Search strategies

MEDLINE

1. exp Diabetes Mellitus Type 2/
2. Diabetes Mellitus/
3. ((diabetes or diabetes mellitus or diabetic*) adj1 (type 2 or type II or type ii or non-insulin dependent or noninsulin dependent or adult onset or mature onset or late onset)).tw.
4. NIDDM.tw.
5. Diabetic Nephropathies/
6. (diabetic nephropath* or diabetic kidney disease).tw.
7. or/1-6
8. exp Insulin, Long Acting/
9. ((long acting or longer acting or intermediate acting) adj insulin*).tw.
10. (insulin adj1 degludec).tw.
11. (insulin adj1 glargine).tw.
12. (insulin adj1 detemir).tw.
13. (insulin adj1 zinc).tw.
14. (insulin adj1 isophane).tw.
15. (insulin adj1 aspart).tw.
16. (insulin adj1 lispro).tw.
17. (insulin adj1 lente).tw.
18. (insulin adj1 ultralente).tw.
19. Sulfonylurea Compounds/
20. Acetohexamide/
21. Carbutamide/
22. Chlorpropamide/
23. Gliclazide/
24. Glipizide/
25. Glyburide/
26. Tolazamide/
27. (sulphonylurea or sulphonylureas).tw.
28. acetohexamide.tw.
29. carbutamide.tw.
30. chlorpropamide.tw.
31. glibenclamide.tw.
32. gliclazide.tw.
33. glimepiride.tw.
34. glibornuride.tw.
35. glipizide.tw.
36. gliquidone.tw.
37. glyburide.tw.
38. glycopyramide.tw.
39. tolazamide.tw.
40. Biguanides/
41. biguanides.tw.
42. Metformin/
43. metformin.tw.
44. alpha-Glucosidases/ai
45. alpha glucosidase inhibitor*.tw.

46. Acarbose/
47. acarbose.tw.
48. miglitol.tw.
49. voglibose.tw.
50. Thiazolidinediones/
51. thiazolidinedione*.tw.
52. pioglitazone.tw.
53. rivoglitazone.tw.
54. rosiglitazone.tw.
55. meglitinide*.tw.
56. repaglinide.tw.
57. nateglinide.tw.
58. mitiglinide.tw.
59. Receptors, Glucagon/
60. Glucagon-like Peptide 1/
61. (glucagon-like peptide 1 receptor inhibitor* or glucagon-like peptide 1 receptor agonist* or glucagon-like peptide 1 inhibitor* or glucagon-like peptide 1 agonist* or GLP-1 receptor inhibitor* or GLP-1 receptor agonist* or GLP-1 inhibitor* or GLP-1 agonist*).tw.
62. dulaglutide.tw.
63. (exenatide or exendin 4).tw.
64. liraglutide.tw.
65. semaglutide.tw.
66. taspoglutide.tw.
67. lixisenatide.tw.
68. albiglutide.tw.
69. Dipeptidyl-peptidase IV Inhibitors/
70. (dipeptidyl-peptidase IV Inhibitor* or dipeptidyl-peptidase 4 Inhibitor* or ((DPP4 or DPP 4 or DPP IV) adj inhibitor*)).tw.
71. omarigliptin.tw.
72. vildagliptin.tw.
73. sitagliptin.tw.
74. saxagliptin.tw.
75. linagliptin.tw.
76. alogliptin.tw.
77. septagliptin.tw.
78. gemigliptin.tw.
79. anagliptin.tw.
80. teneligliptin.tw.
81. evogliptin.tw.
82. dutogliptin.tw.
83. retagliptin.tw.
84. Sodium-Glucose Transporter 2/
85. (sodium glucose transporter 2 inhibitor* or sodium glucose transporter ii inhibitor* or SGLT 2 inhibitor*).tw.
86. (sodium glucose cotransporter adj3 inhibitor*).tw.
87. (sodium glucose co transporter adj3 inhibitor*).tw.
88. canagliflozin.tw.
89. dapagliflozin.tw.
90. empagliflozin.tw.
91. ertugliflozin.tw.

92. tofogliflozin.tw.
93. bexagliflozin.tw.
94. henagliflozin.tw.
95. ipragliflozin.tw.
96. licogliflozin.tw.
97. luseogliflozin.tw.
98. remogliflozin.tw.
99. sergliflozin.tw.
100. sotagliflozin.tw.
101. (amylin adj1 (analogue* or derivative*)).tw.
102. pramlintide.tw.
103. Insulins/
104. Hypoglycemic Agents/
105. or/8-104
106. and/7,105
107. randomized controlled trial.pt.
108. controlled clinical trial.pt.
109. pragmatic clinical trial.pt.
110. randomized.ab.
111. randomised.ab
112. placebo.ab.
113. clinical trials as topic/
114. randomly.ab.
115. trial.ti.
116. or/107-115
117. animals/ not (humans/ and animals/)
118. 116 not 117
119. and/106,118

Embase

1. diabetes mellitus/
2. non insulin dependent diabetes mellitus/
3. ((diabetes or diabetes mellitus or diabetic*) adj1 (type 2 or type II or type ii or non-insulin dependent or noninsulin dependent or adult onset or mature onset or late onset)).tw.
4. NIDDM.tw.
5. Diabetic Nephropathy/
6. (diabetic nephropath* or diabetic kidney disease).tw.
7. Or/1-6
8. long acting insulin/
9. ((long acting or longer acting or intermediate acting) adj insulin*).tw.
10. insulin degludec/
11. (insulin adj1 degludec).tw.
12. insulin detemir/
13. (insulin adj1 detemir).tw.
14. insulin glargine/
15. (insulin adj1 glargine).tw.
16. insulin zinc suspension/
17. (insulin adj1 zinc).tw.
18. insulin aspart/
19. (insulin adj1 aspart).tw.
20. insulin lispro/
21. (insulin adj1 lispro).tw.
22. isophane insulin/
23. (insulin adj1 isophane).tw.
24. (insulin adj1 lente).tw.
25. (insulin adj1 ultralente).tw.
26. meglitinide/
27. meglitinide*.tw.
28. mitiglinide/
29. mitiglinide.tw.
30. nateglinide/
31. nateglinide.tw.
32. repaglinide/
33. repaglinide.tw.
34. amylin derivative/
35. (amylin analogue* or amylin derivative*).tw.
36. pramlintide/
37. pramlintide.tw.
38. biguanide derivative/
39. biguanide*.tw.
40. metformin.tw,sh.
41. sulphonylurea derivative/
42. sulphonylurea*.tw.
43. acetohexamide/
44. carbutamide/
45. chlorpropamide/
46. glibenclamide/
47. glibornuride/
48. gliclazide/

49. glimepiride.sh,tw.
50. glipizide/
51. gliquidone/
52. tolazamide/
53. acetohexamide.tw.
54. carbutamide.tw.
55. chlorpropamide.tw.
56. glibenclamide.tw.
57. gliclazide.tw.
58. glimepiride.tw.
59. glibornuride.tw.
60. glipizide.tw.
61. gliquidone.tw.
62. glyburide.tw.
63. glycopyramide.tw.
64. tolazamide.tw.
65. alpha glucosidase inhibitor/
66. alpha glucosidase inhibitor*.tw.
67. acarbose/
68. miglitol/
69. voglibose/
70. acarbose.tw.
71. miglitol.tw.
72. voglibose.tw.
73. glitazone derivative/
74. (glitazone adj1 (derivative* or analogue*)).tw.
75. thiazolidinedione*.tw.
76. pioglitazone/
77. rivoglitazone/
78. rosiglitazone/
79. pioglitazone.tw.
80. rivoglitazone.tw.
81. rosiglitazone.tw.
82. glucagon like peptide 1 receptor agonist/
83. (glucagon-like peptide 1 receptor inhibitor* or glucagon-like peptide 1 receptor agonist* or glucagon-like peptide 1 inhibitor* or glucagon-like peptide 1 agonist* or GLP-1 receptor inhibitor* or GLP-1 receptor agonist* or GLP-1 inhibitor* or GLP-1 agonist*).tw.
84. albiglutide/
85. dulaglutide/
86. exendin 4/
87. liraglutide/
88. lixisenatide/
89. semaglutide/
90. taspoglutide/
91. albiglutide.tw.
92. dulaglutide.tw.
93. (exenatide or exendin 4).tw.
94. liraglutide.tw.
95. lixisenatide.tw.
96. semaglutide.tw.

97. taspoglutide.tw.
98. dipeptidyl peptidase IV inhibitor/
99. (dipeptidyl-peptidase IV Inhibitor* or dipeptidyl-peptidase 4 Inhibitor* or ((DPP4 or DPP 4 or DPP IV) adj inhibitor*)).tw.
100. alogliptin/
101. anagliptin/
102. gemigliptin/
103. linagliptin/
104. omarigliptin/
105. saxagliptin/
106. sitagliptin/
107. teneligliptin/
108. vildagliptin/
109. alogliptin.tw.
110. anagliptin.tw.
111. gemigliptin.tw.
112. linagliptin.tw.
113. omarigliptin.tw.
114. saxagliptin.tw.
115. sitagliptin.tw.
116. teneligliptin.tw.
117. vildagliptin.tw.
118. evogliptin.tw.
119. dutogliptin.tw.
120. retagliptin.tw.
121. sodium glucose cotransporter 2 inhibitor/
122. (sodium glucose transporter 2 inhibitor* or sodium glucose transporter ii inhibitor* or SGLT 2 inhibitor*).tw.
123. (sodium glucose cotransporter adj3 inhibitor*).tw.
124. (sodium glucose co transporter adj3 inhibitor*).tw.
125. canagliflozin/
126. dapagliflozin.tw.
127. empagliflozin/
128. ertugliflozin/
129. tofogliflozin/
130. canagliflozin.tw.
131. dapagliflozin.tw.
132. empagliflozin.tw.
133. ertugliflozin.tw.
134. tofogliflozin.tw.
135. bexagliflozin.tw.
136. henagliflozin.tw.
137. ipragliflozin.tw.
138. licogliflozin.tw.
139. luseogliflozin.tw.
140. remogliflozin.tw.
141. sergliflozin.tw.
142. sotagliflozin.tw.
143. antidiabetic agent/
144. oral antidiabetic agent/
145. or/8-144

146. and/7,145
147. randomized controlled trial/
148. double-blind procedure/
149. single-blind procedure/
150. random$.tw.
151. factorial$.tw.
152. placebo$.tw.
153. (double$ adj blind$).tw.
154. (singl$ adj blind$).tw.
155. assign$.tw.
156. allocat$.tw.
157. or/147-156
158. and/146,157
159. MEDLINE.cr.
160. 158 not 159
161. (mouse or mice or murine or rat or rats or dog or dogs or animal*).ti.
162. 160 not 161

Cochrane Central Register of Controlled Trials (CENTRAL)

#1. MeSH descriptor: [Diabetes Mellitus] this term only
#2. ((diabetes or diabetic* or "diabetes mellitus") near/1 ("type 2" or "type ii" or "non-insulin dependent" or "non insulin dependent" or "noninsulin dependent" or "adult onset" or "mature onset" or "late onset")):ti,ab,kw
#3. ("diabetes mellitus" not "insulin dependent diabetes mellitus"):kw
#4. #3 and EMBASE
#5. NIDDM:ti,ab,kw
#6. ((diabetic next nephropath*) or "diabetic kidney disease"):ti,ab,kw
#7. {or #1-#2, #4-#6}
#8. ((long acting or longer acting or intermediate acting) near/1 insulin*):ti,ab,kw
#9. insulin near/1 degludec:ti,ab,kw
#10. insulin near/1 detemir:ti,ab,kw
#11. insulin near/1 glargine:ti,ab,kw
#12. insulin near/1 zinc
#13. insulin near/1 aspart:ti,ab,kw
#14. insulin near/1 lispro:ti,ab,kw
#15. insulin near/1 isophane:ti,ab,kw
#16. insulin near/1 ultralente:ti,ab,kw
#17. insulin near/1 lente
#18. meglitinide*:ti,ab,kw
#19. mitiglinide:ti,ab,kw
#20. nateglinide:ti,ab,kw
#21. repaglinide:ti,ab,kw
#22. (amylin next analogue* or amylin next derivative*):ti,ab,kw
#23. pramlintide:ti,ab,kw
#24. biguanide*:ti,ab,kw
#25. metformin:ti,ab,kw
#26. (sulfonylurea* or sulphonylurea*):ti,ab,kw
#27. acetohexamide:ti,ab,kw
#28. carbutamide:ti,ab,kw
#29. chlopropramide:ti,ab,kw
#30. glibenclamide:ti,ab,kw
#31. gliclazide:ti,ab,kw
#32. glimepiride:ti,ab,kw
#33. glibornuride:ti,ab,kw
#34. glipizide:ti,ab,kw
#35. gliquidone:ti,ab,kw
#36. glyburide:ti,ab,kw
#37. glycopyramide:ti,ab,kw
#38. tolazimide:ti,ab,kw
#39. MeSH descriptior: [alpha-Glucosidases] this term only and with qualifier(s): [Antagonists & inhibitors
#40. alpha next glucosidase next inhibitor*:ti,ab,kw
#41. acarbose:ti,ab,kw
#42. miglitol:ti,ab,kw
#43. voglibose:ti,ab,kw
#44. (glitazone near/1 (derivative* or analogue*)):ti,ab,kw
#45. thiazolidinedione:ti,ab,kw
#46. pioglitazone:ti,ab,kw
#47. rivoglitazone:ti,ab,kw

#48. rosiglitazone:ti,ab,kw
#49. MeSH descriptor: [Receptors, Glucagon] explode all trees and with qualifier(s): [Agonists - AG]
#50. MeSH descriptor: [Glucagon-Like Peptide 1] explode all trees and with qualifier(s): [Antagonists & inhibitors - AI]
#51. ("glucagon-like peptide 1 receptor inhibitor" or "glucagon-like peptide 1 receptor agonist" or "glucagon-like peptide 1 inhibitor" or "glucagon-like peptide 1 agonist" or "GLP-1 receptor inhibitor" or "GLP-1 receptor agonist" or "GLP-1 inhibitor" or "GLP-1 agonist"):ti,ab,kw
#52. ("glucagon-like peptide 1 receptor inhibitors" or "glucagon-like peptide 1 receptor agonists" or "glucagon-like peptide 1 inhibitors" or "glucagon-like peptide 1 agonists" or "GLP-1 receptor inhibitors" or "GLP-1 receptor agonists" or "GLP-1 inhibitors" or "GLP-1 agonists"):ti,ab,kw
#53. albiglutide:ti,ab,kw
#54. dulaglutide:ti,ab,kw
#55 (exenatide or "exendin 4"):ti,ab,kw
#56 liraglutide:ti,ab,kw
#57 lixisenatide:ti,ab,kw
#58 semaglutide:ti,ab,kw
#59 taspoglutide:ti,ab,kw
#60 ("dipeptidyl-peptidase IV Inhibitor" or "dipeptidylpeptidase 4 Inhibitor" or "dipeptidyl-peptidase IV Inhibitors" or "dipeptidyl-peptidase 4 Inhibitors"):ti,ab,kw
#61 ((DPP4 or DPP 4 or DPP IV) next inhibitor*):ti,ab,kw
#62 alogliptin:ti,ab,kw
#63 anagliptin:ti,ab,kw
#64 gemigliptin:ti,ab,kw
#65 linagliptin:ti,ab,kw
#66 omarigliptin:ti,ab,kw
#67 saxagliptin:ti,ab,kw
#68 sitagliptin:ti,ab,kw
#69 teneligliptin:ti,ab,kw
#70 vildagliptin:ti,ab,kw
#71 evogliptin:ti,ab,kw
#72 dutogliptin:ti,ab,kw
#73 retagliptin:ti,ab,kw
#74 MeSH descriptor: [Sodium-Glucose Transporter 2] explode all trees and with qualifier(s): [Antagonists & inhibitors - AI]
#75 ("sodium glucose transporter 2 inhibitor" or "sodium glucose transporter ii inhibitor" or "SGLT 2 inhibitor" or "sodium glucose transporter 2 inhibitors" or "sodium glucose transporter ii inhibitors" or "SGLT 2 inhibitors"):ti,ab,kw
#76 ("sodium glucose cotransporter" near/3 inhibitor*):ti,ab,kw
#77 ("sodium glucose co-transporter" near/3 inhibitor*):ti,ab,kw
#78 canagliflozin:ti,ab,kw
#79 dapagliflozin:ti,ab,kw
#80 empagliflozin:ti,ab,kw
#81 ertugliflozin:ti,ab,kw
#82 tofogliflozin:ti,ab,kw
#83 bexagliflozin:ti,ab,kw
#84 henagliflozin:ti,ab,kw
#85 ipragliflozin:ti,ab,kw

#86 licogliflozin:ti,ab,kw
#87 luseogliflozin:ti,ab,kw
#88 remogliflozin:ti,ab,kw
#89 sergliflozin:ti,ab,kw
#90 sotagliflozin:ti,ab,kw
#91 MeSH descriptor: [Insulins] this term only
#92 MeSH descriptor: [Hypoglycemic Agents] this term only
#93 (antidiabetic next agent*):kw
#94 (oral next antidiabetic next agent*):kw
#95 {or #8-#94}
#96 {and #7, #95}

Appendix 2 Included studies

Study	Trial registration	Number of participants	Year	Duration of follow-up (months)	Country	Randomised treatments	Dose	Setting	Age (mean), years	Age (SD)	% men	HbA1C (mean), %	HbA1C (SD)	BMI (mean), kg/m2	BMI (SD)	Duration of diabetes (years)	Cardiovascular disease (%)	Estimated glomerular filtration rate	Albumin : creatinine ratio	Additional non-randomised glucose-lowering interventions
3D	UMIN000003784	80	2015	5.5	Japan	Sitagliptin	50 mg daily	Heart failure	67.8	10.5	50	7.1	0.7	27.7	4.1	48	13	74.8		Metformin, sulfonylurea, or pioglitazone
3D						Voglibose	0.6 mg daily		66.7	9.8	65	6.9	0.5	25.7	4.3	38.5	5	70.5		
4B	NCT00960661	627	2014	7.5	Multinational	Exenatide	10-20 mcg daily		59.5	9.6	52	8.3	1	32.7	4.7	12				Metformin + insulin glargine
4B						Insulin lispro	Titrated		59.4	9.3	51	8.2	1	32.3	4.7	11				
4T	ISCRTN51125379	473	2007	12	Multinational	Insulin detemir	Titrated		61.9	10	61.1	8.4	0.8	29.7	4.6	9				Metformin + sulfonylurea
4T						Insulin aspart	Titrated		61.6	10.5	63.6	8.6	0.8	29.6	4.5	9				
1860-LIRA-DPP-4	NCT00700817	665	2010	6	Multinational	Sitagliptin	100 mg daily		55	9	55	8.5	0.7	32.6	5.4	6.3				Metformin
1860-LIRA-DPP-4						Liraglutide	1.8 mg daily		55	9.1	52	8.4	0.7	33.1	5.1	6.4				
1860-LIRA-DPP-4						Liraglutide	1.2 mg daily		55.9	9.6	52	8.4	0.8	32.6	5.2	6				
Abe 2008	Not provided	63	2008	22	Japan	Pioglitazone	15-30 mg daily	Haemodialysis	65.2	12.1	67.7			22.2	2.5	16.6				Alpha glucosidase inhibitor ± meglitinide
Abe 2008						Control			67.2	9.4	68.9			22.2	2.7	16.3				
Abe 2016	UMIN000018445	82	2016	5.5	Japan	Saxagliptin	2.5 mg daily	Haemodialysis	66.9	9.4	65.9	6.5	0.8	22.8	3.7		17.1			Oral drugs and/or insulin
Abe 2016						Control			66.3	9.3	68.3	6.5	0.7	22.9	3.7		14.6			
ACTION-J	UMIN000002333	54	2011	11	Japan	Pioglitazone	15-30 mg daily		56	9.7	81.8	8.59	1.3	25.5	3.1	13.4				Insulin
ACTION-J						Control			57.2	11.3	69.2	8.64	1.2	26.9	4.4	14.8				
ADOPT	NCT00279045	4360	2006	48	Multinational	Metformin	500-2000 mg daily		57.9	9.9	59.4	7.36	0.9	32.1	6.1					None
ADOPT						Glyburide	2.5-15 mg daily		56.4	10.2	58	7.35	0.9	32.2	6.3					
ADOPT						Rosiglitazone	4-8 mg daily		56.3	10	55.7	7.36	0.9	32.2	6.7					
Ahmann 2015	NCT01617434	450	2015	5.5	Multinational	Liraglutide	1.8 mg daily		59.3	9.2	53.3	8.2	0.8	32.3	5.6	12.1				Metformin + basal insulin
Ahmann 2015						Placebo			57.5	11.1	60.4	8.3	0.9	32.2	5.7	12.1				
Ahrén 2004	Not applicable	71	2004	12	Sweden	Vildagliptin	50 mg daily		58.4	9.2	61.9	7.6	0.6	29.6	3.7	5.8				Metformin
Ahrén 2004						Placebo			54.3	12.2	75.9	7.8	0.6	29.9	3.6	4.6				
Allegretti 2019	NCT02836873	312	2019	6	Multinational	Bexagliflozin	20 mg daily	Chronic kidney disease	69.3	8.36	58.6	8.01	0.79	30.3	5.99	15.5		45.4		Oral hypoglycaemic agents
Allegretti 2019						Placebo			69.9	8.29	67.1	7.95	0.81	30.1	5.77	16.3		44.78		
Alogliptin Study 007	NCT00286468	500	2009	6	Multinational	Alogliptin	25 mg daily		56.5	11.7	50	8.09	0.9	30	4.8	7.6				Sulfonylurea
Alogliptin Study 007						Alogliptin	12.5 mg daily		56.5	11.1	54.7	8.08	0.83	30.2	4.8	7.8				
Alogliptin Study 007						Placebo			57.1	10	51.5	8.15	0.85	30	5.3	7.7				
Alogliptin Study 009	NCT00286494	493	2009	6	Multinational	Alogliptin	25 mg daily		55.4	10.2	62.8	8	0.8	33.1	5.4	7.4				Thiazolidinedione ± metformin or sulfonylurea
Alogliptin Study 009						Alogliptin	12.5 mg daily		55.5	9.4	55.3	8.1	0.9	32.3	5.7	7.7				
Alogliptin Study 009						Placebo			55.2	10.8	54.6	8	0.8	33.2	6.2	7.8				
Alogliptin Study 010	NCT00286455	328	2008	6	Multinational	Alogliptin	25 mg daily													None
Alogliptin Study 010						Alogliptin	12.5 mg daily													
Alogliptin Study 010						Placebo														
Alvarsson 2003	Not applicable	51	2003	12	Sweden	Glibenclamide	1.75-3.5 mg daily		55.6	7.3	71.4	6.9	0.9	27.8	3.7					None
Alvarsson 2003						Mixtard 30/70 insu	Titrated		51.1	7.2	61.1	7.3	1.7	27.3	3					
APOLLO	NCT00311818	415	2008	12	Multinational	Insulin glargine	Titrated		60	9	52	8.7	0.96	29.2	3.7	9				Oral agents excluding alpha-glucosidase inhibitors
APOLLO						Insulin lispro	Titrated		59.7	9	59	8.67	0.97	29.4	3.5	8.5				
Apovian 2010	Not provided	194	2010	5.5	USA	Exenatide	10 mcg daily		54.5	10	37	7.7	0.9	33.6	3.7	5.7				Metformin or sulfonylurea
Apovian 2010						Placebo			55.1	9	38	7.5	0.8	33.9	4.3	5.3				
APPROACH	NCT00116831	672	2010	18	Multinational	Glipizide	5-15 mg daily	Coronary artery disease	60.2	9	65.8	7.2	0.9	29.8	5.3					1-2 oral agents
APPROACH						Rosiglitazone	4-8 mg daily		61.8	8.4	70	7.1	0.8	29.3	5.5					
APRIME	UMIN000004367	63	2011	12	Japan	Metformin	500-750 mg daily	Chronic kidney disease	62.5	10.2	75	7.9	1.1	24.5	3.4	9.5	0	75	111	Insulin or oral hypoglycemic agents other than thiazolidinediones/metformin
APRIME						Pioglitazone	15 mg daily		62.4	8.4	67.7	8	1.1	25.6	3.3	11.6	0	79	143	
Araki 2015	NCT01368081	336	2015	12	Japan	Metformin	500-2250 mg daily		60	10.2	75	7.93	0.79	25.2	3.6			86.9		Monotherapy with sulfonylurea, biguanide, thiazolidinedione, alpha glucosidase inhibitor, DPP-4 inhibitor or glinide
Araki 2015						Empagliflozin	25 mg daily		61.8	9.6	70	8.06	0.76	25.2	4.2			85.6		
Araki 2015						Empagliflozin	10 mg daily		61.3	9.9	73	7.99	0.73	24.6	3.8			87.1		
Araki 2015a	NCT01584232	361	2015	5.5	Japan	Dulaglutide	0.75 mg weekly		57.5	10.5	69	8.1	0.8	26.1	3.6	8.9				Biguanide and/or sulphonylurea
Araki 2015a						Insulin glargine	Titrated		56.1	11.3	74	8	0.9	25.9	3.9	8.8				
Arechavaleta 2011	NCT00701090	1035	2011	7	Multinational	Glimepiride	1-6 mg daily		56.2	10.1	53.8	7.5	0.8	30.2	4.4	6.7				Metformin
Arechavaleta 2011						Sitagliptin	100 mg daily		56.3	9.7	55	7.5	0.7	29.7	4.5	6.8				
Arjona Ferreira 2013	NCT00509236	129	2013	12.4	Multinational	Glipizide	2.5-20 mg daily	Dialysis	58.5	9.9	56.9	7.8	0.7	26.3	4.3		27.7			None
Arjona Ferreira 2013						Sitagliptin	25 mg daily		60.5	9.1	62.5	7.9	0.7	27.3	5.7		32.8			
Arjona Ferreira 2013a	NCT00509262	423	2013	12.4	Multinational	Glipizide	2.5-20 mg daily	Chronic kidney disease	64.3	9.2	54.9	7.8	0.7	27	4.8	10.1				None
Arjona Ferreira 2013a						Sitagliptin	25-50 mg daily		64.8	10.6	59.3	7.8	0.7	26.5	4.8	10.7				
Arturi 2017	Not provided	32	2017	12	Italy	Insulin glargine	Titrated	Heart failure	60		75	7.9			30.8					Metformin +/- sulfonylurea
Arturi 2017						Sitagliptin	100 mg daily		60.5		60	8.3			30.9					
Arturi 2017						Liraglutide	1.8 mg daily		59.5		70	8.2			33.2					
Asian Acarbose Study	Not provided	121	1998	5.5	Multinational	Acarbose	300 mg daily		54	10	51.6	8.6	1.1	25.6	3.8	2.1				None
Asian Acarbose Study						Placebo			52.8	10.2	51.6	8.2	1	25.4	3.9	2.7				
Aso 2019	Not provided	57	2019	5.5	Unclear	Dapagliflozin	5 mg daily													Unclear
Aso 2019						Control														
Avilés-Santa 1999	Not provided	43	1999	5.5	USA	Metformin	2000 mg daily		53.1	9.4	28.6	9	1.4			9.2				Insulin
Avilés-Santa 1999						Placebo			54.6	7.8	45.5	9.1	1.5			10.1				
AWARD-1	NCT01064687	976	2014	6	Multinational	Exenatide	10-20 mcg daily		55	10	57	8.1	1.3	34	5	9				Metformin + thiazolidinedione
AWARD-1						Dulaglutide	1.5 mg weekly		56	10	58	8.1	1.3	33	5	9				
AWARD-1						Dulaglutide	0.75 mg weekly		56	9	60	8.1	1.2	33	6	9				
AWARD-1						Placebo			55	10	59	8.1	1.3	33	6	9				
AWARD-2	NCT01075282	807	2015	17.7	Multinational	Dulaglutide	1.5 mg weekly		56	10	53	8.2	1	31	5	9				Metformin + sulfonylurea
AWARD-2						Dulaglutide	0.75 mg weekly		57	9	50	8.1	1	32	5	9				
AWARD-2						Insulin glargine	Titrated		57	9	52	8.1	1	32	6	9				
AWARD-3	NCT01126580	807	2014	12	Multinational	Metformin	2000 mg daily		55	10	45	7.6	0.8	33	5	3				None
AWARD-3						Dulaglutide	1.5 mg weekly		56	10	42	7.6	0.9	34	6	3				
AWARD-3						Dulaglutide	0.75 mg weekly		56	11	44	7.6	0.9	33	6	3				
AWARD-4	NCT01191268	884	2015	12	Multinational	Dulaglutide	1.5 mg weekly		58.9	9.6	54	8.46	1.08	32	5.1	12.8				Insulin + metformin
AWARD-4						Dulaglutide	0.75 mg weekly		59.3	9	50	8.4	1.03	33.1	5.2	12.4				
AWARD-4						Insulin glargine	Titrated		59.9	9.1	56	8.53	1.03	32.4	5.3	13				
AWARD-5	NCT00734474	1098	2014	6	Multinational	Sitagliptin	100 mg daily		54	10	48	8.1	1.1	31	4	7				Metformin
AWARD-5						Dulaglutide	1.5 mg weekly		54	10	48	8.1	1.1	31	5	7				
AWARD-5						Dulaglutide	0.75 mg weekly		54	10	44	8.2	1.1	31	4	7				
AWARD-5						Placebo			55	9	51	8.1	1.1	31	4	7				
AWARD-7	NCT01621178	577	2018	5.5	Multinational	Dulaglutide	1.5 mg weekly	Chronic kidney disease	64.7	8.83	54	8.59	0.9	32.1	4.8	17.57		38.1		Insulin +/- hypoglycaemic agent
AWARD-7						Dulaglutide	0.75 mg weekly		64.7	8.61	55	8.6	1.1	33	5.5	17.95		38.3		
AWARD-7						Insulin glargine	Titrated		64.3	8.41	48	8.6	5.3	1	32.4	18.7		38.5		
AWARD-8	NCT01769378	299	2016	5.5	Multinational	Dulaglutide	1.5 mg weekly		57.7	10.2	43.5	8.4	0.7	30.9	5.2	7.8				Sulfonylurea
AWARD-8						Placebo			58.2	7.4	46.7	8.4	0.7	32.4	5.9	6.8				
AWARD-9	NCT02152371	300	2017	6	Multinational	Dulaglutide	1.5 mg weekly		60.2	9.5	56.7	8.4	0.9	32.8	4.9	13				Insulin glargine ± metformin
AWARD-9						Placebo			60.6	10.1	58.7	8.3	0.8	32.6	4.9	13.3				
AWARD-10	NCT02597049	424	2018	5.5	Multinational	Dulaglutide	1.5 mg weekly		56.2	9.26	54	8.04	0.65	32.87	5.56	9.21				SGLT2 inhibitor +/- metformin
AWARD-10						Dulaglutide	0.75 mg weekly		58.6	9.14	49	8.04	0.61	32.77	6.27	10.05				
AWARD-10						Placebo			57.1	9.59	47	8.05	0.66	32.39	4.98	8.87				
AWARD-CHN1	NCT01644500	737	2018	6	China, South	Glimepiride	1-3 mg daily		52	10.1	53.7	7.9	1	25.7	3.1	3.8				None
AWARD-CHN1						Dulaglutide	1.5 mg weekly		52.7	10.8	56.1	8	1	25.8	3.4	4				
AWARD-CHN1						Dulaglutide	0.75 mg weekly		53.8	10.1	53.1	8	1	26.2	3.5	3.5				
Ba 2017	NCT01590771	498	2017	5.5	China	Sitagliptin	100 mg daily		57.5	9.5	47	8.61	1.06	25.4	3.2	7.1				Sulfonylurea ± metformin
Ba 2017						Placebo			56.5	9.3	53	8.48	0.91	25.3	3.2	6.9				
Bachmann 2003	Not applicable	373	2003	18	Europe	Acarbose	100 mg daily		63.8	7.1	47.6	9.42	0.66	29	3.1					Sulfonylurea
Bachmann 2003						Placebo			63.3	7.2	43.4	9.38	0.73	29	2.9					
Bailey 2010	NCT00528879	546	2010	5.5	Multinational	Dapagliflozin	10 mg daily		52.7	9.9	57	7.92	0.8	31.2	5.1	6.1				Metformin

