet match protocol
Göke 2010	Glipizide v Saxagliptin	All-cause mortality	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention.	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Göke 2010	Glipizide v Saxagliptin	Cardiovascular mortality	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention.	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Göke 2010	Glipizide v Saxagliptin	HbA1c change	High	High number of participants did not complete treatment, and there were no analyses that	Directly applicable	Population, intervention, comparator, and outcome match protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				estimated the effect of adhering to the intervention.		
Göke 2010	Glipizide v Saxagliptin	Hypoglycaemia episodes	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention.	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Göke 2010	Glipizide v Saxagliptin	Weight change	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention.	Directly applicable	Population, intervention, comparator, and outcome match protocol.
Goodman 2009	Vildagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment and randomisation.	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Goodman 2009	Vildagliptin v Placebo	Severe hypoglycaemic episodes	High	Lack of information around allocation concealment and randomisation. 77.6% of participants did not complete the study.	Directly applicable	Population, intervention, comparator and outcome matched the protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				As this was a rare outcome, it was not judged that it may have a substantial effect		
Goodman 2009	Vildagliptin v Placebo	HbA1c change	High	Lack of information around allocation concealment and randomisation. There were missing data, however, discontinuation due to adverse events was low and similar in both arms.	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Gough 2014	Insulin degludec/liraglutide v Insulin	3-point MACE	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	3-point MACE	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	3-point MACE	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	All-cause mortality	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gough 2014	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	HbA1c change	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Insulin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Gough 2014	Liraglutide v Insulin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Gough 2014	Insulin degludec/liraglutide v Liraglutide	Weight change	Low	None specified	Directly applicable	None specified
Gough 2014	Liraglutide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Gram 2011	Metformin v Placebo	HbA1c change	Some concerns	Total attrition around 20%	Directly applicable	None specified
Gram 2011	Metformin v Placebo	Hypoglycaemia episodes	Some concerns	Total attrition around 20%	Directly applicable	None specified
Gram 2011	Metformin v Placebo	Weight change	Some concerns	Total attrition around 20%	Directly applicable	None specified
Grey 2014	Pioglitazone v Placebo	HbA1c change	Some concerns	Differences in baseline cointerventions not accounted for	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Grey 2014	Pioglitazone v Placebo	Weight change	Some concerns	Differences in baseline cointerventions not accounted for	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	4-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	Hypoglycaemia episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	Severe hypoglycaemic episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	Unstable angina	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	HbA1c change	High	Open-label study where there was a high level of discontinuation of study medication. There was also a	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				high proportion of missing data.		
Group 2022	Liraglutide v Insulin	Health-related quality of life - subscale mental component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	Health-related quality of life - subscale physical component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Group 2022	Liraglutide v Insulin	3-point MACE	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	All-cause mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	Cardiovascular mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	None specified
Group 2022	Liraglutide v Insulin	Hospitalisation for heart failure	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				for ITT and per-protocol analysis.		
Group 2022	Sitagliptin v Insulin	4-point MACE	High	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	HbA1c change	High	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	Health-related quality of life - subscale mental component	High	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	Health-related quality of life - subscale physical component	High	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	Hypoglycaemia episodes	High	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome match protocol
Group 2022	Sitagliptin v Insulin	Unstable angina	High	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	3-point MACE	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	All-cause mortality	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	Cardiovascular mortality	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Sitagliptin v Insulin	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	4-point MACE	High	Open-label study where there was a high level of	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		outcome match protocol
Group 2022	Glimepiride v Liraglutide	4-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	4-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Liraglutide v Sitagliptin	4-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Hypoglycaemia episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	Hypoglycaemia episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Hypoglycaemia episodes	High	Open-label study where there was a high level of	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		outcome match protocol
Group 2022	Liraglutide v Sitagliptin	Hypoglycaemia episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Severe hypoglycaemic episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	Severe hypoglycaemic episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Severe hypoglycaemic episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Unstable angina	High	Open-label study where there was a high level of	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		outcome match protocol
Group 2022	Glimepiride v Liraglutide	Unstable angina	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Unstable angina	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Liraglutide v Sitagliptin	Unstable angina	High	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	HbA1c change	High	Open-label study where there was a high level of discontinuation of study medication. There was also a high proportion of missing data.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	HbA1c change	High	Open-label study where there was a high level of discontinuation of study medication. There was also a	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				high proportion of missing data.		
Group 2022	Glimepiride v Sitagliptin	HbA1c change	High	Open-label study where there was a high level of discontinuation of study medication. There was also a high proportion of missing data.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Liraglutide v Sitagliptin	HbA1c change	High	Open-label study where there was a high level of discontinuation of study medication. There was also a high proportion of missing data.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Health-related quality of life - subscale mental component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				were not available at all timepoints.		
Group 2022	Glimepiride v Liraglutide	Health-related quality of life - subscale mental component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Health-related quality of life - subscale mental component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Group 2022	Liraglutide v Sitagliptin	Health-related quality of life - subscale mental component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Health-related quality of life - subscale physical component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	Health-related quality of life -	High	Open-label study where there was a high level of	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale physical component		discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.		outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Health-related quality of life - subscale physical component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Liraglutide v Sitagliptin	Health-related quality of life - subscale physical component	High	Open-label study where there was a high level of discontinuation of study medication. Outcome was also subjective, and the	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				open-label design could have biased the result. There was selective reporting as data were not available at all timepoints.		
Group 2022	Glimepiride v Insulin	3-point MACE	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	3-point MACE	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	3-point MACE	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Group 2022	Liraglutide v Sitagliptin	3-point MACE	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	All-cause mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	All-cause mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	All-cause mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				for ITT and per-protocol analysis.		
Group 2022	Liraglutide v Sitagliptin	All-cause mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Cardiovascular mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	Cardiovascular mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Cardiovascular mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication.	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Results were similar for ITT and per-protocol analysis.		
Group 2022	Liraglutide v Sitagliptin	Cardiovascular mortality	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Insulin	Hospitalisation for heart failure	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Liraglutide	Hospitalisation for heart failure	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022	Glimepiride v Sitagliptin	Hospitalisation for heart failure	Some concerns	Open-label study where there was a high level of discontinuation of	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				study medication. Results were similar for ITT and per-protocol analysis.		outcome match protocol
Group 2022	Liraglutide v Sitagliptin	Hospitalisation for heart failure	Some concerns	Open-label study where there was a high level of discontinuation of study medication. Results were similar for ITT and per-protocol analysis.	Directly applicable	Population, intervention, comparator and outcome match protocol
Group 2022 - with obesity	Liraglutide v Insulin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	None specified
Group 2022 - with obesity	Liraglutide v Insulin	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	None specified
Group 2022 - with obesity	Liraglutide v Insulin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	None specified
Group 2022 - with obesity	Liraglutide v Insulin	Hospitalisation for heart failure	High	Open-label study where there was a high level of	Partially applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		
Group 2022 - with obesity	Sitagliptin v Insulin	3-point MACE	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Sitagliptin v Insulin	All-cause mortality	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Sitagliptin v Insulin	Cardiovascular mortality	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Sitagliptin v Insulin	Hospitalisation for heart failure	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Insulin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Liraglutide	3-point MACE	High	Open-label study where there was a high level of	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Sitagliptin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Liraglutide v Sitagliptin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Insulin	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Liraglutide	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Sitagliptin	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Liraglutide v Sitagliptin	All-cause mortality	High	Open-label study where there was a high level of	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Insulin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Liraglutide	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Sitagliptin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Liraglutide v Sitagliptin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Insulin	Hospitalisation for heart failure	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Liraglutide	Hospitalisation for heart failure	High	Open-label study where there was a high level of	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Glimepiride v Sitagliptin	Hospitalisation for heart failure	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - with obesity	Liraglutide v Sitagliptin	Hospitalisation for heart failure	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Liraglutide v Insulin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	None specified
Group 2022 - without obesity	Liraglutide v Insulin	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	None specified
Group 2022 - without obesity	Liraglutide v Insulin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	None specified
Group 2022 - without obesity	Liraglutide v Insulin	Hospitalisation for heart failure	High	Open-label study where there was a high level of	Partially applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		
Group 2022 - without obesity	Sitagliptin v Insulin	3-point MACE	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Sitagliptin v Insulin	All-cause mortality	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Sitagliptin v Insulin	Cardiovascular mortality	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Sitagliptin v Insulin	Hospitalisation for heart failure	High	None specified	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Insulin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Liraglutide	3-point MACE	High	Open-label study where there was a high level of	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Sitagliptin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Liraglutide v Sitagliptin	3-point MACE	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Insulin	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Liraglutide	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Sitagliptin	All-cause mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Liraglutide v Sitagliptin	All-cause mortality	High	Open-label study where there was a high level of	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Insulin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Liraglutide	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Sitagliptin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Liraglutide v Sitagliptin	Cardiovascular mortality	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Insulin	Hospitalisation for heart failure	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Liraglutide	Hospitalisation for heart failure	High	Open-label study where there was a high level of	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				discontinuation of study medication.		kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Glimepiride v Sitagliptin	Hospitalisation for heart failure	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Group 2022 - without obesity	Liraglutide v Sitagliptin	Hospitalisation for heart failure	High	Open-label study where there was a high level of discontinuation of study medication.	Partially applicable	Subgroup analysis uses a BMI threshold of 30.7 kg/m2 rather than 30 kg/m2
Gu 2019	Glimepiride v Saxagliptin	HbA1c change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Gu 2019	Glimepiride v Saxagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Gu 2019	Glimepiride v Saxagliptin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Gu 2019	Glimepiride v Saxagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome match protocol
Gu 2019	Glimepiride v Saxagliptin	Weight change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Guja 2017	Exenatide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	Population, intervention, comparator and outcome mathced protocol
Guja 2017	Exenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome mathced protocol
Guja 2017	Exenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome mathced protocol
Guja 2017	Exenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome mathced protocol
Guja 2017	Exenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome mathced protocol
Guja 2017	Exenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome mathced protocol
Guja 2017	Exenatide v Placebo	Weight change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome mathced protocol
Gullaksen 2023	Empagliflozin v Placebo	Weight change	High	Concerns around allocation conceallment as report did not state that envelopes were opaque.	Directly applicable	None specified
Guo 2020	Liraglutide v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Guo 2020	Liraglutide v Placebo	BMI change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Guo 2020	Liraglutide v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Guo 2020	Liraglutide v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Guo 2020	Liraglutide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Guo 2020	Liraglutide v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Guo 2020	Liraglutide v Placebo	Weight change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Guo 2020	Liraglutide v Insulin	All-cause mortality	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Guo 2020	Liraglutide v Insulin	BMI change	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Guo 2020	Liraglutide v Insulin	Cardiovascular mortality	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Guo 2020	Liraglutide v Insulin	HbA1c change	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Guo 2020	Liraglutide v Insulin	Hypoglycaemia episodes	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Guo 2020	Liraglutide v Insulin	Severe hypoglycaemic episodes	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Guo 2020	Liraglutide v Insulin	Weight change	Low	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Gurkan 2014	Exenatide v Insulin	BMI change	Some concerns	Lack of information around allocation concealment and method of randomisation	Directly applicable	Population, intervention, comparator, and outcome match protocol
Gurkan 2014	Exenatide v Insulin	HbA1c change	Some concerns	Lack of information around allocation concealment and method of randomisation	Directly applicable	Population, intervention, comparator, and outcome match protocol
Gurkan 2014	Exenatide v Insulin	Weight change	Some concerns	Lack of information around allocation concealment and method of randomisation	Directly applicable	Population, intervention, comparator, and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Guzman 2017	Sitagliptin v Placebo	HbA1c change	High	Lack of information around allocation concealment. The trial was also stopped early, meaning that 12month outcome data were limited.	Directly applicable	Population, intervention, comparator and outcome matched protocol
Guzman 2017	Sitagliptin v Placebo	Severe hypoglycaemic episodes	High	Lack of information around allocation concealment. The trial was also stopped early, meaning that 12month outcome data were limited.	Directly applicable	Population, intervention, comparator and outcome matched protocol
Guzman 2017	Sitagliptin v Placebo	Weight change	High	Lack of information around allocation concealment. The trial was also stopped early, meaning that 12month outcome data were limited.	Directly applicable	Population, intervention, comparator and outcome matched protocol
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	Acute kidney injury	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				was higher in the sitagliptin arm		
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	All-cause mortality	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm	Directly applicable	Population, intervention, comparator and outcome match protocol
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	Cardiac arrhythmia	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm	Directly applicable	Population, intervention, comparator and outcome match protocol
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	Cardiovascular mortality	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	HbA1c change	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm	Directly applicable	Population, intervention, comparator and outcome match protocol
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	Hypoglycaemia episodes	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm	Directly applicable	Population, intervention, comparator and outcome match protocol
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	Severe hypoglycaemic episodes	High	The proportion of participants who discontinued due to lack of glycaemic conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm	Directly applicable	Population, intervention, comparator and outcome match protocol
Handelsman 2019	Dapagliflozin + Saxagliptin v Sitagliptin	Weight change	High	The proportion of participants who discontinued due to lack of glycaemic	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				conrol or rescued for not achieving per-specified targes was higher in the sitagliptin arm		outcome match protocol
Hanefeld 2004	Pioglitazone v Metformin	HbA1c change	High	No information about randomisation/allocation concealment, mITT LOCF analysis, no protocol available	Directly applicable	None specified
Hanefeld 2004	Pioglitazone v Metformin	All-cause mortality	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified
Hanefeld 2004	Pioglitazone v Metformin	Hypoglycaemia episodes	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified
Hanefeld 2004	Pioglitazone v Metformin	Severe hypoglycaemic episodes	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Hanefeld 2011	Pioglitazone + Metformin v Pioglitazone	HbA1c change	Some concerns	Lack of information around randomisation and allocation concealment.	Directly applicable	None specified
Hanefeld 2011	Pioglitazone + Metformin v Pioglitazone	Hypoglycaemia episodes	Some concerns	Lack of information around randomisation and allocation concealment.	Directly applicable	None specified
Hanefeld 2011	Pioglitazone + Metformin v Metformin	HbA1c change	Some concerns	Lack of information around randomisation and allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Hanefeld 2011	Pioglitazone + Metformin v Metformin	Hypoglycaemia episodes	Some concerns	Lack of information around randomisation and allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Hanefeld 2011	Pioglitazone v Metformin	HbA1c change	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Hanefeld 2011	Pioglitazone v Metformin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Hao 2022	Dapagliflozin v Liraglutide	HbA1c change	High	None specified	Directly applicable	None specified
Hao 2022	Dapagliflozin v Liraglutide	Hospitalisation for heart failure	High	None specified	Directly applicable	None specified
Hao 2022	Dapagliflozin v Liraglutide	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Hao 2022	Dapagliflozin v Liraglutide	Non-fatal myocardial infarction	High	None specified	Directly applicable	None specified
Hao 2022	Dapagliflozin v Liraglutide	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Hao 2022	Dapagliflozin v Liraglutide	Unstable angina	High	None specified	Directly applicable	None specified
Hao 2022	Dapagliflozin v Liraglutide	Weight change	High	None specified	Directly applicable	None specified
Haring 2013	Empagliflozin v Placebo	All-cause mortality	High	High proportion of participants did not complete treatment period	Directly applicable	None specified
Haring 2013	Empagliflozin v Placebo	Cardiovascular mortality	High	High proportion of participants did not complete treatment period	Directly applicable	None specified
Haring 2013	Empagliflozin v Placebo	Hypoglycaemia episodes	High	High proportion of participants did not complete treatment period	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Haring 2013	Empagliflozin v Placebo	Severe hypoglycaemic episodes	High	High proportion of participants did not complete treatment period	Directly applicable	None specified
Haring 2013	Empagliflozin v Placebo	HbA1c change	Some concerns	High proportion of participants did not complete treatment period, however, results are similar between MMRM analyses in the FAS and FAS-completers data	Directly applicable	None specified
Haring 2013	Empagliflozin v Placebo	Weight change	Some concerns	High proportion of participants did not complete treatment period, however, results are similar between MMRM analyses in the FAS and FAS-completers data	Directly applicable	None specified
Haring 2014	Empagliflozin v Placebo	All-cause mortality	High	34% of participants did not complete the study	Directly applicable	Population, intervention, comparator and outcome match protocol
Haring 2014	Empagliflozin v Placebo	Cardiovascular mortality	High	34% of participants did not complete the study	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome match protocol
Haring 2014	Empagliflozin v Placebo	HbA1c change	High	34% of participants did not complete the study	Directly applicable	Population, intervention, comparator and outcome match protocol
Haring 2014	Empagliflozin v Placebo	Hypoglycaemia episodes	High	34% of participants did not complete the study	Directly applicable	Population, intervention, comparator and outcome match protocol
Haring 2014	Empagliflozin v Placebo	Severe hypoglycaemic episodes	High	34% of participants did not complete the study	Directly applicable	Population, intervention, comparator and outcome match protocol
Haring 2014	Empagliflozin v Placebo	Weight change	High	34% of participants did not complete the study	Directly applicable	Population, intervention, comparator and outcome match protocol
Harreiter 2021	Exenatide v Placebo	BMI change	Some concerns	The report states that adherence was monitored, and that a per-protocol analysis was performed. However, the results of the per-protocol analysis have not	Directly applicable	Population, intervention, comparator and outcome match review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				been reported for this outcome.		
Harreiter 2021	Exenatide v Placebo	Diabetic ketoacidosis	Some concerns	The report states that adherence was monitored, and that a per-protocol analysis was performed. However, the results of the per-protocol analysis have not been reported for this outcome.	Directly applicable	Population, intervention, comparator and outcome match review protocol
Harreiter 2021	Exenatide v Placebo	HbA1c change	Some concerns	The report states that adherence was monitored, and that a per-protocol analysis was performed. However, the results of the per-protocol analysis have not been reported for this outcome.	Directly applicable	Population, intervention, comparator and outcome match review protocol
Harreiter 2021	Exenatide v Placebo	Hypoglycaemia episodes	Some concerns	The report states that adherence was monitored, and that a per-protocol analysis was performed. However, the results	Directly applicable	Population, intervention, comparator and outcome match review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				of the per-protocol analysis have not been reported for this outcome.		
Harreiter 2021	Exenatide v Placebo	Severe hypoglycaemic episodes	Some concerns	The report states that adherence was monitored, and that a per-protocol analysis was performed. However, the results of the per-protocol analysis have not been reported for this outcome.	Directly applicable	Population, intervention, comparator and outcome match review protocol
Harreiter 2021	Exenatide v Placebo	Weight change	Some concerns	The report states that adherence was monitored, and that a per-protocol analysis was performed. However, the results of the per-protocol analysis have not been reported for this outcome.	Directly applicable	Population, intervention, comparator and outcome match review protocol
Hartemann-Heurtier 2009	Pioglitazone v Insulin	HbA1c change	High	Allocation was not judged to be concealed as envelopes were not	Directly applicable	Population, intervention, comparator and outcome match protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				specifically reported as opaque.		
Hartemann-Heurtier 2009	Pioglitazone v Insulin	Hypoglycaemia episodes	High	Allocation was not judged to be concealed as envelopes were not specifically reported as opaque.	Directly applicable	Population, intervention, comparator and outcome match protocol.
Hartemann-Heurtier 2009	Pioglitazone v Insulin	Severe hypoglycaemic episodes	High	Allocation was not judged to be concealed as envelopes were not specifically reported as opaque.	Directly applicable	Population, intervention, comparator and outcome match protocol.
Hartemann-Heurtier 2009	Pioglitazone v Insulin	Weight change	High	Allocation was not judged to be concealed as envelopes were not specifically reported as opaque.	Directly applicable	Population, intervention, comparator and outcome match protocol.
Hattori 2018	Empagliflozin v Placebo	BMI change	High	None specified	Partially applicable	Assumption made that all people were on antihyperglycaemia medication or insulin treatment at baseline, as empagliflozin described as an 'add-on' treatment and population

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						described as "HbA1c > 6.2% regardless of diet, exercise, and medical treatment other than SGLT2 inhibitors for at least 12 weeks". However, not completely clear as baseline characteristics only report the type of AHA on for ~60% of people.
Hattori 2018	Empagliflozin v Placebo	HbA1c change	High	None specified	Partially applicable	Assumption made that all people were on antihyperglycaemia medication or insulin treatment at baseline, as empagliflozin described as an 'add-on' treatment and population described as "HbA1c > 6.2% regardless of diet, exercise, and medical treatment other than SGLT2

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						inhibitors for at least 12 weeks". However, not completely clear as baseline characteristics only report the type of AHA on for ~60% of people.
Heine 2005	Exenatide v Insulin	Severe hypoglycaemic episodes	High	There were concerns around randomisation as a higher number of participants were allocated to the exenatide arm. More participants withdrew due to adverse events in the exenatide compared with the insulin arm.	Directly applicable	Protocol, intervention, comparator and outcome matched the protocol.
Heine 2005	Exenatide v Insulin	Health-related quality of life - overall	High	There were concerns around randomisation as a higher number of participants were allocated to the exenatide arm. More participants withdrew due to adverse events in	Directly applicable	Protocol, intervention, comparator and outcome matched the protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				the exenatide compared with the insulin arm. A per-protocol analysis was used, and it wasn't clear why results from an ITT analysis were not reported.		
Heine 2005	Exenatide v Insulin	Weight change	High	There were concerns around randomisation as a higher number of participants were allocated to the exenatide arm. More participants withdrew due to adverse events in the exenatide compared with the insulin arm.	Directly applicable	Protocol, intervention, comparator and outcome matched the protocol.
Heine 2005	Exenatide v Insulin	HbA1c change	High	There were concerns around randomisation as a higher number of participants were allocated to the exenatide arm. There was a lack of information around adherence,	Directly applicable	Protocol, intervention, comparator and outcome matched the protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				however, data were similar between the ITT and per-protocol analyses. There was higher attrition in the exenatide arm due to adverse events		
Heise 2022	Semaglutide v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Heise 2022	Semaglutide v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Heise 2022	Semaglutide v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Heise 2022	Semaglutide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Heise 2022	Semaglutide v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Heise 2022	Semaglutide v Placebo	Weight change	Some concerns	Lack of information around allocation concealment.	Directly applicable	None specified
Heise 2022	Tirzepatide v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome match protocol
Heise 2022	Tirzepatide v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Placebo	Weight change	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Semaglutide	All-cause mortality	Some concerns	None specified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome match protocol
Heise 2022	Tirzepatide v Semaglutide	Cardiovascular mortality	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Semaglutide	HbA1c change	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Semaglutide	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Semaglutide	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Heise 2022	Tirzepatide v Semaglutide	Weight change	Some concerns	None specified	Directly applicable	Population, intervention, comparator and outcome match protocol
Henriksen 2011	Pioglitazone v Placebo	Weight change	High	Lack of information around allocation concealment and	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				adherence. Attrition was higher in the placebo arm than the pioglitazone arm.		outcome match the review protocol
Henriksen 2011	Pioglitazone v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match the review protocol
Henriksen 2011	Pioglitazone v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match the review protocol
Henriksen 2011	Pioglitazone v Placebo	Non-fatal myocardial infarction	Some concerns	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome match the review protocol
Henriksen 2011	Pioglitazone v Placebo	HbA1c change	High	Lack of information around allocation concealment. Attrition was higher in the placebo arm than the pioglitazone arm.	Directly applicable	Population, intervention, comparator and outcome match the review protocol
Hermansen 2007 - Stratum 1	Sitagliptin v Placebo	HbA1c change	High	Attrition was high. Discontinuation due to exceeding of prespecified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				glycaemic criteria was higher in the placebo group, bu discontinuation due to adverse events was higher in the sitagliptin group		outcome matched the protocol
Hermansen 2007 - Stratum 1	Sitagliptin v Placebo	Weight change	High	Attrition was high. Discontinuation due to exceeding of prespecified glycaemic criteria was higher in the placebo group, bu discontinuation due to adverse events was higher in the sitagliptin group	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 1	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 1	Sitagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 1	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome matched the protocol
Hermansen 2007 - Stratum 1	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 2	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 2	Sitagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 2	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 2	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hermansen 2007 - Stratum 2	Sitagliptin v Placebo	Weight change	Low	None specified	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						outcome matched the protocol
Hollander 2009	Saxagliptin v Placebo	All-cause mortality	High	The methods state that randomisation was 1:1:1, however, more participants were randomised to the saxagliptin 2.5 mg arm. A high proportion of participants discontinued.	Directly applicable	Population, intervention, comparator, and outcome match the review protocol
Hollander 2009	Saxagliptin v Placebo	Cardiovascular mortality	High	The methods state that randomisation was 1:1:1, however, more participants were randomised to the saxagliptin 2.5 mg arm. A high proportion of participants discontinued.	Directly applicable	Population, intervention, comparator, and outcome match the review protocol
Hollander 2009	Saxagliptin v Placebo	Hypoglycaemia episodes	High	The methods state that randomisation was 1:1:1, however, more participants were randomised to the saxagliptin 2.5 mg arm. A high proportion of	Directly applicable	Population, intervention, comparator, and outcome match the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				participants discontinued.		
Hollander 2009	Saxagliptin v Placebo	HbA1c change	High	The methods state that randomisation was 1:1:1, however, more participants were randomised to the saxagliptin 2.5 mg arm. Despite greater attrition in the placebo group, more participants discontinued due to adverse events in the 5mg saxagliptin arm and more participants received rescue therapy in the placebo arm.	Directly applicable	Population, intervention, comparator, and outcome match the review protocol
Hollander 2009	Saxagliptin v Placebo	Weight change	High	The methods state that randomisation was 1:1:1, however, more participants were randomised to the saxagliptin 2.5 mg arm. Despite greater attrition in the placebo group, more participants discontinued due to adverse events in	Directly applicable	Population, intervention, comparator, and outcome match the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				the 5mg saxagliptin arm and more participants received rescue therapy in the placebo arm.		
Hollander 2018	Glimepiride v Ertugliflozin	Hypoglycaemia episodes	High	Reasons for discontinuation of intervention differed between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in the 15 mg ertugliflozin arm.	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hollander 2018	Glimepiride v Ertugliflozin	HbA1c change	High	Although randomisation was 1:1:1, the number of participants allocated to each arm was different. Attrition was high, and reasons for discontinuation of intervention differed	Directly applicable	Population, intervention, comparator and outcome matched the protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in the 15 mg ertugliflozin arm.		
Hollander 2018	Glimepiride v Ertugliflozin	Weight change	High	Attrition was high, and reasons for discontinuation of intervention differed between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in the 15 mg ertugliflozin arm. Although the methods states that	Directly applicable	Population, intervention, comparator and outcome matched the protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				a per-protocol analysis was performed, data from this analysis of this outcome were not presented.		
Hollander 2018	Glimepiride v Ertugliflozin	Cardiovascular mortality	High	Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in the 15 mg ertugliflozin arm.	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hollander 2018	Glimepiride v Ertugliflozin	Acute kidney injury	High	Reasons for discontinuation of intervention differed between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in	Directly applicable	Population, intervention, comparator and outcome matched the protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				the 15 mg ertugliflozin arm.		
Hollander 2018	Glimepiride v Ertugliflozin	All-cause mortality	High	Reasons for discontinuation of intervention differed between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in the 15 mg ertugliflozin arm.	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Hollander 2018	Glimepiride v Ertugliflozin	Diabetic ketoacidosis	High	Reasons for discontinuation of intervention differed between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in	Directly applicable	Population, intervention, comparator and outcome matched the protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				the 15 mg ertugliflozin arm.		
Hollander 2018	Glimepiride v Ertugliflozin	Severe hypoglycaemic episodes	High	Reasons for discontinuation of intervention differed between the arms. Discontinuation due to protocol non-compliance and hyperglycaemia were higher in was higher in the 5mg ertugliflozin arm, and discontinuation due to adverse events was higher in the 15 mg ertugliflozin arm.	Directly applicable	Population, intervention, comparator and outcome matched the protocol
Holman 2017	Exenatide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Death from renal causes	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Holman 2017	Exenatide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Holman 2017	Exenatide v Placebo	Unstable angina	Low	None specified	Partially applicable	Outcome indirectness - The outcome is for people who received PCI and CABG only.
Holman 2017 no CVD	Exenatide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Holman 2017 no HF	Exenatide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Home 2015	Pioglitazone v Placebo	3-point MACE	High	High attrition rates overall with >10% difference between placebo and pioglitazone rates (19% discontinuation in piog, 30% discontinuation in placebo)	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Home 2015	Pioglitazone v Placebo	All-cause mortality	High	High attrition rates overall with >10% difference between placebo and pioglitazone rates (19% discontinuation in piog, 30% discontinuation in placebo)	Directly applicable	None specified
Home 2015	Pioglitazone v Placebo	Hypoglycaemia episodes	High	High attrition rates overall with >10% difference between placebo and pioglitazone rates (19% discontinuation in piog, 30% discontinuation in placebo)	Directly applicable	None specified
Home 2015	Pioglitazone v Placebo	Severe hypoglycaemic episodes	High	High attrition rates overall with >10% difference between placebo and pioglitazone rates (19% discontinuation in piog, 30% discontinuation in placebo)	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Home 2015	Pioglitazone v Placebo	HbA1c change	Some concerns	High attrition rates overall with >10% difference between placebo and pioglitazone rates (19% discontinuation in piog, 30% discontinuation in placebo)	Directly applicable	None specified
Home 2015	Pioglitazone v Placebo	Weight change	Some concerns	High attrition rates overall with >10% difference between placebo and pioglitazone rates (19% discontinuation in piog, 30% discontinuation in placebo)	Directly applicable	None specified
Hong 2012	Sitagliptin v Insulin	HbA1c change	Some concerns	No details given on randomisation protocol or concealment	Directly applicable	None specified
Hong 2012	Sitagliptin v Insulin	Hypoglycaemia episodes	Some concerns	No details given on randomisation protocol or concealment	Directly applicable	None specified
Hong 2012	Sitagliptin v Insulin	Severe hypoglycaemic episodes	Some concerns	No details given on randomisation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				protocol or concealment		
Hong 2012	Sitagliptin v Insulin	Weight change	Some concerns	No details given on randomisation protocol or concealment	Directly applicable	None specified
Hong 2023	Dapagliflozin v Sitagliptin	BMI change	Some concerns	No info about allocation concealment	Directly applicable	None specified
Hong 2023	Dapagliflozin v Sitagliptin	HbA1c change	Some concerns	No info about allocation concealment	Directly applicable	None specified
Hong 2023	Dapagliflozin v Sitagliptin	Hospitalisation for heart failure	Some concerns	No info about allocation concealment	Directly applicable	None specified
Hong 2023	Dapagliflozin v Sitagliptin	Hypoglycaemia episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Hong 2023	Dapagliflozin v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	5-point MACE	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Husain 2019	Semaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Husain 2019	Semaglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Iacobellis 2017	Liraglutide + Metformin v Metformin	BMI change	High	Lack of detail around allocation concealment. The number of participants randomised to the intervention group was higher than the number of patients randomised to the control group, indicating there was a problem with the randomisation process.	Directly applicable	Population, intervention, comparator and outcome match review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Iacobellis 2017	Liraglutide + Metformin v Metformin	HbA1c change	High	Lack of detail around allocation concealment. The number of participants randomised to the intervention group was higher than the number of patients randomised to the control group, indicating there was a problem with the randomisation process.	Directly applicable	Population, intervention, comparator and outcome match review protocol
Iacobellis 2020	Dapagliflozin v Placebo	BMI change	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Iacobellis 2020	Dapagliflozin v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome matched the review protocol
Iacobellis 2020	Dapagliflozin v Placebo	Weight change	Some concerns	Lack of information around allocation concealment	Directly applicable	Population, intervention, comparator and outcome matched the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Iijima 2023	Semaglutide v Dulaglutide	HbA1c change	Some concerns	No details on randomisation or concealment	Directly applicable	None specified
Iijima 2023	Semaglutide v Dulaglutide	Hypoglycaemia episodes	Some concerns	No details on randomisation or concealment	Directly applicable	None specified
Iijima 2023	Semaglutide v Dulaglutide	Weight change	Some concerns	No details on randomisation or concealment	Directly applicable	None specified
Ikonomidis 2020	Empagliflozin v Insulin	BMI change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	None specified
Ikonomidis 2020	Empagliflozin v Insulin	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	None specified
Ikonomidis 2020	Empagliflozin v Insulin	Weight change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	None specified
Ikonomidis 2020	Empagliflozin + Liraglutide v Empagliflozin	BMI change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ikonomidis 2020	Empagliflozin + Liraglutide v Liraglutide	BMI change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin v Liraglutide	BMI change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Liraglutide v Insulin	BMI change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin + Liraglutide v Empagliflozin	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin + Liraglutide v Liraglutide	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin v Liraglutide	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ikonomidis 2020	Liraglutide v Insulin	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin + Liraglutide v Empagliflozin	Weight change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin + Liraglutide v Liraglutide	Weight change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin v Liraglutide	Weight change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Liraglutide v Insulin	Weight change	Some concerns	Lack of information around method of randomisation and allocation conceallment.	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin + Liraglutide v Insulin	BMI change	Some concerns	None specified	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ikonomidis 2020	Empagliflozin + Liraglutide v Insulin	HbA1c change	Some concerns	None specified	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Ikonomidis 2020	Empagliflozin + Liraglutide v Insulin	Weight change	Some concerns	None specified	Directly applicable	Population, intervention, comparator, and outcome matched the review protocol
Inagaki 2012	Exenatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Inagaki 2012	Exenatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Inagaki 2013	Linagliptin v Metformin	HbA1c change	Some concerns	No detail recorded of randomisation process or concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Inagaki 2013	Linagliptin v Metformin	Hypoglycaemia episodes	Some concerns	No detail recorded of randomisation process or concealment	Directly applicable	None specified
Inagaki 2013	Linagliptin v Metformin	Severe hypoglycaemic episodes	Some concerns	No detail recorded of randomisation process or concealment	Directly applicable	None specified
Jabbour 2014	Dapagliflozin v Placebo	All-cause mortality	Some concerns	Randomised double blin placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method or randomisation method	Directly applicable	None specified
Jabbour 2014	Dapagliflozin v Placebo	HbA1c change	Some concerns	Randomised double blin placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method or randomisation method	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Jabbour 2014	Dapagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	Randomised double blin placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method or randomisation method	Directly applicable	None specified
Jabbour 2014	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	Randomised double blin placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method or randomisation method	Directly applicable	None specified
Jabbour 2014	Dapagliflozin v Placebo	Weight change	Some concerns	Randomised double blin placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method or	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomisation method		
Ji 2016B	Vildagliptin v Metformin	All-cause mortality	High	No detail regarding randomisation of concealment. Although iTT analysis performed still a high attrition rate for a 24 week trial	Directly applicable	None specified
Ji 2016B	Vildagliptin v Metformin	Cardiovascular mortality	High	No detail regarding randomisation of concealment. Although iTT analysis performed still a high attrition rate for a 24 week trial	Directly applicable	None specified
Ji 2016B	Vildagliptin v Metformin	HbA1c change	High	No detail regarding randomisation of concealment. Although iTT analysis performed still a high attrition rate for a 24 week trial	Directly applicable	None specified
Ji 2016B	Vildagliptin v Metformin	Hypoglycaemia episodes	High	No detail regarding randomisation of concealment. Although iTT analysis performed	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				still a high attrition rate for a 24 week trial		
Ji 2016B	Vildagliptin v Metformin	Weight change	High	No detail regarding randomisation of concealment. Although iTT analysis performed still a high attrition rate for a 24 week trial	Directly applicable	None specified
Ji 2019	Ertugliflozin v Placebo	All-cause mortality	Low	double blind placebo controlled study. Clearly descirbied rationale and process of a registered trial. Low attrition rates	Directly applicable	None specified
Ji 2019	Ertugliflozin v Placebo	Cardiovascular mortality	Low	double blind placebo controlled study. Clearly descirbied rationale and process of a registered trial. Low attrition rates	Directly applicable	None specified
Ji 2019	Ertugliflozin v Placebo	HbA1c change	Low	double blind placebo controlled study. Clearly descirbied rationale and process of a	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				registered trial. Low attrition rates		
Ji 2019	Ertugliflozin v Placebo	Hypoglycaemia episodes	Low	double blind placebo controlled study. Clearly descirbied rationale and process of a registered trial. Low attrition rates	Directly applicable	None specified
Ji 2019	Ertugliflozin v Placebo	Weight change	Low	double blind placebo controlled study. Clearly descirbied rationale and process of a registered trial. Low attrition rates	Directly applicable	None specified
Ji 2021A	Semaglutide v Sitagliptin	All-cause mortality	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2021A	Semaglutide v Sitagliptin	BMI change	Low	Randomised double blind placebo control trial reporting	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described		
Ji 2021A	Semaglutide v Sitagliptin	Cardiovascular mortality	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2021A	Semaglutide v Sitagliptin	HbA1c change	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				on clinical outcomes described		
Ji 2021A	Semaglutide v Sitagliptin	Hypoglycaemia episodes	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2021A	Semaglutide v Sitagliptin	Weight change	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2023	Empagliflozin v Placebo	Acute kidney injury	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described		
Ji 2023	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2023	Empagliflozin v Placebo	HbA1c change	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ji 2023	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2023	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of concealment method. Likely to have minimal impact on clinical outcomes described	Directly applicable	None specified
Ji 2023	Empagliflozin v Placebo	Weight change	Low	Randomised double blind placebo control trial reporting clinical outcomes clearly defined in methods. However no discussion of	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concealment method. Likely to have minimal impact on clinical outcomes described		
Jiang 2021B	Dapagliflozin v Liraglutide	All-cause mortality	High	No detail regarding randomisation of concealment, little detail regarding statistical analysis. Small study sample size and recruited from only 2 sites	Partially applicable	All patients are also receiving repaglinide
Jiang 2021B	Dapagliflozin v Liraglutide	Cardiovascular mortality	High	No detail regarding randomisation of concealment, little detail regarding statistical analysis. Small study sample size and recruited from only 2 sites	Partially applicable	All patients are also receiving repaglinide
Jiang 2021B	Dapagliflozin v Liraglutide	Diabetic ketoacidosis	High	No detail regarding randomisation of concealment, little detail regarding statistical analysis. Small study sample size and recruited from only 2 sites	Partially applicable	All patients are also receiving repaglinide

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Jiang 2021B	Dapagliflozin v Liraglutide	Severe hypoglycaemic episodes	High	No detail regarding randomisation of concealment, little detail regarding statistical analysis. Small study sample size and recruited from only 2 sites	Partially applicable	All patients are also receiving repaglinide
Jiang 2021B	Dapagliflozin v Liraglutide	Weight change	High	No detail regarding randomisation of concealment, little detail regarding statistical analysis. Small study sample size and recruited from only 2 sites	Partially applicable	All patients are also receiving repaglinide
Joubert 2021	Exenatide v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	BMI change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Joubert 2021	Exenatide v Placebo	Health-related quality of life - subscale barriers to activity	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Health-related quality of life - subscale disinhibited eating	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Health-related quality of life - subscale psychological distress	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Hospitalisation for heart failure	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Joubert 2021	Exenatide v Placebo	Weight change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Kadowaki 2011	Exenatide v Placebo	All-cause mortality	High	Lack of information around allocation concealment. Discontinuation due to adverse events	Directly applicable	Population, intervention, comparator and outcomes match the review protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				was higher in the exenatide compared to placebo arms.		
Kadowaki 2011	Exenatide v Placebo	Cardiovascular mortality	High	Lack of information around allocation concealment. Discontinuation due to adverse events was higher in the exenatide compared to placebo arms.	Directly applicable	Population, intervention, comparator and outcomes match the review protocol.
Kadowaki 2011	Exenatide v Placebo	Diabetic ketoacidosis	High	Lack of information around allocation concealment. Discontinuation due to adverse events was higher in the exenatide compared to placebo arms.	Directly applicable	Population, intervention, comparator and outcomes match the review protocol.
Kadowaki 2011	Exenatide v Placebo	HbA1c change	High	Lack of information around allocation concealment. Discontinuation due to adverse events was higher in the exenatide compared to placebo arms.	Directly applicable	Population, intervention, comparator and outcomes match the review protocol.
Kadowaki 2011	Exenatide v Placebo	Hypoglycaemia episodes	High	Lack of information around allocation concealment. Discontinuation due	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				to adverse events was higher in the exenatide compared to placebo arms.		outcomes match the review protocol.
Kadowaki 2011	Exenatide v Placebo	Severe hypoglycaemic episodes	High	Lack of information around allocation concealment. Discontinuation due to adverse events was higher in the exenatide compared to placebo arms.	Directly applicable	Population, intervention, comparator and outcomes match the review protocol.
Kadowaki 2011	Exenatide v Placebo	Weight change	High	Lack of information around allocation concealment. Discontinuation due to adverse events was higher in the exenatide compared to placebo arms.	Directly applicable	Population, intervention, comparator and outcomes match the review protocol.
Kadowaki 2017	Canagliflozin v Placebo	All-cause mortality	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Kadowaki 2017	Canagliflozin v Placebo	Cardiovascular mortality	Low	Randomised double blind placebo trial with low attrition. Methods of protocol	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				and analysis clearly stated		
Kadowaki 2017	Canagliflozin v Placebo	Diabetic ketoacidosis	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Kadowaki 2017	Canagliflozin v Placebo	HbA1c change	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Kadowaki 2017	Canagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Kadowaki 2017	Canagliflozin v Placebo	Weight change	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Kaku 2009A	Pioglitazone v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment and randomisation	Directly applicable	Population, intervention, comparator, and outcome match the protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kaku 2009A	Pioglitazone v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment and randomisation	Directly applicable	Population, intervention, comparator, and outcome match the protocol
Kaku 2010	Liraglutide v Placebo	Weight change	High	Lack of information around method of randomisation and allocation concealment. In the per-protocol set, the number of participants were higher in the intervention arms compared with the placebo arm, however, the results from this analysis did not appear to be reported. 52-week data were not adequately reported for this outcome.	Directly applicable	Population, intervention, comparator and outcome matched protocol
Kaku 2010	Liraglutide v Placebo	All-cause mortality	High	Lack of information around method of randomisation and allocation concealment. Results could have been biased by	Directly applicable	Population, intervention, comparator and outcome matched protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				higher withrawal by participants in the placebo arm, where most withdrawals were due to lack of effectiveness.		
Kaku 2010	Liraglutide v Placebo	Cardiovascular mortality	High	Lack of information around method of randomisation and allocation concealment. Results could have been biased by higher withrawal by participants in the placebo arm, where most withdrawals were due to lack of effectiveness.	Directly applicable	Population, intervention, comparator and outcome matched protocol
Kaku 2010	Liraglutide v Placebo	HbA1c change	High	Lack of information around method of randomisation and allocation concealment. Results could have been biased by higher withrawal by participants in the placebo arm, where most withdrawals were due to lack of effectiveness.	Directly applicable	Population, intervention, comparator and outcome matched protocol