Bailey 2010						Dapagliflozin	5 mg daily		54.3	9.4	50	8.17	1	31.4	5	6.4						
Bailey 2010						Dapagliflozin	2.5 mg daily		55	9.3	51	7.99	0.9	31.6	4.8	6						
Bailey 2010						Placebo			53.7	10.3	55	8.11	1	31.8	5.3	5.8						
Bailey 2012	Not provided	282	2012	5.5	Multinational	Dapagliflozin	5 mg daily		51.3	11.51	47.1	7.9	1.03	30.97	5.68	1.4						None
Bailey 2012						Dapagliflozin	2.5 mg daily		53.5	10.6	45.9	8.1	1.07	31.13	5.47	1.5						
Bailey 2012						Dapagliflozin	1 mg daily		53.7	9.04	52.8	7.8	0.98	32.53	5.68	1.6						
Bailey 2012						Placebo			53.5	11.08	54.4	7.8	1.12	32.47	4.91	1.1						
Bajaj 2014	NCT00996658	272	2014	5.5	Multinational	Linagliptin	5 mg daily		53.1	9.7	45.4	8.39	0.84	28.2	5.2							Metformin + thiazolidinedione
Bajaj 2014						Placebo			55.2	8.4	55.1	8.47	0.78	28.1	5.5							
Bakris 2006	Not provided	389	2006	7.4	Multinational	Glyburide	5 mg daily	Chronic kidney disease	58.8	9.8	69	8.3	1.6	31.8	6	7.6				63.5		Metformin
Bakris 2006						Rosiglitazone	4 mg daily		60	9.6	63	8.5	1.7	31.6	5.6	8				65.94		
BALANCE	NCT02126358	193	2018	5.5	Korea	Gemigliptin	50 mg daily		55.5	11	56.4	7.79	0.79	25.6	3.6	6.2						Metformin
BALANCE						Standard care			56.2	9.2	51	7.78	0.78	25.2	3.3	6.8						
Banerji 1995	Not applicable	20	1995	36	United Kingdom	Glipizide					70	14	3	26.7	2.5							None
Banerji 1995						Placebo					30	12	2	27.5	3.2							
Barnett 2003	Not applicable	171	2003	5.5	United Kingdom	Rosiglitazone	4 mg daily		54.1	32-78	75	9.06	1.3	26.4	20-45	6.5						Sulphonylurea
Barnett 2003						Placebo			54.3	28-76	80	9.21	1.27	26.8	21-39	6.5						
Barnett 2012	NCT00757588	455	2012	5.5	Multicentre	Saxagliptin	5 mg daily		57.2	9.43	40	8.7	0.9	32.6	5.65	11.8						Metformin ± insulin
Barnett 2012						Placebo			57.3	9.27	45	8.6	0.9	31.8	4.76	12.2						
Barnett 2013	NCT01084005	241	2013	6	Multinational	Linagliptin	5 mg daily		74.9	4.4	71.6	7.8	0.8	29.6	4.7							Metformin ± sulfonylurea ± basal insulin
Barnett 2013						Placebo			74.9	4.2	62	7.7	0.7	29.8	4.5							
Barzilai 2011	NCT00305604	206	2011	5.5	USA	Sitagliptin	50-100 mg daily		71.6	6.1	47	7.8	0.8	30.8	5.9	7.2		70				None
Barzilai 2011						Placebo			72.1	6	47	7.8	0.7	31.1	7.2	7		72				
Bayrasheva 2020	Not provided	44	2020	6	Russia	Vildagliptin	50 mg daily		62.0	58-63	39.1	7.3	6.9-7.6	31.6	30.3-34.9	8.0		90	27.2			Insulin
Bayrasheva 2020						Control			60.0	54-66	42.9	7.2	6.6-7.6	31.5	28.0-35.4	10.0		91	26.7			
BEGIN: ADD TO GLP-1	NCT01664247	346	2016	6	Multinational	Insulin degludec	Titrated		57	10	56.3	7.6	0.6	32	5.7	9.7						Metformin ± sulfonylurea, glinide, DPP-4 inhibitor, or exenatide plus liraglutide
BEGIN: ADD TO GLP-1						Placebo			57.3	9.4	60.5	7.6	0.6	32.4	5.4	9.3						
BEGIN: VICTOZA ADD	NCT01388361	177	2014	6	Multinational	Liraglutide	1.8 mg daily		61.1	9.5	71.6	7.7	0.6	32.5	5.4	12.9						Metformin + basal insulin
BEGIN: VICTOZA ADD-ON						Insulin aspart	Titrated		60.9	8.8	59.6	7.7	0.8	32	4.8	11.8						
Berberoglu 2010	Not provided	49	2010	24	Turkey	Rosiglitazone	4 mg daily		60.7	6.4	0	6.3	0.5	35	4.1							None
Berberoglu 2010						Control			59.8	7.6	0	6	0.5	34.6	3.3							
Bergenstal 2009	NCT00097877	372	2009	6	USA	Exenatide	10-20 mcg daily		52.5	10.62	48.4	10.2	1.5	34.2	7.1	8.6						Metformin + sulfonylurea
Bergenstal 2009						Insulin aspart 70/3	Titrated		51.8	10.9	48.4	10.1	1.8	33.7	7.1	8.4						
Bergenstal 2009						Insulin aspart 70/3	Titrated		53.4	9.96	47.6	10.3	1.9	33.5	7.4	9.9						
Berndt-Zipfel 2013	Not provided	44	2013	5.5	Germany	Glimepiride	4 mg daily		60	7	59	7.3	0.6	33.3	6.7	6.1						Metformin
Berndt-Zipfel 2013						Vildagliptin	100 mg daily		57	0.9	68	7.4	0.7	34.6	5.9	8.4						
BEST	NCT00420511	21	2010	11.2	Canada	Sitagliptin	100 mg daily		61.3	45.5-69.5	60	6.2	5.8-6.9	34.3	27.3-42.6	2.8						Metformin
BEST						Placebo			60.8	51.3-61.4	72.7	6.1	5.9-6.9	32.7	31.0-41.1	3.5						
BETA	NCT00562172	75	2010	12	Republic of Korea	Glimepiride	8 mg daily		54.9	8.6	34	8.9	1.3	25.5	3.6	7.97						Metformin
BETA						Insulin glargine	Titrated		51.3	8.1	38	8.8	1.2	24.4	2.7	6.58q						
Bi 2013	ChiCTR-TRC-	160	2013	5.5	China	Metformin	1500 mg daily		55.6	9.9		8.1	1.6	24.6	2.5							None
Bi 2013						Glipizide	15 mg daily		54.5	9.9		8	1.6	25.2	2.5							
Bilezikian 2013	NCT00679939	225	2013	12	USA	Metformin	1000-2000 mg daily		64	6.46	0	6.8	0.74	31.5	5.79	3.3						None
Bilezikian 2013						Rosiglitazone	4-8 mg daily		63.6	6.61	0	6.8	0.73	31.2	5.86	3.9						
Birkeland 1994a	Not applicable	36	1994	12	Norway	Glibenclamide	10.5 mg daily					8.6	1.2	26.3	4							None
Birkeland 1994a						Basal and bolus ins	Titrated					8.8	1.3	26.4	3							
Bode 2013	NCT01106651	714	2013	6	Multinational	Canagliflozin	300 mg daily		63.4	6	54.7	7.7	0.8	31.5	4.6	11.3		78.7				None or monotherapy/combination therapy (including metformin, sulfonylurea, DPP-4 inhibitor, alpha glucosidase inhibitor, GLP-1 agonist, or insulin)
Bode 2013						Canagliflozin	100 mg daily		64.3	6.5	51.5	7.8	0.8	31.4	4.4	12.3		77.6				
Bode 2013						Placebo			63.2	6.2	60.3	7.8	0.8	31.8	4.8	11.4		76.1				
Bolinder 2012	NCT00855166	182	2012	24	Multinational	Dapagliflozin	10 mg daily		60.6	8.2	55.1	7.19	0.4	32.1	3.9	6	23.6					Metformin
Bolinder 2012						Placebo			60.8	6.9	56	7.16	0.5	31.7	3.9	5.5	28.6					
Bolli 2009	Not provided	576	2009	12	Italy	Pioglitazone	30 mg daily		57	9.7	64.1	8.4	0.9	32.1	5.1	6.4						Metformin
Bolli 2009						Vildagliptin	100 mg daily		56.3	9.3	61.7	8.4	1	32.2	5.6	6.4						
Borges 2011	NCT00386100	688	2011	20	Multinational	Rosiglitazone	4-8 mg daily		51.5	10.5	53	8.6	0.9	32.2	6.8	2.3						None
Borges 2011						Control			50.7	10.5	53	8.6	0.9	33.1	7.1	2.6						
Bosi 2007	NCT00099892	544	2007	5.5	Multinational	Vildagliptin	100 mg daily		53.9	9.5	61.5	8.4	1	32.9	5	5.8						Metformin
Bosi 2007						Vildagliptin	50 mg daily		54.3	9.7	57.3	8.4	0.9	32.1	5.3	6.8						
Bosi 2007						Placebo			54.5	10.3	53.1	8.3	0.9	33.2	6.1	6.2						
Bosi 2009	NCT00382096 and	589	2009	6	Multinational	Vildagliptin	100 mg daily		52.8	10.84	58	8.7	1.02	31.37	4.75	1.9						None
Bosi 2009						Control			52.4	10.71	58.2	8.62	0.93	31.31	4.58	2.2						
Bosi 2011	NCT00432276	803	2011	12	Multinational	Alogliptin	25 mg daily		54.3	9.86	52	8.3	0.82	31.5	5.25	7.5						Metformin + thiazolidinedione
Bosi 2011						Control			55.9	9.94	51.1	8.1	0.83	31.6	5.18	6.9						
Bouchi 2017	UMIN000015867	19	2017	5.5	Japan	Liraglutide	0.9 mg daily		57	16	8	8.2	0.5	27.7	2.5			71	220			Insulin
Bouchi 2017						Control			60	22	9	7.9	0.7	28.2	2.5			66.3	254			
Braun 1996	Not applicable	152	1996	5.5	Germany	Acarbose	300 mg daily		60	47-75	61.9	10	1.5	26	20-32	16						None
Braun 1996						Placebo			61	42-74	54.5	9.9	1.5	26	22-31	17						
BRL-049653/334	Not provided	200	2007	12	Sweden	Rosiglitazone	4 mg daily	Coronary artery disease	67	6	51	6.93	0.825	30	4	3.7						Metformin or sulfonylurea
BRL-049653/334						Placebo			66	8	59	6.94	0.832	29	5	4.5						
Bryson 2016	Not provided	447	2016	5.5	Multinational	Tenegliptin	40 mg daily		58.2		59.1	7.87		32.18		5.1						Metformin
Bryson 2016						Tenegliptin	20 mg daily		58.3		61.5	7.96		32.98		5.3						
Bryson 2016						Tenegliptin	10 mg daily		58.5		54.8	7.78		32.21		4.8						
Bryson 2016						Tenegliptin	5 mg daily		58.8		52.9	7.96		32.23		4.7						
Bryson 2016						Placebo			58.9		53.4	7.88		31.98		4.8						
Bunck 2009	NCT00097500	69	2009	12	Multinational	Exenatide	60 mcg daily		58.4	1.4	63.9	7.6	0.6	30.9	4.2	5.7						Metformin
Bunck 2009						Insulin glargine	Titrated		58.3	1.3	66.7	7.4	0.6	30.1	3.6	4						
Buse 2011	NCT00765817	260	2011	7	Multinational	Exenatide	20 mcg daily		59	9	51.1	8.32	0.85	33.8	5.8	12						Metformin ± thiazolidinedione ± insulin
Buse 2011						Placebo			59	10	63.9	8.5	0.96	33.1	6.2	12						
Camerini-Davalos 198	Not applicable	147	1988	24	USA	Glipizide	20-40 mg daily		46.8	6.8		12.7	1.4	25.4	2	4.8						None
Camerini-Davalos 1988						Placebo			47.1	8.4		12.9	1.7	25.4	2	5.6						
Camerini-Davalos 198	Not applicable	70	1984	36	USA	Glipizide	5 mg daily		45.2	10.8	44.1	11.3	1.9	25.1	1.3	10.8						Oral drugs ± insulin
Camerini-Davalos 1984						Placebo			46.4	10.8	37	10.3	1.6	24.3	2.2	14.5						
Campbell 1994	Not applicable	48	1994	12	UK	Metformin	3000 mg daily		57	10	33.3	11.5	1.9	29.6	5.6	2.3						None
Campbell 1994						Glipizide	30 mg daily		57	9	33.3	11.8	2.11	31.2	6.6	2.8						
CANDLE	UMIN000017669	245	2020	5.5	Japan	Glimepiride	6 mg daily	Heart failure	68.9	10.4	86	71.7	7.1	0.9	25.4	4.8						Oral drugs ± insulin
CANDLE						Canagliflozin	100 mg daily		68.3	9.8	88	77.9	6.9	0.7	24.1	6.4						
CANATATA-D	NCT01106677	1284	2013	6	Multinational	Sitagliptin	100 mg daily		55.5	9.6	47	7.9	0.9	32	6.1	6.8						Metformin
CANATATA-D						Canagliflozin	300 mg daily		55.3	9.2	45	7.9	0.9	31.4	6.3	7.1						
CANATATA-D						Canagliflozin	100 mg daily		55.5	9.4	47.3	7.9	0.9	32.4	6.4	6.7						
CANATATA-D						Placebo			55.3	9.8	51.4	8	0.9	31.1	6.1	6.8						
CANTATA-D2	NCT01137812	756	2013	12	Multinational	Sitagliptin	100 mg daily		56.7	9.3	56.9	8.1	0.9	31.7	6.9	9.7						Metformin + sulfonylurea
CANTATA-D2						Canagliflozin	300 mg daily		56.6	9.6	54.9	8.1	0.9	31.5	6.9	9.4						
CANTATA-M	NCT01081834	584	2013	6	Multinational	Canagliflozin	300 mg daily		55.3	10.2	45.2	8	1	31.7	6	4.3						None
CANTATA-M						Canagliflozin	100 mg daily		55.1	10.8	41.5	8.1	1	31.3	6.6	4.5						
CANTATA-M						Placebo			55.7	10.9	45.8	8	1	31.8	6.2	4.2						
CANTATA-MSU	NCT01106625	469	2013	5.5	Multinational	Canagliflozin	300 mg daily		56.1	8.9	55.8	8.1	0.9	33.2	6.3	9.4						Metformin + sulfonylurea
CANTATA-MSU						Canagliflozin	100 mg daily		57.4	10.5	48.4	8.1	0.9	33.3	6.3	9						
CANTATA-MSU						Placebo			56.8	8.3	48.7	8.1	0.9	32.7	6.8	10.3						
CANTATA-SU	NCT00968812	1450	2013	12	Multinational	Glimepiride	6-8 mg daily		56.3	9	54.6	7.8	0.8	30.9	5.5	6.6						Metformin
CANTATA-SU						Canagliflozin	300 mg daily		55.8	9.2	49.6	7.8	0.8	31.2	5.4	6.7						
CANTATA-SU						Canagliflozin	100 mg daily		54.6	9.5	52.1	7.8	0.8	31	5.3	6.5						
CANVAS/CANVAS-R	NCT01032629/NC	10142	2017	43	Multinational	Canagliflozin	100-300 mg daily	High cardiovascular risk	63.2	8.3	64.9	8.2	0.9	31.9	5.9	13.5	55.8	76.7	12.1			Monotherapy or combination therapy of any approved agent
CANVAS/CANVAS-R						Placebo			63.4	8.2	63.3	8.2	0.9	32	6	13.7	57.2	76.2	12.4			
Carlson 2019	Not provided	33	2019	7.8	USA	Exenatide	10-20 mcg		58.6	7.8	62.5	6.4	0.2	32.6	4.7	7.5						Metformin and/or sulfonylurea
Carlson 2019						Insulin glargine			53.8	7.4	41.2	7.5	0.4	33.7	5.9	6.8						
CARMELINA	NCT01897532	6991	2019	26.4	Multinational	Linagliptin	5 mg daily	High cardiovascular/renal ris	66.1	9.1	61.5	7.9	1	31.4	5.3	15	58.1	54.7	162			Additional medications except DPP-4 inhibitors, GLP 1 receptor agonists or SGLT-2 inhibitors
CARMELINA						Placebo			65.6	9.1	64.3	8	1	31.3	5.4	14.5	58.9	54.5	162			
CAROLINA	NCT01243424	6042	2019	75.6	Multinational	Glimepiride	1-4 mg daily	High cardiovascular risk	63.9	9.5	60.8	7.2	0.6	30.2	5.2	6.3	42.2	76.5	9.7			Additional medications including adjustment of background therapy, or addition of pioglitazone, metformin, alpha glucosidase inhibitor or basal insulin
CAROLINA						Linagliptin	5 mg daily		64.2	9.5	59.2	7.2	0.6	30	5.1	6.2	41.7	77	9.7			
Casner 1988	Not applicable	64	1988	12	USA	Glyburide	5 mg daily					10.85	0.51									Insulin