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kaku 2010	Liraglutide v Placebo	Severe hypoglycaemic episodes	High	Lack of information around method of randomisation and allocation concealment. Results could have been biased by higher withrawal by participants in the placebo arm, where most withdrawals were due to lack of effectiveness.	Directly applicable	Population, intervention, comparator and outcome matched protocol
Kaku 2019A	Insulin degludec/liraglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Kaku 2019A	Insulin degludec/liraglutide v Liraglutide	HbA1c change	Low	None specified	Directly applicable	None specified
Kaku 2019A	Insulin degludec/liraglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Kaku 2019A	Insulin degludec/liraglutide v Liraglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Kaku 2019A	Insulin degludec/liraglutide v Insulin	Weight change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kaku 2019A	Insulin degludec/liraglutide v Liraglutide	Weight change	Low	None specified	Directly applicable	None specified
Kanazawa 2010	Pioglitazone v Metformin	BMI change	High	Small study with analysis poorly described, randomisation not described and significaint difference between arms for BMI at baseline	Directly applicable	None specified
Kanazawa 2010	Pioglitazone v Metformin	HbA1c change	High	Small study with analysis poorly described, randomisation not described and significaint difference between arms for BMI at baseline	Directly applicable	None specified
Kanazawa 2010	Pioglitazone v Metformin	Weight change	High	Small study with analysis poorly described, randomisation not described and significaint difference between arms for BMI at baseline	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kaneto 2020	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Low	No concerns	Directly applicable	No concerns
Kaneto 2020	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Low	No concerns	Directly applicable	No concerns
Kaneto 2020	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Low	No concerns	Directly applicable	No concerns
Kaneto 2020	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Low	No concerns	Directly applicable	No concerns
Kaneto 2020	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Low	No concerns	Directly applicable	No concerns
Kaneto 2020	Insulin glargine/Lixisenatide v Insulin	Weight change	Low	No concerns	Directly applicable	No concerns
Kang 2021	Exenatide v Insulin	BMI change	High	Concerns about allocation concealment, missing data strategy unclear, info about trial registration etc not available	Directly applicable	None specified
Kang 2021	Exenatide v Insulin	HbA1c change	High	Concerns about allocation concealment, missing data	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				strategy unclear, info about trial registration etc not available		
Kang 2021	Exenatide v Insulin	Weight change	High	Concerns about allocation concealment, missing data strategy unclear, info about trial registration etc not available	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	Acute kidney injury	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	All-cause mortality	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	Cardiovascular mortality	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	HbA1c change	Low	Randomised double blind placebo trial	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				for 52 weeks with low attrition		
Kawamori 2018	Empagliflozin v Placebo	Hospitalisation for heart failure	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	Non-fatal stroke	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kawamori 2018	Empagliflozin v Placebo	Weight change	Low	Randomised double blind placebo trial for 52 weeks with low attrition	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	All-cause mortality	Some concerns	No info about randomisation/allocation concealment	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	Hypoglycaemia episodes	Some concerns	No info about randomisation/allocation concealment	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	Severe hypoglycaemic episodes	Some concerns	No info about randomisation/allocation concealment	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	Unstable angina	Some concerns	No info about randomisation/allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kellerer 2022	Semaglutide v Insulin	BMI change	High	No info about randomisation/allocation concealment; mITT LOCF analysis	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	HbA1c change	High	No info about randomisation/allocation concealment; mITT LOCF analysis	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	Weight change	High	No info about randomisation/allocation concealment; mITT LOCF analysis	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	Health-related quality of life - subscale mental component	High	No info about randomisation/allocation concealment; mITT LOCF analysis; open-label trial/patient-reported outcome	Directly applicable	None specified
Kellerer 2022	Semaglutide v Insulin	Health-related quality of life - subscale physical component	High	No info about randomisation/allocation concealment; mITT LOCF analysis; open-label trial/patient-reported outcome	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kendall 2005	Exenatide v Placebo	Hypoglycaemia episodes	High	No info about randomsiation/allocation; trial not registered	Directly applicable	None specified
Kendall 2005	Exenatide v Placebo	Severe hypoglycaemic episodes	High	No info about randomsiation/allocation; trial not registered	Directly applicable	None specified
Kendall 2005	Exenatide v Placebo	HbA1c change	High	No info about randomsiation/allocation; trial not registered; mITT LOCF analysis, high proportion missing data	Directly applicable	None specified
Kendall 2005	Exenatide v Placebo	Weight change	High	No info about randomsiation/allocation; trial not registered; mITT LOCF analysis, high proportion missing data	Directly applicable	None specified
Kesavadev 2017	Glimepiride v Sitagliptin	BMI change	High	Open-label trial with per protocol analysis, baseline difference on BMI	Directly applicable	None specified
Kesavadev 2017	Glimepiride v Sitagliptin	HbA1c change	High	Open-label trial with per protocol analysis, baseline difference on BMI	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kesavadev 2017	Glimepiride v Sitagliptin	Weight change	High	Open-label trial with per protocol analysis, baseline difference on BMI	Directly applicable	None specified
Kesavadev 2017	Glimepiride v Sitagliptin	Hypoglycaemia episodes	High	Open-label trial, baseline difference on BMI	Directly applicable	None specified
Kesavadev 2017	Glimepiride v Sitagliptin	Severe hypoglycaemic episodes	High	Open-label trial, baseline difference on BMI	Directly applicable	None specified
Khaloo 2019	Pioglitazone v Sitagliptin	BMI change	High	Baseline differences on several variables; trial retrospectively registered	Directly applicable	None specified
Khaloo 2019	Pioglitazone v Sitagliptin	HbA1c change	High	Baseline differences on several variables; trial retrospectively registered	Directly applicable	None specified
Khaloo 2019	Pioglitazone v Sitagliptin	Weight change	High	Baseline differences on several variables; trial retrospectively registered	Directly applicable	None specified
Khan 2022	Empagliflozin v Vildagliptin	HbA1c change	High	No info about allocation concealment, trial retrospectively registered	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Khan 2022	Empagliflozin v Vildagliptin	Weight change	High	No info about allocation concealment, trial retrospectively registered	Directly applicable	None specified
Kim 2018	Glimepiride + Metformin slow release v Glimepiride + Metformin standard release	At night hypoglycaemic episodes	High	Randomisation and concealment process not described. No details on co-interventions for patients in either arm	Directly applicable	None specified
Kim 2018	Glimepiride + Metformin slow release v Glimepiride + Metformin standard release	Hypoglycaemia episodes	High	Randomisation and concealment process not described. No details on co-interventions for patients in either arm	Directly applicable	None specified
Kim 2020	Pioglitazone v Glimepiride	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Kim 2020	Pioglitazone v Glimepiride	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Kinoshita 2020	Glimepiride v Dapagliflozin	HbA1c change	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Pioglitazone v Dapagliflozin	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kinoshita 2020	Pioglitazone v Glimepiride	HbA1c change	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Glimepiride v Dapagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Pioglitazone v Dapagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Pioglitazone v Glimepiride	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Glimepiride v Dapagliflozin	Weight change	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Pioglitazone v Dapagliflozin	Weight change	Low	None specified	Directly applicable	None specified
Kinoshita 2020	Pioglitazone v Glimepiride	Weight change	Low	None specified	Directly applicable	None specified
Komorizono 2020	Linagliptin v Metformin	All-cause mortality	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Komorizono 2020	Linagliptin v Metformin	BMI change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Komorizono 2020	Linagliptin v Metformin	Cardiovascular mortality	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Komorizono 2020	Linagliptin v Metformin	HbA1c change	Low	Randomised open label trial with low	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				attrition. Analysis clearly described		
Komorizono 2020	Linagliptin v Metformin	Weight change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Kooy 2009	Metformin v Placebo	All-cause mortality	Some concerns	High attrition rates with less than 400 patients included in total. However the method and design clearly states, follow-up was 4.3 years and an iTT analysis performed	Directly applicable	None specified
Kooy 2009	Metformin v Placebo	BMI change	Some concerns	High attrition rates with less than 400 patients included in total. However the method and design clearly states, follow-up was 4.3 years and an iTT analysis performed	Directly applicable	None specified
Kooy 2009	Metformin v Placebo	Cardiovascular mortality	Some concerns	High attrition rates with less than 400 patients included in total. However the method and design clearly states, follow-up was 4.3	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				years and an iTT analysis performed		
Kooy 2009	Metformin v Placebo	HbA1c change	Some concerns	High attrition rates with less than 400 patients included in total. However the method and design clearly states, follow-up was 4.3 years and an iTT analysis performed	Directly applicable	None specified
Kooy 2009	Metformin v Placebo	Hospitalisation for heart failure	Some concerns	High attrition rates with less than 400 patients included in total. However the method and design clearly states, follow-up was 4.3 years and an iTT analysis performed	Directly applicable	None specified
Kooy 2009	Metformin v Placebo	Weight change	Some concerns	High attrition rates with less than 400 patients included in total. However the method and design clearly states, follow-up was 4.3 years and an iTT analysis performed	Directly applicable	None specified
Kothny 2013	Vildagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Kothny 2013	Vildagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Kothny 2013	Vildagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Kothny 2013	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Kovacs 2014	Empagliflozin v Placebo	HbA1c change	High	Double blind placebo trial but high attrition rates. Authors state exploratorty nature of of of the analyses and large amount of missing data	Directly applicable	None specified
Kovacs 2014	Empagliflozin v Placebo	Weight change	High	Double blind placebo trial but high attrition rates. Authors state exploratorty nature of of of the analyses and large amount of missing data	Directly applicable	None specified
Kovacs 2014	Empagliflozin v Placebo	All-cause mortality	High	Double blind placebo trial but high attrition rates. Authors state exploratorty nature of of of the analyses and large amount of	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				missing data. The different timpoints for each arm favouring placebo is a concern		
Kovacs 2014	Empagliflozin v Placebo	Hypoglycaemia episodes	High	Double blind placebo trial but high attrition rates. Authors state exploratorty nature of of of the analyses and large amount of missing data. The different timpoints for each arm favouring placebo is a concern	Directly applicable	None specified
Koyama 2014	Pioglitazone v Glimepiride	HbA1c change	High	Lack of clarity and method of analysis. Report states that analysis was per-protocol. There was also a lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome matched protocol.
Koyama 2014	Pioglitazone v Glimepiride	Non-fatal myocardial infarction	High	Lack of clarity and method of analysis. Report states that analysis was per-protocol. There was	Directly applicable	Population, intervention, comparator and outcome matched protocol.

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				also a lack of information around allocation concealment.		
Koyama 2014	Pioglitazone v Glimepiride	Non-fatal stroke	High	Lack of clarity and method of analysis. Report states that analysis was per-protocol. There was also a lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome matched protocol.
Koyama 2014	Pioglitazone v Glimepiride	Weight change	High	Lack of clarity and method of analysis. Report states that analysis was per-protocol. There was also a lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and outcome matched protocol.
Langenfeld 2005	Pioglitazone v Glimepiride	BMI change	High	No info about randomisation etc; per protocol analysis; protocol not available	Directly applicable	None specified
Langenfeld 2005	Pioglitazone v Glimepiride	HbA1c change	High	No info about randomisation etc; per protocol	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				analysis; protocol not available		
Langenfeld 2005	Pioglitazone v Glimepiride	Hospitalisation for heart failure	High	No info about randomisation etc; type of analysis unclear; protocol not available	Directly applicable	None specified
Langenfeld 2005	Pioglitazone v Glimepiride	Hypoglycaemia episodes	High	No info about randomisation etc; type of analysis unclear; protocol not available	Directly applicable	None specified
Langenfeld 2005	Pioglitazone v Glimepiride	Severe hypoglycaemic episodes	High	No info about randomisation etc; type of analysis unclear; protocol not available	Directly applicable	None specified
Lavalle-Gonzalez 2013A	Canagliflozin v Placebo	All-cause mortality	Low	Randomised placebo controlled trial. Attrition <20% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013A	Sitagliptin v Placebo	All-cause mortality	Low	Randomised placebo controlled trial. Attrition <20% overall and <3% difference between arms	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Lavalle-Gonzalez 2013A	Canagliflozin v Placebo	HbA1c change	Low	Randomised placebo controlled trial. Attrition <20% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013A	Sitagliptin v Placebo	HbA1c change	Low	Randomised placebo controlled trial. Attrition <20% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013A	Canagliflozin v Placebo	Weight change	Low	Randomised placebo controlled trial. Attrition <20% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013A	Sitagliptin v Placebo	Weight change	Low	Randomised placebo controlled trial. Attrition <20% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013B	Canagliflozin v Sitagliptin	All-cause mortality	Low	Randomised placebo controlled trial. Attrition <10% overall and <3% difference between arms	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Lavalle-Gonzalez 2013B	Canagliflozin v Sitagliptin	HbA1c change	Low	Randomised placebo controlled trial. Attrition <10% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013B	Canagliflozin v Sitagliptin	Hypoglycaemia episodes	Low	Randomised placebo controlled trial. Attrition <10% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013B	Canagliflozin v Sitagliptin	Severe hypoglycaemic episodes	Low	Randomised placebo controlled trial. Attrition <10% overall and <3% difference between arms	Directly applicable	None specified
Lavalle-Gonzalez 2013B	Canagliflozin v Sitagliptin	Weight change	Low	Randomised placebo controlled trial. Attrition <10% overall and <3% difference between arms	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	HbA1c change	Some concerns	mITT analysis but unclear what missing data strategy is	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	4-point MACE	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ledesma 2019	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Ledesma 2019	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Lee 2022	Dapagliflozin v Sitagliptin	Diabetic ketoacidosis	High	Lack of details about randomisation. Trial retrospectively registered	Directly applicable	None specified
Lee 2022	Dapagliflozin v Sitagliptin	HbA1c change	High	Lack of details about randomisation; mITT LOCF analysis; Trial retrospectively registered	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Lee 2022	Dapagliflozin v Sitagliptin	Weight change	High	Lack of details about randomisation; mITT LOCF analysis; Trial retrospectively registered	Directly applicable	None specified
Li 2014A	Vildagliptin v Saxagliptin	BMI change	High	None specified	Directly applicable	None specified
Li 2014A	Vildagliptin v Saxagliptin	HbA1c change	High	None specified	Directly applicable	None specified
Li 2014A	Vildagliptin v Saxagliptin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Li 2014A	Vildagliptin v Saxagliptin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Li 2014A	Vildagliptin v Saxagliptin	Weight change	High	None specified	Directly applicable	None specified
Li 2014A	Liraglutide v Saxagliptin	BMI change	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Vildagliptin	BMI change	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Li 2014A	Liraglutide v Saxagliptin	HbA1c change	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Vildagliptin	HbA1c change	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Saxagliptin	Hypoglycaemia episodes	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Vildagliptin	Hypoglycaemia episodes	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Saxagliptin	Severe hypoglycaemic episodes	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Vildagliptin	Severe hypoglycaemic episodes	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Li 2014A	Liraglutide v Saxagliptin	Weight change	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014A	Liraglutide v Vildagliptin	Weight change	High	Poorly described analysis methods which appear to be inappropriate from the data presented	Directly applicable	None specified
Li 2014B	Sitagliptin v Saxagliptin	All-cause mortality	High	None specified	Directly applicable	None specified
Li 2014B	Sitagliptin v Saxagliptin	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Li 2014B	Sitagliptin v Saxagliptin	HbA1c change	High	None specified	Directly applicable	None specified
Li 2014B	Sitagliptin v Saxagliptin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Li 2014B	Vildagliptin v Saxagliptin	All-cause mortality	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified
Li 2014B	Vildagliptin v Sitagliptin	All-cause mortality	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Li 2014B	Vildagliptin v Saxagliptin	Cardiovascular mortality	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified
Li 2014B	Vildagliptin v Sitagliptin	Cardiovascular mortality	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified
Li 2014B	Vildagliptin v Saxagliptin	HbA1c change	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified
Li 2014B	Vildagliptin v Sitagliptin	HbA1c change	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified
Li 2014B	Vildagliptin v Saxagliptin	Hypoglycaemia episodes	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified
Li 2014B	Vildagliptin v Sitagliptin	Hypoglycaemia episodes	High	Randomisation process not reported and no compliance data collected	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Li 2017	Vildagliptin v Placebo	Weight change	High	Lack of information on analysis methods; small sample size; did not state in the protocol that weight would be assessed so unclear if study is pwered effectively	Directly applicable	None specified
Li 2017	Vildagliptin v Placebo	HbA1c change	Some concerns	No information on analysis methods; small sample size	Directly applicable	None specified
Li 2017	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	No information on analysis methods; small sample size	Directly applicable	None specified
Lind 2015	Liraglutide v Placebo	BMI change	Low	Central randomisation, mITT analysis	Directly applicable	NA
Lind 2015	Liraglutide v Placebo	Weight change	Low	Central randomisation, mITT analysis	Directly applicable	NA
Lind 2015	Liraglutide v Placebo	HbA1c change	Low	Central randomisation, mITT analysis	Directly applicable	None specified
Lind 2015	Liraglutide v Placebo	Severe hypoglycaemic episodes	Low	Central randomisation, mITT analysis	Directly applicable	None specified
Lingvay 2016	Insulin degludec/liraglutide v Insulin	Health-related quality of life -	High	For questionnaire knowledge of	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale mental component		intervention could influence outcome		
Lingvay 2016	Insulin degludec/liraglutide v Insulin	Health-related quality of life - subscale physical component	High	For questionnaire knowledge of intervention could influence outcome	Directly applicable	None specified
Lingvay 2016	Insulin degludec/liraglutide v Insulin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Lingvay 2016	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Lingvay 2016	Insulin degludec/liraglutide v Insulin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Lingvay 2016	Insulin degludec/liraglutide v Insulin	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Lingvay 2016	Insulin degludec/liraglutide v Insulin	Weight change	Some concerns	None specified	Directly applicable	None specified
Lingvay 2019	Canagliflozin v Semaglutide	Acute kidney injury	Low	None specified	Directly applicable	NA
Lingvay 2019	Canagliflozin v Semaglutide	Cardiovascular mortality	Low	None specified	Directly applicable	NA
Lingvay 2019	Canagliflozin v Semaglutide	HbA1c change	Low	None specified	Directly applicable	NA
Lingvay 2019	Canagliflozin v Semaglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	NA

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Lingvay 2019	Canagliflozin v Semaglutide	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	NA
Lingvay 2019	Canagliflozin v Semaglutide	Weight change	Low	None specified	Directly applicable	NA
Lingvay 2019	Canagliflozin v Semaglutide	All-cause mortality	Low	None specified	Directly applicable	None specified
Liu 2013	Pioglitazone v Sitagliptin	Weight change	Some concerns	Some baseline differences	Directly applicable	NA
Liu 2013	Pioglitazone v Sitagliptin	HbA1c change	Some concerns	Some baseline differences	Directly applicable	None specified
Liu 2013	Pioglitazone v Sitagliptin	Hypoglycaemia episodes	Some concerns	Some baseline differences	Directly applicable	None specified
Liu 2013	Pioglitazone v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	Some baseline differences	Directly applicable	None specified
Liu 2021	Empagliflozin v Linagliptin	All-cause mortality	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Liu 2021	Empagliflozin v Linagliptin	Cardiovascular mortality	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Liu 2021	Empagliflozin v Linagliptin	Diabetic ketoacidosis	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Liu 2021	Empagliflozin v Linagliptin	HbA1c change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Liu 2021	Empagliflozin v Linagliptin	Hypoglycaemia episodes	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Liu 2021	Empagliflozin v Linagliptin	Severe hypoglycaemic episodes	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Liu 2021	Empagliflozin v Linagliptin	Weight change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Liutkus 2010	Exenatide v Placebo	All-cause mortality	Some concerns	Lack of info on allocation concealment	Directly applicable	None specified
Liutkus 2010	Exenatide v Placebo	Cardiovascular mortality	Some concerns	Lack of info on allocation concealment	Directly applicable	None specified
Liutkus 2010	Exenatide v Placebo	HbA1c change	Some concerns	Lack of info on allocation concealment	Directly applicable	None specified
Liutkus 2010	Exenatide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of info on allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Liutkus 2010	Exenatide v Placebo	Weight change	Some concerns	Lack of info on allocation concealment	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Ludvik 2018	Dulaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Ludvik 2021	Tirzepatide v Insulin	4-point MACE	Low	None specified	Directly applicable	None specified
Ludvik 2021	Tirzepatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Ludvik 2021	Tirzepatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Ludvik 2021	Tirzepatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ludvik 2021	Tirzepatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Ludvik 2021	Tirzepatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Ludvik 2021	Tirzepatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Lukashevich 2011 moderate renal impairment	Vildagliptin v Placebo	All-cause mortality	High	Poorly described analysis, no detail on randomisation, concealment or statistical analysis	Directly applicable	None specified
Lukashevich 2011 moderate renal impairment	Vildagliptin v Placebo	Hypoglycaemia episodes	High	Poorly described analysis, no detail on randomisation, concealment or statistical analysis. High attrition rates	Directly applicable	None specified
Lukashevich 2011 moderate renal impairment	Vildagliptin v Placebo	Severe hypoglycaemic episodes	High	Poorly described analysis, no detail on randomisation, concealment or statistical analysis. High attrition rates	Directly applicable	None specified
Lukashevich 2014	Vildagliptin v Placebo	All-cause mortality	High	Lack of information on randomisation and allocation. Some baseline imbalances.	Directly applicable	NA
Lukashevich 2014	Vildagliptin v Placebo	Hypoglycaemia episodes	High	Lack of information on randomisation	Directly applicable	NA