Casner 1988						Placebo						10.1	0.43								
Cefalu 2015	NCT01031680	922	2015	12	Multinational	Dapagliflozin	10 mg daily	High cardiovascular risk	62.8	7	67.9	8.18	0.84	32.6	5.9	12.6	100				Drugs excluding thiazolidinedione
Cefalu 2015						Placebo			63	7.7	67.9	8.08	0.8	32.9	6.1	12.3	100				
Chacra 2017	NCT01698775	213	2017	5.5	Multinational	Omarigliptin	12.5-25 mg daily	Chronic kidney disease	65.9	9.4	63.6	8.3	0.8	29.4	4.5	14.9					None, 1, or 2 oral agents
Chacra 2017						Placebo			64.5	9.7	59.4	8.3	0.8	30.7	6.8	15.1					
Chakraborty 2011	Not provided	208	2011	5.5	India	Metformin	850-2000 mg daily				55.5	8.7	1.4	27	2.4						None
Chakraborty 2011						Placebo					46	8.7	1.5	27	1.3						
Charbonnel 2013	NCT01296412	653	2013	6	Multinational	Sitagliptin	100 mg daily		56.9	10	55	8.2	1.1	32.6	5.9						Metformin
Charbonnel 2013						Liraglutide	0.6-1.2 mg daily		57.6	10.8	55	8.1	0.9	32.7	6.1						
Charpentier 2009	Not provided	299	2009	7	France	Pioglitazone	30-45 mg daily		59.2	9.6	66.2	8.2	0.6	29.2	3.1	12.1					Metformin + sulfonylurea or metiglinide
Charpentier 2009						Placebo			60.2	9.3	64.6	8.1	0.7	29.1	3.3	12.5					
Charpentier 2017	Not provided	359	2017	6	Multinational	Metformin	1000 mg daily														None
Charpentier 2017						Glimepiride	4 mg daily														
Chavez 2015	Not provided	21	2015	5.5	Unclear	Pioglitazone	45 mg daily														None
Chavez 2015						Exenatide	20 mcg daily														
Chen 2015	NCT01214239	299	2015	5.5	Multinational	Linagliptin	5 mg daily		54.6	10.1	58	7.95	0.89	25.5	3.3						None
Chen 2015						Placebo			54.1	9.3	59.6	8.09	0.91	25.1	3.4						
Chen 2016	NCT01175486	60	2016	6	Taiwan	Pioglitazone	30 mg daily		66.3	8.8	26.7	8.3	0.8	26	3.4	11.6					Metformin + sulfonylurea
Chen 2016						Acarbose	150 mg daily		67.2	7.6	30	8.2	0.8	30.1	18.4	12.3					
Chiasson 1994	Not applicable	354	1994	12	Canada	Acarbose	600 mg daily														Metformin, sulfonylurea, and insulin
Chiasson 1994						Placebo															
Chiasson 2001	Not applicable	248	2001	8.3	Canada	Metformin	1500 mg daily		57.9	8.6	73.5	8.2	0.9	30.7	5.1	7.5					None
Chiasson 2001						Miglitol	300 mg daily		57.3	9	78	8.2	0.9	31.1	4.5	5.2					
Chiasson 2001						Placebo			57.7	9.9	67.5	8.1	0.7	31.1	4.4	5.1					
CHICAGO	NCT00225264	462	2006	18	USA	Glimepiride	1-4 mg daily		59.9	8.2	62.7	7.4	0.97	31.9	5	7.5	13.6				Metformin ± sulfonylurea ± insulin
CHICAGO						Pioglitazone	15-45 mg daily		59.3	8	63.5	7.43	0.99	32	5.2	8	7.8				
Chien 2011	Not provided	97	2011	5.5	Taiwan	Sitagliptin	100 mg daily		73.5	5.9	36.7	9.5	1.3	26.2	2.2	13.2					Metformin, sulfonylurea, alpha-glucosidase inhibitors
Chien 2011						Standard care			72.5	5.2	47.9	10	1.6	26	2.3	14.2					
Cho 2019	UMIN000022804	71	2019	5.5	Japan	Pioglitazone	15-30 mg daily		63.6	10.2	54.3	6.9	0.6	28.5	4.2		17.1	67.1	26.5		Other hypoglycemic agents
Cho 2019						Dapagliflozin	5 mg daily		63.1	10	63.9	6.9	0.6	28.7	6.2		13.9	72.4	22.1		
Choi 2004	Not applicable	55	2004	6	Republic of Korea	Rosiglitazone	4 mg daily	Coronary artery disease	60.9	9.3	63.2	7.79	1.3	24.9	2.96	7.5	100				Metformin, sulphonylurea, and/or alpha-glucosidase inhibitor or insulin
Choi 2004						Standard care			59.9	9.3	75.6	7.72	1.13	24.8	3.35	7.2	100				
Chou 2008	SB-797620/004	457	2008	6.4	Multinational	Glimepiride	4 mg daily		53	11	57.7	9	1.3	31.8	7.2						None
Chou 2008						Rosiglitazone	8 mg daily		53.6	10.7	60	9.1	1.3	31.3	5.8						
Chou 2012	NCT00484198	1912	2012	6	Multinational	Rivoglitazone	1.5 mg daily		55.1	10.59	50.9	7.7	0.57	29.6	5.27	4.3					None
Chou 2012						Rivoglitazone	1.0 mg daily		55	10.51	48.2	7.7	0.53	29.7	5.63	5					
Chou 2012						Pioglitazone	45 mg daily		55	10.84	53	7.7	0.58	30	5.8	4.4					
Chou 2012						Placebo			55.4	12.32	48.9	7.7	0.54	30.1	5.43	4.9					
CIMT	NCT00657943	412	2016	18	Denmark	Metformin	2000 mg daily		61	8.7	68	8.6	1.1	32.3	4.2	13.5	22	44			Oral drugs ± insulin
CIMT						Placebo			60.3	9.1	68	8.5	1	32.1	4.2	12.2	27	45			
Civera 2008	Not provided	24	2008	5.5	Spain	Repaglinide	6 mg daily		60.3	7.7	50	9.6	0.6	30.6	4.8	8					Metformin + insulin
Civera 2008						Standard care			61.6	9.2	60	9.6	0.7	27.9	3.8	7.9					
COMPASS	UMIN000004716	130	2013	5.5	Japan	Pioglitazone	30 mg daily		60.7	9.5	56.1	7.4	0.61	25.8	4.8			87.6	80.8		Metformin ± sulfonylurea
COMPASS						Sitagliptin	100 mg daily		60.3	7.5	62.1	7.47	0.66	24.6	3.3			88.1	100.5		
CompoSIT-I	NCT02738879	746	2018	7	Multinational	Sitagliptin	100 mg daily		58.6	9.5	45.6	8.8	0.9	31.2	5.8	10.4		103.7			Metformin + DPP-4 inhibitor and/or sulphonylurea
CompoSIT-I						Placebo			58.1	9.7	51.4	8.8	10	31.1	5.7	11.1		106.4			
CompoSIT-R	NCT02532855	614	2018	5	Multinational	Sitagliptin	100 mg daily		67.7	8.5	55	7.7	0.7	31.8	5.7	10.5		79.4			Metformin alone or with sulfonylurea
CompoSIT-R						Dapagliflozin	10 mg daily		66.6	8.6	60.8	7.8	0.7	31.5	5.3	10.7		76.9			
CONFIDENCE	NCT01147627	416	2015	11	China	Pioglitazone	30-45 mg daily		50	9.3	61	8	1.2	25.8	3.5						None
CONFIDENCE						Exenatide	10-20 mcg daily		50	9.5	69	8	1.2	26.1	3.6						
CONFIDENCE						Premixed lispro/lis	Titrated		51	9.4	61.6	8.1	1.2	25.6	3.5						
Coniff 1994	Not applicable	189	1994	8.4	USA	Acarbose	900 mg daily		56	9.5	45	6.78		32		4					None
Coniff 1994						Placebo			55.6	9.9	54	6.65		31.5		3					
Coniff 1995	Not applicable	129	1995	5.5	USA	Acarbose	600 mg daily		56.2		39	6.88		29.7		5.1					None
Coniff 1995						Placebo					52	7.1		29.9		5.5					
Coniff 1995a	Not applicable	207	1995	8.4	USA	Acarbose	900 mg daily														Insulin
Coniff 1995a						Placebo															
Costa 1997	Not applicable	65	1997	6	Spain	Acarbose	300 mg daily		60.2	8.4	33.3	9	1.2	28.7	4.2						None
Costa 1997						Placebo			61.7	9.69	31	8.8	0.54	27.4	3.23						
CREDENCE	NCT02065791	4401	2019	31.4	Multinational	Canagliflozin	100 mg daily	Chronic kidney disease	62.9	9.2	65.4	8.3	1.3	31.4	6.2	15.5	50.5	56.3	923		Background therapy consistent with guidelines
CREDENCE						Placebo			63.2	9.2	66.7	8.3	1.3	31.3	6.2	16	50.3	56	931		
Cusi 2019	NCT02009488	56	2019	5.5	USA	Canagliflozin	300 mg daily		58	9	62	7.6	0.8	32.2	4.1			92			Metformin ± DPP-4 inhibitor
Cusi 2019						Placebo			58	10	70	7.7	0.7	31	4.9			89			
CV181-011	NCT00121641	401	2009	5.5	Multinational	Saxagliptin	10 mg daily		52.72	11.27	45.9	7.8	0.9	31.71	4.71	2.3					None
CV181-011						Saxagliptin	5 mg daily		53.91	11.57	50.9	8	1.1	32.24	4.5	2.5					
CV181-011						Saxagliptin	2.5 mg daily		53.27	10.06	56.9	7.9	0.9	31.9		3.1					
CV181-011						Placebo			53.91	12.3	49.5	7.9	0.9	31.7		2.3					
CV181-013	NCT00295633	565	2011	17.5	Multinational	Saxagliptin	5 mg daily		53.2	10.6	47.8	8.4	1.1	29.8	5.3	5.2					Thiazolidinedione
CV181-013						Saxagliptin	2.5 mg daily		54.9	9.7	54.4	8.3	1.1	30	5.8	5.3					
CV181-013						Placebo			54	10.1	46.2	8.2	1.1	30.3	5.8	5.2					
CV181-039	NCT00327015	971	2011	18	Multinational	Saxagliptin	10 mg daily		52.1	11.6	45.2	9.5	1.2	30.4	4.9	1.4					Metformin
CV181-039						Saxagliptin	5 mg daily		52	10.4	51.6	9.4	1.2	29.9	4.5	2					
CV181-039						Placebo			51.8	10.7	49.7	9.4	1.3	30.2	4.9	1.7					
da Silva 2016	NCT02607410	35	2016	12	Brazil	Sitagliptin	100 mg daily		55.1	6.7	50	8	0.6	26.5	2.7	10.9					Metformin + sulfonylurea
da Silva 2016						Insulin NPH			58.4	6.9	35	8.1	0.7	27.5	2.5	10.9					
Dailey 2004	Not applicable	365	2004	5.5	USA	Rosiglitazone	4-8 mg daily		57	9	58	8.1	0.9	32	5	9					Metformin + sulfonylurea
Dailey 2004						Placebo			57	10	61	8.1	0.8	32	5	9					
Dapagliflozin 006	NCT00673231	807	2012	11	Multinational	Dapagliflozin	10 mg daily		59.3	8.8	44.8	8.57	0.82	33.4	5.1	14.2					Insulin
Dapagliflozin 006						Dapagliflozin	5 mg daily		59.3	7.9	47.4	8.62	0.89	33	5.3	13.1					
Dapagliflozin 006						Dapagliflozin	2.5 mg daily		59.8	7.6	49.5	8.46	0.78	33	5	13.6					
Dapagliflozin 006						Placebo			58.8	8.6	49.2	8.47	0.77	33.1	5.9	13.5					
DAPA-HF	NCT03036124	2139	2019	24	Multinational	Dapagliflozin	10 mg daily	Heart failure	66.3	9.9	77.7	7.4	1.5	29.3	5.9		100	64			Glucose lowering treatment
DAPA-HF						Placebo			66.7	9.8	77.7	7.4	1.6	29.4	6.1		100	63			
Dargie 2007	GSK 49653/211	224	2007	12	Europe	Rosiglitazone	4-8 mg daily	Heart failure	64.3	8.8	84.3	7.8	1.3	28.8	3.7	4.5	100				Antidiabetes treatment except thiazolidinedione or insulin + acarbose
Dargie 2007						Placebo			63.9	8.6	79.1	7.8	1.3	28.6	3.5		100				
Davidson 2007	Not provided	245	2007	5.5	USA	Rosiglitazone	8 mg daily		52	11.9	45.3	9.2	1.3	31.3	5.7	6					Sulfonylurea
Davidson 2007						Placebo			53	10.4	48.3	9.4	1.4	31.9	5.6	6.2					
Davies 2013	NCT01003184	216	2013	5.5	United	Exenatide	2 mg weekly					8.37	0.85	33.7	4.7						Metformin ± sulfonylurea
Davies 2013						Insulin detemir	Titrated					8.35	0.88	33.7	4.7						
Davies 2017	NCT01923181	421	2017	5.5	Multinational	Semaglutide	20 mg daily		56.5	10.2	60.6	8	0.7			7.7					Metformin
Davies 2017						Semaglutide	20 mg daily		58.3	10.4	62.9	7.9	0.7			7					
Davies 2017						Semaglutide	10 mg daily		56.5	10.1	62.3	7.8	0.7			5.8					
Davies 2017						Semaglutide	5 mg daily		55.7	11	67.1	7.8	0.6			5.3					
Davies 2017						Semaglutide	2.5 mg daily		56.7	9.9	64.3	8	0.7			6.1					
Davies 2017						Placebo			58.9	10.3	56.3	8	0.8			6.7					
DECLARE-TIMI 58	NCT01730534	17160	2019	50.4	Multinational	Dapagliflozin	10 mg daily	High cardiovascular risk	63.9	6.8	63.1	8.3	1.2	32.1	6	11	40.5	85.4			Use of other glucose lowering agents at discretion (other than SGLT-2 inhibitor, pioglitazone or rosiglitazone
DECLARE-TIMI 58						Placebo			64	6.8	62.1	8.3	1.2	32	6.1	10	40.8	85.1			
DeFronzo 1995	Not applicable	419	1995	6.7	USA	Metformin	500-2500 mg daily		55	14.5	45.7	8.4	5.8	29.4	4.3	8.4					None
DeFronzo 1995						Glyburide	10-20 mg daily		56	14.5	49.3	8.5	1.4	29.1	4.3	8.7					
DeFronzo 2005	Not applicable	336	2005	7	USA	Exenatide	20 mcg daily		52	11	60.2	8.2	1	34	6	4.9					Metformin
DeFronzo 2005						Exenatide	10 mcg daily		53	11	51.8	8.3	1.1	34	6	6.2					
DeFronzo 2005						Placebo			54	9	59.3	8.2	1	34	6	6.6					
DeFronzo 2012	NCT00328627	386	2012	6	Multinational	Alogliptin	25 mg daily		53.7	9.3	38.8	8.6	0.7	31.5	5.7	5.6					Metformin
DeFronzo 2012						Alogliptin	12.5 mg daily		53.1	9.6	52.3	8.6	0.7	31	5.1	6.2					
DeFronzo 2012						Placebo			55.2	9.9	47.3	8.5	0.6	30.6	4.8	6					
DeFronzo 2015	NCT01422876	405	2015	12	Multinational	Linagliptin	5 mg daily		56.2	10	50	8.02	0.9	30.6	5.4			90			Metformin
DeFronzo 2015						Empagliflozin	25 mg daily		55.5	10	46.4	8.02	0.83	31.8	5.3			90.2			
DeFronzo 2015						Empagliflozin	10 mg daily		56.1	10.5	56.9	8	0.93	30.9	5.4			91.2			
Del Cas 2017	NCT01822548	64	2017	12	Italy	Glibeclamide	5-20 mg daily		63	10	71	7.7		28.9		5					Metformin

Dei Cas 2017						Vildagliptin	100 mg daily		61	9	65	7.7		29		7						
Dejager 2007	NCT00099905	632	2007	5.5	Multinational	Vildagliptin	100 mg daily		53.6	10.8	53.3	8.4	0.8	32.4	6.1	2.4						None
Dejager 2007						Vildagliptin	100 mg daily		52.8	9.6	46.7	8.6	0.8	33.3	4.8	2.1						
Dejager 2007						Vildagliptin	50 mg daily		55.3	11.4	41.3	8.2	0.8	32.9	6	2.1						
Dejager 2007						Placebo			52.2	11.2	47.9	8.4	0.8	32.6	5.6	1.6						
Del Prato 2003	Not applicable	428	2003	6	Multinational	Metformin	2550 mg daily		56	9	59	7.79	1.61	29.7	4.2							None
Del Prato 2003						Placebo			56	9	63	7.43		29.9	3.9							
Del Prato 2011	Not provided	503	2011	5.5	Multinational	Linagliptin	5 mg daily		56.4	10.1	48.8	8	0.9	29.04	4.8							None
Del Prato 2011						Placebo			54.4	10.3	47.3	8	0.9	29.1	4.8							
Del Prato 2014	NCT00856284	2639	2014	24	Multinational	Glipizide	5 mg daily		55.4	9.6	50.5	7.6	0.62	31.1	5.32	5.5						Metformin
Del Prato 2014						Alogliptin	25 mg daily		55.5	9.81	51.1	7.6	0.6	31.3	5.34	5.4						
Del Prato 2014						Alogliptin	12.5 mg daily		55.2	9.6	47.6	7.6	0.6	31.3	5.42	5.7						
DELIGHT	NCT02547935	293	2018	5.5	Multinational	Dapagliflozin	10 mg daily	Chronic kidney disease	64.7	8.6	70	8.44	1	30.19	5.3	17.55	40			270		Stable glucose-lowering therapy
DELIGHT						Placebo			64.7	8.5	71	8.57	1.2	30.34	5.6	17.71	28			257.5		
Deng 2017	Not provided	72	2017	12	China	Sitagliptin	100 mg daily		63.7	10.7	77.8	7.3	0.7									None
Deng 2017						Standard care			64.1	11.2	72.2	7.4	0.8									
DERIVE	NCT02413398	321	2019	5.5	Multinational	Dapagliflozin	10 mg daily	Chronic kidney disease	65.3		56.9	8.33	1.08	32.6	4.7	14.3		53.3	23.5			Stable glucose-lowering therapy
DERIVE						Placebo			66.2		56.5	8.03	1.08	31.6	5	14.5		53.6	29			
Derosa 2003	Not applicable	124	2003	6	Italy	Glimepiride	1 mg daily		54	10	48.4	7.8	1.2	26.4	7.9							None
Derosa 2003						Repaglinide	1 mg daily		56	9	50	8	1.2	26.12	9.45							
Derosa 2003a	Not applicable	112	2003	12	Italy	Metformin	1500-2500 mg daily		52	9	48.2	7.4	0.9	24.7	1.2							None
Derosa 2003a						Repaglinide	2-4 mg daily		55	10	51.8	7.6	0.9	25.2	1.1							
Derosa 2004	Not applicable	164	2004	12	Italy	Metformin	3000 mg daily															None
Derosa 2004						Glimepiride	4 mg daily															
Derosa 2005	Not applicable	95	2005	12	Italy	Glimepiride	2 mg daily		52	5	48.9	7.9	0.6	16.8	1.5	4						Metformin
Derosa 2005						Rosiglitazone	4 mg daily		54	4	52.1	8	0.7	26.6	1.3	5						
Derosa 2007	Not provided	248	2007	6	Italy	Glibeclamide	12.5 mg daily		56	4	50.9	8.2	1.1	26.5	1.5	4						Metformin
Derosa 2007						Nateglinide	300 mg daily		55	5	48.7	8.1	1	26.4	1.4	5						
Derosa 2009	Not provided	350	2009	6	Italy	Pioglitazone	45 mg daily		55	8	49.1	7.9	0.5	26.18	0.6							Oral hypoglycaemic agents
Derosa 2009						Acarbose	300 mg daily		57	6	49.7	8	0.6	26.97	0.8							
Derosa 2009a	Not provided	271	2009	15	Italy	Metformin	3000 mg daily		55	5	50.7	9.1	1.2	27.2	1.5							None
Derosa 2009a						Pioglitazone	45 mg daily		54	6	46.3	9.2	1.3	27.5	1.7							
Derosa 2009a			2009	15	Italy	Glimepiride	6 mg daily		57.7	7	48.5	9	1.1	27.1	1.4							Metformin
Derosa 2009a						Pioglitazone	45 mg daily		57	7	49.3	9.3	1.4	27.4	1.6							
Derosa 2010	Not provided	151	2010	12	Italy	Metformin	1700 mg daily		58	6	51.3	8.4	0.8	27.7	1.3	6						Pioglitazone
Derosa 2010						Sitagliptin	100 mg daily		57	5	49.3	8.5	0.9	27.9	1.5	5						
Derosa 2010a	Not provided	128	2010	12	Italy	Glibeclamide	15 mg daily		56	7	50.8	8.9	0.8	28.5	1.4							Metformin
Derosa 2010a						Exenatide	20 mcg daily		57	8	47.6	8.8	0.7	28.7	1.5							
Derosa 2011	Not provided	188	2011	7	Italy	Acarbose	300 mg daily				48.9	6.8	0.6	26.6	0.8							None
Derosa 2011						Placebo					48.9	6.7	0.5	26.8	0.9							
Derosa 2011a	Not provided	111	2011	12	Italy	Glimepiride	6 mg daily		55	6	48.1	8.8	0.8	28.5	1.4							Metformin
Derosa 2011a						Exenatide	20 mcg daily		56.7	7	49.1	8.7	0.7	28.4	1.3							
Derosa 2012	Not provided	178	2012	12	Italy	Sitagliptin	100 mg daily		55.9	8.8	46	8.1	0.8	28.1	1.2							Metformin
Derosa 2012						Placebo			54.8	7.9	50.6	8	0.7	28.9	2							
Derosa 2012a	Not provided	167	2012	12	Italy	Vildagliptin	100 mg daily		54.2	8.3	50	8.1	0.6	27.9	1.5	6.1						Metformin
Derosa 2012a						Placebo			52.4	7.1	51.8	8.2	0.7	27.8	1.4	6.3						
Derosa 2013	Not provided	171	2013	12	Italy	Exenatide	20 mcg daily				50	8.1	0.8	31.9	1.7					98.2		Metformin
Derosa 2013						Placebo					48.2	7.9	0.6	31.7	1.5					93.6		
Derosa 2014	Not provided	167	2014	5.5	Italy	Glimepiride	6 mg daily		57.2	9	49.4	7.7	0.7	27.6	1.3	0.57						Metformin
Derosa 2014						Vildagliptin	100 mg daily		59.8	9.9	48.8	7.9	0.9	27.9	1.6	0.58						
Derosa 2014a	Not provided	205	2014	24	Italy	Sitagliptin	100 mg daily				49	8	0.8	29.2	3.1							Oral antidiabetic drugs
Derosa 2014a						Placebo					48.5	8.1	0.9	29.4	3.2							
DIA3004	NCT01064414	269	2014	12	Multinational	Canagliflozin	300 mg daily	Chronic kidney disease	67.9	8.2	53.9	8	0.8	33.4	6.5	17		38.5	228.1			AHA monotherapy or combination therapy
DIA3004						Canagliflozin	100 mg daily		69.5	8.2	64.4	7.9	0.9	32.4	5.5	15.6		39.7	285.9			
DIA3004						Placebo			68.2	8.4	63.3	8	0.9	33.1	6.5	16.4		40.1	255.1			
Distiller 2014	Not provided	28	2014	6	South Africa	Exenatide	20 mcg daily		49.1	36-65	50	8.7		41.9	33.3-47	12.3						Metformin + insulin
Distiller 2014						Standard care			54.3	41-71	50	9.2		40.2	34.5-46.6	12.4						
DIVERSITY-CVR	UMIN000028014	340	2020	5.5	Japan	Sitagliptin	50-100 mg daily		57.9	12.1	58.3	7.8	0.8	27.9	4.2		2.5	79				Metformin or no treatment
DIVERSITY-CVR						Dapagliflozin	5-10 mg daily		58.3	12.4	61.9	7.8	0.8	27.8	4.0		4.2	79				
Dobs 2013	NCT00350779	278	2013	12.4	Multinational	Sitagliptin	100 mg daily		54.4	8.8	56	8.8	1	30.1	6.2	9.3						Metformin + PPAR gamma agonist, metformin + sulfonylurea, sulfonylurea + PPAR gamma agonist
Dobs 2013						Control			54.8	9.5	60	8.7	1	30.8	5.6	9.4						
Dorkhan 2009	Not provided	30	2009	6	Sweden	Pioglitazone	45 mg daily		60.8	7.1	73.3	8.1	1.5	30.8	5.5	11.1						Metformin with or without sulfonylurea /meglitinide
Dorkhan 2009						Insulin glargine	Titrated		61.5	8.2	60	8.3	1.4	31.6	6.1	9.5						
Douek 2005	Not provided	183	2005	12	United Kingdom	Metformin	2000 mg daily		58	8.9	67.4	9.7	1.3	30.9	4.5	9						Sulfonylurea ± thiazolidinedione
Douek 2005						Placebo			58	7.7	62.6	10	1.5	31.5	4.3	10						
Drent 2002	Not applicable	465	2002	5.5	The Netherlands	Miglitol	600 mg daily		64	10	63.8	8.1	1.01	26.9	3.5							None
Drent 2002						Miglitol	300 mg daily		63	11	52.1	8	1.21	27.8	3.2							
Drent 2002						Miglitol	150 mg daily		63	9	56	8.09	1.23	26.8	3.2							
Drent 2002						Miglitol	75 mg daily		64	10	48.8	8.14	1.14	27.4	3.7							
Drent 2002						Placebo			63	11	56.3	7.94	1.15	27.2	3.4							
DUAL-I	NCT01336023	829	2014	6	Multinational	Liraglutide	1.8 mg daily		55	10.2	50	8.3	0.9	31.3	4.8	7.2						Metformin ± thiazolidinedione
DUAL-I						Insulin degludec	Titrated		54.9	9.7	48	8.3	1	31.2	5.3	7						
DUAL-I CHINA	NCT03172494	359	2020	6	China	Liraglutide	1.8 mg daily		54.1	10.2	60.0	8.2	0.8									Metformin
DUAL-I CHINA						Insulin degludec	Titrated		55.7	10.2	55.9	8.3	0.8									
DUAL-I JAPAN	NCT02607306	544	2019	12	Japan	Liraglutide	1.8 mg daily		56.8	10.1	70.3	8.3	1.0	26.5	4.5	9.4						Oral antidiabetic drugs
DUAL-I JAPAN						Insulin degludec	Titrated		57.8	9.9	72.0	8.5	1.1	26.6	4.8	9.7						
DUAL-II	NCT01392573	398	2014	6	Multinational	Liraglutide	1.8 mg daily		57	9	56	8.7	0.7	33.6	6	10						Metformin + insulin degludec
DUAL-II						Control			58	11	53	8.8	0.7	33.8	6	11						
DUAL-II CHINA	NCT03175120	453	2020	6	China	Liraglutide	1.8 mg daily		54.5	9.8	60.6	8.9	1.2									Metformin + insulin degludec
DUAL-II CHINA						Control			55.3	10.0	60.3	9.0	1.2									
DUAL-III	NCT01676116	438	2017	6	Multinational	Liraglutide	1.8 mg daily		58.3	9.9	52.4	7.8	0.6	32.9	4.4	10.4						Metformin ± pioglitazone ± sulphonylurea
DUAL-III						Control			58.4	8.8	48.6	7.7	0.6	33	4.1	10.4						
DUAL-VIII	NCT02501161	1012	2019	24	Multinational	Liraglutide	1.8 mg daily		56.8	10.0	55.0	8.4	1.0	32.0	6.2	10.0						Antidiabetic treatment except DPP-4 inhibitor or glinide
DUAL-VIII						Control	Control		56.4	10.1	54.0	8.6	1.0	31.9	5.8	10.2						
DUAL-IX	NCT02773368	420	2019	6	Multinational	Liraglutide			56.1	10.4	57.6	8.2	0.9	31.5	4.8	9.8						SGLT2 inhibitor
DUAL-IX						Control			57.2	10.2	60	8.4	1.1	30.9	4.8	9.3						
DUET-beta	Not provided	48	2019	5.5	Unclear	Trelagliptin	100 mg weekly															Metformin ± basal insulin
DUET-beta						Dulaglutide	0.75 mg weekly															
DURATION-2	NCT00637273	491	2010	6	Multinational	Pioglitazone	45 mg daily		53	10	48	8.5	1.1	32	6	6						Metformin
DURATION-2						Sitagliptin	100 mg daily		52	11	52	8.5	1.2	32	5	5						
DURATION-2						Exenatide	2 mg weekly		52	10	56	8.6	1.2	32	5	6						
DURATION-3	NCT00641056	456	2010	6	Multinational	Exenatide	2 mg weekly		58	10	52	8.3	1.1	32	5	8						Metformin ± sulfonylurea
DURATION-3						Insulin glargine	Titrated		58	9	55	8.3	1	32	5	7.8						
DURATION-4	NCT00676338	820	2012	6	Multinational	Metformin	2000 mg daily		54	11	62.6	8.6	1.2	30.7	5.5	2.6						None
DURATION-4						Pioglitazone	45 mg daily		55	11	59.5	8.5	1.2	31.1	5.3	2.7						
DURATION-4						Sitagliptin	100 mg daily		52	11	57.7	8.5	1.3	31.8	5.4	2.7						
DURATION-4						Exenatide	2.0 mg weekly		54	11	56	8.5	1.2	31.4	5.3	2.7						
DURATION-7	NCT02229383	461	2018	6.8	Multinational	Exenatide	2.0 mg weekly		57.8	9.0	49.4	8.5	0.9	33.3	6.1	11.5						Metformin ± sulfonylurea
DURATION-7						Placebo			57.6	10.3	46.5	8.5	0.9	34.1	6.6	11.1						
DURATION-8	NCT02229396	464	2016	6	Multinational	Dapagliflozin	10 mg daily		55	9	48	9.3	1	33	6.1	7.1		97.5				Metformin
DURATION-8						Exenatide	2 mg weekly		54	10	51	9.3	1	32	5.9	7.4		99.4				
DURATION-NEO-2	NCT01652729	364	2017	6	USA	Sitagliptin	100 mg daily		54.3	9	54.1	8.5	1	31.6	5.8	7.9						Metformin
DURATION-NEO-2						Exenatide	2 mg weekly		53.4	9.8	49.2	8.4	1	32.1	5.4	8.5						
DURATION-NEO-2						Placebo			53.4	9.5	60.7	8.5	1	31.5	5.1	8.7						
EAGLE	Not provided	978	2015	5.5	Multinational	Liraglutide	1.8 mg daily		57.4	8.9	56			31.8	4.1	8.4	4					Metformin ± sulfonylurea
EAGLE						Insulin glargine	Titrated		57.1	8.8	52.7			32	4.2	8.5	4					
EASIE	NCT00751114	515	2012	5.5	Multinational	Sitagliptin	100 mg daily		53.3	8.7	52.2	8.5	1.1	31.3	4.9		6					Metformin
EASIE						Insulin glargine	Titrated		53.9	8.9	50.2	8.5	1	31.1	4.9		5					
Ebato 2009	Not provided	26	2009	5.5	Japan	Glimepiride	3 mg daily		62.4	7.8	50	8.34	1.1	25.3	2.43	14.2		75.4				Insulin with or without biguanides and/or alpha glucosidase inhibitors