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				and allocation. Some baseline imbalances.		
Lukashevich 2014	Vildagliptin v Placebo	Severe hypoglycaemic episodes	High	Lack of information on randomisation and allocation. Some baseline imbalances.	Directly applicable	NA
Lundby-Christensen 2016	Metformin v Placebo	All-cause mortality	Low	Randomised placebo controlled trial. Attrition higher in one arm but no evidence to suggest that outcomes were affected as a result. Analysis clearly described	Directly applicable	None specified
Lundby-Christensen 2016	Metformin v Placebo	BMI change	Low	Randomised placebo controlled trial. Attrition higher in one arm but no evidence to suggest that outcomes were affected as a result. Analysis clearly described	Directly applicable	None specified
Lundby-Christensen 2016	Metformin v Placebo	HbA1c change	Low	Randomised placebo controlled trial. Attrition higher in one arm but no evidence to suggest	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				that outcomes were affected as a result. Analysis clearly described		
Lundby-Christensen 2016	Metformin v Placebo	Hypoglycaemia episodes	Low	Randomised placebo controlled trial. Attrition higher in one arm but no evidence to suggest that outcomes were affected as a result. Analysis clearly described	Directly applicable	None specified
Lundby-Christensen 2016	Metformin v Placebo	Severe hypoglycaemic episodes	Low	Randomised placebo controlled trial. Attrition higher in one arm but no evidence to suggest that outcomes were affected as a result. Analysis clearly described	Directly applicable	None specified
Lundby-Christensen 2016	Metformin v Placebo	Weight change	Low	Randomised placebo controlled trial. Attrition higher in one arm but no evidence to suggest that outcomes were affected as a result. Analysis clearly described	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Macauley 2015	Vildagliptin v Placebo	All-cause mortality	High	None specified	Partially applicable	The population had vildagliptin added to metformin to assess the possible effects of vildagliptin on hepatic stenosis and insulin sensitivity rather than because their diabetes was uncontrolled on metformin
Macauley 2015	Vildagliptin v Placebo	Cardiovascular mortality	High	None specified	Partially applicable	The population had vildagliptin added to metformin to assess the possible effects of vildagliptin on hepatic stenosis and insulin sensitivity rather than because their diabetes was uncontrolled on metformin
Macauley 2015	Vildagliptin v Placebo	HbA1c change	High	None specified	Partially applicable	The population had vildagliptin added to metformin to assess the possible effects of vildagliptin on hepatic stenosis and insulin sensitivity rather than because their diabetes was

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						uncontrolled on metformin
Macauley 2015	Vildagliptin v Placebo	Hypoglycaemia episodes	High	None specified	Partially applicable	The population had vildagliptin added to metformin to assess the possible effects of vildagliptin on hepatic stenosis and insulin sensitivity rather than because their diabetes was uncontrolled on metformin
Macauley 2015	Vildagliptin v Placebo	Weight change	High	None specified	Partially applicable	The population had vildagliptin added to metformin to assess the possible effects of vildagliptin on hepatic stenosis and insulin sensitivity rather than because their diabetes was uncontrolled on metformin
Mahaffey 2018	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mahaffey 2018	Canagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Mahaffey 2018	Canagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no CVD	Canagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no HF	Canagliflozin v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no HF	Canagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no HF	Canagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Mahaffey 2018 no HF	Canagliflozin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Marre 2009	Liraglutide v Placebo	All-cause mortality	Some concerns	Lack of info on randomisation and allocation concealment. Also, although it was a double-blinded trial the mode of	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				administeration differed between intervention (subcutaneous) and placebo (oral).		
Marre 2009	Liraglutide v Placebo	Cardiovascular mortality	Some concerns	Lack of info on randomisation and allocation concealment. Also, although it was a double-blinded trial the mode of administeration differed between intervention (subcutaneous) and placebo (oral).	Directly applicable	None specified
Marre 2009	Liraglutide v Placebo	HbA1c change	Some concerns	Lack of info on randomisation and allocation concealment. Also, although it was a double-blinded trial the mode of administeration differed between intervention (subcutaneous) and placebo (oral).	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Marre 2009	Liraglutide v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of info on randomisation and allocation concealment. Also, although it was a double-blinded trial the mode of administeration differed between intervention (subcutaneous) and placebo (oral).	Directly applicable	None specified
Marre 2009	Liraglutide v Placebo	Weight change	Some concerns	Lack of info on randomisation and allocation concealment. Also, although it was a double-blinded trial the mode of administeration differed between intervention (subcutaneous) and placebo (oral).	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Death from renal causes	High	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Marso 2016A	Liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Marso 2016A	Liraglutide v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Marso 2016A no HF	Liraglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Marso 2016A no HF	Liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Marso 2016A no HF	Liraglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Marso 2016A no HF	Liraglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Marso 2016A no HF	Liraglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Marso 2016A no HF	Liraglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Marso 2016A no HF	Liraglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	5-point MACE	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Marso 2016B	Semaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Health-related quality of life - subscale mental component	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Health-related quality of life - subscale physical component	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Marso 2016B	Semaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Marso 2016B no HF	Semaglutide v Placebo	3-point MACE	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mathieu 2014	Insulin degludec/liraglutide v Insulin	All-cause mortality	Some concerns	Concerns regarding allocation concealment.	Directly applicable	None specified
Mathieu 2014	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Some concerns	Concerns regarding allocation concealment.	Directly applicable	None specified
Mathieu 2014	Insulin degludec/liraglutide v Insulin	HbA1c change	Some concerns	Concerns regarding allocation concealment.	Directly applicable	None specified
Mathieu 2014	Insulin degludec/liraglutide v Insulin	Non-fatal stroke	Some concerns	Concerns regarding allocation concealment.	Directly applicable	None specified
Mathieu 2014	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	Some concerns	Concerns regarding allocation concealment.	Directly applicable	None specified
Mathieu 2014	Insulin degludec/liraglutide v Insulin	Weight change	Some concerns	Concerns regarding allocation concealment.	Directly applicable	None specified
Mathieu 2015A	Dapagliflozin v Placebo	All-cause mortality	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Mathieu 2015A	Dapagliflozin v Placebo	HbA1c change	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mathieu 2015A	Dapagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Mathieu 2015A	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Mathieu 2015A	Dapagliflozin v Placebo	Weight change	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Mathieu 2015B	Sitagliptin v Placebo	All-cause mortality	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Mathieu 2015B	Sitagliptin v Placebo	HbA1c change	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Mathieu 2015B	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Mathieu 2015B	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Matthaei 2015A	Saxagliptin v Placebo	All-cause mortality	Some concerns	Some baseline imbalances for HbA1c categories	Directly applicable	None specified
Matthaei 2015A	Saxagliptin v Placebo	Cardiac arrhythmia	Some concerns	Some baseline imbalances for HbA1c categories	Directly applicable	None specified
Matthaei 2015A	Saxagliptin v Placebo	HbA1c change	Some concerns	Some baseline imbalances for HbA1c categories	Directly applicable	None specified
Matthaei 2015A	Saxagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Some baseline imbalances for HbA1c categories	Directly applicable	None specified
Matthaei 2015A	Saxagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Some baseline imbalances for HbA1c categories	Directly applicable	None specified
Matthaei 2015B	Dapagliflozin v Placebo	HbA1c change	High	Attrition is high and no evidence in analysis results that	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				this has been accounted for		
Matthaei 2015B	Dapagliflozin v Placebo	Weight change	High	Attrition is high and no evidence in analysis results that this has been accounted for	Directly applicable	None specified
Matthaei 2015B	Dapagliflozin v Placebo	All-cause mortality	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Matthaei 2015B	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Matthaei 2015B	Dapagliflozin v Placebo	Health-related quality of life - overall	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Matthaei 2015B	Dapagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Matthaei 2015B	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Matthews 2005	Pioglitazone v Gliclazide	All-cause mortality	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified
Matthews 2005	Pioglitazone v Gliclazide	HbA1c change	High	No information about	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomisation/allocation concealment, no protocol available		
Matthews 2005	Pioglitazone v Gliclazide	Hypoglycaemia episodes	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified
Matthews 2005	Pioglitazone v Gliclazide	Non-fatal myocardial infarction	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified
Matthews 2005	Pioglitazone v Gliclazide	Severe hypoglycaemic episodes	High	No information about randomisation/allocation concealment, no protocol available	Directly applicable	None specified
Matthews 2010	Glimepiride v Vildagliptin	All-cause mortality	Some concerns	Higher attrition	Directly applicable	None specified
Matthews 2010	Glimepiride v Vildagliptin	HbA1c change	Some concerns	Higher attrition	Directly applicable	None specified
Matthews 2010	Glimepiride v Vildagliptin	Hypoglycaemia episodes	Some concerns	Higher attrition	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Matthews 2010	Glimepiride v Vildagliptin	Severe hypoglycaemic episodes	Some concerns	Higher attrition	Directly applicable	None specified
Matthews 2010	Glimepiride v Vildagliptin	Weight change	Some concerns	Higher attrition	Directly applicable	None specified
Mattoo 2005	Pioglitazone v Placebo	All-cause mortality	Low	Attrition <20%	Directly applicable	None specified
Mattoo 2005	Pioglitazone v Placebo	HbA1c change	Low	Attrition <20%	Directly applicable	None specified
Mattoo 2005	Pioglitazone v Placebo	Hypoglycaemia episodes	Low	Attrition <20%	Directly applicable	None specified
Mattoo 2005	Pioglitazone v Placebo	Weight change	Low	Attrition <20%	Directly applicable	None specified
Mazzone 2006	Pioglitazone v Glimepiride	3-point MACE	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall)	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
Mazzone 2006	Pioglitazone v Glimepiride	All-cause mortality	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall)	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
Mazzone 2006	Pioglitazone v Glimepiride	Cardiovascular mortality	High	Lack of information on methods of randomisation and allocation. Higher	Partially applicable	10% of the population was naïve to antidiabetic oral treatment

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				attrition (30% overall)		
Mazzone 2006	Pioglitazone v Glimepiride	Hospitalisation for heart failure	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall)	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
Mazzone 2006	Pioglitazone v Glimepiride	Hypoglycaemia episodes	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall)	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
Mazzone 2006	Pioglitazone v Glimepiride	Non-fatal myocardial infarction	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall)	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
Mazzone 2006	Pioglitazone v Glimepiride	Non-fatal stroke	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall)	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
Mazzone 2006	Pioglitazone v Glimepiride	Unstable angina	High	Lack of information on methods of randomisation and allocation. Higher	Partially applicable	10% of the population was naïve to antidiabetic oral treatment

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				attrition (30% overall)		
Mazzone 2006	Pioglitazone v Glimepiride	Weight change	High	Lack of information on methods of randomisation and allocation. Higher attrition (30% overall) . Also no reporting of baseline weight.	Partially applicable	10% of the population was naïve to antidiabetic oral treatment
McCluskey 2004	Glimepiride v Placebo	HbA1c change	High	Lack of info on randomisation and allocation concealment. Baseline imbalances present. Lack of reporting on analysis methods.	Directly applicable	None specified
Meneghini 2010	Pioglitazone v Insulin	HbA1c change	High	Lack of information on allocation and randomisation; high attrition; mITT was used but still less than 80% of overall sample size included; generally unclear reporting	Directly applicable	NA
Meneghini 2010	Pioglitazone v Insulin	Hypoglycaemia episodes	High	Lack of information on allocation and randomisation; high attrition; mITT was	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				used but still less than 80% of overall sample size included; generally unclear reporting		
Meneghini 2010	Pioglitazone v Insulin	Severe hypoglycaemic episodes	High	Lack of information on allocation and randomisation; high attrition; mITT was used but still less than 80% of overall sample size included; generally unclear reporting	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	All-cause mortality	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	Cardiovascular mortality	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	HbA1c change	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	Health-related quality of life -	Low	Randomised double blind placebo	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale mental component		controlled trial with low attrition, balance between both arms		
Meneilly 2017	Lixisenatide v Placebo	Health-related quality of life - subscale physical component	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Meneilly 2017	Lixisenatide v Placebo	Weight change	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	All-cause mortality	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Miras 2019	Liraglutide v Placebo	HbA1c change	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale barriers to activity	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale emotional effects	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale fatigue	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life -	Some concerns	Randomisation method not reported,	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale general health		differences in baseline HbA1c between arms apparent		
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale pain	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale physical functioning	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale social	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Health-related quality of life - subscale well being	Some concerns	Randomisation method not reported, differences in baseline HbA1c	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				between arms apparent		
Miras 2019	Liraglutide v Placebo	Hypoglycaemia episodes	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Persistent signs of worsening kidney disease	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Miras 2019	Liraglutide v Placebo	Weight change	Some concerns	Randomisation method not reported, differences in baseline HbA1c between arms apparent	Directly applicable	None specified
Moon 2014	Glimepiride v Insulin	HbA1c change	High	Lack of information on randomisation and allocation; some baseline imbalances	Directly applicable	None specified
Moon 2014	Glimepiride v Insulin	Hypoglycaemia episodes	High	Lack of information on randomisation and allocation;	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				some baseline imbalances		
Moon 2014	Glimepiride v Insulin	Severe hypoglycaemic episodes	High	Lack of information on randomisation and allocation; some baseline imbalances	Directly applicable	None specified
Moon 2014	Glimepiride v Insulin	Weight change	High	Lack of information on randomisation and allocation; some baseline imbalances	Directly applicable	None specified
Morikawa 2011	Pioglitazone v Metformin	All-cause mortality	High	None specified	Directly applicable	None specified
Morikawa 2011	Pioglitazone v Metformin	HbA1c change	High	None specified	Directly applicable	None specified
Morikawa 2011	Pioglitazone v Metformin	Persistent signs of worsening kidney disease	High	None specified	Directly applicable	None specified
Morikawa 2011	Pioglitazone v Metformin	Unstable angina	High	None specified	Directly applicable	None specified
Moses 2014	Saxagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Moses 2014	Saxagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Moses 2014	Saxagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Moses 2014	Saxagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Moses 2014	Saxagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Moses 2017	Sitagliptin v Placebo	All-cause mortality	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Moses 2017	Sitagliptin v Placebo	HbA1c change	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Moses 2017	Sitagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Moses 2017	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Moses 2017	Sitagliptin v Placebo	Weight change	Some concerns	Lack of information on randomisation and allocation.	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Dapagliflozin	HbA1c change	Low	None specified	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Dapagliflozin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Dapagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Dapagliflozin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Dapagliflozin	Weight change	Low	None specified	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Glimepiride	HbA1c change	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Glimepiride v Dapagliflozin	HbA1c change	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Glimepiride	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Glimepiride v Dapagliflozin	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Glimepiride	Severe hypoglycaemic episodes	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Muller-Wieland 2018	Glimepiride v Dapagliflozin	Severe hypoglycaemic episodes	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Glimepiride	Weight change	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Glimepiride v Dapagliflozin	Weight change	Low	Randomised double blind placebo controlled trial with low attrition, balance between both arms	Directly applicable	None specified
Muller-Wieland 2018	Dapagliflozin + Saxagliptin v Glimepiride	Hospitalisation for heart failure	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified
Muller-Wieland 2018	Glimepiride v Dapagliflozin	Hospitalisation for heart failure	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nahra 2021	Liraglutide v Placebo	HbA1c change	Some concerns	Concerns regarding differential attrition between arms	Directly applicable	None specified
Nahra 2021	Liraglutide v Placebo	Weight change	Some concerns	Concerns regarding differential attrition between arms	Directly applicable	None specified
Nahra 2021	Liraglutide v Placebo	All-cause mortality	High	Concerns regarding differential attrition between arms - likley to have impact on rare events such as mortality	Directly applicable	None specified
Nahra 2021	Liraglutide v Placebo	Cardiovascular mortality	High	Concerns regarding differential attrition between arms - likley to have impact on rare events such as mortality	Directly applicable	None specified
Nakaguchi 2020	Empagliflozin v Liraglutide	BMI change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Nakaguchi 2020	Empagliflozin v Liraglutide	HbA1c change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Nakaguchi 2020	Empagliflozin v Liraglutide	Severe hypoglycaemic episodes	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nakaguchi 2020	Empagliflozin v Liraglutide	Weight change	Low	Randomised open label trial with low attrition. Analysis clearly described	Directly applicable	None specified
Nauck 2007A	Exenatide v Insulin	All-cause mortality	High	High attrition which was imbalanced between arms owing to greater adverse events in exenatide arm	Directly applicable	None specified
Nauck 2007A	Exenatide v Insulin	At night hypoglycaemic episodes	High	High attrition which was imbalanced between arms owing to greater adverse events in exenatide arm	Directly applicable	None specified
Nauck 2007A	Exenatide v Insulin	Severe hypoglycaemic episodes	High	High attrition which was imbalanced between arms owing to greater adverse events in exenatide arm	Directly applicable	None specified
Nauck 2007A	Exenatide v Insulin	HbA1c change	Some concerns	High attrition which was imbalanced between arms owing to greater adverse events in exenatide arm	Directly applicable	None specified
Nauck 2007A	Exenatide v Insulin	Weight change	Some concerns	High attrition which was imbalanced	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				between arms owing to greater adverse events in exenatide arm		
Nauck 2007B	Glipizide v Sitagliptin	HbA1c change	High	Lack of clarity around allocation concealment. Although there was high discontinuation, the mean difference for this outcome was similar between APT and per-protocol analyses.	Directly applicable	Population, intervention, comparator and outcome match protocol
Nauck 2007B	Glipizide v Sitagliptin	All-cause mortality	High	Lack of information around allocation concealment. Discontinuation was also high, with no alternitive analyses for this outcome.	Directly applicable	Population, intervention, comparator and outcome match protocol
Nauck 2007B	Glipizide v Sitagliptin	Cardiovascular mortality	High	Lack of information around allocation concealment. Discontinuation was also high, with no alternitive analyses for this outcome.	Directly applicable	Population, intervention, comparator and outcome match protocol
Nauck 2007B	Glipizide v Sitagliptin	Hypoglycaemia episodes	High	Lack of information around allocation concealment.	Directly applicable	Population, intervention, comparator and