Ebato 2009						Control			60.5	8.2	58.3	8.33	0.73	25.7	2.4	13.1		74.5				
EDIT	UMIN000004678	50	2015	5.5	Japan	Sitagliptin	50 mg daily		66	8	64	7.9	1	24.5	2	19	56	64				Insulin
EDIT						Control			66	13	75	7.8	0.7	26.8	4.3	20	46	63.9				
Efstathiou 2015	Not provided	66	2015	5.5	Greece	Saxagliptin	5 mg daily															Metformin
Efstathiou 2015						Dapagliflozin	10 mg daily															
ELEGANT	NCT01392898	50	2014	12	The Netherlands	Liraglutide	1.8 mg daily		57	10	61.5	7.2	0.6	34	7	8.3						Antidiabetic medications (metformin, sulfonylurea, insulin)
ELEGANT						Standard care			59	8	60	7.5	0.7	32	5	7.6						
ELIXA	NCT01147250	6068	2015	25	Multinational	Lixisenatide	10-20 mcg daily	Coronary artery disease	59.9	9.7	69.6	7.7	1.3	30.1	5.6	9.2						Antidiabetic medications with the exception of other incretin therapies
ELIXA						Placebo			60.6	9.6	69.1	7.6	1.3	30.2	5.8	9.4						
ELLENA-IT	UMIN000027614	61	2020	5.5	Japan	Empagliflozin	10 mg daily		66.3	9.5	67.7	8.1	0.8	25.8	3.9	19.0						Standard therapy
ELLENA-IT						Liraglutide	0.9 mg daily		67.2	9.0	70.0	8.0	0.8	26.4	4.6	18.8						
EMBLEM	UMIN000024502	117	2019	5.5	Japan	Empagliflozin	10 mg daily	Cardiovascular disease	65	11	69.2	7.2	0.8	26	5	14	100		67			Standard therapy
EMBLEM						Placebo			64	10	67.9	7.2	0.9	27	6	13	100		69			
EMIT	NCT01242215	243	2015	5.5	Japan	Ipragliflozin	50 mg daily		59.6	10.02	67.3	8.38	0.641	25.8	3.6	10.3						Sulphonylurea
EMIT						Placebo			59.8	8.6	62.7	8.34	0.727	24.2	3	10.8						
EMLIA001	NCT02637973	84	2020	5.5	Germany	Empagliflozin	25 mg daily		62.7	7.0	69.0	6.7	0.7	32.1	4.6	3.0						None
EMLIA001						Placebo			61.5	10.0	69.0	6.8	0.5	32.4	4.2	3.3						
EMPA-HEART	NCT01011868	97	2019	6.0	Canada	Empagliflozin	10 mg daily	Coronary artery disease			90.0	7.9	0.8	27.7	4.7							Stable glucose-lowering therapy
EMPA-HEART						Placebo					96.0	8.0	0.9	27.4	5.4							
EMPA-REG BASAL	NCT01011868	494	2015	18	Multinational	Empagliflozin	25 mg daily		59.9	10.5	60	8.2	0.8	32.7	5.9			83				Insulin ± metformin ± sulphonylurea
EMPA-REG BASAL						Empagliflozin	10 mg daily		58.6	9.8	55	8.3	0.8	32.1	5.8			85				
EMPA-REG BASAL						Placebo			58.1	9.4	53	8.2	0.8	31.8	6			84				
EMPA-REG H2H-SU	NCT02998970	1549	2014	24	Multinational	Glimepiride	1-4 mg daily		55.7	10.4	54	7.92	0.86	30.3	5.3			88.1	39.8			Metformin
EMPA-REG H2H-SU						Empagliflozin	25 mg daily		56.2	10.3	56	7.92	0.81	30	5.3			87.9	40.7			
EMPA-REG MDI	NCT01306214	563	2014	12	Multinational	Empagliflozin	25 mg daily		58	9.4	44	8.29	0.72	35	4			84.4				Insulin ± metformin
EMPA-REG MDI						Empagliflozin	10 mg daily		56.7	8.7	52	8.39	0.74	34.7	3.8			84.1				
EMPA-REG MDI						Placebo			55.3	10.1	40	8.33	0.72	34.7	4.3			83.4				
EMPA-REG MET	NCT01159600	637	2014	5.5	Multinational	Empagliflozin	25 mg daily		55.6	10.2	56	7.86	0.87	29.7	5.7			87.7				Metformin
EMPA-REG MET						Empagliflozin	10 mg daily		55.5	9.9	58	7.94	0.79	29.1	5.5			89.5				
EMPA-REG MET						Placebo			56	9.7	56	7.9	0.88	28.7	5.2			89.7				
EMPA-REG METSU	NCT01159600	669	2013	5.5	Multinational	Empagliflozin	25 mg daily		57.4	9.3	53	8.1	0.83	28.3	5.5			88.3				Metformin + sulfonylurea
EMPA-REG METSU						Empagliflozin	10 mg daily		57	9.2	50	8.07	0.81	28.3	5.4			86.5				
EMPA-REG METSU						Placebo			56.9	9.2	50	8.15	0.83	27.9	4.9			86.9				
EMPA-REG MONO	NCT01177813	899	2013	5.5	Multinational	Sitagliptin	100 mg daily		55.1	9.9	63	7.85	0.79	28.2	5.2			87.6				None
EMPA-REG MONO						Empagliflozin	25 mg daily		53.8	11.6	65	7.86	0.85	28.2	5.5			87.6				
EMPA-REG MONO						Empagliflozin	10 mg daily		56.2	11.6	63	7.87	0.88	28.3	5.5			87.7				
EMPA-REG MONO						Placebo			54.9	10.9	54	7.91	0.78	28.7	6.2			86.8				
EMPA-REG OUTCOMI	NCT01131676	7020	2015	36	Multinational	Empagliflozin	10-25 mg daily	Cardiovascular disease	63.1	8.6	71.2	8.07	0.85	30.6	5.3		75.6	74.2				No or stable glucose lowering therapy
EMPA-REG OUTCOME				34.8		Placebo			63.2	8.8	72	8.08	0.84	30.7	5.2		75.6	73.8				
EMPA-REG PIO	NCT01210001	498	2014	5.5	Multinational	Empagliflozin	25 mg daily		54.2	8.9	50.6	8.1	0.82	29.1	5.5			87.4				Thiazolidinedione ± metformin
EMPA-REG PIO						Empagliflozin	10 mg daily		54.7	9.9	50.3	8.1	0.89	29.2	5.6			84.3				
EMPA-REG PIO						Placebo			54.6	10.5	44.2	8.2	0.92	29.3	5.4			85.5				
EMPA-REG RENAL - C	NCT01164501	741	2014	12	Multinational	Empagliflozin	25 mg daily	Chronic kidney disease	62	8.4	62.9	7.96	0.73	31.3	5.8			72.3				Antidiabetes treatment excluding SGLT-2 inhibitors
EMPA-REG RENAL - CKD2						Empagliflozin	10 mg daily		63.2	8.5	61.2	8.02	0.84	32.4	5.4			70.8				
EMPA-REG RENAL - CKD2						Placebo			62.6	8.1	58.9	8.09	0.8	30.8	5.6			71.8				
EMPA-REG RENAL - CKD3						Empagliflozin	25 mg daily		64.6	8.9	57.2	8.02	0.84	30.2	5.3			45.4				
EMPA-REG RENAL - CKD3						Placebo			65.1	8.2	56.7	8.09	0.8	30.3	5.3			44.3				
EMPA-REG RENAL - CKD4						Empagliflozin	25 mg daily		65.4	10.2	56.8	8.06	1.05	29	4.9			24.4				
EMPA-REG RENAL - CKD4						Placebo			62.9	11.9	51.4	8.16	0.99	31.8	6			22				
Engelbrechtsen 2016	NCT02094183	42	2016	12	Denmark	Liraglutide	1.2 mg daily		46	2	18.5											None
Engelbrechtsen 2016						Control			45	2	12											
Erem 2014	Not provided	57	2015	12	Turkey	Metformin	2000 mg daily		52.2	10.5	31.6	7.62	1.06	33.56	4.6		10.5					None
Erem 2014						Gliclazide	60 mg daily		55	8.7	36.8	8.26	1.65	32.72	3.9		10.5					
Erem 2014						Pioglitazone	30 mg daily		52.5	5.2	26.3	8.03	1.7	31.31	4.7		0					
ESPECIAL-ACS	UMIN000007900	41	2017	6	Japan	Sitagliptin	50-100 mg daily	Acute coronary syndrome			95.2	6.7	0.5	25.1	3.2		100					None
ESPECIAL-ACS						Control					100	6.8	0.6	24.3	2.9		100					
Esposito 2004	Not applicable	175	2004	12	Italy	Glyburide	20 mg daily		51.3	5.9	52.9	7.4	1.1	28.3	4.1							Oral drugs
Esposito 2004						Repaglinide	12 mg daily		52	6.4	53.4	7.5	1.1	28.5	4.3							
Esposito 2011	Not provided	110	2011	5.5	Italy	Metformin	2000 mg daily		54.9	6.6	50.9	8.1	1	29.1	3.3							None
Esposito 2011						Pioglitazone	45 mg daily		54.2	6.1	54.5	8	1	28.9	3.5							
Essen Study	Not applicable	85	1994	5.5	Germany	Glibenclamide	10.5 mg daily		59.5	5.7	48	8.3	0.37	26.5	2.1	1.5						None
Essen Study						Acarbose	300 mg daily		58.8	6.9	46	8.29	0.42	26.5	1.6	1.1						
Essen Study						Placebo			56.9	6.7	40	8.29	0.37	26.8	1.5	1						
EUREXA	NCT00359762	1029	2012	26	Multinational	Glimepiride	Titrated		56.8	9.14	52	7.4	0.7	32.3	3.9	5.5						Metformin
EUREXA				23.4		Exenatide	10-20 mcg daily		56.1	10.03	56	7.5	0.7	32.6	4.2	5.8						
EUREXA extension	NCT00359762	154	2015	24	Multinational	Glimepiride	Titrated		56	10	54.1	7.6	0.6	32.6	4.1	7.2						Metformin + exenatide
EUREXA extension						Pioglitazone	45 mg daily		55.7	9.2	65.8	7.7	0.7	32.8	4.3	6.9						
EXAMINE	NCT00968708	5380	2013	19	Multinational	Alogliptin	6.25-25mg daily	Acute coronary syndrome			67.7				28.7		87.5	71.1				Anti-diabetic therapy other than DPP-4 inhibitor or GLP-1 receptor agonist
EXAMINE				18		Placebo					68				28.7		88.4	71.2				
Exenatide-113	Not applicable	377	2004	7	USA	Exenatide	20 mcg daily		56	11	57.4	8.6	1.2	33	6	6.6						Sulfonylurea
Exenatide-113						Exenatide	10 mcg daily		55	10	59.2	8.5	1.1	33	6	6.3						
Exenatide-113						Placebo			55	11	62.6	8.7	1.2	34	5	5.7						
EXSCEL	NCT01144338	14752	2017	38.4	Multinational	Exenatide	2 mg weekly		62		62	8		31.8		12	73.3	76.6				Up to three oral glucose-lowering agents or insulin plus two oral glucose-lowering agents
EXSCEL						Placebo					62	8		31.7		12	72.9	76				
Feng 2017	NCT03068065	93	2017	5.5	China	Metformin	1000 mg twice daily		46.31	12.3	65.5	9.36	1.78	26.82	3.66							None
Feng 2017						Gliclazide	120 mg daily		48.07	12.6	68.9	9.03	1.24	27.85	3.02							
Feng 2017						Liraglutide	1.8 mg daily		46.79	9.7	72.4	8.91	1.72	28.1	3.02							
Ferdinand 2019	NCT02182830	150	2019	5.5	USA	Empagliflozin	10-25 mg daily		56.5	9.3	55.1	8.66	0.92			9.3	7.7	91.2				None or stable oral hypoglycemic drug
Ferdinand 2019						Placebo			57.2	9.3	50	8.51	1.09			9.3	6.9	91.49				
Fernandez 2008	Not provided	20	2008	8.4	USA	Pioglitazone	45 mg daily					9	0.7									Insulin
Fernandez 2008						Placebo						9.2	0.4									
Ferrannini 2010	NCT00528372	485	2010	5.5	Multinational	Dapagliflozin	10 mg daily		50.6	9.97	48.6	8.01	0.96	33.6	5.4							None
Ferrannini 2010						Dapagliflozin	5 mg daily		52.6	10.9	48.4	7.86	0.94	31.9	4.8							
Ferrannini 2010						Dapagliflozin	2.5 mg daily		53	11.7	55.4	7.92	0.9	32.6	5.5							
Ferrannini 2010						Placebo			52.7	10.3	41.3	7.84	0.87	32.3	5.5							
FIGHT	NCT01800968	178	2018	6	USA	Liraglutide	1.8 mg daily	Heart failure	63.0	57-69	75.0	7.3	6.6-8.5	32.0	27-37		100					Antidiabetic therapy
FIGHT						Placebo			62.0	54-68	77.0	7.6	6.8-8.5	34.0	28-40		100					
Filozof 2010	Not provided	1007	2010	12	Multinational	Gliclazide	80-320 mg daily		59.7	10.2	51.8	8.5	1	30.8	5	6.8						Metformin
Filozof 2010						Vildagliptin	50 mg daily		59.2	9.9	52.2	8.5	1	31.2	5	6.4						
Finn 2009	NCT00116792	65	2009	8	USA	Rosiglitazone	4 mg daily	Coronary artery disease	65.7	9.6	75			30.9	6.2							Thiazolidinediones excluded
Finn 2009						Placebo			59.7	9.3	78.8			32.7	6.5							
Fischer 1998	Not applicable	495	1998	5.5	Germany	Acarbose	75 mg daily		59.4	8.6	51	7.51	1.1	27.2	3.3	1.8						None
Fischer 1998						Acarbose	150 mg daily		56.8	9.4	59	7.43	1.1	27.6	3.7	1.4						
Fischer 1998						Acarbose	300 mg daily		55.5	8.4	49	7.52	1.09	27.6	3.5	1.7						
Fischer 1998						Acarbose	600 mg daily		58.5	8.4	53	7.42	1.09	27.3	3.5	2.2						
Fischer 1998						Placebo			52.7	8.7	53	7.26	1.09	26.9	2.9	2						
Foley 2009	NCT00102388	1092	2009	24	Multinational	Gliclazide	80-320 mg daily		54.3	10.4	52.7	8.69	1.1	30.8	5.5	1.9						None
Foley 2009						Vildagliptin	100 mg daily		55.2	10.6	58.8	8.6	1	30.6	5	2.4						
Foley 2011	NCT00260156	59	2011	12	The Netherlands	Vildagliptin	100 mg daily		57.4	9.4	58.6	6	0.7	29.9	4.9	1.4						None
Foley 2011						Placebo			57	6.7	60	6	0.7	29.2	4.4	0.6						
Fonseca 2000	Not applicable	348	2000	6	USA	Rosiglitazone	8 mg daily		58.3	8.8	68.2	8.9	1.5	29.8	3.9	8.3						Metformin
Fonseca 2000						Rosiglitazone	4 mg daily		57.5	10.5	62.1	8.9	1.3	30.2	4.2	7.5						
Fonseca 2000						Placebo			58.8	9.2	74.3	8.6	1.3	30.3	4.4	7.3						
Fonseca 2003	Not applicable	402	2003	5.5	USA	Naglitinide	120 mg daily		56.5	11.3		8.3	1.4	31.6	4.2	5.9						Rosiglitazone
Fonseca 2003						Placebo			56.8	11.4		8.4	1.4	30.5	4.3	5.8						
Fonseca 2007	NCT00099931	296	2007	5.5	Multinational	Vidagliptin	50 mg twice daily		59.6	10.3	47.9	8.4	1	33.3	5.2	14.4						Insulin
Fonseca 2007						Placebo			58.9	10.8	54.6	8.4	1.1	32.9	5.9	14.9						
Fonseca 2013	NCT00885352	313	2013	6	Multinational	Sitagliptin	100 mg daily		55.7	8.7	61.8	8.8	1	29.9	5.2	9.4						Metformin + PPARγ or sulfonylurea
Fonseca 2013						Placebo			56.4	9.4	62.8	8.7	1	30	5.2	10.2						