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Discontinuation was also high, with no alternitive analyses for this outcome.		outcome match protocol
Nauck 2007B	Glipizide v Sitagliptin	Severe hypoglycaemic episodes	High	Lack of information around allocation concealment. Discontinuation was also high, with no alternitive analyses for this outcome.	Directly applicable	Population, intervention, comparator and outcome match protocol
Nauck 2007B	Glipizide v Sitagliptin	Weight change	High	Lack of information around allocation concealment. Discontinuation was also high, with no alternitive analyses for this outcome.	Directly applicable	Population, intervention, comparator and outcome match protocol
Nauck 2009A	Alogliptin v Placebo	All-cause mortality	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified
Nauck 2009A	Alogliptin v Placebo	Cardiovascular mortality	Low	Randomised double blind placebo controlled trial with low attrition, balanced between	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				both arms. Analysis clearly described		
Nauck 2009A	Alogliptin v Placebo	HbA1c change	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified
Nauck 2009A	Alogliptin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified
Nauck 2009A	Alogliptin v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified
Nauck 2009A	Alogliptin v Placebo	Weight change	Low	Randomised double blind placebo controlled trial with low attrition, balanced between both arms. Analysis clearly described	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nauck 2009B	Glimepiride v Placebo	Death from renal causes	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Liraglutide v Placebo	Death from renal causes	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Glimepiride v Placebo	HbA1c change	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Liraglutide v Placebo	HbA1c change	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Glimepiride v Placebo	Hypoglycaemia episodes	High	High attrition particularly in placebo group	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				skews data. Duration of exposure to therapy in each arm differs		
Nauck 2009B	Liraglutide v Placebo	Hypoglycaemia episodes	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Glimepiride v Placebo	Severe hypoglycaemic episodes	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Liraglutide v Placebo	Severe hypoglycaemic episodes	High	High attrition particularly in placebo group skews data. Duration of exposure to therapy in each arm differs	Directly applicable	None specified
Nauck 2009B	Glimepiride v Liraglutide	Death from renal causes	High	None specified	Directly applicable	None specified
Nauck 2009B	Glimepiride v Liraglutide	HbA1c change	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nauck 2009B	Glimepiride v Liraglutide	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Nauck 2009B	Glimepiride v Liraglutide	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Nauck 2011	Glipizide v Dapagliflozin	All-cause mortality	High	None specified	Directly applicable	None specified
Nauck 2011	Glipizide v Dapagliflozin	HbA1c change	High	None specified	Directly applicable	None specified
Nauck 2011	Glipizide v Dapagliflozin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Nauck 2011	Glipizide v Dapagliflozin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Nauck 2011	Glipizide v Dapagliflozin	Weight change	High	None specified	Directly applicable	None specified
Nauck 2014 Dulaglutide v Placebo	Dulaglutide v Placebo	HbA1c change	Some concerns	High attrition (LOCF used) but sensitivity analysis done and reasons for missing outcome data is reported; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Dulaglutide v Placebo	Dulaglutide v Placebo	All-cause mortality	High	High attrition (LOCF used) reasons for missing outcome data is reported ; lack of information	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				on allocation concealment.		
Nauck 2014 Dulaglutide v Placebo	Dulaglutide v Placebo	Severe hypoglycaemic episodes	High	High attrition (LOCF used) reasons for missing outcome data is reported ; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Dulaglutide v Sitagliptin	Dulaglutide v Sitagliptin	HbA1c change	Some concerns	High attrition (LOCF used) but sensitivity analysis done; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Dulaglutide v Sitagliptin	Dulaglutide v Sitagliptin	All-cause mortality	High	High attrition (LOCF used) reasons for missing outcome data is reported but slightly more in the sitagliptin arm discontinued due to patient decision in the sitagliptin arm than the dulaglutide arms; lack of information on allocation concealment.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nauck 2014 Dulaglutide v Sitagliptin	Dulaglutide v Sitagliptin	Cardiovascular mortality	High	High attrition (LOCF used) reasons for missing outcome data is reported but slightly more in the sitagliptin arm discontinued due to patient decision in the sitagliptin arm than the dulaglutide arms; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Dulaglutide v Sitagliptin	Dulaglutide v Sitagliptin	Severe hypoglycaemic episodes	High	High attrition (LOCF used) reasons for missing outcome data is reported but slightly more in the sitagliptin arm discontinued due to patient decision in the sitagliptin arm than the dulaglutide arms; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Dulaglutide v Sitagliptin	Dulaglutide v Sitagliptin	Weight change	High	High attrition (LOCF used) reasons for missing outcome	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				data is reported but slightly more in the sitagliptin arm discontinued due to patient decision in the sitagliptin arm than the dulaglutide arms; lack of information on allocation concealment.		
Nauck 2014 Sitagliptin v Placebo	Sitagliptin v Placebo	HbA1c change	Some concerns	High attrition (LOCF used) 46% attrition in the placebo group and 41% in sitagliptin, reasons for missing outcome data is reported and sensitivity analysis conducted; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Sitagliptin v Placebo	Sitagliptin v Placebo	All-cause mortality	High	High attrition (LOCF used)46% attrition in the placebo group and 41% in sitagliptin, reasons for missing outcome data is reported ; lack of information	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				on allocation concealment.		
Nauck 2014 Sitagliptin v Placebo	Sitagliptin v Placebo	Cardiovascular mortality	High	High attrition (LOCF used)46% attrition in the placebo group and 41% in sitagliptin, reasons for missing outcome data is reported ; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2014 Sitagliptin v Placebo	Sitagliptin v Placebo	Severe hypoglycaemic episodes	High	High attrition (LOCF used)46% attrition in the placebo group and 41% in sitagliptin, reasons for missing outcome data is reported ; lack of information on allocation concealment.	Directly applicable	None specified
Nauck 2016B	Lixisenatide v Liraglutide	Cardiac arrhythmia	High	None specified	Directly applicable	None specified
Nauck 2016B	Lixisenatide v Liraglutide	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Nauck 2016B	Lixisenatide v Liraglutide	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Nauck 2016B	Lixisenatide v Liraglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Nauck 2016B	Lixisenatide v Liraglutide	Weight change	Low	None specified	Directly applicable	None specified
Nesti 2022	Empagliflozin v Sitagliptin	HbA1c change	High	Low study numbers and no baseline or results data providedfor approx 25% of patients who either did not complete trial or whose data was deemed to be poor quality. Statistical analysis poorly described	Directly applicable	None specified
Nesti 2022	Empagliflozin v Sitagliptin	Weight change	High	Low study numbers and no baseline or results data providedfor approx 25% of patients who either did not complete trial or whose data was deemed to be poor quality. Statistical analysis poorly described	Directly applicable	None specified
Ning 2016	Vildagliptin v Placebo	All-cause mortality	Low	Randomised double bind placebo controlled trial.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Methods of analysis and results clearly explained		
Ning 2016	Vildagliptin v Placebo	Cardiovascular mortality	Low	Randomised double bind placebo controlled trial. Methods of analysis and results clearly explained	Directly applicable	None specified
Ning 2016	Vildagliptin v Placebo	Hypoglycaemia episodes	Low	Randomised double bind placebo controlled trial. Methods of analysis and results clearly explained	Directly applicable	None specified
Ning 2016	Vildagliptin v Placebo	HbA1c change	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Ning 2016	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Nogueira 2014	Sitagliptin v Insulin	BMI change	High	Lack of information around randomisation method, allocation concealment, adherence,	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				deviations, and analysis plan		
Nogueira 2014	Sitagliptin v Insulin	HbA1c change	High	Lack of information around randomisation method, allocation concealment, adherence, deviations, and analysis plan	Directly applicable	None specified
Nogueira 2014	Sitagliptin v Insulin	Weight change	High	Lack of information around randomisation method, allocation concealment, adherence, deviations, and analysis plan	Directly applicable	None specified
Ohira 2014A	Pioglitazone v Glimepiride	BMI change	High	There was a lack of information around allocation concealment, and the type of analysis that was performed	Directly applicable	None specified
Ohira 2014A	Pioglitazone v Glimepiride	HbA1c change	High	There was a lack of information around allocation concealment, and the type of analysis that was performed	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Ohira 2014A	Pioglitazone v Glimepiride	Weight change	High	There was a lack of information around allocation concealment, and the type of analysis that was performed	Directly applicable	None specified
Ohira 2014B	Sitagliptin v Metformin	BMI change	High	Methods state that participants were randomised using the 'envelope method' however, this wsa deemed not to provide sufficient information to say that participants were adequately randomised or could not be subverted. The study was unblinded. There was no information around adherence or whether there were any deviations. There was also a lack of information around the analysis used.	Directly applicable	None specified
Ohira 2014B	Sitagliptin v Metformin	HbA1c change	High	Methods state that participants were	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomised using the 'envelope method' however, this wsa deemed not to provide sufficient information to say that participants were adequately randomised or could not be subverted. The study was unblinded. There was no information around adherence or whether there were any deviations. There was also a lack of information around the analysis used.		
Ohira 2014B	Sitagliptin v Metformin	Weight change	High	Methods state that participants were randomised using the 'envelope method' however, this wsa deemed not to provide sufficient information to say that participants were adequately	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				randomised or could not be subverted. The study was unblinded. There was no information around adherence or whether there were any deviations. There was also a lack of information around the analysis used.		
Owens 2011	Linagliptin v Placebo	HbA1c change	Some concerns	Lack of information around randomisation and allocation concealment	Directly applicable	None specified
Owens 2011	Linagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around randomisation and allocation concealment	Directly applicable	None specified
Owens 2011	Linagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information around randomisation and allocation concealment	Directly applicable	None specified
Owens 2011	Linagliptin v Placebo	Weight change	Some concerns	Lack of information around randomisation and	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				allocation concealment		
Pan 2012B	Vildagliptin v Placebo	All-cause mortality	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2012B	Vildagliptin v Placebo	Cardiovascular mortality	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2012B	Vildagliptin v Placebo	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2012B	Vildagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2012B	Vildagliptin v Placebo	Non-fatal stroke	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2012B	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of information around method of randomisation and	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				allocation concealment		
Pan 2012B - no obesity	Vildagliptin v Placebo	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2012B - obesity	Vildagliptin v Placebo	HbA1c change	Some concerns	Lack of information around method of randomisation and allocation concealment	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Pan 2014	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pan 2014	Lixisenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Papathanassiou 2009	Pioglitazone v Glimepiride	BMI change	High	Randomised on basis of order of presentation; trial not registered	Directly applicable	None specified
Papathanassiou 2009	Pioglitazone v Glimepiride	HbA1c change	High	Randomised on basis of order of presentation; trial not registered	Directly applicable	None specified
Papathanassiou 2009	Pioglitazone v Glimepiride	Weight change	High	Randomised on basis of order of presentation; trial not registered	Directly applicable	None specified
Park 2011	Pioglitazone v Metformin	BMI change	High	No info about randomisation etc; protocol not available	Directly applicable	None specified
Park 2011	Pioglitazone v Metformin	HbA1c change	High	No info about randomisation etc; protocol not available	Directly applicable	None specified
Park 2014	Glimepiride v Metformin	At night hypoglycaemic episodes	High	Open-label study with noteable protocol violations and prohibited medication	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Glimepiride	At night hypoglycaemic episodes	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Park 2014	Glimepiride + Metformin v Glimepiride	HbA1c change	High	None specified	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Glimepiride	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Glimepiride	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Glimepiride	Weight change	High	None specified	Directly applicable	None specified
Park 2014	Glimepiride v Metformin	HbA1c change	High	Open-label study with noteable protocol violations and prohibited medication	Directly applicable	None specified
Park 2014	Glimepiride v Metformin	Hypoglycaemia episodes	High	Open-label study with noteable protocol violations and prohibited medication	Directly applicable	None specified
Park 2014	Glimepiride v Metformin	Severe hypoglycaemic episodes	High	Open-label study with noteable protocol violations and prohibited medication	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Metformin	At night hypoglycaemic episodes	Some concerns	Open-label study with noteable protocol violations	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				that were balanced between groups.		
Park 2014	Glimepiride + Metformin v Metformin	HbA1c change	Some concerns	Open-label study with noteable protocol violations that were balanced between groups.	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Metformin	Hypoglycaemia episodes	Some concerns	Open-label study with noteable protocol violations that were balanced between groups.	Directly applicable	None specified
Park 2014	Glimepiride + Metformin v Metformin	Severe hypoglycaemic episodes	Some concerns	Open-label study with noteable protocol violations that were balanced between groups.	Directly applicable	None specified
Park 2023	Glimepiride v Dapagliflozin	All-cause mortality	Low	None specified	Directly applicable	None specified
Park 2023	Glimepiride v Dapagliflozin	BMI change	Low	None specified	Directly applicable	None specified
Park 2023	Glimepiride v Dapagliflozin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Park 2023	Glimepiride v Dapagliflozin	HbA1c change	Low	None specified	Directly applicable	None specified
Park 2023	Glimepiride v Dapagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Park 2023	Glimepiride v Dapagliflozin	Weight change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pasquel 2021	Liraglutide v Insulin	Acute kidney injury	High	Unclear whether allocation could be subverted. Open label study with high attrition, no information around adherence, and no evidence that resuts weren't biased by missing data.	Partially applicable	16%/18% of participants had not received previous treatment for diabetes
Pasquel 2021	Liraglutide v Insulin	All-cause mortality	High	Unclear whether allocation could be subverted. Open label study with high attrition, no information around adherence, and no evidence that resuts weren't biased by missing data.	Partially applicable	16%/18% of participants had not received previous treatment for diabetes
Pasquel 2021	Liraglutide v Insulin	HbA1c change	High	Unclear whether allocation could be subverted. Open label study with high attrition, no information around adherence, and no evidence that resuts weren't biased by missing data.	Partially applicable	16%/18% of participants had not received previous treatment for diabetes

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pasquel 2021	Liraglutide v Insulin	Hypoglycaemia episodes	High	Unclear whether allocation could be subverted. Open label study with high attrition, no information around adherence, and no evidence that resuts weren't biased by missing data.	Partially applicable	16%/18% of participants had not received previous treatment for diabetes
Pasquel 2021	Liraglutide v Insulin	Severe hypoglycaemic episodes	High	Unclear whether allocation could be subverted. Open label study with high attrition, no information around adherence, and no evidence that resuts weren't biased by missing data.	Partially applicable	16%/18% of participants had not received previous treatment for diabetes
Pasquel 2021	Liraglutide v Insulin	Weight change	High	Unclear whether allocation could be subverted. Open label study with high attrition, no information around adherence, and no evidence that resuts weren't biased by missing data.	Partially applicable	16%/18% of participants had not received previous treatment for diabetes

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pei 2021	Insulin degludec/liraglutide v Insulin	3-point MACE	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	All-cause mortality	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	HbA1c change	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	Hypoglycaemia episodes	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	Non-fatal myocardial infarction	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	Non-fatal stroke	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	Severe hypoglycaemic episodes	Low	No concerns	Directly applicable	No concerns
Pei 2021	Insulin degludec/liraglutide v Insulin	Weight change	Low	No concerns	Directly applicable	No concerns
Petrica 2011	Pioglitazone v Glimepiride	BMI change	High	Small study sample with little detail	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				reported on methods of randomisation, concealment, analysis, or compliance		
Petrica 2011	Pioglitazone v Glimepiride	HbA1c change	High	Small study sample with little detail reported on methods of randomisation, concealment, analysis, or compliance	Directly applicable	None specified
Pf?tzner 2005	Pioglitazone v Glimepiride	BMI change	High	Randomisation and concealment process not described. No details on co-intervetions for patients in either arm	Directly applicable	None specified
Pf?tzner 2005	Pioglitazone v Glimepiride	HbA1c change	High	Randomisation and concealment process not described. No details on co-intervetions for patients in either arm	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pf?tzner 2005	Pioglitazone v Glimepiride	Hospitalisation for heart failure	High	Randomisation and concealment process not described. No details on co-intervetions for patients in either arm	Directly applicable	None specified
Pf?tzner 2005	Pioglitazone v Glimepiride	Severe hypoglycaemic episodes	High	Randomisation and concealment process not described. No details on co-intervetions for patients in either arm	Directly applicable	None specified
Pf?tzner 2011B	Pioglitazone v Glimepiride	Acute kidney injury	Some concerns	High overall attrition, lack of detail regarding randomisation and concealment, however a power calculation shows study is suitably powered to detect true effects	Directly applicable	None specified
Pf?tzner 2011B	Pioglitazone v Glimepiride	HbA1c change	Some concerns	High overall attrition, lack of detail regarding randomisation and concealment,	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				however a power calculation shows study is suitably powered to detect true effects		
Pf?tzner 2011B	Pioglitazone v Glimepiride	Hospitalisation for heart failure	Some concerns	High overall attrition, lack of detail regarding randomisation and concealment, however a power calculation shows study is suitably powered to detect true effects	Directly applicable	None specified
Pf?tzner 2011B	Pioglitazone v Glimepiride	Hypoglycaemia episodes	Some concerns	High overall attrition, lack of detail regarding randomisation and concealment, however a power calculation shows study is suitably powered to detect true effects	Directly applicable	None specified
Pf?tzner 2011B	Pioglitazone v Glimepiride	Weight change	Some concerns	High overall attrition, lack of detail regarding randomisation and concealment, however a power	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				calculation shows study is suitably powered to detect true effects		
Philis-Tsimikas 2013	Sitagliptin v Insulin	All-cause mortality	Some concerns	~24% missing data, unclear whether withdrawals followed up	Directly applicable	None specified
Philis-Tsimikas 2013	Sitagliptin v Insulin	At night hypoglycaemic episodes	Some concerns	~24% missing data, unclear whether withdrawals followed up	Directly applicable	None specified
Philis-Tsimikas 2013	Sitagliptin v Insulin	Hypoglycaemia episodes	Some concerns	~24% missing data, unclear whether withdrawals followed up	Directly applicable	None specified
Philis-Tsimikas 2013	Sitagliptin v Insulin	Severe hypoglycaemic episodes	Some concerns	~24% missing data, unclear whether withdrawals followed up	Directly applicable	None specified
Philis-Tsimikas 2013	Sitagliptin v Insulin	HbA1c change	High	mITT LOCF analysis, ~24% missing data	Directly applicable	None specified
Philis-Tsimikas 2013	Sitagliptin v Insulin	Weight change	High	mITT LOCF analysis, ~24% missing data	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	HbA1c change	Some concerns	mITT analysis with imputation for missing values	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	Weight change	Some concerns	mITT analysis with imputation for missing values	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	3-point MACE	Low	None specified	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	Acute kidney injury	Low	None specified	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Philis-Tsimikas 2019	Insulin degludec/liraglutide v Insulin	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	BMI change	Low	ITT analysis with multiple imputation	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	HbA1c change	Low	ITT analysis with multiple imputation	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	Weight change	Low	ITT analysis with multiple imputation	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	Health-related quality of life -	High	ITT analysis with multiple imputation;	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale mental component		Patient-reported outcome and open-label trial		
Pieber 2019	Semaglutide v Sitagliptin	Health-related quality of life - subscale physical component	High	ITT analysis with multiple imputation; Patient-reported outcome and open-label trial	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	Acute kidney injury	Low	None specified	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Pieber 2019	Semaglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Pinget 2013	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Pinget 2013	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pinget 2013	Lixisenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pinget 2013	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pinget 2013	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Pinget 2013	Lixisenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Health-related quality of life - overall	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Weight change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pozzilli 2017	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Pozzilli 2017	Dulaglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Pratley 2009A	Alogliptin v Placebo	All-cause mortality	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Pratley 2009A	Alogliptin v Placebo	Hospitalisation for heart failure	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Pratley 2009A	Alogliptin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Pratley 2009A	Alogliptin v Placebo	Non-fatal myocardial infarction	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pratley 2009A	Alogliptin v Placebo	Weight change	Low	Randomised double blind placebo trial with low attrition. Methods of protocol and analysis clearly stated	Directly applicable	None specified
Pratley 2009B	Alogliptin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Pratley 2009B	Alogliptin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Pratley 2009B	Alogliptin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Pratley 2009B	Alogliptin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Pratley 2009B	Alogliptin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Pratley 2009B	Alogliptin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Pratley 2010	Liraglutide v Sitagliptin	All-cause mortality	Some concerns	High attrition rate that results in reduction of power to detect true effect	Directly applicable	None specified
Pratley 2010	Liraglutide v Sitagliptin	Cardiovascular mortality	Some concerns	High attrition rate that results in reduction of power to detect true effect	Directly applicable	None specified
Pratley 2010	Liraglutide v Sitagliptin	HbA1c change	Some concerns	High attrition rate that results in reduction of power to detect true effect	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pratley 2010	Liraglutide v Sitagliptin	Hypoglycaemia episodes	Some concerns	High attrition rate that results in reduction of power to detect true effect	Directly applicable	None specified
Pratley 2010	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Some concerns	High attrition rate that results in reduction of power to detect true effect	Directly applicable	None specified
Pratley 2010	Liraglutide v Sitagliptin	Weight change	Some concerns	High attrition rate that results in reduction of power to detect true effect	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	HbA1c change	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified
Pratley 2018A	Ertugliflozin v Sitagliptin	HbA1c change	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	Hypoglycaemia episodes	High	Data were censored for participants who required rescue therapy, and rescue	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				therapy was higher in the sitagliptin arms.		
Pratley 2018A	Ertugliflozin v Sitagliptin	Hypoglycaemia episodes	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	Severe hypoglycaemic episodes	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified
Pratley 2018A	Ertugliflozin v Sitagliptin	Severe hypoglycaemic episodes	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	Weight change	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pratley 2018A	Ertugliflozin v Sitagliptin	Weight change	High	Data were censored for participants who required rescue therapy, and rescue therapy was higher in the sitagliptin arms.	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	HbA1c change	High	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	Weight change	High	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	All-cause mortality	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Ertugliflozin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin + Sitagliptin v Sitagliptin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Pratley 2018A	Ertugliflozin v Sitagliptin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Pratley 2018B	Semaglutide v Dulaglutide	All-cause mortality	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Pratley 2018B	Semaglutide v Dulaglutide	BMI change	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Pratley 2018B	Semaglutide v Dulaglutide	Cardiovascular mortality	Low	Randomised open label trial with low attrition, clearly	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				reported protocol, analysis and results		
Pratley 2018B	Semaglutide v Dulaglutide	HbA1c change	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Pratley 2018B	Semaglutide v Dulaglutide	Severe hypoglycaemic episodes	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Pratley 2018B	Semaglutide v Dulaglutide	Weight change	Low	Randomised open label trial with low attrition, clearly reported protocol, analysis and results	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Weight change	High	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	Acute kidney injury	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pratley 2019	Semaglutide v Liraglutide	All-cause mortality	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	BMI change	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	HbA1c change	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Pratley 2019	Semaglutide v Liraglutide	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Pratley 2019	Liraglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	Unstable angina	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Liraglutide	Weight change	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Pratley 2019	Semaglutide v Placebo	HbA1c change	Some concerns	The estimated treatment difference was greater in the trial product estimand compared with the treatment policy estimand.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				This appears to be due to higher rescue medication use in the placebo arm.		
Punthakee 2012	Pioglitazone v Placebo	3-point MACE	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	All-cause mortality	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	BMI change	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	Cardiovascular mortality	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	HbA1c change	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	Hospitalisation for heart failure	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Punthakee 2012	Pioglitazone v Placebo	Non-fatal myocardial infarction	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	Non-fatal stroke	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	Persistent signs of worsening kidney disease	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	Severe hypoglycaemic episodes	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Punthakee 2012	Pioglitazone v Placebo	Weight change	High	High attrition without any further analysis to assess the effect of attrition	Directly applicable	None specified
Raz 2008	Sitagliptin v Placebo	All-cause mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Raz 2008	Sitagliptin v Placebo	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Raz 2008	Sitagliptin v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Raz 2008	Sitagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Raz 2008 - no obesity	Sitagliptin v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Raz 2008 - obesity	Sitagliptin v Placebo	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Retnakaran 2010	Sitagliptin v Placebo	Hypoglycaemia episodes	High	None specified	Partially applicable	although switched from their original therapy to a new therapeutic plan, this included an initial high intensity insulin boost followed by the randomised treatment
Ridderstrale 2014	Glimepiride v Empagliflozin	Hypoglycaemia episodes	Low	Low	Directly applicable	NA
Ridderstrale 2014	Glimepiride v Empagliflozin	All-cause mortality	Low	Low	Directly applicable	None specified
Ridderstrale 2014	Glimepiride v Empagliflozin	HbA1c change	Low	Low	Directly applicable	None specified
Ridderstrale 2014	Glimepiride v Empagliflozin	Weight change	Low	Low	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	All-cause mortality	High	No info about randomisation/alloc	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				ation; trial not registered		
Riddle 1998	Glimepiride v Placebo	Cardiovascular mortality	High	No info about randomisation/allocation; trial not registered	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	HbA1c change	High	No info about randomisation/allocation; trial not registered	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	Non-fatal myocardial infarction	High	No info about randomisation/allocation; trial not registered	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	Non-fatal stroke	High	No info about randomisation/allocation; trial not registered	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	Severe hypoglycaemic episodes	High	No info about randomisation/allocation; trial not registered	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	Weight change	High	No info about randomisation/allocation; trial not registered	Directly applicable	None specified
Riddle 1998	Glimepiride v Placebo	Hypoglycaemia episodes	High	No info about randomisation/allocation; trial not registered; self-	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				reported symptoms only for this outcome		
Riddle 2013A	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Riddle 2013A	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Riddle 2013A	Lixisenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Riddle 2013A	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Riddle 2013A	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Riddle 2013A	Lixisenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Riddle 2013B	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Riddle 2013B	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Riddle 2013B	Lixisenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Riddle 2013B	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Riddle 2013B	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Riddle 2013B	Lixisenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	All-cause mortality	High	No info about randomisation etc and no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	Cardiovascular mortality	High	No info about randomisation etc and no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	Hypoglycaemia episodes	High	No info about randomisation etc and no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	Non-fatal myocardial infarction	High	No info about randomisation etc and no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	Severe hypoglycaemic episodes	High	No info about randomisation etc and no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	BMI change	High	No info about randomisation etc; missing data strategy not clear; no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	HbA1c change	High	No info about randomisation etc;	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				missing data strategy not clear; no available protocol		
Roberts 2005	Glimepiride v Placebo	Health-related quality of life - overall	High	No info about randomisation etc; missing data strategy not clear; no available protocol	Directly applicable	None specified
Roberts 2005	Glimepiride v Placebo	Weight change	High	No info about randomisation etc; missing data strategy not clear; no available protocol	Directly applicable	None specified
Rodbard 2016	Canagliflozin v Placebo	All-cause mortality	High	No info about allocatino concealment, trial not registered	Directly applicable	None specified
Rodbard 2016	Canagliflozin v Placebo	Cardiovascular mortality	High	No info about allocatino concealment, trial not registered	Directly applicable	None specified
Rodbard 2016	Canagliflozin v Placebo	Diabetic ketoacidosis	High	No info about allocatino concealment, trial not registered	Directly applicable	None specified
Rodbard 2016	Canagliflozin v Placebo	HbA1c change	High	No info about allocatino	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concealment, trial not registered		
Rodbard 2016	Canagliflozin v Placebo	Hypoglycaemia episodes	High	No info about allocatino concealment, trial not registered	Directly applicable	None specified
Rodbard 2016	Canagliflozin v Placebo	Severe hypoglycaemic episodes	High	No info about allocatino concealment, trial not registered	Directly applicable	None specified
Rodbard 2016	Canagliflozin v Placebo	Weight change	High	No info about allocatino concealment, trial not registered	Directly applicable	None specified
Rodbard 2017	Insulin degludec/liraglutide v Placebo	HbA1c change	Some concerns	ITT LOCF analysis	Directly applicable	None specified
Rodbard 2017	Insulin degludec/liraglutide v Placebo	Weight change	High	Missing data with LOCF for this outcome, no sensitivity analysis	Directly applicable	None specified
Rodbard 2017	Insulin degludec/liraglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Rodbard 2017	Insulin degludec/liraglutide v Placebo	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rodbard 2017	Insulin degludec/liraglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rodbard 2017	Insulin degludec/liraglutide v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Rodbard 2017	Insulin degludec/liraglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	HbA1c change	Some concerns	mITT analysis with imputation for missing values	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	Weight change	Some concerns	mITT analysis with imputation for missing values	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Rodbard 2018	Semaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	HbA1c change	Some concerns	ITT analysis with multiple imputation	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Weight change	Some concerns	ITT analysis with multiple imputation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rodbard 2019	Empagliflozin v Semaglutide	BMI change	High	ITT analysis with multiple imputation; No info about missing data for this outcome	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Health-related quality of life - subscale mental component	High	ITT analysis with multiple imputation; No info about missing data for this outcome, open-label trial/patient-reported outcome	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Health-related quality of life - subscale physical component	High	ITT analysis with multiple imputation; No info about missing data for this outcome, open-label trial/patient-reported outcome	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Acute kidney injury	Low	None specified	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	All-cause mortality	Low	None specified	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Rodbard 2019	Empagliflozin v Semaglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rodbard 2019	Empagliflozin v Semaglutide	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Roden 2005 1.2	Pioglitazone v Metformin	Weight change	High	Allocation concealment unclear, unclear reporting of attrition and methods of analysis	Directly applicable	None specified
Rosenstock 2006	Sitagliptin v Placebo	HbA1c change	High	Lack of information around allocation concealment and method of randomisation. A greater number of participants had missing data due to inititaion of rescue therapy in the control arm.	Directly applicable	None specified
Rosenstock 2006	Sitagliptin v Placebo	All-cause mortality	High	Lack of information around allocation concealment or method of randomisation. The method of analysis was 'as-treated', however, protocol violations were low and it was judged as unlikely that this	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				would have a substantial effect.		
Rosenstock 2006	Sitagliptin v Placebo	Cardiovascular mortality	High	Lack of information around allocation concealment or method of randomisation. The method of analysis was 'as-treated', however, protocol violations were low and it was judged as unlikely that this would have a substantial effect.	Directly applicable	None specified
Rosenstock 2006	Sitagliptin v Placebo	Severe hypoglycaemic episodes	High	Lack of information around allocation concealment or method of randomisation. The method of analysis was 'as-treated', however, protocol violations were low and it was judged as unlikely that this would have a substantial effect.	Directly applicable	None specified
Rosenstock 2006	Sitagliptin v Placebo	Weight change	High	Lack of information around allocation concealment or	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				method of randomisation. There was also a lack of information around adherence, however, as the outcome was continuous this was not judged to have a substantial effect. The method of analysis was 'as-treated', however, protocol violations were low and it was judged as unlikely that this would have a substantial effect.		
Rosenstock 2006	Sitagliptin v Placebo	Hypoglycaemia episodes	High	Lack of information around allocation concealment or method of randomisation.The method of analysis was 'as-treated', however, protocol violations were low and it was judged as unlikely that this would have a substantial effect.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2009B	Alogliptin v Placebo	All-cause mortality	High	High proportion of participants discontinued. The proportion of participants withdrawn from the study due to hyperglycaemia has higher in the placebo arm.	Directly applicable	None specified
Rosenstock 2009B	Alogliptin v Placebo	Cardiovascular mortality	High	High proportion of participants discontinued. The proportion of participants withdrawn from the study due to hyperglycaemia has higher in the placebo arm.	Directly applicable	None specified
Rosenstock 2009B	Alogliptin v Placebo	HbA1c change	High	High proportion of participants discontinued. The proportion of participants withdrawn from the study due to hyperglycaemia has higher in the placebo arm.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2009B	Alogliptin v Placebo	Hypoglycaemia episodes	High	High proportion of participants discontinued. The proportion of participants withdrawn from the study due to hyperglycaemia has higher in the placebo arm.	Directly applicable	None specified
Rosenstock 2009B	Alogliptin v Placebo	Severe hypoglycaemic episodes	High	High proportion of participants discontinued. The proportion of participants withdrawn from the study due to hyperglycaemia has higher in the placebo arm.	Directly applicable	None specified
Rosenstock 2009B	Alogliptin v Placebo	Weight change	High	High proportion of participants discontinued. The proportion of participants withdrawn from the study due to hyperglycaemia has higher in the placebo arm.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2012	Dapagliflozin v Placebo	Weight change	Some concerns	No detail on randomisation or concealment, 25% attrition in placebo arm and 16% in treatment arm	Directly applicable	None specified
Rosenstock 2012	Dapagliflozin v Placebo	All-cause mortality	High	No detail on randomisation or concealment, 25% attrition in placebo arm and 16% in treatment arm may affect rare events	Directly applicable	None specified
Rosenstock 2012	Dapagliflozin v Placebo	Hypoglycaemia episodes	High	No detail on randomisation or concealment, 25% attrition in placebo arm and 16% in treatment arm may affect rare events	Directly applicable	None specified
Rosenstock 2012	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	High	No detail on randomisation or concealment, 25% attrition in placebo arm and 16% in treatment arm may affect rare events	Directly applicable	None specified
Rosenstock 2012	Dapagliflozin v Placebo	HbA1c change	Some concerns	No detail on randomisation or concelament, 25% attrition in placebo	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				arm and 16% in treatment arm		
Rosenstock 2013	Lixisenatide v Exenatide	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2013	Lixisenatide v Exenatide	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2013	Lixisenatide v Exenatide	All-cause mortality	Low	Separate paper reporting 52 week safety outcomes does not appear to have been published	Directly applicable	None specified
Rosenstock 2013	Lixisenatide v Exenatide	Hypoglycaemia episodes	Low	Separate paper reporting 52 week safety outcomes does not appear to have been published	Directly applicable	None specified
Rosenstock 2013	Lixisenatide v Exenatide	Severe hypoglycaemic episodes	Low	Separate paper reporting 52 week safety outcomes does not appear to have been published	Directly applicable	None specified
Rosenstock 2014A	Lixisenatide v Placebo	All-cause mortality	Some concerns	No detail on randomisation or concelament protocol	Directly applicable	None specified
Rosenstock 2014A	Lixisenatide v Placebo	Cardiovascular mortality	Some concerns	No detail on randomisation or	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concelament protocol		
Rosenstock 2014A	Lixisenatide v Placebo	HbA1c change	Some concerns	No detail on randomisation or concelament protocol	Directly applicable	None specified
Rosenstock 2014A	Lixisenatide v Placebo	Hypoglycaemia episodes	Some concerns	No detail on randomisation or concelament protocol	Directly applicable	None specified
Rosenstock 2014A	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Some concerns	No detail on randomisation or concelament protocol	Directly applicable	None specified
Rosenstock 2014A	Lixisenatide v Placebo	Weight change	Some concerns	No detail on randomisation or concelament protocol	Directly applicable	None specified
Rosenstock 2014B	Empagliflozin v Placebo	All-cause mortality	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Rosenstock 2014B	Empagliflozin v Placebo	HbA1c change	Low	Randomised double blind placebo controlled trial with low attrition, balanced between	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				arms. Analysis clearly described		
Rosenstock 2014B	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Rosenstock 2014B	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Rosenstock 2014B	Empagliflozin v Placebo	Weight change	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	All-cause mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin v Saxagliptin	All-cause mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin v Saxagliptin	Cardiovascular mortality	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin v Saxagliptin	HbA1c change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin v Saxagliptin	Hypoglycaemia episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	Persistent signs of worsening kidney disease	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin v Saxagliptin	Persistent signs of worsening kidney disease	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2015A	Dapagliflozin v Saxagliptin	Severe hypoglycaemic episodes	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Dapagliflozin	Weight change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin v Saxagliptin	Weight change	Some concerns	Lack of information around allocation concealment	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	Persistent signs of worsening kidney disease	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2015A	Dapagliflozin + Saxagliptin v Saxagliptin	Weight change	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2015B	Empagliflozin v Placebo	All-cause mortality	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention	Directly applicable	None specified
Rosenstock 2015B	Empagliflozin v Placebo	Diabetic ketoacidosis	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention	Directly applicable	None specified
Rosenstock 2015B	Empagliflozin v Placebo	Hypoglycaemia episodes	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention	Directly applicable	None specified
Rosenstock 2015B	Empagliflozin v Placebo	Severe hypoglycaemic episodes	High	High number of participants did not complete treatment, and there were no	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				analyses that estimated the effect of adhering to the intervention		
Rosenstock 2015B	Empagliflozin v Placebo	Weight change	High	High number of participants did not complete treatment, and there were no analyses that estimated the effect of adhering to the intervention	Directly applicable	None specified
Rosenstock 2015B	Empagliflozin v Placebo	HbA1c change	High	High number of participants did not complete treatment. Data were presented from completers only, and although the report states that sensitivity analyses measured the impact of attrition, the results of these analyses were not reported.	Directly applicable	None specified
Rosenstock 2016A	Lixisenatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2016A	Lixisenatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2016A	Lixisenatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2016A	Lixisenatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2016A	Lixisenatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2016A	Lixisenatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Lixisenatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Lixisenatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	All-cause mortality	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Lixisenatide	Unstable angina	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Lixisenatide v Insulin	All-cause mortality	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Some concerns	Participants were analysed according to the treatment they received rather than the treatment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Lixisenatide v Insulin	Cardiovascular mortality	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Hospitalisation for heart failure	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016B	Lixisenatide v Insulin	Hospitalisation for heart failure	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016B	Lixisenatide v Insulin	Hypoglycaemia episodes	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Non-fatal myocardial infarction	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016B	Lixisenatide v Insulin	Non-fatal myocardial infarction	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Non-fatal stroke	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016B	Lixisenatide v Insulin	Non-fatal stroke	Some concerns	Participants were analysed according	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				with those randomised.		
Rosenstock 2016B	Lixisenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016B	Insulin glargine/Lixisenatide v Insulin	Unstable angina	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment,	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				however, the numbers in the safety analysis seemed consistent with those randomised.		
Rosenstock 2016B	Lixisenatide v Insulin	Unstable angina	Some concerns	Participants were analysed according to the treatment they received rather than the treatment to which they were assigned. There is no information around whether or how many participants switched treatment, however, the numbers in the safety analysis seemed consistent with those randomised.	Directly applicable	None specified
Rosenstock 2016C	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2016C	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2016C	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2016C	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2016C	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2016C	Insulin glargine/Lixisenatide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2018A	Exenatide v Placebo	All-cause mortality	Low	Na	Directly applicable	None specified
Rosenstock 2018A	Exenatide v Placebo	Cardiovascular mortality	Low	Na	Directly applicable	None specified
Rosenstock 2018A	Exenatide v Placebo	HbA1c change	Low	Na	Directly applicable	None specified
Rosenstock 2018A	Exenatide v Placebo	Hypoglycaemia episodes	Low	Na	Directly applicable	None specified
Rosenstock 2018A	Exenatide v Placebo	Severe hypoglycaemic episodes	Low	Na	Directly applicable	None specified
Rosenstock 2018A	Exenatide v Placebo	Weight change	Low	Na	Directly applicable	None specified
Rosenstock 2018B	Ertugliflozin v Placebo	HbA1c change	Low	Power calculcation clearly showing stdy well powered to identify true effects.	Directly applicable	None specified
Rosenstock 2018B	Ertugliflozin v Placebo	Hypoglycaemia episodes	Low	Power calculcation clearly showing stdy	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				well powered to identify true effects.		
Rosenstock 2018B	Ertugliflozin v Placebo	All-cause mortality	Low	Power calculcation clearly showing study well powered to identify true effects.	Directly applicable	None specified
Rosenstock 2018B	Ertugliflozin v Placebo	Cardiovascular mortality	Low	Power calculcation clearly showing study well powered to identify true effects.	Directly applicable	None specified
Rosenstock 2019A	Linagliptin v Placebo	3-point MACE	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	4-point MACE	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Acute kidney injury	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	All-cause mortality	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Cardiovascular mortality	Low	Study described as multicentre, randomized, double-	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Death from renal causes	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Development of end stage kidney disease	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	HbA1c change	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Hospitalisation for heart failure	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Hypoglycaemia episodes	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Non-fatal myocardial infarction	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Non-fatal stroke	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2019A	Linagliptin v Placebo	Persistent signs of worsening kidney disease	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A	Linagliptin v Placebo	Unstable angina	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A no CKD	Linagliptin v Placebo	Hospitalisation for heart failure	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				(using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A no HF	Linagliptin v Placebo	Cardiovascular mortality	Low	Study described as multicentre, randomized, double-blind, active controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019A no HF	Linagliptin v Placebo	Hospitalisation for heart failure	Low	Study described as multicentre, randomized, double-blind, active	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				controlled clinical trial indicating adequate allocation concealment, but specific methods not outlined; ITT undertaken; Data provided for all primary (Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke [3P-MACE]) and secondary end points accounting for 99.9% (6033/6042) of participants randomized. Clinical event rates and objective measures of safety coded (using the Medical Dictionary for Drug Regulatory Activities version) were utilized to measure pre-specified outcomes. Evidence of prespecified		

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				analytical plan and prespecified outcomes (Marx et al 2015), and the data presented, and methods of analysis outlined aligns with prespecified plans		
Rosenstock 2019B	Glimepiride v Linagliptin	3-point MACE	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	4-point MACE	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Non-fatal stroke	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2019B	Glimepiride v Linagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Unstable angina	Low	None specified	Directly applicable	None specified
Rosenstock 2019B	Glimepiride v Linagliptin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2019B no CVD	Glimepiride v Linagliptin	3-point MACE	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	HbA1c change	Some concerns	Estimated treatment differences were different between the treatment policy and trial policy estimands.	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Acute kidney injury	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	BMI change	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Death from renal causes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2019C	Semaglutide v Sitagliptin	Health-related quality of life - subscale mental component	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Health-related quality of life - subscale physical component	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Unstable angina	Low	None specified	Directly applicable	None specified
Rosenstock 2019C	Semaglutide v Sitagliptin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Dapagliflozin	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Dapagliflozin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Dapagliflozin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Dapagliflozin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Dapagliflozin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Dapagliflozin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin + Saxagliptin v Saxagliptin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2019D	Dapagliflozin v Saxagliptin	Weight change	Low	None specified	Directly applicable	None specified
Rosenstock 2023	Tirzepatide v Insulin	Acute kidney injury	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2023	Tirzepatide v Insulin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2023	Tirzepatide v Insulin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2023	Tirzepatide v Insulin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Rosenstock 2023	Tirzepatide v Insulin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Rosenstock 2023	Tirzepatide v Insulin	Weight change	Some concerns	None specified	Directly applicable	None specified
Roussel 2019	Sitagliptin v Placebo	All-cause mortality	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Roussel 2019	Sitagliptin v Placebo	Cardiovascular mortality	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Roussel 2019	Sitagliptin v Placebo	HbA1c change	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Roussel 2019	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial with low attrition, balanced between	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				arms. Analysis clearly described		
Roussel 2019	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Roussel 2019	Sitagliptin v Placebo	Weight change	Low	Randomised double blind placebo controlled trial with low attrition, balanced between arms. Analysis clearly described	Directly applicable	None specified
Russell-Jones 2009	Liraglutide v Placebo	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None
Russell-Jones 2009	Liraglutide v Placebo	Weight change	Some concerns	mITT LOCF analysis	Directly applicable	None
Russell-Jones 2009	Liraglutide v Placebo	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None
Russell-Jones 2009	Liraglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None
Russell-Jones 2009	Liraglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Russell-Jones 2009	Liraglutide v Insulin	At night hypoglycaemic episodes	Low	Double-blind comparison with mITT analysis and low attrition	Directly applicable	None specified
Russell-Jones 2009	Liraglutide v Insulin	HbA1c change	Low	Double-blind comparison with mITT analysis and low attrition	Directly applicable	None specified
Russell-Jones 2009	Liraglutide v Insulin	Hypoglycaemia episodes	Low	Double-blind comparison with mITT analysis and low attrition	Directly applicable	None specified
Russell-Jones 2009	Liraglutide v Insulin	Severe hypoglycaemic episodes	Low	Double-blind comparison with mITT analysis and low attrition	Directly applicable	None specified
Russell-Jones 2009	Liraglutide v Insulin	Weight change	Low	Double-blind comparison with mITT analysis and low attrition	Directly applicable	None specified
Sathyanarayana 2011	Pioglitazone + Exenatide v Pioglitazone	BMI change	High	Lack of information on baseline characteristics; lack of information on allocation	Partially applicable	not all patients were also on metformin (2 patients in each group)
Sathyanarayana 2011	Pioglitazone + Exenatide v Pioglitazone	HbA1c change	High	Lack of information on baseline characteristics; lack of information on allocation	Partially applicable	not all patients were also on metformin (2 patients in each group)