Forst 2003	Not applicable	143	2003	6	Germany,	Glibenclamide	3.5-10.5 mg daily		56.6	8.6	57.4	7.7	1.2	28.7	3.9	4.3					Oral antidiabetic drugs
Forst 2003						Insulin lispro	Titrated		58.7	7.3	68	7.5	1	29.7	3.6	4.4					
Forst 2005	Not applicable	173	2005	5.5	Germany	Glimepiride	1-6 mg daily		63	7.4	61.9	7.44	0.89	31.8	4.3	6.9					Additional antidiabetic medication
Forst 2005						Pioglitazone	45 mg daily		62.2	8.4	61.8	7.52	0.85	31.7	5	7.4					
Forst 2014	NCT01106690	342	2014	6	Multinational	Canagliflozin	300 mg daily		57	10.2	55.3	7.9	0.9	32.8	7.7	11		87.4			Metformin + pioglitazone
Forst 2014						Canagliflozin	100 mg daily		56.7	10.4	68.1	8	0.9	32.3	6.2	10.5		84.6			
Forst 2014						Placebo			58.3	9.6	66.1	8	1	32.5	6.4	10.1		87.2			
Forst 2015	NCT01649466	161	2015	5.5	Germany	Vildagliptin	50 mg daily		65.9	9.8	56.1	7.6	0.5	29.7	4.5	7.3					Sulfonylurea
Forst 2015						NPH insulin	Titrated		67.6	11.9	60.8	7.7	0.5	31.4	5.2	8.6					
Frederich 2012	NCT00316082	365	2012	5.5	Multinational	Saxagliptin	5 mg daily		54.7	9.71	51.4	8	0.9	31	5.23	1.7	10.8				None
Frederich 2012						Saxagliptin	5 mg daily		55.1	10.35	45.8	7.9	0.9	29.6	5.37	2	11.1				
Frederich 2012						Saxagliptin	2.5 mg daily		55.2	10.44	33.8	8	0.8	30.4	4.84	1.2	12.2				
Frederich 2012						Saxagliptin	2.5-5mg daily		54.3	10.93	52.1	8	1.1	30.6	4.72	2	21.1				
Frederich 2012						Placebo			55.6	10.32	47.3	7.8	1	31.1	4.54	1.7	12.2				
FREEDOM-1	NCT01455857	460	2018	9.1	USA	Exenatide	60 mcg daily		54.7	9.6	59.5	8.5	0.8	33.8	5.2	8.9		87.6			Diet and exercise alone or with metformin, sulfonylureas or pioglitazone monotherapy or in combination
FREEDOM-1						Exenatide	40 mcg daily		55.5	10.3	58.2	8.5	0.8	33.1	5.1	9.1		86.5			
FREEDOM-1						Placebo			54.7	9.1	59.7	8.5	0.8	33.7	5.5	8.6		89.3			
Frias 2018	NCT03131687	105	2018	6	Multinational	Dulaglutide	1.5 mg weekly		58.7	7.8	44.0	8.1	1.0	32.4	5.4	9.3					Metformin
Frias 2018						Placebo			56.6	8.9	57.0	8.0	0.9	32.4	6.0	8.6					
Gaal 2001	Not applicable	152	2001	6.4	Multinational	Miglitol	300 mg daily		57.9	10	41.6	8.5	1	30	4						Metformin
Gaal 2001						Placebo			57.9	8.5	49.3	8.4	1	29.7	3.9						
Gallwitz 2011	NCT00434954	494	2011	6	Germany	Exenatide	10-20 mcg daily		57.2	10.03	59.7	7.89	0.8	33.4	4.23	4.8					Metformin
Gallwitz 2011						Insulin aspart 70/3	Titrated		56.9	9.94	55.5	7.88	0.9	32.9	4.37	5.2					
Gallwitz 2012	NCT00622284	1552	2012	24	Multinational	Glimepiride	1 mg daily		59.8	9.4	61	7.7	0.9	30.3	4.6						Metformin
Gallwitz 2012						Linagliptin	5 mg daily		59.8	9.4	60	7.7	0.9	30.2	4.8						
Gantz 2017	NCT01703208	4202	2017	22.3	Multinational	Omarigliptin	25 mg daily	Cardiovascular disease	63.7	8.5	69.6	8	0.9	31.2	5.5	12		85.7			Diet and exercise alone or on monotherapy or dual combination therapy with metformin, pioglitzone, alpha glucosidase inhibitor, or SGLT2 inhibitor
Gantz 2017						Placebo			63.6	8.5	70.7	8	0.9	31.4	5.6	12.1		86.6			
Gantz 2017a	NCT01814748	303	2017	5.5	Multinational	Omarigliptin	25 mg daily		38.8	4.7	65.7	7.9	0.8	32.9	5.8	2.9					Background therapy
Gantz 2017a						Placebo			39.5	4.5	59.4	8.1	0.9	32.1	5	3.3					
Garber 2006	Not provided	318	2006	5.5	USA	Glibenclamide	5 mg daily		56	31-78	56	8.5	1.2	32	5	5					Metformin
Garber 2006						Rosiglitazone	4 mg daily		56	24-78	65	8.4	1.1	32	5	6					
Garber 2007	NCT00099853	463	2007	5.5	Multinational	Vildagliptin	100 mg daily		54	9.2	44.9	8.7	1.2	32.2	5.8	4.6					Thiazolidinedione
Garber 2007						Vildagliptin	50 mg daily		54	8.2	54.8	8.6	1	32.6	5	4.7					
Garber 2007						Placebo			54.8	10.6	50.7	8.7	1.2	32.3	5.8	4.8					
Garber 2008	NCT00099944	515	2008	5.5	Multinational	Vildagliptin	100 mg daily		58.2	11.1	59.8	8.6	1	30.8	5.3	6.7					Sulfonylurea
Garber 2008						Vildagliptin	50 mg daily		58.6	10.6	59.1	8.5	0.9	32.2	4.9	6.9					
Garber 2008						Placebo			57.9	10.5	58.3	8.5	1	31	5.5	7.8					
Gastaldelli 2014	NCT00381342	79	2014	5.5	USA	Exenatide	10 mcg daily		59	10.8	37.9	7.73	0.92	30.3	5.4						None
Gastaldelli 2014						Exenatide	5 mcg daily		57	10.2	38.5	7.78	0.92	31.2	4.6						
Gastaldelli 2014						Placebo			54	9.8	50	7.77	0.8	32.9	4.9						
GENERATION	NCT01006603	720	2015	12	Multinational	Glimepiride	1-6 mg daily		72.7	5.4	63.3	7.58	0.67	29.9	5	7.6	10				Metformin
GENERATION						Saxagliptin	5 mg daily		72.5	5.7	60.3	7.62	0.65	29.3	4.7	7.6	8.6				
Gentile 2001	Not applicable	100	2001	6.5	Italy	Acarbose	300 mg daily					8.9	0.8								Insulin
Gentile 2001						Placebo						8.7	0.8								
GetGoal-Duo-1	NCT00975286	446	2013	5.5	Multinational	Lixisenatide	20 mcg daily		56	10	49	7.6	0.5	32	6.6	9.6					Metformin ± thiazolidinedione + insulin
GetGoal-Duo-1						Placebo			56	10	51	7.6	0.5	31.7	6	8.7					
GetGoal-Duo-2	NCT01768559	894	2016	5.5	Multinational	Lixisenatide	20 mcg daily		59.8	8.6	46.3	8.5	0.7	32.3	4.6	11.9					Metformin + insulin glargine
GetGoal-Duo-2						Insulin glulisine			60.2	8.6	45.3	8.5	0.7	31.9	4.4	12.3					
GetGoal-Duo-2						Insulin glulisine			59.4	9.5	44.3	8.5	0.8	32.5	4.6	12.4					
GetGoal-F1	NCT00763451	482	2014	17.5	Multinational	Lixisenatide	10-20 mcg daily		54.6	8.9	45	8.1	0.9	32.1	4.8	6					Metformin
GetGoal-F1						Lixisenatide	10-20 mcg daily		55.4	8.9	44	8	0.9	33	5.8	5.8					
GetGoal-F1						Placebo			58.2	9.8	45	8	0.8	32.4	5.5	6.2					
GetGoal-L	NCT00715624	496	2013	6	Multinational	Lixisenatide	10-20 mcg daily		57	10	45	8.4	0.9	31.9	6.2	12.5					Insulin ± metformin
GetGoal-L						Placebo			57	10	49	8.4	0.8	32.6	6.3	12.4					
GetGoal-L-C	NCT01632163	448	2018	5.5	Multinational	Lixisenatide	10-20 mcg daily		53.9	9.9	46.9	7.9	0.66	27.5	4.39	10.3					Insulin with or without metformin
GetGoal-L-C						Placebo			56.2	9.1	43.8	8.6	0.86	27.9	4.48	10.2					
GetGoal-L Asia	NCT00866658	311	2012	6	Multinational	Lixisenatide	10-20 mcg daily		58.7	10.2	44.8	8.54	0.73	25.4	3.7	13.7					Insulin ± sulfonylurea
GetGoal-L Asia						Placebo			58	10.1	51	8.52	0.78	25.2	3.9	14.1					
GetGoal-M	NCT00712673	680	2013	5.5	Multinational	Lixisenatide	20 mcg daily		54.8	10.4	38.4	8.1	0.9	32.5	5.8	6.2					Metformin
GetGoal-M						Lixisenatide	20 mcg daily		54.5	9.2	44.7	8	0.9	33.2	6.9	6.2					
GetGoal-M						Placebo			55	9.4	47.6	8.1	0.9	33.1	6.5	5.9					
GetGoal-M-Asia	NCT01169779	390	2014	5.5	Multinational	Lixisenatide	10-20 mcg daily		54.5	10.3	51.5	7.95	0.81	26.8	3.9	6.5					Metformin ± sulfonylurea
GetGoal-M-Asia						Placebo			55.1	10.5	46.9	7.85	0.71	27.1	3.8	6.8					
GetGoal-O	NCT01798706	350	2017	5.5	Multinational	Lixisenatide	20 mcg daily		74	4	52.3	8.1	0.7	29.9	3.7	13.6					Permitted therapies were metformin, sulfonylurea (except glibenclamide >10 mg and gliclazide >160 mg), meglitininde (excet repaglinide >6 mg), pioglitazone, and basal insulin)
GetGoal-O						Placebo			74.4	3.8	51.7	8.1	0.7	30.1	4.5	14.6					
GetGoal-P	NCT00763815	484	2013	5.5	Multinational	Lixisenatide	10-20 mcg daily		56	9.5	53	8.1	0.9	33.7	6.7	8.1					Thiazolidinedione ± metformin
GetGoal-P						Placebo			55.3	9.5	51	8.1	0.8	34.4	7	8.1					
GetGoal-S	NCT00713830	859	2014	5.5	Multinational	Lixisenatide	10-20 mcg daily		57	9.8	49.5	8.3	0.9	30.1	6.6	9.1					Sulfonylurea ± metformin
GetGoal-S						Placebo			57.8	10.1	52.6	8.2	0.8	30.4	6.6	9.8					
Giles 2008	NCT00521820	518	2008	6	Multinational	Glyburide	10-15 mg daily	Heart failure	63.4	9.38	77	7.95	1.8	29.7	5.37	11.7	100				Thiazolidinedione or sulfonylurea ± insulin
Giles 2008						Pioglitazone	30-45 mg daily		64.2	9.92	70.2	8.74	1.6	29.6	5.2	11.8	100				
Giugliano 1993	Not applicable	50	1993	6	Italy	Metformin	1500 mg daily		60	1	37	11.5	1.2	33	3.1	11.9					Insulin
Giugliano 1993						Placebo			60.8	1.1	39.1	11.7	1.3	32.7	3.2	11.5					
GLAC	Not applicable	200	2004	9	Multinational	Glibenclamide	10.5 mg daily		57.9	9.2	73	8.5	0.8	29.6	4.8						No therapy or monotherapy
GLAC						Pioglitazone	45 mg daily		60	8.5	62	8.4	0.7	30.2	5.6						
GLAD	Not applicable	244	2004	12	Mexico	Glimepiride	8 mg daily		55.7	9.3	53	8.45	1.02	28.8	3.2	6.8					None
GLAD						Pioglitazone	45 mg daily		55.1	8	45	8.54	0.9	29.3	3.3	6.5					
GLAL	Not applicable	567	2005	12	Multinational	Gliclazide	320 mg daily		56	9.9	61.3			31	5.6	2.9					None
GLAL						Pioglitazone	45 mg daily		57	9.8	63.3			32	6.4	2.7					
Glimepiride Combina	Not applicable	145	1998	5.5	USA	Glimepiride	8 mg twice daily		58	8	62.5	9.7		32.2	4.4	4					None
Glimepiride Combination	Group					Placebo			58	8	54.8	9.9		33.7	5.4	7					
Göke 2002	Not applicable	265	2002	6	Germany	Pioglitazone	45 mg daily		58.9	9.1	53.5	8.98	1.2	30.9	5.3	4.75					None
Göke 2002						Acarbose	300 mg daily		58.8	9.1	54.5	9.03	1.32	30.8	4.4	4.9					
Göke 2010	Not provided	858	2010	12	Multinational	Glipizide	5-20 mg daily		57.6	10.37	54	7.7	0.9	31.3	6.17	5.4					Metformin
Göke 2010						Saxagliptin	5 mg daily		57.5	10.26	49.5	7.7	0.9	31.5	5.7	5.5					
Gómez-Perez 2002	Not applicable	105	2002	5.5	Mexico	Rosiglitazone	8 mg daily		54.2	9.3	19.4			27.6	3.2	10.7					Metformin
Gómez-Perez 2002						Rosiglitazone	4 mg daily		51.7	8.6	28.6			28	4	11.1					
Gómez-Perez 2002						Placebo			53.4	7.5	29.4			28.5	3.9	9.1					
Gomis 2011	NCT00641043	389	2011	5.5	Multinational	Linagliptin	5 mg daily		57.7	9.6	58.7	8.6	0.79	28.7	4.8						Pioglitazone
Gomis 2011						Placebo			57.1	10.1	65.4	8.58	0.87	29.7	4.8						
Goodman 2009	Not provided	370	2009	5.5	Multinational	Vildagliptin	100 mg daily		54.7	10.3	52.8	8.5	1	31.7	4.6						Metformin
Goodman 2009						Vildagliptin	100 mg daily		55.2	11.4	52.8	8.5	0.9	31	4.8						
Goodman 2009						Placebo			54.5	9.7	67.2	8.7	1.1	31.7	4.3						
Grant 1996	Not applicable	75	1996	6	UK	Metformin	3000 mg daily														None
Grant 1996						Metformin	1500 mg daily														
Grant 1996						Placebo															
GRAVITAS	ISCTRN13643081	80	2019	6	UK	Liraglutide	1.8 mg daily		55		38	7.9	1.39	36.1	7.8	16.4					Glucose lowering drugs based on guidelines
GRAVITAS						Placebo			57		48	7.4	0.75	37	7.7	19.6					
Grey 2014	ACTRN126070006	86	2014	12	New Zealand	Pioglitazone	15-30 mg daily				49	7.4	3.5	31	5						Insulin; thiazolidinedione excluded
Grey 2014						Placebo					53	7.5	3.2	31	5						
Gudipaty 2014	NCT00775684	47	2014	5.5	USA	Glimepiride	4 mg daily		52	7.4	57	6.7	0.4	31	7.5	3.4					None
Gudipaty 2014						Sitagliptin	100 mg daily		57	10.4	66	6.5	0.4	33	3.5	5.3					
Gudipaty 2014						Exenatide	20 mcg daily		57	7.5	64	6.4	0.4	33	7.5	3.3					
Gurkan 2014	Not provided	34	2014	6	Turkey	Exenatide	20 mcg daily		52.2	7.3	29.4	7.95	0.81	35.9	3.7		12				Metformin
Gurkan 2014						Insulin glargine	Titrated		53.1	7	42	8.11	0.76	33.2	4.5		6				
Gutniak 1987	Not applicable	20	1987	12	Sweden	Glyburide	10.5 mg daily		56.1	4.74		11.1	0.4								Insulin
Gutniak 1987						Placebo			58	2		10.3	0.5								
Güvener 1999	Not applicable	40	1999	6	Turkey	Gliclazide	320 mg daily		53.1	6.1	22.2	8.32	1.1	28.04	4.29	11.86					Insulin
Güvener 1999						Acarbose	150 mg daily		59.61	9.3	20	8.6	0.67	27.6	5.41	10.15					

Guzman 2017	NCT02111096	174	2017	6	Multinational	Sitagliptin	100 mg daily		57.1	9	75.6	8.3	0.9	31.8	6.1	10.9						Metformin + sulfonylurea
Guzman 2017						LY2409021	20 mg daily		56.9	8.3	63.1	8.1	1	32.6	5.5	10.2						
Guzman 2017						Placebo			57.8	8.2	54.4	8.3	0.9	31.2	4.9	12.4						
Haak 2012	NCT00798161	791	2012	6	Multinational	Linagliptin	2.5 mg daily		55.6	11.2	51	8.7	1	29.7	5.3							Metformin
Haak 2012						Linagliptin	2.5 mg daily		56.4	10.7	53.8	8.7	1	28.6	4.8							
Haak 2012						Standard care			55.2	10.6	53.1	8.5	0.9	29.5	5.3							
Haak 2012						Standard care			52.9	10.4	56.9	8.7	0.9	28.9	4.8							
Haak 2012			2012	6	Multinational	Linagliptin	5 mg		56.2	10.8	56.3	8.7	1	29	4.7							None
Haak 2012						Placebo			55.7	11	50	8.7	1	28.6	5.2							
Hadjadj 2016	NCT01719003	665	2016	5.5	Multinational	Metformin	1000 mg daily		51.6	10.8	51.2	8.69	1.04	30.3	5.8			90.9				None
Hadjadj 2016						Metformin	2000 mg daily		53.4	10.9	56.1	8.58	1.13	30.5	5.9			93.2				
Hadjadj 2016						Empagliflozin	10 mg daily		53.1	10.7	57.4	8.62	1.24	30.3	5.2			94				
Hadjadj 2016						Empagliflozin	25 mg daily		53.3	10.7	50.6	8.86	1.29	30.6	5.9			91.7				
Halimi 2000	Not applicable	152	2000	6	France	Acarbose	300 mg daily		56	9.2	47.5	8.6	1.1	30.1	3.3	9.5						None
Halimi 2000						Placebo			55	10	62.9	8.5	1.1	29.7	3.3	9						
Hällsten 2002	Not applicable	31	2002	6	Finland	Metformin	1000-2000 mg daily		57.8	7.9	61.5	6.9	0.7	29.9	4							None
Hällsten 2002						Rosiglitazone	4-8 mg daily		58.6	7.5	71.4	6.8	0.7	29.3	3.7							
Hällsten 2002						Placebo			57.7	7.1	71.4	6.3	0.4	30.3	4.5							
Halvorsen 2019	NCT01377844	286	2019	22.3	Mexico and	Bexagliflozin	20 mg daily		56.2	10.9	46.2			29.7	5.35	7.55						None
Halvorsen 2019						Placebo			54.9	10.3	35.5			30.6	5.46	7.38						
Halvorsen 2019a	NCT03115112	384	2019	5.5	Multinational	Sitagliptin	100 mg daily		59.6	9.8	65.3	8.0	0.9	31.4	5.3	9.36						Metformin
Halvorsen 2019a						Bexagliflozin	20 mg daily		59.3	9.7	62.8	7.9	0.8	32.1	6.1	8.22						
Han 2016	Not provided	219	2016	5.5	Unclear	Gemigliptin	50 mg daily															Metformin + glimepiride
Han 2016						Placebo																
Han 2018	NCT02452632	143	2018	5.5	Republic of Korea	Ipragliflozin	50 mg daily		57.62	8.26	50.7	7.9	0.69	25.5	3.07	11.62		89.4				Metformin + sitagliptin
Han 2018						Placebo			57.44	7.88	48.5	7.92	0.79	26.05	3.79	11.3		90.7				
Handelsman 2017	NCT01682759	751	2017	12	Multinational	Glimepiride	6 mg daily		58	9	56.3	7.4	0.7	31.7	6	7.7						Metformin
Handelsman 2017						Omarigliptin	25 mg weekly		58	10	54	7.5	0.8	31.2	5.3	7.6						
Handelsman 2019	NCT02284893	461	2019	5.5	Multinational	Dapagliflozin	10 mg daily		55.9	8.9	43.1	8.8	0.8	33.3	6.1	7.9		92.2				Metformin plus saxagliptin
Handelsman 2019						Control			55.8	9.6	48	8.9	0.9	32.8	6.3	8.2		92.9				
Haneda 2016	JapicCTI-111507	145	2016	5.5	Japan	Luseogliflozin	2.5-5 mg daily		67.9	8.9	75.8	7.72	0.68	25.45	4.18	10.4	20.2	52	335.7			No therapy or 1-2 oral drugs
Haneda 2016						Placebo			68.4	8.9	78	7.69	0.65	25.81	3.95	12.6	20	52.4	231.9			
Hanefeld 1991	Not applicable	100	1991	5.5	Germany	Acarbose	300 mg daily		60	43-70	49	9.2		27.4		5.8						None
Hanefeld 1991						Placebo			59	43-70	47	9.5		27.7		4.1						
Hanefeld 2004	Not applicable	639	2004	12	Multinational	Metformin	850-2550 mg daily		60	8	54.7	8.8	0.97	30	4.6	7.1				0.11		Sulfonylurea
Hanefeld 2004						Pioglitazone	15-45 mg daily		60	8.8	53.6	8.82	0.98	30.2	4.4	7				0.07		
Hanefeld 2007	Not provided	598	2007	12	Multinational	Glibenclamide	15 mg daily		60.1	8.3	70.4	8.2	1.3	28.7	3.9	6.4						None
Hanefeld 2007						Rosiglitazone	8 mg daily		60.4	8.2	57.1	8.1	1.3	28.7	3.7	5.9						
Hanefeld 2007						Rosiglitazone	4-8 mg daily															
HARMONY 1	NCT00849056	310	2014	12	Multinational	Albiglutide	30 mg weekly		55.2	9.98	61.3	8.1	1	33.6	5.9	8						Thiazolidinedione ± metformin
HARMONY 1						Placebo			54.9	9.4	58.3	8.1	0.9	34.7	24.5	7.9						
HARMONY 2	NCT00849017	301	2016	12	Multinational	Albiglutide	50 mg weekly		52	11.8	50.5	8.2	0.9	33.9	5.5	4.2						None
HARMONY 2						Albiglutide	30 mg weekly		53.6	10.9	57.4	8	0.8	33.7	5.1	3.4						
HARMONY 2						Placebo			53.1	11.7	57.4	8	0.9	33	5.4	4.3						
HARMONY 3	NCT00838903	1012	2014	24	Multinational	Glimepiride	2-4 mg daily		54.4	10	51.5	8.1	0.8	32.5	5.5	6						Metformin
HARMONY 3						Sitagliptin	100 mg daily		54.3	9.8	46	8.1	0.8	32.5	5.4	5.8						
HARMONY 3						Albiglutide	30-50 mg weekly		54.3	10.1	44.7	8.1	0.8	32.7	5.6	6						
HARMONY 3						Placebo			56.1	10	49.5	8.2	0.9	32.8	5.4	6.7						
HARMONY 4	NCT00838916	745	2014	12	Multinational	Albiglutide	30 mg weekly		55.8	9.3	56.7	8.28	0.9	33.2	5.6	8.9	5.3					Metformin ± sulfonylurea
HARMONY 4						Insulin glargine	Titrated		54.7	9.8	54.8	8.36	0.95	33	5.4	8.4	4.6					
HARMONY 5	NCT00839527	685	2015	12	Multinational	Pioglitazone	30 mg daily		55.7	9.4	53.4	8.29	0.88	32.2	5.7	9.2	5.1					Metformin + sulfonylurea
HARMONY 5						Albiglutide	30 mg weekly		54.5	9.5	49.8	8.19	0.91	32.4	5.5	8.5	3.7					
HARMONY 5						Placebo			55.7	9.6	60.9	8.26	0.98	31.8	4.9	9.3	3.5					
HARMONY 6	NCT00976391	566	2014	12	Multinational	Albiglutide	30-50 mg weekly		54.8	9.1	46	8.5	0.9			11	7.7					Insulin ± oral drugs
HARMONY 6						Lispro Insulin	Titrated		56.3	8.9	48	8.4	0.9			11	9.6					
HARMONY OUTCOMI	NCT02465515	9463	2018	19.2	Mutlinational	Albuglutide	30-50 mg weekly	Cardiovascular disease	64.1	8.7	70	8.76	1.5	32.3	5.9	14.1	70	79.1				Standard therapy
HARMONY OUTCOMES						Placebo			64.2	8.7	69	8.72	1.5	32.3	5.9	14.2	71	78.9				
Hartemann-Heurtier	NCT00159211	27	2009	5.5	France	Pioglitazone	30 mg daily		62	10	64.2	8.3	0.5	30	5	12						Metformin + sulfonylurea
Hartemann-Heurtier	2009					NPH insulin	0.2 IU/kg/day		58	10	53.8	8.6	0.5	32	4	12						
Hartley 2015	NCT01189890	480	2015	7	USA	Glimepiride	Titrated		70.8	4.9	40.3	7.8	0.7	29.7	5.1	9.4						None
Hartley 2015						Sitagliptin	50-100 mg daily		70.6	4.8	47.2	7.8	0.7	29.7	4	8						
Hasche 1999	Not applicable	74	1999	24	Germany	Acarbose	100-600 mg daily		63.8	9.8	47.2	8.5	0.7	26.1	2.9							None
Hasche 1999						Placebo			63.1	10.5	50	8.3	0.7	26.7	2.8							
Hattori 2017	UMIN000004674	74	2017	5.5	Japan	Sitagliptin	50 mg daily		65.7	5.4	51.5	7.3	0.6	23.4	3.4							Sulphonylurea
Hattori 2017						Voglibose or migli	0.2 mg or 150 mg daily		63.1	9.8	72.9	7	0.5	24.5	3.9							
Hattori 2018	UMIN000021552	102	2018	12	Japan	Empagliflozin	10 mg daily		57.4	12.3	74.5	7.01	1.1	30	4.9							Medical treatment other than SGLT2 inhibitors
Hattori 2018						Placebo			58.1	9.71	80.4	6.84	0.85	30	4.4							
HEELA	Not provided	235	2009	6	UK	Exenatide	10-20 mcg daily		56.8	10.2	70.3	8.65	0.7	34.6	5.7	9	13.6					2-3 oral drugs (metformin, sulfonylurea, thiazolidinedione)
HEELA						Insulin glargine	Titrated		56.2	7.9	66.4	8.48	0.7	33.7	4.9	8.4	18.1					
Hegele 1995	Not applicable	141	1995	12	Canada	Acarbose	Not reported		53.7	4.8	48.6	12.2	2.1									None
Hegele 1995						Placebo			55.5	5.1	46.5	12.4	2.9									
Heine 2005	NCT00082381	549	2005	6	Multinational	Exenatide	20 mcg daily		59.8	8.8	55	8.2	1	31.4	4.4	9.9						Metformin + sulfonylurea
Heine 2005						Insulin glargine	Titrated		58	9.5	56.6	8.3	1	31.3	4.6	9.2						
Heliövaara 2007	Not provided	59	2007	12	Multinational	Glibenclamide	1.75-10.5 mg daily		57.2	9.9	73.333333	8.35	0.66	30.5	4.9							None
Heliövaara 2007						Pioglitazone	30-45 mg daily		57.4	7.5	58.62069	8.18	0.48	32.3	7							
Henry 2012	NCT00643851	831	2012	5.5	USA	Metformin	500-2000 mg daily		51.8	9.8	47.3	9.2	1.3			1.6						None
Henry 2012						Dapagliflozin	5 mg daily		52.3	10.2	45.3	9.1	1.4			1.6						
Henry 2012						Metformin	500-2000 mg daily		52.7	10.4	46.6	9.1	1.3			1.9						
Henry 2012						Dapagliflozin	10 mg daily		51.1	11.5	47.9	9.1	1.3			2.1						
Henry 2014	NCT00722371	751	2014	12	USA	Pioglitazone	45 mg daily		52.5		50.5	8.7	1.2	31.2	5.1	3.7						None
Henry 2014						Pioglitazone	30 mg daily		51.8		54.1	8.9	1.1	30.9	5.6	3.9						
Henry 2014						Pioglitazone	15 mg daily		50.3		65	8.8	1	30.7	5.2	3.7						
Henry 2014						Sitagliptin	100 mg daily		51		60.2	8.6	1.2	31.4	5.7	4.5						
Hermann 1999	Not applicable	35	1999	12	Sweden	Metformin	1700 mg daily		56.9	10.2	43.75	9.1	1.3	33.6	3.5	13						Insulin
Hermann 1999						Placebo			58.1	9.7	63.16	8.7	1	32.6	3.8	13						
Hiramatsu 2018	Not provided	139	2018	48	Japan	Sitagliptin	50 mg daily	Chronic kidney disease	69.9	8.5		6.72	0.72	24.2	3.8	8.8		46.1	300			None, insulin, alphaglucosidase inhibitor, or glinide
Hiramatsu 2018						Linagliptin	5 mg daily		69	7.7		6.71	0.75	23.8	4.8	8.3		45.2	289			
Hiramatsu 2018						Liraglutide	0.9 mg daily		70.5	5.7		6.75	0.62	23.5	3.5	9.2		40.2	380			
Hirano 2009	Not provided	61	2009	6	Japan	Pioglitazone	15-30 mg daily	Acute coronary syndrome	65	13	77			24.6	3.3		100					Anti-diabetic medications (sulfonylurea; alpha-glucosidase inhibitor; biguanide; insulin)
Hirano 2009						Placebo			62	12	70			24.9	3		100					
Hirano 2012	Not provided	44	2012	6	Japan	Acarbose	150-300 mg daily	Acute coronary syndrome	65	10	82	8	1.8	25	3.9		100					OADs except alpha-glucosidase inhibitor
Hirano 2012						Control			65	11	77	8.1	1.7	24.9	3.8		100					
Hollander 2007	NCT00054782	670	2007	5.5	USA	Rosiglitazone	4 mg daily		52.6	10.1	48.1	9	1.2	33.7	7.1	13						Insulin
Hollander 2007						Rosiglitazone	2 mg daily		52.7	9.6	57	8.9	1.1	32.8	7.4	12.5						
Hollander 2007						Placebo			53.8	10.2	46.2	9.1	1.3	33	6.5	12.6						
HOME	NCT00375388	390	2009	51.6	Netherlands	Metformin	850-2550 mg daily		64	10	41.3	7.9	1.2	30	5	14						Insulin
HOME						Placebo			59	11	50	7.9	1.2	30	5	12						
Home 2018	NCT01717313	329	2018	5.5	Multinational	Omarigliptin	25 mg weekly		57.4	9.2	57.6	8	0.9	31.1	6.1	5.4						None
Home 2018						Placebo			57	9.7	59.1	8.1	1	30.8	6.6	5.7						
Hong 2013	Not provided	50	2013	6	Korea	Pioglitazone	Not reported															Unclear
Hong 2013			2013	6	Korea	Placebo																Unclear
Hong 2015	Not provided	72	2015	9	Republic of Korea	Pioglitazone	15 mg daily	Coronary artery disease	58.3	11.8	52.8	7.6	1.6	24.6	3.9	2.33	100					Treated/untreated
Hong 2015						Control			60	12.7	58.3	7.5	1.9	24.4	3.5	2.17	100					
Hong 2016	Not provided	142	2016	5.5	Republic of Korea	Teneglitpin	20 mg daily		56.64	10.07	52.5	7.74	0.61	24.96	2.5	55.07						None
Hong 2016						Placebo			57.93	11.9	65.1	7.74	0.58	25.1	3.2	55.09						
Horton 2000	Not applicable	529	2000	5.5	USA	Metformin	1500 mg daily		56.8	10.9	68	8.4	1.2	29.6	4.3	4.5						None
Horton 2000						Nateglinide	360 mg daily		58.6	10.7	61.5	8.3	1	29.6	3.8	4.7						
Horton 2000						Placebo			59.6	10.9	60.5	8.3	1.1	29.2	3.9	4.6						
Hotta 1993	Not applicable	37	1993	5.5	Japan	Acarbose	300 mg daily		49.8		73.6	11.1	2	23.5		4.6						None