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Sathyanarayana 2011	Pioglitazone + Exenatide v Pioglitazone	Weight change	High	Lack of information on baseline characteristics; lack of information on allocation	Partially applicable	not all patients were also on metformin (2 patients in each group)
Savvidou 2016	Exenatide v Insulin	BMI change	High	Randomisation method no approprirate and significant differences in baseline values for weight. Discontiuations only occurred in one arm(13%) with no explanation as to reasons why. Inappropraite anayses used	Directly applicable	None specified
Savvidou 2016	Exenatide v Insulin	HbA1c change	High	Randomisation method no approprirate and significant differences in baseline values for weight. Discontiuations only occurred in one arm(13%) with no explanation as to reasons why.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				Inappropraite anayses used		
Savvidou 2016	Exenatide v Insulin	Weight change	High	Randomisation method no approprirate and significant differences in baseline values for weight. Discontiuations only occurred in one arm(13%) with no explanation as to reasons why. Inappropraite anayses used	Directly applicable	None specified
Schernthaner 2013	Canagliflozin v Sitagliptin	All-cause mortality	High	High attrition with attrition higher in the sitagliptin arm and no analysis to assess the impact of adherence	Directly applicable	None specified
Schernthaner 2013	Canagliflozin v Sitagliptin	Cardiovascular mortality	High	High attrition with attrition higher in the sitagliptin arm and no analysis to assess the impact of adherence	Directly applicable	None specified
Schernthaner 2013	Canagliflozin v Sitagliptin	Hypoglycaemia episodes	High	High attrition with attrition higher in the sitagliptin arm and	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				no analysis to assess the impact of adherence		
Schernthaner 2013	Canagliflozin v Sitagliptin	Severe hypoglycaemic episodes	High	High attrition with attrition higher in the sitagliptin arm and no analysis to assess the impact of adherence	Directly applicable	None specified
Schernthaner 2013	Canagliflozin v Sitagliptin	HbA1c change	High	High attrition with attrition higher in the sitagliptin arm. ITT analysis indicated greater difference in mean change between sitagliptin and canagliflozin.	Directly applicable	None specified
Schernthaner 2013	Canagliflozin v Sitagliptin	Weight change	High	High attrition with attrition higher in the sitagliptin arm. ITT analysis indicated greater difference in mean change between sitagliptin and canagliflozin.	Directly applicable	None specified
Schernthaner 2015A	Glimepiride v Saxagliptin	All-cause mortality	Some concerns	Only around 80% of participants completed the 52-week study period, however, reasons for discontinuation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				were similar in study arms.		
Schernthaner 2015A	Glimepiride v Saxagliptin	Cardiovascular mortality	Some concerns	Only around 80% of participants completed the 52-week study period, however, reasons for discontinuation were similar in study arms.	Directly applicable	None specified
Schernthaner 2015A	Glimepiride v Saxagliptin	Hypoglycaemia episodes	Some concerns	Only around 80% of participants completed the 52-week study period, however, reasons for discontinuation were similar in study arms.	Directly applicable	None specified
Schernthaner 2015A	Glimepiride v Saxagliptin	Weight change	Some concerns	Only around 80% of participants completed the 52-week study period, however, reasons for discontinuation were similar in study arms.	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	3-point MACE	High	Problems with adherence to outcome	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Scirica 2013	Saxagliptin v Placebo	All-cause mortality	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	BMI change	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Cardiovascular mortality	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Death from renal causes	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Development of end stage kidney disease	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	HbA1c change	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Hospitalisation for heart failure	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Hypoglycaemia episodes	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Non-fatal myocardial infarction	High	Problems with adherence to outcome	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Scirica 2013	Saxagliptin v Placebo	Non-fatal stroke	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Persistent signs of worsening kidney disease	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Severe hypoglycaemic episodes	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Unstable angina	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013	Saxagliptin v Placebo	Weight change	High	Problems with adherence to outcome	Directly applicable	None specified
Scirica 2013 no CVD	Saxagliptin v Placebo	3-point MACE	High	Problems with adherence to outcome	Directly applicable	None specified
Scott 2018	Dapagliflozin v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Scott 2018	Dapagliflozin v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Scott 2018	Dapagliflozin v Sitagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Scott 2018	Dapagliflozin v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Scott 2018	Dapagliflozin v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Seino 2012	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Seino 2012	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Seino 2012	Lixisenatide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Seino 2012	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Seino 2012	Lixisenatide v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Seino 2012	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Seino 2012	Lixisenatide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Seino 2016	Liraglutide v Placebo	All-cause mortality	Some concerns	As treated' analysis was conducted for the safety set, however, the same number of participants were in the 'as randomised' and 'as treated' datasets, so this is unlikely to have a substantial effect.	Directly applicable	None specified
Seino 2016	Liraglutide v Placebo	At night hypoglycaemic episodes	Some concerns	As treated' analysis was conducted for the safety set, however, the same	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				number of participants were in the 'as randomised' and 'as treated' datasets, so this is unlikely to have a substantial effect.		
Seino 2016	Liraglutide v Placebo	Cardiovascular mortality	Some concerns	As treated' analysis was conducted for the safety set, however, the same number of participants were in the 'as randomised' and 'as treated' datasets, so this is unlikely to have a substantial effect.	Directly applicable	None specified
Seino 2016	Liraglutide v Placebo	Hypoglycaemia episodes	Some concerns	As treated' analysis was conducted for the safety set, however, the same number of participants were in the 'as randomised' and 'as treated' datasets, so this is unlikely to have a substantial effect.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Seino 2016	Liraglutide v Placebo	Severe hypoglycaemic episodes	Some concerns	As treated' analysis was conducted for the safety set, however, the same number of participants were in the 'as randomised' and 'as treated' datasets, so this is unlikely to have a substantial effect.	Directly applicable	None specified
Seino 2016	Liraglutide v Placebo	HbA1c change	Low	Lack of information around adherence, however, this was judged not to have a substantial effect on non-rare outcomes.	Directly applicable	None specified
Seino 2016	Liraglutide v Placebo	Weight change	Low	Lack of information around adherence, however, this was judged not to have a substantial effect on non-rare outcomes.	Directly applicable	None specified
Seino 2021	Sitagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Seino 2021	Sitagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Seino 2021	Sitagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Seino 2021	Sitagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Seino 2021	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Seino 2021	Sitagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	All-cause mortality	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	Cardiovascular mortality	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	Diabetic ketoacidosis	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	HbA1c change	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	Non-fatal myocardial infarction	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Shankar 2017A	Sitagliptin v Placebo	Weight change	Some concerns	Protocol registered NCT01590797	Directly applicable	None specified
Sivalingam 2023	Semaglutide v Placebo	All-cause mortality	Some concerns	Lack of information arounf allocation concealment	Directly applicable	None specified
Sivalingam 2023	Semaglutide v Placebo	HbA1c change	Some concerns	Lack of information arounf allocation concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Sivalingam 2023	Semaglutide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of information arounf allocation concealment	Directly applicable	None specified
Sivalingam 2023	Semaglutide v Placebo	Weight change	Some concerns	Lack of information arounf allocation concealment	Directly applicable	None specified
Skrivanek 2014	Dulaglutide v Placebo	Weight change	High	Attrition >20% and no sensitivity analyses; baseline weight is also not reported; lack of information on adherence	Directly applicable	None specified
Skrivanek 2014	Sitagliptin v Placebo	Weight change	High	Attrition >20% and no sensitivity analyses; baseline weight is also not reported; lack of information on adherence	Directly applicable	None specified
Skrivanek 2014	Dulaglutide v Placebo	HbA1c change	High	Attrition >20% and no sensitivity analyses; lack of information on adherence	Directly applicable	None specified
Skrivanek 2014	Sitagliptin v Placebo	HbA1c change	High	Attrition >20% and no sensitivity analyses; lack of information on adherence	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Softeland 2017	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Softeland 2017	Empagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Softeland 2017	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Softeland 2017	Empagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Softeland 2017	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Softeland 2017	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Softeland 2017	Empagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Sone 2019	Empagliflozin v Placebo	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Sone 2019	Empagliflozin v Placebo	Weight change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Sone 2019	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Sone 2019	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Sone 2019	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Sone 2019	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Sone 2019	Empagliflozin v Placebo	Unstable angina	Low	None specified	Directly applicable	None specified
Sridhar 2013	Pioglitazone v Placebo	BMI change	High	No info on randomisation; baseline difference on age, no available protocol	Directly applicable	None specified
Sridhar 2013	Pioglitazone v Placebo	HbA1c change	High	No info on randomisation; baseline difference on age, no available protocol	Directly applicable	None specified
Sridhar 2013	Pioglitazone v Placebo	Hypoglycaemia episodes	High	No info on randomisation; baseline difference on age, no available protocol	Directly applicable	None specified
Sridhar 2013	Pioglitazone v Placebo	Weight change	High	No info on randomisation; baseline difference on age, no available protocol	Directly applicable	None specified
Strain 2013	Vildagliptin v Placebo	All-cause mortality	Low	None specified	Partially applicable	Population indirectness (unclear proportion of people who were receiving medication before trial)
Strain 2013	Vildagliptin v Placebo	Cardiovascular mortality	Low	None specified	Partially applicable	Population indirectness