Hotta 1993						Placebo			47.9		77.8	10.4	1.6	22.9		4.8						
Hsieh 2011	Not provided	105	2011	5.5	Taiwan	Miglitol	150-300 mg daily		58.4	10.5	44	8.14	0.72	25.3	3.1							Sulfonylurea
Hsieh 2011						Placebo			59	10.7	34	8.11	0.77	26.1	2.9							
Hu 2007	Not provided	78	2007	6	China	Rosiglitazone	4 mg daily	Chronic kidney disease	62	10	55	8.6	2.2									None
Hu 2007						Placebo			62	9	52	8.5	2.1									
Hwang 2008	Not provided	90	2008	12	Korea	Rosiglitazone	4-8 mg daily		55.1	10	53.4	7.81	0.73	26.5	2.8							Glibenclamide
Hwang 2008						Placebo			53.4	9.7	45.6	7.9	1.12	26.6	2.5							
Hygum 2020	NCT02473809	60	2020	6.0	Denmark	Liraglutide	1.8 mg daily		62	53.3				33		6.0						Background therapy
Hygum 2020						Placebo			64	46.7				31.3		7.0						
Iacobellis 2017	NCT02014740	95	2017	6	USA	Liraglutide	1.8 mg daily		50	10	41	6.6	0.8	37.8	7.3							Metformin
Iacobellis 2017						Control			52	10	37	6.4	0.6	32.6	6.7							
Ikonomidis 2018	Not provided	60	2018	6	Greece	Metformin																None
Ikonomidis 2018						Liraglutide																
Ikonomidis 2020	NCT03878706	80	2020	12	Greece	Empagliflozin	25 mg daily	High cardiovascular risk	58.0	10.0	75.0	7.8	0.9	29.8	3.0	6.6		85				Metformin + basal insulin
Ikonomidis 2020						Liraglutide	1.8 mg daily		57.0	9.0	67.5	8.0	1.1	30.0	4.0	5.9		85				
ILLUMINATE	NCT01135433	168	2015	5.5	Japan	Ipragliflozin	50 mg daily		57.7	9.24	58.9	8.25	0.72	25.96	4.4	7.5						Metformin
ILLUMINATE						Placebo			56.2	10.7	58.9	8.38	0.74	25.47	3.1	8.1						
Inagaki 2012	NCT00935532	427	2012	6	Japan	Exenatide	2 mg weekly		57.07	10.44	66	8.51	0.82	26.11	4.03	8.86						Metformin ± sulfonylurea ± thiazolidinedione
Inagaki 2012						Insulin glargine	Titrated		56.44	11.16	69.8	8.5	0.79	26.18	3.77	9.21						
Inagaki 2013	NCT01204294	206	2013	12	Japan	Metformin	500-2250 mg daily		61.2	10.6	69.8	8	0.1	25.8	4							Monotherapy with an SU, biguanide, TZD, α glucosidase inhibitor, DPP-4 inhibitor or glinide
Inagaki 2013						Linagliptin	5 mg daily		61.8	10.8	73.4	8.1	0.8	24.5	4.2							
Inagaki 2014	NCT01413204	272	2014	5.5	Japan	Canagliflozin	200 mg daily		57.4	11.1	81.8	8.04	0.77	25.43	4.18	5.88		87.2				None
Inagaki 2014						Canagliflozin	100 mg daily		58.4	10.4	65.6	7.98	0.73	25.59	4.2	4.72		81.4				
Inagaki 2014						Placebo			58.2	11	64.5	8.04	0.7	25.85	4.39	5.63		84.7				
Inagaki 2015	NCT01632007	245	2015	5.5	Japan	Tretagliptin	100 mg daily		58		72	7.73	0.85	25.4	4.42	6.3		113.3				None
Inagaki 2015						Alogliptin	25 mg daily		60		75	7.87	0.86	24.7	3.79	7.1		109.1				
Inagaki 2015						Placebo			62		86	7.72	0.77	24.6	4.3	7.5		98.4				
INICOM	NCT01787396	292	2016	5.5	Republic of Korea	Metformin	1000-2000 mg daily		54	11.3	60.1	8.73	0.91			4.1						None
INICOM						Gemigliptin	50 mg daily		53.4	11	57.1	8.7	0.9			3.5						
Inoue 2019	UMIN000018839	49	2018	5.5	Japan	Ipragliflozin	50 mg daily		60.5	9.8	54.2	8.12	0.93	27.9	4	15.9		91				Insulin therapy alone or with insulin plus oral hypoglycemic agents other than SGLT2 inhibitors
Inoue 2019						Control			60.8	12.1	58.3	8.3	0.65	27.7	4.5	19.1		82.9				
Insulin Glargine 4014	Not provided	216	2006	5.5	USA	Rosiglitazone	8 mg daily		55.3	11.4	58	8.7	1	33.6	6.3	8.1						Metformin + sulfonylurea
Insulin Glargine 4014						Insulin glargine	Titrated		55.9	10.5	45	8.8	1	34.6	7	8.5						
INTERVAL	NCT01257451	278	2013	5.5	Europe	Vildagliptin	50-100 mg daily		75.1	4.3	52.5	7.9	0.8	29.1	3.8	12.2						Oral drugs
INTERVAL						Placebo			74.4	4	38.1	7.9	0.7	30.5	4.8	10.6						
Ito 2011	Not provided	60	2011	5.5	Japan	Vildagliptin	50-100 mg daily	Haemodialysis	67	10.95	70	6.7	0.55	22.7	2.74			<15				Mitiglinide or Voglibose
Ito 2011						Conrol			68	9.17	67	6.7	0.46	22.4	2.29			<15				
Ito 2017	UMIN000022651	66	2017	5.5	Japan	Pioglitazone	15-30 mg daily		59.1	9.8	53	8.3	1.4	29.9	6.2	9.5						Diet and exercise therapy alone or with oral hypoglycemic agents other than SGLT2 inhibitors and thiazolidinediones and/or insulin
Ito 2017						Ipragliflozin	50 mg daily		57.3	12.1	44	8.5	1.5	30.7	5	8.7						
Jabbour 2014	NCT00984867	451	2014	11	Multinational	Dapagliflozin	10 mg daily		54.8	10.4	57	7.9	0.8			5.7						DPP-4 inhibitor ± metformin
Jabbour 2014						Placebo			55	10.2	52.7	8	0.8			5.64						
Jacob 2007	Not provided	57	2007	6	USA	Metformin	2000 mg daily		47	10	61	11.1	1.4	31.9	7.1	8						Insulin
Jacob 2007						Pioglitazone	30 mg daily		47	11	72	11.2	1.7	30.7	8.5	5						
Jacob 2007						Standard care			44	13	57	11.2	1.8	32.3	5.6	9						
Jain 2006	Not provided	502	2006	12.9	Multinational	Glyburide	5-15 mg daily		52.1	12.39	56.2	9.2	1.26	32.8	5.71	0.78						None
Jain 2006						Pioglitazone	15-45 mg daily		52.1	11.28	53	9.2	1.2	32.5	5.75	0.8						
JEDIS-1	Not provided	49	2017	24	Japan	Metformin	2250 mg daily															None
JEDIS-1						Gliclazide	120 mg daily															
JEDIS-1						Acarbose or miglit	300 mg daily/225 mg daily															
JEDIS-1						Standard care																
Jeon 2011	Not provided	102	2011	7.5	Republic of Korea	Glimepiride	4 mg daily		55.38	10.98	60.8	8.13	0.86	23.1	4.24	5.92						Metformin
Jeon 2011						Vildagliptin	100 mg daily		53.51	10.41	68.6	8.01	1.2	22.69	7.75	5.89						
Jeon 2018	Not provided	310	2018	5.5	Republic of Korea	Dapagliflozin	10 mg daily		59.24	12.69	54.3	8.5	0.93			12.14		99.69				Metformin, glimepiride + DPP-4 inhibitor
Jeon 2018						Insulin glargine			56.13	15.17	47.3	8.82	1.36			12.79		98.6				
Jerums 1987	Not applicable	40	1987	24	Germany;Australi	Gliclazide	Not provided	Chronic kidney disease	49	4	58.8	10.5	2.1			12.7						Insulin
Jerums 1987						Placebo	Not provided		53	5	37.5	9.6	1.9			11.7						
Ji 2014	NCT01095653	393	2014	5.5	China	Dapagliflozin	10 mg daily		51.2	9.89	64.7	8.28	0.85	25.76	3.43	1.67						None
Ji 2014						Dapagliflozin	5 mg daily		53	11.07	65.6	8.14	0.74	25.2	3.29	1.15						
Ji 2014						Placebo			49.9	10.87	65.9	8.35	0.85	25.93	3.64	1.3						
Ji 2016	Not provided	497	2016	5.5	China	Metformin	1700 mg daily		53	10.3	60.5	8.7	1.1	25.8	3.5	1.1						None
Ji 2016						Metformin	1000 mg daily		52.6	9.5	54.8	8.7	1	26	3.6	1						
Ji 2016						Sitagliptin	100 mg daily		51.7	10.2	61.7	8.7	1.1	26	3.5	1.1						
Ji 2016						Placebo			53.6	9.7	68.5	9	1.1	25.4	3.4	1.1						
Ji 2017	Not provided	484	2017	5.5	Multinational	Metformin	1000 mg daily		53.6	9.91	50.6	8.4	0.78	26.3	3.57							None
Ji 2017						Alogliptin	25 mg daily		55.4	9.62	60.1	8.48	0.7	26.16	3.92							
Ji 2017						Placebo			52.2	10.17	58.3	8.21	0.77	26.56	4.22							
Jian 2018	Not provided	126	2018	6	China	Dapagliflozin																Insulin
Jian 2018						Control																
Jibran 2006	Not provided	100	2006	12	Pakistan	Glibenclamide	5-15 mg daily		45.8	8.8	20	10.2	1.6	30.4	5.6							None
Jibran 2006						Repaglinide	0.5-2 mg three times daily		46.6	10.5	32	9.9	1.6	27.1	3.5							
Johnston 1998	Not applicable	385	1997	12	USA	Placebo			52.9		60	8.7		31.8	-9	5.7						No treatment or sulfonylurea
Johnston 1998						Miglitol	150-600 mg daily		53.9		52	8.53		30.6	-9	4.8						
Johnston 1998a	Not applicable	340	1998	12	USA	Miglitol	150-300 mg daily		55	14.28	50	8.69	2	31.9	10	5.1			158			No treatment or sulfonylurea
Johnston 1998a						Placebo			56.9	13.32	51	8.62	1.84	32	9.22	4.5			215			
Johnston 1998b	Not applicable	364	1998	12	USA	Glyburide	1.25-20 mg daily		67.7	5.75	64.1	8.4	0.96	29.3	5.75	7.2						None
Johnston 1998b						Miglitol	150 mg daily		67.8	6.45	71.8	8.4	0.92	29.4	5.53	6.8						
Johnston 1998b						Miglitol	75 mg daily		67.2	5.85	63.2	8.3	0.97	29.7	5.85	7.5						
Johnston 1998b						Placebo			68.5	5.75	71.7	8.4	0.96	30.4	5.75	7						
Josse 2003	Not applicable	192	2003	12	Canada	Acarbose	300 mg daily		69.7	5	69.9	7.4	1	28.3	4	5.8						None
Josse 2003						Placebo			70.3	5	60.6	7.3	1	28.6	4	4.8						
Jovanovic 2000	Not applicable	361	2000	5.5	USA	Repaglinide	4 mg daily		57.6		60	8.7	1.7	29.5	4.4	6.3						None
Jovanovic 2000						Repaglinide	1 mg daily		57.9		69	8.9	1.9	29.4	4.5	6.6						
Jovanovic 2000						Placebo			58.5		65	8.6	1.4	29.8	4.3	6.8						
Jovanovic 2004	Not applicable	123	2004	5.5	USA	Pioglitazone	30 mg daily		56.2	12.2	50	9.3		32.1	5.3	6.1						None
Jovanovic 2004						Repaglinide	12 mg daily		57.8	13.1	59	9		31.2	5.3	6.9						
Jung 2005	Not applicable	30	2005	6	Korea	Metformin	500 mg twice daily		54	14	46	9	0.8	24.6	2.4	7	15.4					Glimepiride
Jung 2005						Rosiglitazone	4 mg daily		60	8	43	9.3	0.9	23.3	2.6	9	14.3					
Juurinen 2009	Not provided	81	2009	5.5	Finland	Nateglinide	360 mg daily		55.3	8.2	60	7.5	0.63	33.6	4.4	9.5						Metformin + insulin
Juurinen 2009						Placebo			56.6	8.3	51	7.4	0.64	32.1	4.5	9.3						
Kadoglou 2007	NCT00306176	50	2007	8	Greece	Rosiglitazone	8 mg daily		59.04	7.35	40	8.53	1.26	30.04	2.99	5.29						Metformin; Gliclazide
Kadoglou 2007						Control			60.32	9.28	39	8.03	0.91	28.96	1.03	5.78						
Kadoglou 2008	Not provided	70	2008	6	Greece	Rosiglitazone	8 mg daily		63.8	7.3	40	8.2	1.2	29.5	3.82	8.5						Metformin; Gliclazide
Kadoglou 2008						Control			66.7	9.6	45	8	0.8	29.9	4.3	7.5						
Kadoglou 2011	Not provided	140	2011	6	Greece	Rosiglitazone	4 mg daily		62	8.3	27	7.58	0.6	29.68	2.47	1.8						Metformin
Kadoglou 2011						Control			62.7	6.8	28	7.56	0.64	30.04	4.85	2.7						
Kadowaki 2011	NCT00577824	179	2011	5.5	Japan	Exenatide	20 mcg daily		59.4	89.8	68.1	8.2	1	25.8	3.9	11.6						Sulphonylurea ± biguanide or thiazolidinedione
Kadowaki 2011						Exenatide	10 mcg daily		58.5	9.3	68.1	8.3	0.8	25	4.1	12.2						
Kadowaki 2011						Placebo			56.3	11.4	68.6	8.1	0.9	25.8	4.2	12.4						
Kadowaki 2017	NCT02354235	138	2017	5.5	Japan	Canagliflozin	100 mg daily		58.4	8.9	77.1	8.18	0.9	25.53	4.21	8.34						DPP-4 inhibitor
Kadowaki 2017						Placebo			56	9.5	77.9	7.87	0.83	26.44	3.87	6.5						
Kadowaki 2018	NCT02354222	154	2018	5.5	Japan	Teneglitin	20 mg daily		55.9	8.3	83.1	7.98	0.8	25.53	3.95	8.15						Canagliflozin
Kadowaki 2018						Placebo			54.1	10.2	75.3	8.09	0.85	26.5	4.82	7.34						
Kaku 2009	UMIN000001110	169	2009	6.5	Japan	Pioglitazone	15-30 mg daily		52	8.6	66.3	7.58	1	25.6	4.2	4.5						Metformin
Kaku 2009						Control			53	7.5	43	7.55	0.9	25.4	3.6	5.6						
Kaku 2009a	UMIN000001363	587	2009	12	Japan	Pioglitazone	15-30 mg daily	Cardiovascular disease	58.1		63	7.6		26.51	-9		9.6					None
Kaku 2009a						Control			57.9		62	7.53		26.92	-9		7.5					
Kaku 2011	NCT00393718	400	2011	12	Japan	Glibenclamide	1.25-2.5 mg daily		58.5	10.4	65.2	9.18	0.97	24.6	3.8	8.5						None
Kaku 2011						Liraglutide	0.3-0.9 mg daily		58.2	10.4	68.3	9.32	1.08	24.9	3.7	8.1						
Kaku 2014	Not provided	261	2014	5.5	Japan	Dapagliflozin	10 mg daily		57.5	9.3	60.2	7.46	0.61	26.06	4.52	4.93	50	66.9				None

Kaku 2014						Dapagliflozin	5 mg daily		58.6	10.4	58.1	7.5	0.72	24.88	3.91	4.59	44.2	66.5				
Kaku 2014						Placebo			60.4	9.7	59.8	7.5	0.63	25.22	4.39	5.29	42.5	67.8				
Kaku 2017	Not provided	374	2017	5.5	Japan	Metformin	500 mg daily		57.6	9.72	70.2	7.89	0.79			7.02						DPP-4 inhibitor
Kaku 2017						Metformin	500 mg daily		56.9	8.79	72.4	7.82	0.82			7.04						
Kaku 2017						Control	50 mg daily		57.2	10.07	73.2	7.77	0.78			7.73						
Kaku 2019	NCT02489968	447	2019	5.5	Japan	Linagliptin	5 mg daily		58	9.3	79.4	8.34	0.54	24.9	4	8.4		97				Empaglifozin
Kaku 2019						Control			56.3	9.9	78.7	8.4	0.68	25.1	3.6	7.6		96.4				
Kaku 2019			2019	12	Japan	Linagliptin	5 mg daily		56.8	10.6	75	8.27	0.59	25	4.3	8.5		96.4				Empaglifozin
Kaku 2019						Control			58.4	9.2	68.1	8.26	0.68	24.7	3.7	8.3		94.7				
Kanazawa 2010	UMIN000001997	55	2010	12	Japan	Metformin	500-750 mg daily		66	10	56.5	7.9	1.3	24.9	3.7	12						Insulin, Sulphonylurea, Alpha-glucosidase inhibitor
Kanazawa 2010						Pioglitazone	15-30 mg daily		67	10	63.6	7.9	1.7	22	2.3	14						
Kanazawa 2011	UMIN000002099	66	2011	6	Japan	Metformin	2250 mg daily		64	6.9	50	7.7	1.9	24.4	4.2	13.8						Sulphonylurea, Insulin, Alpha-glucosidase inhibitor
Kanazawa 2011						Pioglitazone	30 mg daily		65.2	10.1	63.6	7.9	1.4	24.6	3.9	13.9						
Kanazawa 2011						Control			65.4	9.1	54.5	7.9	1.7	23.7	3.7	14						
Kato 2015	UMIN000013356	20	2015	5.5	Japan	Glimepiride	1 mg daily		55	42-62	50	7.3	6.8-7.4	26.6	25.0-32.4							None
Kato 2015						Sitagliptin	50 mg daily		62	56-70	60	7.2	7.0-7.5	25.6	24.7-32.5							
Kawamori 2018	NCT02453555	275	2018	5.5	Japan	Empagliflozin	25 mg daily		60	9.9	78	8.27	0.65	26	3.8	9		89.3				None or oral antidiabetic drug (one drug at stable dosage)
Kawamori 2018						Placebo			59.8	10.8	77.4	8.36	0.74	26.6	4.5	8.7		86.3				
Kelly 2007	NCT00123643	36	2007	6	USA, India,	Glyburide	20 mg daily		63.1	7.8	62.5	7.3	0.7									Metformin
Kelly 2007						Rosiglitazone	8 mg daily		57.9	8.2	45	7.8	1.1									
Kendall 2005	Not applicable	733	2005	6	USA	Exenatide	20 mcg daily		55	10	59.3	8.5	1.1	34	6	8.7						Metformin + sulfonylurea
Kendall 2005						Exenatide	10 mcg daily		55	9	59.2	8.5	1	33	6	8.7						
Kendall 2005						Placebo			56	10	55.9	8.5	1	34	5	9.4						
Khaloo 2019	NCT03125694	250	2019	12	Iran	Pioglitazone	30 mg daily		62.7	8.2	41.5	9	1.2	29	4.8	14.3						Metformin + Gliclazide
Khaloo 2019						Sitagliptin	100 mg daily		60.8	8.1	58.5	8.8	1.1	29.7	4.3	11.3						
Khanolkar 2008	Not provided	50	2008	6	UK	Gliclazide	80 mg daily		56	37.55	60	7.08	0.65	33.66	7.76							Metformin
Khanolkar 2008						Rosiglitazone	4 mg daily		59	37.55	56	7.33	0.5	34.55	8.38							
Kikuchi 2012	NCT00297063	372	2012	7	Japan	Rosiglitazone	4 mg daily		55	10.6	62.9	8.9	1.3	24.5	3.7	5						None
Kikuchi 2012						Pioglitazone	30 mg daily		56	10.3	62.3	8.8	1.3	24.9	3.5	4.2						
Kikuchi 2012						Placebo			53.9	10	61.1	9	1.4	25	3.6	4.2						
Kim 2014	NCT01001611	173	2014	5.5	Republic of Korea	Lobeglitazone	0.5 mg daily		56.36	9.28	57.39	7.95	1.03	25.25	2.75	4.31						None
Kim 2014						Placebo			54.72	9.7	55.17	8.05	0.9	25.11	2.24	4.9						
Kim 2019	NCT02426294	135	2019	6	Republic of Korea	Glimepiride	4 mg daily		58.5	10.4	45.5	8.16	0.61	24.9	2.8	9.7						Metformin + alogliptin
Kim 2019						Pioglitazone	30 mg daily		60.7	9.1	49.3	8.25	0.58	24.4	3.2	10.6						
Kim 2020	Not provided	243	2020	5.5	Republic of Korea	Sitagliptin	100 mg daily		58.0	9.9	44.0	7.8	0.7	26.5	3.3	7.0						Metformin
Kim 2020						Lobeglitazone	0.5 mg daily		57.8	8.8	54.2	7.9	0.7	26.3	3.9	7.9						
KIND-LM	UMIN000004243	46	2015	5.5	Japan	Metformin	2250 mg daily		51	11	66.7			28.7	3.7	4.7						None
KIND-LM						Liraglutide	0.9 mg daily		55	11	59.1			28.6	4.2	5.6						
Kinoshita 2020	UMIN000021291	98	2020	6.8	Japan	Glimepiride	0.5-1 mg daily		58	13.2	45.5	7.6	1.14	28.4	4	7.2						Antidiabetic drugs
Kinoshita 2020						Pioglitazone	7.5-15 mg daily		59	10.9	45.5	7.4	1.15	28.7	5.2	7.9						
Kinoshita 2020						Dapagliflozin	5 mg daily		58.7	9.05	46.9	7.4	1.13	29.5	4.5	6.6						
Kiyici 2009	Not provided	50	2009	12	Turkey	Metformin	850 mg daily		52.4	8.3		6.7	0.9	31.6	3.6							Standard care
Kiyici 2009						Rosiglitzone	4mg daily		50.7	6.4		7.1	0.9	31.2	5.9							
Kiyici 2009						Control			52.1	5.1		6.4	0.6	30	3.2							
Ko 2006	Not provided	112	2006	12	China	Rosiglitazone	8 mg daily		56.6	10.7	57.1	10.1	1	25.3	3.8	11.8						Oral antidiabetic drugs
Ko 2006						Isophane insulin	Titrated		59.8	11.2	42.9	9.6	0.9	24	2.7	13.6						
Koffert 2017	NCT02526615	41	2017	6	Finland	Metformin	2000 mg daily		57.8	7.9	61.5	6.9	0.72	29.9	13.7							None
Koffert 2017						Rosiglitazone	8 mg daily		58.6	7.5	71.4	6.8	0.75	29.1	14.2							
Koffert 2017						Placebo			57.5	7.1	71.4	6.3	0.4	30.3	16.3							
Kohan 2014	NCT00663260	252	2014	24	Multinational	Dapagliflozin	10 mg daily	Chronic kidney disease	68	7.7	65.9	8.22	0.98			18.2		43.9	73			Antidiabetic drugs including insulin
Kohan 2014						Dapagliflozin	5 mg daily		66	8.9	66.3	8.3	1.04			16.9		44.2	79			
Kohan 2014						Placebo			67	8.6	63.1	8.53	1.28			15.7		45.6	67			
Kondo 2016	UMIN00004791	171	2016	12	Japan	Glimepiride	1 mg daily		64	8	72.1	7.5	0.5	24.7	3.3	6		74.9				None
Kondo 2016						Sitagliptin	100 mg daily		63	9	75.4	7.4	0.5	24.1	3.8	6.2		76.2				
Kothny 2013	Not provided	449	2013	6	Multinational	Vildagliptin	100 mg daily		59.3	9.9	47.8	8.8	1	28.9	4.4	12.9		77.6				Insulin ± metformin
Kothny 2013						Placebo			59.1	10.1	52	8.8	1	29	4.6	13.2		82.2				
Krawczyk 2005	Not applicable	40	2005	6	Poland	Metformin	1500 mg daily		55.8	8.14	40	8.58	1.89	35.4	3.83	12.2						Insulin
Krawczyk 2005						Control			58.4	5.96	60	8.44	1.64	33	3.67	11.9						
Kudo-Fujimaki 2014	UMIN000004010	40	2014	5.5	Japan	Nateglinide	270 mg daily		66.3	10	58.8	7.6	0.6	25	4.1	11.8						Vildagliptin
Kudo-Fujimaki 2014						Standard care			63	13.2	78.9	7.5	0.6	24.7	2.6	11.6						
Kumashiro 2018	Not provided	34	2018	5.5	Japan	Canaglifozin	100 mg daily															Basal insulin
Kumashiro 2018						Liraglutide	0.9 mg daily															
Laberge 2016	Not provided	116	2016	12	Canada	Rosiglitazone	8 mg daily	Coronary artery disease									100					Unclear
Laberge 2016						Placebo											100					
Lam 1998	Not applicable	89	1998	5.5	China	Acarbose	300 mg daily		57.8	8.7	44.4	9.4	0.7	24.8	3.4	10.1						Metformin + sulfonylurea
Lam 1998						Placebo			56.9	8.6	43.2	9.4	0.7	24.1	2.6	10.2						
Lambadiari 2018	NCT03010683	60	2018	6	Greece	Metformin	2000 mg daily		50	12	66.7	8.4	1.2	27.7	2			83				None
Lambadiari 2018						Liraglutide	1.8 mg daily		51	10	66.7	8.6	2	32.9	5			85				
Langenfeld 2005	Not applicable	179	2005	6	Germany	Glimepiride	1-6 mg daily		63	7	61.9	7.44	0.89	31.8	4.3	6.9						Oral drugs excluding thiazolidinediones
Langenfeld 2005						Pioglitazone	45 mg daily		62	8	61.8	7.52	0.85	31.7	5	7.4						
LANTERN	NCT01316094	165	2015	5.5	Japan	Ipragliflozin	50 mg daily	Chronic kidney disease	63.9	6.59	78	7.53	0.538	25.84	3.45	9.5		60.2				AGI, sulphonylurea or pioglitazone
LANTERN						Placebo			65.7	6.93	78.3	7.55	0.526	24.96	3.36	9.4		62.7				
Lawrence 2004	Not applicable	65	2004	6	United Kingdom	Metformin	1000-3000 mg daily		59.5	9.3	60	8.04	0.9	29.2	28.1-31.6							Metformin, sulfonylurea or no treatment
Lawrence 2004						Gliclazide	80-160 mg daily		63.5	11.4	65	7.95	0.9	28.7	28.3-34.4							
Lawrence 2004						Pioglitazone	30-45 mg daily		60.4	7.5	70	7.43	0.9	30.6	29.4-35.2							
LEAD-1	Not provided	809	2009	5.5	Multinational	Rosiglitazone	4 mg daily		55.6	9.8	47	8.4	1	29.4	4.8	6.6						Oral drugs
LEAD-1						Liraglutide	1.8 mg daily		55.6	10	53	8.5	0.9	30	5	6.5						
LEAD-1						Liraglutide	1.2 mg daily		57.7	9	45	8.5	1.1	29.8	5.1	6.7						
LEAD-1						Liraglutide	0.6 mg daily		55.7	9.9	54	8.4	1	30	5	6.5						
LEAD-1						Placebo			56	9.8	47	8.4	1	29.4	4.8	6.6						
LEAD-2	NCT00318461	1091	2009	6	Multinational	Glimepiride	4mg daily		57	9	57	8.4	1	31.2	4.6	8						Oral drugs
LEAD-2						Liraglutide	1.8 mg daily		57	9	57	8.4	1	30.9	4.6	8						
LEAD-2						Liraglutide	1.2 mg daily		57	9	54	8.3	1	31.1	4.8	7						
LEAD-2						Liraglutide	0.6 mg daily		56	11	62	8.4	0.9	30.5	4.8	7						
LEAD-2						Placebo			56	9	60	8.4	1.1	31.6	4.4	8						
LEAD-3	NCT00294723	745	2009	12	Multinational	Glimepiride	8 mg daily		53.4	10.9	54	8.4	1.2	33.2	5.6	5.6						Monotherapy with an SU, biguanide, TZD, α glucosidase inhibitor, DPP-4 inhibitor or glinide
LEAD-3						Liraglutide	1.8 mg daily		52	10.8	49	8.3	1.1	32.8	6.3	5.3						
LEAD-3						Liraglutide	1.2 mg daily		53.7	11	47	8.3	1	33.2	5.6	5.2						
LEAD-4	NCT00333151	533	2009	6	USA	Liraglutide	1.8 mg daily		55	11	51	8.6	1.2	33.5	5.1	9						Metformin + rosiglitazone
LEAD-4						Liraglutide	1.2 mg daily		55	10	57	8.5	1.2	33.2	5.4	9						
LEAD-4						Placebo			55	10	62	8.4	1.2	33.9	5.2	9						
LEAD-5	NCT00331851	581	2009	6	Multinational	Liraglutide	1.8 mg daily		57.6	9.5	57	8.3	0.9	30.4	5.3	9.2						Metformin + glimepiride
LEAD-5						Insulin glargine	Titrated		57.5	10.5	60	8.2	0.9	30.3	5.3	9.1						
LEAD-5						Placebo			57.5	9.6	49	8.3	0.9	31.3	5	9.4						
LEADER	NCT01179048	9340	2016	42	Multinational	Liraglutide	1.8 mg daily	High cardiovascular risk	64.2	7.2	64.5	8.7	1.6	32.5	6.3	12.8	82.1					One or more drugs, insulin, or combination
LEADER						Placebo			64.4	7.2	64	8.7	1.5	32.5	6.3	12.9	80.6					
Lebovitz 2001	Not applicable	493	2001	6	USA	Risiglitazone	8 mg daily		61	9.5	66.9	8.8	1.6	29.1	3.9	5.4						None
Lebovitz 2001						Risiglitazone	4 mg daily		60	9.8	64.5	9	1.5	30.2	4.4	4.8						
Lebovitz 2001						Placebo			59	10.9	65.8	9	1.7	29.9	4.1	4.6						
Ledesma 2019	NCT02240680	302	2019	5.5	Multinational	Linagliptin	5 mg daily		72.3	5.1	60.9	8.2	0.8	28.3	5.62			65.9				Basal insulin
Ledesma 2019						Placebo			72.5	5.6	60.3	8.1	0.7	27.86	5.74			70.3				
Lee 2013	Not provided	121	2013	12	Korea	Pioglitazone	15 mg daily	Coronary artery disease	60.3	9.53	71.7	8.1	1.6	24	2.96	6.03	100					One or more drugs, insulin, or combination
Lee 2013						Placebo			61.9	8.75	75.4	7.4	1.8	23.8	3.23	5.5	100					
Lee 2017	NCT01704261	307	2017	5.5	Multinational	Omarigliptin	25 mg weekly		57.2	8.4	47	8.5	0.8	31.8	6.2	9.8						Metformin + glimepiride
Lee 2017						Placebo			58.4	9.4	48	8.6	0.8	30.6	5.8	10.4						
Leiter 2014	NCT01098539	495	2014	12	Multinational	Sitagliptin	25-100 mg daily		63.5	9.02	52.8	8.23	0.9	30.43	5.828	11.62	8.9					Oral antihyperglycaemic drugs (metformin, thiazolidinedione, sulfonylurea, or combination)
Leiter 2014						Albiglutide	30-50 mg weekly		63.2	8.37	54.6	8.13	1	30.35	5.466	10.83	8.4					
Leiter 2014a	NCT01042977	965	2014	6	Multinational	Dapagliflozin	10 mg daily		63.9	7.6	66.9	8	0.8	33	5.3	13.5						Pre-existing treatment excluding rosiglitazone
Leiter 2014a						Placebo			63.6	7	67	8.1	0.8	32.7	5.7	13						

Leonhardt 1991	Not applicable	94	1991	5.5	Germany	Acarbose	300 mg daily													None
Leonhardt 1991						Placebo														
Lewin 2007	Not provided	575	2007	5.5	USA	Metformin	2000 mg daily		53	10.9	51.4			34	7.1	4.9				Sulphonylurea
Lewin 2007						Metformin	2000 mg daily		53	10.5	58.9			34	6.3	5				
Lewin 2007						Metformin	1500 mg daily		54	10.3	53.5			35	7.1	5.1				
Lewin 2007						Standard care			53	10.7	54.9			34	7.1	5.8				
Lewin 2015	NCT01422876	398	2015	5.5	Multinational	Linagliptin	5 mg daily		53.8	11.5	56.4	8.05	0.89	31.9	5.9			89.5		None
Lewin 2015						Empagliflozin	25 mg daily		56	9.3	57.9	7.99	0.97	31.2	5.7			88.5		
Lewin 2015						Empagliflozin	10 mg daily		53.9	10.5	48.5	8.05	1.03	31.5	5.7			88.4		
Li 2014	Not provided	203	2014	5.5	China	Vildagliptin	100 mg daily		46.4	9.8	60	8.56	0.77	25.9	1.8	5.4				Metformin ± sulfonylurea ± alpha-glucosidase inhibitor or thiazolidinedione
Li 2014						Saxagliptin	5 mg daily		47	11.3	65	8.59	0.87	26.3	2.2	5.4				
Li 2014						Liraglutide	1.2 mg daily		47.9	10.8	59	8.48	0.79	26.7	2.4	5.8				
Li 2014a	Not provided	42	2014	77	China	Insulin glargine	Titrated	High cardiovascular risk												None or oral agents
Li 2014a						Standard care														
Li 2017	Not provided	33	2017	5.5	China	Vildagliptin	100 mg daily		58.9	9	35.3	8.5	0.8	26.1	3.1	8.6				Metformin
Li 2017						Placebo			59.9	7.7	56.3	8.8	0.7	26.1	3.4	8.6				
Li 2019	Not provided	64	2019	5.5	China	Glimepiride	2 mg daily		47.36	9.4	51.5	7.82	0.61	26.46	3.23	0.85				None
Li 2019						Saxagliptin	5 mg daily		46.58	8.15	46.7	7.79	0.52	27.2	4.06	0.94				
Li 2019a	NCT01644500	23	2019	6	China	Glimepiride			53.3	6.6	60	7.91	0.98							None or single oral agent
Li 2019a						Dulaglutide	0.75-1.5 mg weekly		54.75	5.33	53.8	8.38	0.93							
Li 2020	NCT02655757	149	2020	18	China	Sitagliptin	100 mg daily	Coronary artery disease	60.6	9.5	73.3	8.2	1.5	25.1	3.7	6.3	100			0, 1 or 2 oral agents
Li 2020						Control			59.7	10.3	79.7	7.9	0.9	24.9	3.1	9.9	100			
LIBRA	NCT01270789	51	2017	11.2	USA	Liraglutide	1.8 mg daily		58.9	8.7	61.5	6.2	0.4	30	4.3	3				Metformin
LIBRA						Placebo			57.4	7.4	64	6.4	0.5	30.4	5.8	1.5				
Lim 2017	Not applicable	170	2017	5.5	Republic of Korea	Lobeglitazone	0.5 mg daily		56.36	9.29	58	7.68	0.76	25.3	2.8	4.3				None, sulfonylurea, metformin, DPP-4 inhibitor or alphaglucosidase inhibitor
Lim 2017						Placebo			54.72	9.7	55.2	7.86	0.86	25.1	2.2	4.9				
Lin 2003	Not applicable	65	2003	5.5	Multinational	Acarbose	300 mg daily		57.7	7.3	53.1	9.01	1.2	24.8	3	7				Sulfonylurea
Lin 2003						Placebo			55.4	8.5	37.5	8.99	0.95	25.1	2.8	5				
Linagliptin-LTC Trial	NCT02061969	140	2018	6	USA	Linagliptin	5 mg daily		68.0	14.0	48.0	7.9	2.2	29.7	7.0	10.9				Metformin
Linagliptin-LTC Trial						Insulin glargine			71.5	13.0	34.0	7.8	2.2	30.0	8.0	10.6				
Lindström 2000	Not applicable	107	2000	5.5	Finland	Acarbose	300 mg daily		58.3	9		9.8	1.3	29.1	3.3	6.3				Biguanide ± sulfonylurea
Lindström 2000						Placebo			61.8	5.2		10.1	1.5	28.3	3.7	6				
Lingvay 2018	NCT02461589	641	2018	6	Multinational	Liraglutide	1.8 mg daily		55.8	9.2	33	8.1	0.8	32.1	4.5	6.6				None or metformin
Lingvay 2018						Liraglutide	1.2 mg daily		53.7	11.4	53.1	8.1	0.9	33.3	4.3	6.9				
Lingvay 2018						Liraglutide	0.6 mg daily		59.5	9.8	50	8.1	0.8	33	4	6.8				
Lingvay 2018						Liraglutide	0.3 mg daily		57.2	10.8	45.3	8.1	0.9	32.9	3.9	8.1				
Lingvay 2018						Semaglutide	0.3 mg daily		54.8	9.7	50.8	8.2	0.8	33.1	4.7	6.5				
Lingvay 2018						Semaglutide	0.2 mg daily		58.4	9.6	50.8	8	0.8	32.8	4.5	7.2				
Lingvay 2018						Semaglutide	0.1 mg daily		57.5	10	55.6	7.9	0.8	32.4	4.5	8.1				
Lingvay 2018						Semaglutide	0.05 mg daily		57.5	9.8	51.6	7.9	0.7	32.3	4.6	6.5				
Lingvay 2018						Placebo			57.1	9.2	55.8	8.1	0.9	32.8	4.2	7.2				
LIPER2	EudraCT number	24	2019	6	Spain	Liraglutide	Liraglutide		53.2	9.7	41.7	8	0.46	34.98	6.2	8.7				Metformin if tolerated and not contraindicated) or a maximum of two intermediate- or long-acting insulin injections per day, or a combination of both
LIPER2						Placebo	Placebo		52.6	13.8	33.3	8.4	0.8	34.98	6.2	8.7				
LIRA-ADD2SGLT2i	NCT02964247	303	2020	6.0	Multinational	Liraglutide	1.8 mg daily		54.7	10.1	62.0	8.0	0.7	32.0	6.0	10.1				Metformin ± SGLT-2 inhibitor
LIRA-ADD2SGLT2i						Placebo			56.0	9.9	58.0	8.0	0.6	32.6	6.5	9.6				
Liraglutide-Detemir S	NCT00856986	323	2012	6	Multinational	Insulin detemir	Titrated		56.8	9.4	54.3	7.6	0.6	34.9	6.3	8.6				Metformin ± sulfonylurea
Liraglutide-Detemir Study						Control			57.3	9.8	55.3	7.6	0.7	33.9	6	8.5				
LIRA-RENAL	NCT01620489	277	2016	6	Multinational	Liraglutide	1.8 mg daily	Chronic kidney disease	68	8.3	53.6	8.08	0.792	33.4	5.4	15.9				Monotherapy or dual therapy combinations with metformin, sulfonylurea, thiazolidinedione, or insulin
LIRA-RENAL						Placebo			66.3	8	47.4	8	0.853	34.5	5.4	14.2				
LIRA-SWITCH	NCT01907854	406	2016	5.5	Multinational	Sitagliptin	100 mg daily		56.5	9.7	61	8.2	0.6	32.2	6.2	7.6				Metformin
LIRA-SWITCH						Liraglutide	1.8 mg daily		56.3	10.6	57.4	8.3	0.6	31.7	6	7.9				
Liu 2013	NCT01195090	119	2013	5.5	Taiwan	Pioglitazone	30 mg daily		58.1	8.4	38.3	8.54	0.97	25.7	3.7	7.8				Metformin or sulfonylurea
Liu 2013						Sitagliptin	100 mg daily		60.1	8.9	36.7	8.27	0.86	26.6	4.6	7.8				
Liu 2014	Not provided	146	2016	14	China	Pioglitazone	30 mg daily	Atrial fibrillation	60.7	12.25	74.3	6.41	1.83							Unclear
Liu 2014						Placebo			62.25	12.39	65.8	6.19	1.45							
Liu 2020	NCT02303730	71	2020	5.5	China	Exenatide	20 mcg daily		47.6	10.1	54.3	8.3	0.9	28.5	3.0	0.3				None
Liu 2020						Insulin glargine			50.6	11.8	52.8	8.6	0.9	27.8	3.1	0.5				
Liutkus 2010	Not provided	165	2010	6	Multinational	Exenatide	20 mcg daily		55	8	60	8.2	0.9	34	6	6.3				Metformin and thiazolidinedione
Liutkus 2010						Placebo			54	9	57	8.3	0.9	33	5	6.4				
LixiLan-G	NCT02787551	514	2019	6	Multinational	Insulin glargine	Titrated		59.2	9.6	49	7.9	0.6	32.8	4.4	11.2				GLP-1RA in combination with metformin with or without SGLT2 inhibitor with or without pioglitazone
LixiLan-G						Control			60	10.3	56	7.9	0.5	33	4.4	11				
LixiLan JP-L	NCT02752412	512	2020	6.0	Japan	Lixisenatide	20 mcg daily		59.4	10.5	62.4	8.2	0.5	25.3	4.2	11.9				Insulin glargine + metformin
LixiLan JP-L						Control			60.2	10.4	57.2	8.3	0.5	24.9	3.9	12.0				
LixiLan JP-O1	NCT02749890	321	2020	6.0	Japan	Insulin glargine			58.3	9.9	64.6	8.4	0.6	26.8	4.4	8.1				Lixisenatide, and oral antidiabetic drugs except DPP-4 inhibitors. Other drugs decreased by 50% or discontinued
LixiLan JP-O1						Control			57.7	11.5	63.7	8.4	0.6	26.9	4.2	9.2				
LixiLan JP-O2	NCT02752828	521	2020	6.0	Japan	Insulin glargine			59.2	11.0	66.9	8.1	0.5	26.2	4.3	8.9				Lixisenatide, and oral antidiabetic drugs except DPP-4 inhibitors. Other drugs decreased by 50% or discontinued
LixiLan JP-O2						Control			60.2	10.3	64.0	8.0	0.5	25.9	4.3	9.6				
LixiLan-L	NCT02058160	736	2020	7.3	Multinational	Insulin glargine			59.6	9.4	45.0	8.1	0.7	31.3	4.3	12.0				Metformin
LixiLan-L						Control			60.3	8.7	48.5	8.1	0.7	31.0	4.2	12.1				
Lou 2020	Not reported	86	2020	6.0	China	Metformin	1500 mg daily		62.2	7.2	69.0			31.2	1.5	3.3				Unclear
Lou 2020						Liraglutide	1.2 mg daily		61.8	7.7	71.4			31.1	1.7	3.5				
Lu 2016	NCT01505426	170	2016	5.5	Multinational	Ipragliflozin	50 mg daily		53.9	11.3	50.6	7.74	0.78	26.57	4.3	6.5				Metformin
Lu 2016						Placebo			53.4	11.3	39.8	7.75	0.71	27.04	4.06	5.8				
Lukashevich 2011	Not provided	515	2011	5.5	Finland	Vildagliptin	50 mg daily	Chronic kidney disease	67.7	8.8	58.2	7.8	1	30.2	5.1	15				Untreated or treated with sulfonylurea, α glucosidase inhibitor, thiazolidinedione, insulin, meglitinide, or combination
Lukashevich 2011						Placebo			69.7	7.3	62	7.8	0.9	30	5	15.2				
Lukashevich 2011						Vildagliptin	50 mg daily		64.1	9.2	52.4	7.7	1	30.2	5.6	17.3				
Lukashevich 2011						Placebo			64.5	10.8	54.6	7.7	1	29.5	5	19				
Lund 2009	NCT00118963	101	2009	12	Denmark	Metformin	2000 mg daily		63	7.8	59.6	7.8	0.97	24.53	2.33	8				Biphasic insulin
Lund 2009						Repaglinide	6 mg daily		63.7	7.9	63.3	7.82	1.23	24.88	2.45	12				
LYDIA	NCT02043054	76	2020	6.0	United Kingdom	Sitagliptin	100 mg daily		44.8	5.9	39.5	7.6	0.8	34.9	5.3	4.4		89		Metformin and/or sulfonylurea
LYDIA						Liraglutide	1.8 mg daily		43.4	7.0	52.6	7.5	0.8	35.7	7.0	4.5		88		
Ma 2015	Not provided	60	2015	12	China	Metformin	1500 mg daily		53.8	14.7	53.3	7.82	0.54	29.7	2.7					Unclear
Ma 2015						Pioglitazone	15 mg daily		55.3	10.1	60	8.13	0.19	28.5	3.2					
Macauley 2015	NCT01356381	44	2015	6	United Kingdom	Vildagliptin	100 mg daily		65.2	3.3		6.6	0.5	29.4	3.8					Metformin
Macauley 2015						Placebo			58.9	7.5		6.5	0.5	31.1	2.8					
Madsbad 2001	Not applicable	256	2001	12	Europe	Glipizide	5-15 mg daily		62	8.8	64.2	7.2	1.4	28	3.5	7				None or oral agents
Madsbad 2001						Repaglinide	1.5-12 mg daily		60.2	8.1	61.1	7.3	1.2	28	3.6	8.1				
Maffioli 2013	Not provided	170	2013	6	Italy	Glibenclamide	10 mg daily		61.4	5.6	50			30.2	2.9					Metformin
Maffioli 2013						Pioglitazone	30 mg daily		62.8	6.3	47.7			30	3					
MAGNA VICTORIA	NCT01761318	49	2019	6	The Netherlands	Liraglutide	1.8 mg daily		60	6	61	8.4	1.1	32.6	4.4	11				Metformin with or without sulfonylurea and/or insulin
MAGNA VICTORIA						Placebo			59	7	58	8.2	1	31.6	3.4	11				
Marbury 1999	Not applicable	576	1999	12	USA	Glyburide	2.5-15 mg daily		58.7	9	66	8.9	1.6	29.1	3.7	8.3				None or oral agents
Marbury 1999						Repaglinide	1.5-12 mg daily		58.3	9.4	67	8.7	1.7	29.4	3.7	7.2				
MARCH	ChiCTR-TRC-	784	2014	11	China	Metformin	1500 mg daily		50.2	9.3	60	7.59	1.22	25.7	2.7	0.26				None
MARCH						Acarbose	300 mg daily		50.6	9.2	61	7.49	1.26	25.5	2.7	0.22				
Marena 1993	Not applicable	20	1993	5.5	Italy	Glibenclamide	10 mg daily		64	5.1	60	7.8	0.3	26.7	1.3	7				None
Marena 1993						Miglitol	300 mg daily		57	3.8	70	8.2	0.6	26.4	1.3	5				
Mari 2008	NCT00101712	306	2008	12	Multinational	Vildagliptin	50 mg daily		63.3	10.2	59.6	6.7	0.4	30.4	4.9	2.5				None
Mari 2008						Placebo			62.8	11	59.3	6.8	0.4	30	4.9	2.7				
MARLINA-T2D	NCT01792518	360	2017	5.5	Multinational	Linagliptin	5 mg daily	Chronic kidney disease										102.8	120.8	Antidiabetic drugs including insulin
MARLINA-T2D						Placebo												94.4	131.9	
Marre 2002	Not applicable	468	2002	5.5	Multinational	Nateglinide	360 mg daily		57.3	10.5	61.3	8.18		29.3	3.5	6.8				Metformin
Marre 2002						Nateglinide	180 mg daily		57.9	9.9	61.3	7.99		29.4	3.7	7.2				
Marre 2002						Placebo			56.4	10.3	55.3	8.2		29.6	3.9	6.5				
Maruyama 2019	Not provided	44	2019	12	Japan	Canagliflozin	100 mg daily	Chronic kidney disease												Oral antidiabetic drugs and/or insulin
Maruyama 2019						Control														
MASTER	UMIN000001671	28	2014	5.5	Japan	Sitagliptin	50 mg daily		59.2	11.8	78.5	7.45	0.93	28.8	2.5	7.6				Metformin or sulphonylurea or no treatment
MASTER						Miglitol	150 mg daily		58.7	7	78.5	6.9	0.51	29.5	5.5	9.3				
Mathieu 2015	NCT01462266	658	2015	5.5	Unclear	Sitagliptin	100 mg daily		59.3	8.9	45.9	8.7	1	31.9	5.8	13.2				Insulin ± metformin