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
						(unclear proportion of people who were receiving medication before trial)
Strain 2013	Vildagliptin v Placebo	HbA1c change	Low	None specified	Partially applicable	Population indirectness (unclear proportion of people who were receiving medication before trial)
Strain 2013	Vildagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Partially applicable	Population indirectness (unclear proportion of people who were receiving medication before trial)
Strain 2013	Vildagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Partially applicable	Population indirectness (unclear proportion of people who were receiving medication before trial)
Strojek 2011	Dapagliflozin v Placebo	Weight change	High	~43 missing data, no sensitivity analysis	Directly applicable	None specified
Strojek 2011	Dapagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Strojek 2011	Dapagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Strojek 2011	Dapagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Strojek 2011	Dapagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Strojek 2011	Dapagliflozin v Placebo	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Strojek 2011	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Strojek 2011	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Su 2014	Vildagliptin v Placebo	HbA1c change	High	Lack of information on randomisation methods, allocation, analysis	Directly applicable	None specified
Su 2014	Vildagliptin v Placebo	Hypoglycaemia episodes	High	Lack of information on randomisation methods, allocation, analysis	Directly applicable	None specified
Su 2014	Vildagliptin v Placebo	Weight change	High	Lack of information on randomisation methods, allocation, analysis	Directly applicable	None specified
Takihata 2013	Pioglitazone v Sitagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Takihata 2013	Pioglitazone v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Takihata 2013	Pioglitazone v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Takihata 2013	Pioglitazone v Sitagliptin	Weight change	Low	None specified	Directly applicable	None specified
Tan 2004	Pioglitazone v Glimepiride	HbA1c change	Low	Randomised double blind placebo controlled trial. Analysis clearly described	Directly applicable	None specified
Tan 2004	Pioglitazone v Glimepiride	Hypoglycaemia episodes	Low	Randomised double blind placebo controlled trial. Analysis clearly described	Directly applicable	None specified
Tanaka 2017	Vildagliptin v Alogliptin	HbA1c change	High	Lack of information around method of allocation concealment, adherence, and method of analysis.	Directly applicable	None specified
Tanaka 2017	Vildagliptin v Alogliptin	Weight change	High	Lack of information around method of allocation concealment, adherence, and method of analysis.	Directly applicable	None specified
Tanaka 2017	Vildagliptin v Alogliptin	Hypoglycaemia episodes	High	Lack of information around method of allocation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concealment, adherence, and method of analysis. There was also no information around how the outcome was measured and whether this was objective or subjective.		
Tanaka 2017	Vildagliptin v Alogliptin	Severe hypoglycaemic episodes	High	Lack of information around method of allocation concealment, adherence, and method of analysis. There was also no information around how the outcome was measured and whether this was objective or subjective.	Directly applicable	None specified
Tanaka 2019	Empagliflozin v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Tanaka 2019	Empagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Tanaka 2019	Empagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Taskinen 2011	Linagliptin v Placebo	Hypoglycaemia episodes	Some concerns	No info about randomisation/allocation concealment	Directly applicable	None specified
Taskinen 2011	Linagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	No info about randomisation/allocation concealment; LOCF for missing data	Directly applicable	None specified
Taskinen 2011	Linagliptin v Placebo	HbA1c change	High	No info about randomisation/allocation concealment; LOCF for missing data and no info about proportion missing	Directly applicable	None specified
Taskinen 2011	Linagliptin v Placebo	Weight change	High	No info about randomisation/allocation concealment; LOCF for missing data and no info about proportion missing	Directly applicable	None specified
Terauchi 2020	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Terauchi 2020	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Terauchi 2020	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Terauchi 2020	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Terauchi 2020	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Terauchi 2020	Insulin glargine/Lixisenatide v Insulin	Weight change	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Thrasher 2014	Linagliptin v Placebo	All-cause mortality	Some concerns	Randomisation issues and some baseline differences	Directly applicable	None specified
Thrasher 2014	Linagliptin v Placebo	Cardiovascular mortality	Some concerns	Randomisation issues and some baseline differences	Directly applicable	None specified
Thrasher 2014	Linagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Randomisation issues and some baseline differences	Directly applicable	None specified
Thrasher 2014	Linagliptin v Placebo	Non-fatal myocardial infarction	Some concerns	Randomisation issues and some baseline differences	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Thrasher 2014	Linagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	Randomisation issues and some baseline differences	Directly applicable	None specified
Thrasher 2014	Linagliptin v Placebo	HbA1c change	High	Randomisation issues and some baseline differences; mITT analysis with LOCF	Directly applicable	None specified
Thrasher 2014	Linagliptin v Placebo	Weight change	High	Randomisation issues and some baseline differences; mITT analysis with LOCF; high proportion of missing data and no sensitivity analysis	Directly applicable	None specified
Tinahones 2017 Study 1	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 1	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 1	Linagliptin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 1	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 1	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 1	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Tinahones 2017 Study 1	Linagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Tinahones 2017 Study 2	Linagliptin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Tripathy 2013	Pioglitazone v Placebo	BMI change	Some concerns	Trial retrospectively registered	Partially applicable	~15% of participants had received diet only at baseline
Tripathy 2013	Pioglitazone v Placebo	HbA1c change	Some concerns	Trial retrospectively registered	Partially applicable	~15% of participants had received diet only at baseline
Tripathy 2013	Pioglitazone v Placebo	Weight change	Some concerns	Trial retrospectively registered	Partially applicable	~15% of participants had received diet only at baseline
Umpierrez 2006	Pioglitazone v Glimepiride	Hospitalisation for heart failure	High	No info about randomisation/alloc	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				ation concealment; trial not registered		
Umpierrez 2006	Pioglitazone v Glimepiride	Hypoglycaemia episodes	High	No info about randomisation/allocation concealment; trial not registered	Directly applicable	None specified
Umpierrez 2006	Pioglitazone v Glimepiride	Severe hypoglycaemic episodes	High	No info about randomisation/allocation concealment; trial not registered	Directly applicable	None specified
Umpierrez 2006	Pioglitazone v Glimepiride	BMI change	High	No info about randomisation/allocation concealment; trial not registered; missing data strategy not clear	Directly applicable	None specified
Umpierrez 2006	Pioglitazone v Glimepiride	HbA1c change	High	No info about randomisation/allocation concealment; trial not registered; missing data strategy not clear	Directly applicable	None specified
Umpierrez 2006	Pioglitazone v Glimepiride	Weight change	High	No info about randomisation/allocation concealment; trial not registered; missing data strategy not clear	Directly applicable	None specified
Vähätalo 2007	Glipizide v Metformin	HbA1c change	High	Concerns with allocation, baseline	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				values, blinding, method of assessment and attrition		
Vähätalo 2007	Glipizide v Metformin	Weight change	High	Concerns with allocation, baseline values, blinding, method of assessment and attrition	Directly applicable	None specified
van der Meer 2009	Pioglitazone v Metformin	Hospitalisation for heart failure	High	No details on concealment and analysis poorly described	Directly applicable	None specified
van der Meer 2009	Pioglitazone v Metformin	HbA1c change	Some concerns	No details on concealment and analysis poorly described	Directly applicable	None specified
van der Meer 2009	Pioglitazone v Metformin	Weight change	Some concerns	No details on concealment and analysis poorly described	Directly applicable	None specified
van Eyk 2019	Liraglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
van Eyk 2019	Liraglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
van Eyk 2019	Liraglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
van Gaal 2014	Lixisenatide v Sitagliptin	HbA1c change	High	No info about randomisation/alloc	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				ation; mITT LOCF analysis; trial retrospectively registered		
van Gaal 2014	Lixisenatide v Sitagliptin	Weight change	High	No info about randomisation/allocation; mITT LOCF analysis; trial retrospectively registered	Directly applicable	None specified
van Gaal 2014	Lixisenatide v Sitagliptin	All-cause mortality	High	No info about randomisation/allocation; trial retrospectively registered	Directly applicable	None specified
van Gaal 2014	Lixisenatide v Sitagliptin	Cardiovascular mortality	High	No info about randomisation/allocation; trial retrospectively registered	Directly applicable	None specified
van Gaal 2014	Lixisenatide v Sitagliptin	Hypoglycaemia episodes	High	No info about randomisation/allocation; trial retrospectively registered	Directly applicable	None specified
van Gaal 2014	Lixisenatide v Sitagliptin	Severe hypoglycaemic episodes	High	No info about randomisation/allocation; trial retrospectively registered	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Vanderheiden 2016A	Liraglutide v Placebo	BMI change	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	HbA1c change	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale barriers to activity	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale blood glucose control	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale current health perception	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale general health	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale hypoglycaemia fear	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life -	Some concerns	No info about allocation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale lifestyle impact		concealment, some baseline differences		
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale satisfaction	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale social or vocational worry	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Health-related quality of life - subscale social stigma	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Hypoglycaemia episodes	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Severe hypoglycaemic episodes	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vanderheiden 2016A	Liraglutide v Placebo	Weight change	Some concerns	No info about allocation concealment, some baseline differences	Directly applicable	None specified
Vianna 2018	Gliclazide v Vildagliptin	Weight change	High	None specified	Directly applicable	None specified
Vianna 2018	Gliclazide v Vildagliptin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Vianna 2018	Gliclazide v Vildagliptin	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Vianna 2018	Gliclazide v Vildagliptin	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Vianna 2018	Gliclazide v Vildagliptin	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Vianna 2018	Gliclazide v Vildagliptin	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Vianna 2018	Gliclazide v Vildagliptin	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	All-cause mortality	Some concerns	No info about allocatino concealment	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	Cardiovascular mortality	Some concerns	No info about allocatino concealment	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	Hypoglycaemia episodes	Some concerns	No info about allocatino concealment	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	Non-fatal myocardial infarction	Some concerns	No info about allocatino concealment	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	No info about allocatino concealment	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	Unstable angina	Some concerns	No info about allocatino concealment	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Vilsboll 2010	Sitagliptin v Placebo	Weight change	Some concerns	No info about allocatino concealment	Directly applicable	None specified
Vilsboll 2010	Sitagliptin v Placebo	HbA1c change	High	No info about allocatino concealment; changes to outcome reported retrospectively	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	HbA1c change	High	High proportion of missing data	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Weight change	High	High proportion of missing data	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Acute kidney injury	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Health-related quality of life - subscale net benefit score	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Health-related quality of life - subscale regimen acceptance score	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Health-related quality of life - subscale satisfaction	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Vilsboll 2019	Dapagliflozin + Saxagliptin v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
W?gner 2019	Liraglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
W?gner 2019	Liraglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
W?gner 2019	Liraglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	Weight change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	5-point MACE	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wang 2016B	Linagliptin v Placebo	Hospitalisation for heart failure	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Wang 2016B	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Wang 2017	Sitagliptin v Placebo	HbA1c change	Some concerns	Some differential attrition between two groups	Directly applicable	NA
Wang 2017	Sitagliptin v Placebo	Hypoglycaemia episodes	Some concerns	Some differential attrition between two groups	Directly applicable	NA
Wang 2017	Sitagliptin v Placebo	Weight change	Some concerns	Some differential attrition between two groups	Directly applicable	NA
Wang 2019B	Dulaglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Wang 2019B	Dulaglutide v Insulin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Wang 2019B	Dulaglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Wang 2019B	Dulaglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wang 2019B	Dulaglutide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Wang 2019B	Dulaglutide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Wang 2020A	Exenatide v Insulin	HbA1c change	High	No detail on concealment or statisitical analysis	Directly applicable	None specified
Wang 2020A	Exenatide v Insulin	Weight change	High	No detail on concealment or statisitical analysis	Directly applicable	None specified
Wang 2020C	Liraglutide v Sitagliptin	HbA1c change	High	No detail on concealment, analysis or attrition rates	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	All-cause mortality	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	Cardiovascular mortality	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				withdrawal due to adverse events)		
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	HbA1c change	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	Non-fatal stroke	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	Unstable angina	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	Weight change	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	Unstable angina	Low	None specified	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Wang 2022B	Liraglutide v Insulin	All-cause mortality	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wang 2022B	Liraglutide v Insulin	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wang 2022B	Liraglutide v Insulin	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Wang 2022B	Liraglutide v Insulin	Unstable angina	Some concerns	None specified	Directly applicable	None specified
Wang 2022B	Insulin degludec/liraglutide v Insulin	At night hypoglycaemic episodes	Low	None specified	Partially applicable	May also include patients who experienced severe hypoglycaemia
Wang 2022B	Insulin degludec/liraglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Partially applicable	May also include patients who experienced severe hypoglycaemia
Wang 2022B	Liraglutide v Insulin	At night hypoglycaemic episodes	Some concerns	None specified	Partially applicable	May also include patients who experienced severe hypoglycaemia
Wang 2022B	Liraglutide v Insulin	Hypoglycaemia episodes	Some concerns	None specified	Partially applicable	May also include patients who experienced severe hypoglycaemia
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	At night hypoglycaemic episodes	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Partially applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wang 2022B	Insulin degludec/liraglutide v Liraglutide	Hypoglycaemia episodes	Some concerns	Attrition <20% but differential attrition between the liraglutide and degludec, IDegLira arms. (higher in liraglutide due to withdrawal due to adverse events)	Partially applicable	None specified
Wang 2023	Dulaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified
Wang 2023	Dulaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Wang 2023	Dulaglutide v Placebo	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Wang 2023	Dulaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Wang 2023	Dulaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Wang 2023	Dulaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Wang 2023	Dulaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Watada 2019	Insulin degludec/liraglutide v Insulin	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Watada 2019	Insulin degludec/liraglutide v Insulin	Health-related quality of life - overall	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Watada 2019	Insulin degludec/liraglutide v Insulin	Weight change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Watada 2019	Insulin degludec/liraglutide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Watada 2019	Insulin degludec/liraglutide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Watada 2019	Insulin degludec/liraglutide v Insulin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Webb 2020	Liraglutide v Sitagliptin	Hypoglycaemia episodes	Some concerns	Definition of hypoglycaemia not provided so some concerns given open-label trial.	Directly applicable	None specified
Webb 2020	Liraglutide v Sitagliptin	BMI change	Low	None specified	Directly applicable	None specified
Webb 2020	Liraglutide v Sitagliptin	HbA1c change	Low	None specified	Directly applicable	None specified
Webb 2020	Liraglutide v Sitagliptin	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Webb 2020	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Webb 2020	Liraglutide v Sitagliptin	Weight change	Low	None specified	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	HbA1c change	Some concerns	High proportion of missing data	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	Weight change	Some concerns	High proportion of missing data	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Wilding 2012	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Wilding 2013A	Canagliflozin v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Wilding 2013A	Canagliflozin v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Wilding 2013A	Canagliflozin v Placebo	HbA1c change	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wilding 2013A	Canagliflozin v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Wilding 2013A	Canagliflozin v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Wilding 2013A	Canagliflozin v Placebo	Weight change	High	None specified	Directly applicable	None specified
Wilding 2013B	Glipizide v Placebo	All-cause mortality	Some concerns	Lack of info on allocation concealment	Directly applicable	NA
Wilding 2013B	Glipizide v Placebo	Cardiovascular mortality	Some concerns	Lack of info on allocation concealment	Directly applicable	NA
Wilding 2013B	Glipizide v Placebo	Hypoglycaemia episodes	Some concerns	Lack of info on allocation concealment	Directly applicable	NA
Wilding 2013B	Glipizide v Placebo	Severe hypoglycaemic episodes	Some concerns	Lack of info on allocation concealment	Directly applicable	NA
Wiviott 2019	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Acute kidney injury	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Cardiac arrhythmia	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wiviott 2019	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Death from renal causes	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Development of end stage kidney disease	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Diabetic ketoacidosis	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Persistent signs of worsening kidney disease	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Unstable angina	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019	Dapagliflozin v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wiviott 2019 no CKD	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CKD	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CKD	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CKD	Dapagliflozin v Placebo	Diabetic ketoacidosis	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CKD	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CKD	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	Cardiac arrhythmia	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no CVD	Dapagliflozin v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wiviott 2019 no HF	Dapagliflozin v Placebo	3-point MACE	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no HF	Dapagliflozin v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no HF	Dapagliflozin v Placebo	Cardiac arrhythmia	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no HF	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no HF	Dapagliflozin v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no HF	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Wiviott 2019 no HF	Dapagliflozin v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Wu 2014	Pioglitazone v Metformin	BMI change	High	Lack of information on methods of randomisation, blinding and allocation. Lack of information on withdrawals, follow-up and completion rates.	Directly applicable	None specified
Wu 2014	Pioglitazone v Metformin	HbA1c change	High	Lack of information on methods of randomisation, blinding and allocation. Lack of information on	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				withdrawals, follow-up and completion rates.		
Wysham 2014 26 weeks	Dulaglutide v Exenatide	All-cause mortality	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Exenatide	Cardiovascular mortality	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Exenatide	HbA1c change	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Exenatide	Hypoglycaemia episodes	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Exenatide	Weight change	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Placebo	All-cause mortality	High	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Placebo	Cardiovascular mortality	High	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Placebo	HbA1c change	High	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Wysham 2014 26 weeks	Dulaglutide v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Dulaglutide v Placebo	Weight change	High	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Exenatide v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Exenatide v Placebo	Cardiovascular mortality	Some concerns	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Exenatide v Placebo	HbA1c change	Some concerns	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Exenatide v Placebo	Hypoglycaemia episodes	Some concerns	None specified	Directly applicable	None specified
Wysham 2014 26 weeks	Exenatide v Placebo	Weight change	Some concerns	None specified	Directly applicable	None specified
Wysham 2014 52 weeks	Dulaglutide v Exenatide	All-cause mortality	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 52 weeks	Dulaglutide v Exenatide	Cardiovascular mortality	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 52 weeks	Dulaglutide v Exenatide	HbA1c change	Some concerns	Lack of information on allocation concealment, blinding.	Directly applicable	None specified
Wysham 2014 52 weeks	Dulaglutide v Exenatide	Severe hypoglycaemic episodes	Some concerns	Lack of information on allocation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				concealment, blinding.		
Xiao 2015	Pioglitazone v Glipizide	HbA1c change	High	Open-label trial, unclear type of analysis and no available protocol	Directly applicable	None specified
Xiao 2016	Glimepiride v Sitagliptin	HbA1c change	High	No information regarding majority of domains; 52% missing data	Directly applicable	None specified
Xiao 2016	Glimepiride v Sitagliptin	Hospitalisation for heart failure	High	No information regarding majority of domains; 52% missing data	Directly applicable	None specified
Xiao 2016	Glimepiride v Sitagliptin	Non-fatal myocardial infarction	High	No information regarding majority of domains; 52% missing data	Directly applicable	None specified
Xiao 2016	Glimepiride v Sitagliptin	Non-fatal stroke	High	No information regarding majority of domains; 52% missing data	Directly applicable	None specified
Xiao 2016	Glimepiride v Sitagliptin	Weight change	High	No information regarding majority of domains; 52% missing data	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	Weight change	Low	None specified	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	All-cause mortality	High	Open-label study where the analysis	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				did not assess assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.		
Xu 2017	Glimepiride v Gliclazide	Cardiovascular mortality	High	Open-label study where the analysis did not assess assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	Diabetic ketoacidosis	High	Open-label study where the analysis did not assess assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	Hypoglycaemia episodes	High	Open-label study where the analysis did not assess	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.		
Xu 2017	Glimepiride v Gliclazide	Non-fatal myocardial infarction	High	Open-label study where the analysis did not assess assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	Non-fatal stroke	High	Open-label study where the analysis did not assess assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	Severe hypoglycaemic episodes	High	Open-label study where the analysis did not assess assignment to	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				treatment. There was also a high proportion of protocol violations which included non-adherence.		
Xu 2017	Glimepiride v Gliclazide	Unstable angina	High	Open-label study where the analysis did not assess assignment to treatment. There was also a high proportion of protocol violations which included non-adherence.	Directly applicable	None specified
Xu 2017	Glimepiride v Gliclazide	HbA1c change	High	Open-label study where the analysis did not assess assignment to treatment. There was also high attrition, however, attrition was similar between arms.	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	BMI change	Some concerns	mITT analysis with multiple imputation	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	HbA1c change	Some concerns	mITT analysis with multiple imputation	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Weight change	Some concerns	mITT analysis with multiple imputation	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yabe 2020	Semaglutide v Dulaglutide	Health-related quality of life - subscale mental component	High	No info about missing data for this outcome; mITT analysis with multiple imputation	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Health-related quality of life - subscale physical component	High	No info about missing data for this outcome; mITT analysis with multiple imputation	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Acute kidney injury	Low	None specified	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	All-cause mortality	Low	None specified	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Death from renal causes	Low	None specified	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yabe 2020	Semaglutide v Dulaglutide	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yabe 2023	Empagliflozin v Placebo	Health-related quality of life - overall	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	Persistent signs of worsening kidney disease	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Yabe 2023	Empagliflozin v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Yan 2019	Sitagliptin v Insulin	BMI change	Low	None specified	Directly applicable	None specified
Yan 2019	Sitagliptin v Insulin	HbA1c change	Low	None specified	Directly applicable	None specified
Yan 2019	Liraglutide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yan 2019	Liraglutide v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yan 2019	Sitagliptin v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yan 2019	Sitagliptin v Insulin	Weight change	Low	None specified	Directly applicable	None specified
Yan 2019	Liraglutide v Sitagliptin	BMI change	Some concerns	None specified	Directly applicable	None specified
Yan 2019	Liraglutide v Sitagliptin	HbA1c change	Some concerns	Reports data for ITT population but >10% difference in per protocol	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				populations and does not report missing data strategy		
Yan 2019	Liraglutide v Sitagliptin	Weight change	Some concerns	Reports data for ITT population but >10% difference in per protocol populations and does not report missing data strategy	Directly applicable	None specified
Yan 2019	Liraglutide v Insulin	BMI change	Some concerns	Reports data for ITT population but does not report strategy for missing data. >10% difference between groups in per protocol population, but data not reported.	Directly applicable	None specified
Yan 2019	Liraglutide v Insulin	HbA1c change	Some concerns	Reports data for ITT population but does not report strategy for missing data. >10% difference between groups in per protocol population, but data not reported.	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yan 2019	Liraglutide v Insulin	Weight change	Some concerns	Reports data for ITT population but does not report strategy for missing data. >10% difference between groups in per protocol population, but data not reported.	Directly applicable	None specified
Yang 2011	Saxagliptin v Placebo	Hypoglycaemia episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2011	Saxagliptin v Placebo	Non-fatal stroke	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2011	Saxagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2011	Saxagliptin v Placebo	BMI change	High	No info about allocation concealment; mITT analysis with LOCF	Directly applicable	None specified
Yang 2011	Saxagliptin v Placebo	HbA1c change	High	No info about allocation concealment; mITT analysis with LOCF	Directly applicable	None specified
Yang 2011	Saxagliptin v Placebo	Weight change	High	No info about allocation concealment; mITT analysis with LOCF	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yang 2012	Sitagliptin v Placebo	All-cause mortality	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2012	Sitagliptin v Placebo	Cardiovascular mortality	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2012	Sitagliptin v Placebo	Hypoglycaemia episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2012	Sitagliptin v Placebo	Severe hypoglycaemic episodes	Some concerns	No info about allocation concealment	Directly applicable	None specified
Yang 2012	Sitagliptin v Placebo	HbA1c change	High	No info about allocation concealment; mITT analysis with LOCF	Directly applicable	None specified
Yang 2012	Sitagliptin v Placebo	Weight change	High	No info about allocation concealment; mITT analysis with LOCF	Directly applicable	None specified
Yang 2015	Vildagliptin v Placebo	HbA1c change	High	No info about randomisation/allocation concealment; mITT LOCF analysis; trial retrospectively registered	Directly applicable	None specified
Yang 2015	Vildagliptin v Placebo	All-cause mortality	High	No info about randomisation/allocation concealment;	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				trial retrospectively regiestered		
Yang 2015	Vildagliptin v Placebo	Cardiovascular mortality	High	No info about randomisation/allocation concealment; trial retrospectively regiestered	Directly applicable	None specified
Yang 2015	Vildagliptin v Placebo	Hypoglycaemia episodes	High	No info about randomisation/allocation concealment; trial retrospectively regiestered	Directly applicable	None specified
Yang 2015	Vildagliptin v Placebo	Non-fatal stroke	High	No info about randomisation/allocation concealment; trial retrospectively regiestered	Directly applicable	None specified
Yang 2015	Vildagliptin v Placebo	Severe hypoglycaemic episodes	High	No info about randomisation/allocation concealment; trial retrospectively registered	Directly applicable	None specified
Yang 2016	Dapagliflozin v Placebo	All-cause mortality	Some concerns	Baseline differences on some variables	Directly applicable	None specified
Yang 2016	Dapagliflozin v Placebo	Cardiovascular mortality	Some concerns	Baseline differences on some variables	Directly applicable	None specified
Yang 2016	Dapagliflozin v Placebo	Development of end stage kidney disease	Some concerns	Baseline differences on some variables	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yang 2016	Dapagliflozin v Placebo	Hypoglycaemia episodes	Some concerns	Baseline differences on some variables	Directly applicable	None specified
Yang 2016	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Some concerns	Baseline differences on some variables	Directly applicable	None specified
Yang 2016	Dapagliflozin v Placebo	HbA1c change	High	Baseline differences on some variables; mITT LOCF analysis	Directly applicable	None specified
Yang 2016	Dapagliflozin v Placebo	Weight change	High	Baseline differences on some variables; mITT LOCF analysis	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	HbA1c change	High	>10% missing data between groups	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	Weight change	High	>10% missing data between groups	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	Development of end stage kidney disease	Low	None specified	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yang 2018A	Dapagliflozin v Placebo	Non-fatal myocardial infarction	Low	None specified	Directly applicable	None specified
Yang 2018A	Dapagliflozin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Yang 2018B	Lixisenatide v Placebo	HbA1c change	Some concerns	mITT analysis with LOCF	Directly applicable	None specified
Yang 2018B	Lixisenatide v Placebo	Weight change	Some concerns	mITT analysis with LOCF	Directly applicable	None specified
Yang 2018B	Lixisenatide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Yang 2018B	Lixisenatide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Yang 2018B	Lixisenatide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yang 2018B	Lixisenatide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Yang 2021	Linagliptin v Placebo	HbA1c change	Some concerns	mITT analysis, unclear missing data strategy	Directly applicable	None specified
Yang 2021	Linagliptin v Placebo	Weight change	Some concerns	mITT analysis, unclear missing data strategy	Directly applicable	None specified
Yang 2021	Linagliptin v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yang 2021	Linagliptin v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Yang 2021	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yang 2021	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Yang 2022	Insulin glargine/Lixisenatide v Lixisenatide	All-cause mortality	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Yang 2022	Insulin glargine/Lixisenatide v Lixisenatide	Cardiovascular mortality	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Yang 2022	Insulin glargine/Lixisenatide v Lixisenatide	HbA1c change	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Yang 2022	Insulin glargine/Lixisenatide v Lixisenatide	Hypoglycaemia episodes	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Yang 2022	Insulin glargine/Lixisenatide v Lixisenatide	Severe hypoglycaemic episodes	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Yang 2022	Insulin glargine/Lixisenatide v Lixisenatide	Weight change	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	No concerns
Yang 2022	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	None specified
Yang 2022	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	None specified
Yang 2022	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	None specified
Yang 2022	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	None specified
Yang 2022	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	None specified
Yang 2022	Insulin glargine/Lixisenatide v Insulin	Weight change	Some concerns	low attrition, open label due to the mode of administration.	Directly applicable	None specified
Yki-Järvinen 2013	Linagliptin v Placebo	5-point MACE	High	Data for this outcome collected	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				to max 104 weeks, so timepoint for each participant could differ		
Yki-Järvinen 2013	Linagliptin v Placebo	All-cause mortality	High	Data for this outcome collected to max 104 weeks, so timepoint for each participant could differ	Directly applicable	None specified
Yki-Järvinen 2013	Linagliptin v Placebo	Cardiovascular mortality	High	Data for this outcome collected to max 104 weeks, so timepoint for each participant could differ	Directly applicable	None specified
Yki-Järvinen 2013	Linagliptin v Placebo	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Yki-Järvinen 2013	Linagliptin v Placebo	Weight change	High	mITT LOCF analysis; Number of participants for this outcome/missing data not clear	Directly applicable	None specified
Yki-Järvinen 2013	Linagliptin v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yki-Järvinen 2013	Linagliptin v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Yokoyama 2014	Liraglutide v Sitagliptin	Hypoglycaemia episodes	High	No info about randomistion/allocati	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				on concealment; ITT analysis; missing data; trial retrospectively registered		
Yokoyama 2014	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	High	No info about randomistion/allocation concealment; ITT analysis; missing data; trial retrospectively registered	Directly applicable	None specified
Yokoyama 2014	Liraglutide v Sitagliptin	BMI change	High	No info about randomistion/allocation concealment; per protocol analysis; missing data; trial retrospectively registered	Directly applicable	None specified
Yokoyama 2014	Liraglutide v Sitagliptin	HbA1c change	High	No info about randomistion/allocation concealment; per protocol analysis; missing data; trial retrospectively registered	Directly applicable	None specified
Yokoyama 2014	Liraglutide v Sitagliptin	Weight change	High	No info about randomistion/allocation concealment; per protocol analysis; missing data; trial	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				retrospectively registered		
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	HbA1c change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	Weight change	Some concerns	mITT LOCF analysis	Directly applicable	None specified
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	All-cause mortality	Low	None specified	Directly applicable	None specified
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	Death from renal causes	Low	None specified	Directly applicable	None specified
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Yuan 2022	Insulin glargine/Lixisenatide v Insulin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	BMI change	Some concerns	mITT analysis but unclear missing data strategy	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	HbA1c change	Some concerns	mITT analysis but unclear missing data strategy	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Zang 2016	Liraglutide v Sitagliptin	Weight change	Some concerns	mITT analysis but unclear missing data strategy	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	All-cause mortality	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	At night hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	Cardiac arrhythmia	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	Diabetic ketoacidosis	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	Non-fatal stroke	Low	None specified	Directly applicable	None specified
Zang 2016	Liraglutide v Sitagliptin	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	None specified
Zhang 2020B	Exenatide v Insulin	BMI change	High	Lack of info on allocation concealment; lack of information on cointerventions; differential attrition >10%	Directly applicable	NA

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Zhang 2020B	Exenatide v Insulin	HbA1c change	High	Lack of info on allocation concealment; lack of information on cointerventions; differential attrition >10%	Directly applicable	NA
Zhang 2020B	Exenatide v Insulin	Hypoglycaemia episodes	High	Lack of info on allocation concealment; lack of information on cointerventions; differential attrition >10%	Directly applicable	NA
Zhang 2020B	Exenatide v Insulin	Severe hypoglycaemic episodes	High	Lack of info on allocation concealment; lack of information on cointerventions; differential attrition >10%	Directly applicable	NA
Zhang 2020B	Exenatide v Insulin	Weight change	High	Lack of info on allocation concealment; lack of information on cointerventions; differential attrition >10%	Directly applicable	NA
Zhao 2017	Sitagliptin v Placebo	BMI change	High	Concerns in allocation concealment,	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
				method of analysis and attrition.		
Zhao 2017	Sitagliptin v Placebo	HbA1c change	High	Concerns in allocation concealment, method of analysis and attrition.	Directly applicable	None specified
Zhao 2017	Sitagliptin v Placebo	Hypoglycaemia episodes	High	Concerns in allocation concealment, method of analysis and attrition.	Directly applicable	None specified
Zhao 2017	Sitagliptin v Placebo	Weight change	High	Concerns in allocation concealment, method of analysis and attrition.	Directly applicable	None specified
Zinman 2009	Liraglutide v Placebo	HbA1c change	High	None specified	Directly applicable	None specified
Zinman 2009	Liraglutide v Placebo	Hypoglycaemia episodes	High	None specified	Directly applicable	None specified
Zinman 2009	Liraglutide v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Zinman 2009	Liraglutide v Placebo	Weight change	High	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	Acute kidney injury	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Zinman 2019A	Semaglutide v Placebo	All-cause mortality	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	Cardiovascular mortality	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	Health-related quality of life - subscale mental component	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	Health-related quality of life - subscale physical component	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Zinman 2019A	Semaglutide v Placebo	Severe hypoglycaemic episodes	Low	None specified	Directly applicable	Severe or blood glucose-confirmed hypoglycaemia, defined as "an episode that was severe according to the American Diabetes Association classification"

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
Zinman 2019A	Semaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Partially applicable	Hypoglycaemia definition is broad - defined as "American Diabetes Association classified, including hypoglycaemia episodes classified as severe, documented symptomatic, asymptomatic, probable symptomatic, and pseudo-hypoglycaemia"
Zinman 2019B	Semaglutide v Placebo	Severe hypoglycaemic episodes	High	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	BMI change	Low	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	HbA1c change	Low	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Health-related quality of life - subscale mental component	Low	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Health-related quality of life -	Low	None specified	Directly applicable	None specified

Study name	Comparison details	Outcome	Risk of bias	Risk of bias comments	Directness	Directness comments
		subscale physical component				
Zinman 2019B	Semaglutide v Placebo	Hypoglycaemia episodes	Low	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Weight change	Low	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Acute kidney injury	Some concerns	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	All-cause mortality	Some concerns	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Non-fatal myocardial infarction	Some concerns	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Non-fatal stroke	Some concerns	None specified	Directly applicable	None specified
Zinman 2019B	Semaglutide v Placebo	Hospitalisation for heart failure	Some concerns	None specified	Partially applicable	Unclear if heart failure outcome reported was for people hospitalised for heart failure