Mathieu 2015						Placebo			58.3	9.7	49.8	8.8	1	32.2	6.6	13.7						
Mathieu 2016	NCT01646320	320	2016	12	Mexico	Dapagliflozin	10 mg daily		55.2	8.6	43.7	8.24	0.96	31.2	4.7	7.2			93.5			Metformin ± DPP-4 inhibitor
Mathieu 2016						Placebo			55	9.6	47.5	8.17	0.98	32.2	5.3	8			91.6			
Matthaei 2015	NCT01619059	322	2015	12	Multinational	Saxagliptin	5 mg daily		54.7	9.8	47.7	7.97	0.83	31.4	5.2	8.1			92.8			Metformin + dapagliflozin
Matthaei 2015						Placebo			54.5	9.3	46.9	7.86	0.93	31.4	5.3	7.4			93.9			
Matthaei 2015a	NCT01392677	218	2015	5.5	Multinational	Dapagliflozin	10 mg daily		61.1	9.7	42.6	8.08	0.91	31.9	4.8	9.3	84.3					Metformin + sulfonylurea
Matthaei 2015a						Placebo			60.9	9.2	55.6	8.24	0.87	32	4.6	9.6	88					
Matthews 2005	Not applicable	630	2005	12	Multinational	Gliclazide	80-320 mg daily		57	9	49.2	8.53	0.89	32.6	5.8	5.5						Metformin
Matthews 2005						Pioglitazone	15-45 mg daily		56	9.2	50.8	8.71	1	32.6	5	5.8						
Matthews 2010	EudraCT 2004-	3118	2010	24	Multicentre	Glimepiride	2-6 mg daily		57.5	9.19	53.9	7.3	0.7	31.7	5.3	5.7						Metformin
Matthews 2010						Vildagliptin	50 mg twice daily		57.5	9.07	53.1	7.3	0.7	31.9	5.3	5.7						
Mattoo 2005	Not applicable	289	2005	6	Multinational	Pioglitazone	30 mg daily		58.8	7.4	43.7	8.85	1.3	32.5	4.8	13.6						None or oral agents
Mattoo 2005						Placebo			58.9	6.9	42.9	8.79	1.2	31.8	5	13.4						
McCluskey 2004	Not applicable	40	2004	6	USA	Glimepiride	2-8 mg daily		60.2	7.8	44	7.9	0.6			7.2						Rosiglitazone
McCluskey 2004						Placebo			50.8	9.7	40	8.4	0.7			4.6						
McGill 2013	Not provided	133	2013	12	Multinational	Linagliptin	5 mg daily	Chronic kidney disease	64	10.9	66.2	8.2	1.1	32.3	5.8				22.1			Insulin, sulfonylurea, glinides, pioglitazone, and α-glucosidase inhibitors
McGill 2013						Placebo			64.9	9.6	53.8	8.2	0.9	31.7	5.9				25.1			
McGuire 2010	NCT00424762	150	2010	6	USA	Rosiglitazone	4-8 mg daily	High cardiovascular risk	57	8.7	57.4	7.6	1.8	34.1	6.4	9.5						Existing treatment except thiazolidinediones
McGuire 2010						Placebo			55.7	8.3	61.1	7.6	1.8	34.1	7.3	8.7						
MDI Liraglutide	EudraCT 2012-	124	2015	5.5	Sweden	Liraglutide	1.8 mg daily		63.7	8.2	62.5	9	1	33.7	4.3	17.3	9.4					Insulin
MDI Liraglutide						Placebo			63.5	7.7	66.7	9	1.1	33.5	4	17	16.7					
Meneghini 2010	Not provided	247	2010	11	USA	Pioglitazone	45 mg daily		51.8	9.8	49	9.5	1.4	33.5	7.1	5.8						Metformin or sulphonylurea or no treatment
Meneghini 2010						Insulin glargine	Titrated		52.9	10.6	48	9.4	1.2	33.7	6.9	6.5						
Meneilly 2000	Not applicable	45	2000	12	Canada	Acarbose	300 mg daily		68	4.7		7.3	0.5	28	4.7							None
Meneilly 2000						Placebo			70	4.8		7	1	29	4.8							
Milovanova 2019	Not provided	42	2019	36	Russia	Linagliptin	5 mg daily	Chronic kidney disease														Hypoglycaemic drugs except SGLT-2 inhibitors
Milovanova 2019						Control																
Mita 2007	Not provided	70	2007	12	Japan	Nateglinide	270 mg daily		61.3	8.3	52.9	6.13	0.37	23.6	2.7	4.46						None
Mita 2007						Control			61.8	6	52.8	6.04	0.37	23.6	2.7	4.75						
Mita 2019	UMIN000022953	43	2019	5.5	Japan	Metformin	2250 mg daily		58.1	13.8	59	7.5	1.5	26.3	4.9	3.3			92			None or insulin
Mita 2019						Linagliptin	5 mg daily		61.3	8.7	62	7.1	0.7	25.7	4.5	3.4			76.7			
Mitrakou 1998	Not applicable	120	1998	5.5	Greece	Miglitol	300 mg daily		57.4	5.6	48.3	9.9	0.5	24.4	3.1	8.5						Insulin
Mitrakou 1998						Placebo			57.4	5.8	61.7	9.9	0.4	24.5	3.4	7.9						
Miyagawa 2015	NCT01558271	492	2015	6	Japan	Dulaglutide	0.75 mg weekly		57.2	9.6	81	8.15	0.77	25.6	3.6	6.8						None
Miyagawa 2015						Liraglutide	0.9 mg daily		57.9	10.4	83	8.08	0.89	25.5	3.5	6.3						
Miyagawa 2015						Placebo			57.7	8.3	79	8.2	0.83	25.2	3.2	6.3						
Miyazaki 2002	Not applicable	58	2002	6	USA	Pioglitazone	45 mg daily		55	6.6	45.4	9.1	1	30.4	3.3							None
Miyazaki 2002						Pioglitazone	30 mg daily		51	6.6	72.7	8.5	1.7	32.2	5.3							
Miyazaki 2002						Pioglitazone	15 mg daily		57	13.9	66.6	8	1	30.8	4.5							
Miyazaki 2002						Pioglitazone	7.5 mg daily		51	10.8	76.9	8.9	1.4	31.3	4.3							
Miyazaki 2002						Placebo			58	9.9	27.3	8.6	1.7	32.8	5.3							
Mokta 2018	Not provided	217	2018	30	India	Glimepiride	2 mg daily		49.41	8.87	59	9.03		26.44	2.74							Metformin
Mokta 2018						Vildagliptin	100 mg daily		50.88	9.3	60	9.07		26.81	3.15							
Moretto 2008	NCT00381342	233	2008	5.5	USA	Exenatide	10 mcg daily		54	10	63	7.9	1	31	5	2						None
Moretto 2008						Exenatide	5 mcg daily		55	10	52	7.8	1	32	5	2						
Moretto 2008						Placebo			53	9	55	7.8	0.9	32	5	1						
Morino 2018	Not provided	46	2018	5.5	Japan	Ipragliflozin						8.1	0.9									Insulin
Morino 2018						Control						8.3	0.7									
Moriwaki 2018	UMIN000012562	28	2018	5.5	Japan	Sitagliptin	100 mg daily	Coronary artery disease	69	9	79	6.64	0.51			3.1	100	71				None or fixed doses of glucose-lowering drugs
Moriwaki 2018						Voglibose	0.9 mg daily		68	10	71	6.6	0.46			1.3	100	73				
Moses 2014	Not provided	257	2014	5.5	Multinational	Saxagliptin	5 mg daily		57.2	9.6	62	8.4	0.9	29.4	5.3							Metformin + sulfonylurea
Moses 2014						Placebo			56.8	11.5	57.8	8.2	0.8	29.1	4.9							
Moses 2016	NCT01076075	427	2016	5.5	Multinational	Sitagliptin	100 mg daily		54.4	9.6	45.2	8.4	0.8	29.5	4.8	7.5						Metformin + sulfonylurea
Moses 2016						Placebo			55.4	10.2	46.2	8.4	0.9	28.8	5	8						
Mu 2017	NCT01708902	436	2017	5.5	China	Metformin	2000 mg daily		51.4	10.4	63.2	8.6	1	26.1	3.3	8.75						None
Mu 2017						Metformin	1000 mg daily		52.1	9.6	62.8	8.7	1.1	25.8	3.3	9.8						
Mu 2017						Linagliptin	5 mg daily		50.8	10.5	51.7	8.7	0.9	26.2	3.9	9.2						
Müller-Wieland 2018	NCT02471404	939	2018	12	Multinational	Glimepiride	6 mg daily		58.6	8.4	66.5	8.3	0.8	33	5.1	6.7						Metformin
Müller-Wieland 2018						Dapagliflozin	10 mg daily		57.4	9.4	64.3	8.3	0.7	33.1	5.2	6.9						
Nakamura 2001	Not applicable	28	2001	6	Japan	Pioglitazone	30mg daily	Chronic kidney disease				8.4	1.3						104			Sulfonylurea
Nakamura 2001						Placebo						8	1						106			
Nakamura 2004	Not applicable	45	2004	12	Japan	Glibenclamide	5-20 mg daily	Chronic kidney disease	55	11.5	53.3	7.9	1.4			17						None
Nakamura 2004						Pioglitazone	30 mg daily		56.5	12	60	7.9	1.3			17.5						
Nakamura 2004						Voglibose	0.6mg daily		55	11	53.3	8.1	1.6			16.8						
Nakamura 2006	Not provided	68	2006	12	Japan	Glibenclamide	5-20 mg daily	Chronic kidney disease	53.5	12	55.6	7.8	1.3			16.5			109	136.5		None
Nakamura 2006						Pioglitazone	30 mg daily		56	13	52.9	8	1.4			16			110	142.5		
Nakamura 2006						Voglibose	0.6mg daily		55	12.8	58.8	7.6	1.3			16.2			117	140.8		
Nakamura 2006						Netaglinide	270mg daily		53.5	12.2	56.25	7.7	1.4			16.6			114	134.6		
Nar 2009	Not provided	34	2009	6	Turkey	Metformin	850-1700 mg daily		49.4	8.6	21.1	6.9	1.4	31	4	0						None
Nar 2009						Control			44.5	5.9	33.3	6.1	1.1	33.7	6	0						
Nathan 1988	Not applicable	31	1988	9	USA	Glyburide	10.5 mg daily		50.3	5.9	56.3	10.5	2.41	30.2	5.7	5.9						None
Nathan 1988						NPH Insulin	Titrated		53.5	7.1	53.3	10.3	1.52	28.6	5.1	3.7						
Nauck 2007a	Not provided	501	2007	12	Multinational	Exenatide	10-20 mcg daily		59	9	53	8.6	1	30.6	4	9.8						Metformin + sulfonylurea
Nauck 2007a						Biphasic Insulin As	Titrated		58	9	49	8.6	1.1	30.2	4.2	10						
Nauck 2007b	NCT00094770	1172	2007	12	Multinational	Glipizide	5-20 mg daily		56.5	9.8	61.3	7.6	0.9	31.3	5.2	6.2						None, monotherapy or metformin + monotherapy
Nauck 2007b						Sitagliptin	100 mg daily		56.8	9.3	57.1	7.7	0.9	31.5	5	6.5						
Nauck 2009	NCT00286442	527	2009	6	Multinational	Alogliptin	25mg daily		54	11	54.3	7.9	0.8	32	5	6						Metformin
Nauck 2009						Alogliptin	12.5mg daily		55	11	47.4	7.9	0.7	32	5	6						
Nauck 2009						Placebo			56	11	48	8	0.9	32	6	6						
Nauck 2011	NCT00660907	814	2011	12	Multinational	Glipizide	5-20 mg daily		59	10	54.9	7.7	0.9	31.2	5.1	7	19.5					Metformin ± oral agent
Nauck 2011						Dapagliflozin	2.5-10 mg daily		58	9	55.3	7.7	0.9	31.7	5.1	6	18					
Nauck 2016	NCT01183013	544	2016	7	Multinational	Pioglitazone	45 mg daily		56.5	11	52.2	8.1	0.9	33.9	5.5							None
Nauck 2016						Pioglitazone	30 mg daily		57	11.5	52.1	8	0.9	32.2	5.3							
Nauck 2016						Pioglitazone	15 mg daily		56.3	10.4	55.7	8.3	0.9	32.3	5.6							
Nauck 2016						Linagliptin	5 mg daily		56	10.4	61.5	8	0.9	32.7	5.3							
Neff 2016	NCT01847313	20	2016	6	Ireland	Liraglutide	0.6 mg daily	Chronic kidney disease	65	7	70			30	5	8			69	106.9		Usual care
Neff 2016						Control			64	10	30			34	4	9			79	122.8		
Negro 2005	Not applicable	38	2005	12	Italy	Rosiglitazone	8 mg daily		60.3	6.4	52.6	8.4	0.6	28.3	1.7	7.1						Metformin
Negro 2005						Placebo			59	8	63.2	8.1	0.5	28.7	1.9	6.6						
Ning 2016	NCT01582230	293	2016	5.5	Multinational	Vildagliptin	100 mg daily		57.8	9.1	41.8	8.6	0.9	26.2	3.2	11.2						Metformin ± insulin
Ning 2016						Placebo			58.4	9.6	44.9	8.7	0.9	26	3	11.4						
Nino 2017	NCT01733758	387	2017	5.5	Japan	Albiglutide	50 mg weekly		57.7	9.51	76	8.15	0.83	26.1	3.66	6.9						Single oral drug
Nino 2017						Albiglutide	30 mg weekly		59.6	9	78.1	8.07	0.78	25.3	4.17	7.2						
Nino 2017						Placebo			57.3	11.27	67.5	8.16	0.88	25.6	3.42	6.7						
Nishimura 2016	UMIN000011420	40	2016	5.5	Japan	Sitagliptin	50 mg daily		65.2	6.4	75	7.6	0.4	26.6	3.9	6.8	10		72.4			Metformin ± pioglitazone + repaglinide
Nishimura 2016						Control			59.4	8.5	70	7.6	0.4	25.2	3.3	8.5	20		70.9			
Nishio 2006	Not provided	54	2006	6	Japan	Pioglitazone	30 mg daily	Coronary artery disease	66.2	8.6	73.1	7.7	2.2	24.6	3.9		100					α-glucosidase inhibitor ± sulfonylurea
Nishio 2006						Control			67.5	10.3	71.4	6.9	1.6	24.6	3.5		100					
Nogueira 2014	Not provided	35	2014	5.5	Brazil	Sitagliptin	100 mg daily		55.1	6.7	50	8	0.6	26.5	2.7	10.9						Metformin; Glyburide
Nogueira 2014						NPH Insulin	Titrated		58.4	6.9	35	8.1	0.7	27.5	2.5	10.9						
Nowicki 2011	NCT00614939	170	2011	12	Multinational	Saxagliptin	2.5 mg daily	Chronic kidney disease	66.8	8.3	37.6	8.5	1.2	31.2	6.1	15.1			31.5			Excluded metformin therapy, and previous or current DPP-4 inhibitor or GLP1 receptor agonist
Nowicki 2011						Placebo			66.2	9.1	48.2	8.1	1.1	30.2	6.8	18.2			30.4			
Ogasawara 2009	Not provided	54	2009	6	Japan	Pioglitazone	15 mg daily	Coronary artery disease	68.6	7.9	72.7	7.2	0.7	23.8	3							Oral antidiabetic treatments
Ogasawara 2009						Control			66.8	8.1	58.3	6.8	0.9	24.1	2.1							
Oh 2019	NCT01370707	187	2019	5.5	Republic of Korea	Voglibose	0.6 mg daily		51.9	8.8	62.5	8.1	1.0	24.5	2.4				91.3			Metformin
Oh 2019						Control			53.4	8.8	52.4	8.2	1.0	25.1	2.5				100.4			
Ohira 2014	Not provided	70	2014	6	Japan	Metformin	500 mg daily		60.71	11.01	75	8.75	1.27	25.2	4.52							Metformin
Ohira 2014						Sitagliptin	50 mg daily		60.03	12.35	60	9.05	1.69	25.15	3.14							
Ohira 2014a	Not provided	60	2014	6	Japan	Glimepiride	1 mg daily		62.23	12.26	50	8.64	1.34	24.49	4.54							Metformin

Ohira 2014a						Pioglitazone	15 mg daily		63.7	7.94	63.3	8.54	1.06	23.61	4.06							
Omariglitin Study	NCT01697592	585	2017	5.5	Japan	Omagliptin	25 mg daily															Stable dose of an sulfonylurea, glinide, biguanide, thiazolidinedione, or alpha glucosidase inhibitor or dual treatment or additional other treatment depnding on HbA1C
Omariglitin Study						Placebo																
Omariglitpin Protocol	NCT01703221	394	2017	5.5	Japan	Omariglitpin	25 mg daily		60	11	62.7	7.9	0.7	25.2	3.7	7.4						None
Omariglitpin Protocol 2010						Sitagliptin	50 mg daily		60	9	69.7	8	0.8	25.4	4.2	7.4						
Omariglitpin Protocol 2010						Placebo			61	9	68.7	8.1	0.7	24.3	3.3	8.6						
Onoue 2020	UMIN000014531	24	2020	5.5	Japan	Anagliptin	400 mg daily		64.8	12.4	40.0	7.1	0.5	26.9	6.0	7.7						No or stable glucose lowering therapy
Onoue 2020						Control			62.9	14.7	33.0	7.3	0.5	25.6	3.5	7.4						
Onuchin 2010	None	184	2010	12	Russia	Metformin	2500-5000 mg daily		59.4	9.2	0	10.4	1.6	32.8	6.4	7						None
Onuchin 2010						Long acting Insulin	Titrated		61.1	8.5	0	11.03	1.9	31.1	7.6	9						
Onuchin 2010			2010	12	Russia	Gliclaziade	30-90 mg daily		62.3	8.5	0	10.6	1.8	32.1	4.6	7						Metformin
Onuchin 2010						Long-acting insulin	Titrated		61.4	8	0	10.8	1.6	32.3	5.7	8						
Osman 2004	Not applicable	16	2004	6	USA	Rosiglitazone	8mg daily	Coronary artery disease	53.5		14.3	10.3	3.2			7.75	100					Treatment not otherwise specified
Osman 2004						Placebo			57.3		62.5	8.7	1.9			3.25	100					
Ovalle 2004	Not applicable	17	2004	6	USA	Rosiglitazone	8 mg daily		47	12		8.7		31.5	6.9	7.6						Sulphonylurea; Metformin
Ovalle 2004						30/70 Mixed Insuli	Titrated		56	14.1		9		30.8	4.8	7.6						
Owens 2011	NCT00602472	1058	2011	5.5	Multinational	Linagliptin	5 mg daily		58.3	9.9	46.8	8.15	0.8	28.4	4.8							Metformin + sulfonylurea
Owens 2011						Placebo			57.6	9.7	48.3	8.14	0.8	28.2	4.5							
Oyama 2008	Not provided	84	2008	12	Japan	Acarbose	300 mg daily		65	6	29.3	7.5	0.8	23.4	2.5	11.7						Glibenclamide
Oyama 2008						Control			63	4	41.9	7.4	0.7	23.1	3.2	11.3						
Pagano 1995	Not applicable	96	1995	6	Italy	Glibenclamide	5 mg daily		59	7.5	51.1	7.8	0.7	26.7	2.7	7						Metformin
Pagano 1995						Miglitol	300 mg daily		57	8.4	67.3	8.2	1.4	26.4	2.8	5						
Pan 2008	NCT00110240	661	2008	5.5	Multinational	Vildagliptin	100 mg daily		51.8	10.1	60.1	8.6	0.9	26.4	3.6	1.2						None
Pan 2008						Acarbose	300 mg daily		51.9	10.3	63.2	8.6	1	25.8	3.5	1.3						
Pan 2012	Not provided	438	2012	5.5	China	Vildagliptin	100 mg daily		54.2	9.62	50	8.09	0.85	26.01	3.26	4.92						Metformin
Pan 2012						Vildagliptin	50 mg daily		53.7	10	44.6	8.05	0.84	25.03	3.09	5.02						
Pan 2012						Placebo			54.5	9.68	45.8	8.01	0.82	25.46	3.09	5.15						
Pan 2012a	NCT00698932	568	2012	5.5	Multinational	Saxagliptin	5 mg daily		51.2	10	56.3	8.1	0.8	25.9	3.4	0.8			103.1			None
Pan 2012a						Placebo			51.6	10.3	54.6	8.2	0.8	25.9	3.7	1.2			102.2			
Pan 2015	Not provided	461	2015	5.5	China	Retagliptin	100 mg daily															None
Pan 2015						Retagliptin	50 mg daily															
Pan 2015						Placebo																
Park 2011	Not provided	68	2011	5.5	Korea	Metformin	1000 mg daiy		63.1	8.4	51.5	8.2	0.4	25.2	3	4.9						Sulfonylurea
Park 2011						Pioglitazone	15 mg daily		62.3	8	52.9	8.3	0.3	25.5	3.8	5.1						
Park 2014	NCT00708578	67	2014	5.5	Republic of Korea	Metformin	1500 mg daily		55.8	10.5	60.61	8.4	0.9	25.1	3.6	11.3						Oral antidiabetic drugs
Park 2014						Glimepiride	4 mg daily		57.3	9.2	58.82	8.4	1	25.6	2.7	13						
Park 2017	NCT02946541	160	2017	5.5	Republic of Korea	Evogliptin	5 mg daily		57.6	11	48.8	7.21	0.56	25.6	3.2	4.74			88.6			None
Park 2017						Placebo			56.8	9.8	57.5	7.2	0.63	25.4	3.4	4.25			88.6			
Parmar Vinendra	Not provided	130	2019	5.5	India	Tenegliptin	20 mg daily		50.7	12.1	50.0	10.8	2.1	25.8	4.0	4.0						Metformin + glimepiride
Parmar Vinendra						Control			49.8	14.3	56.7	9.9	1.7	25.4	4.0	3.5						
Parthan 2018	NCT02097342	30	2018	6	India	Linagliptin	5 mg daily		49.5	41.5-55.5	50	6.8	6.4-7.1	25.5	23.6-31.1	2.5						Metformin
Parthan 2018						Voglibose	0.6 mg daily		50	45-54	77.8	7	6.8-7.4	25.9	23.8-26.6	2.5						
Parthan 2018						Control			54	48.5-59.5	71	7	6.8-7.1	26.4	23.8-30.5	2						
Patel 2013	Not provided	219	2013	60	USA	Acarbose			53.7	11	33	6.35	0.65	35.1	7.2							None
Patel 2013						Placebo			53.7	11.7	34.6	6.33	0.63	35.2	7.1							
Pavithra 2019	Not provided	80	2019	6.0	India	Sitagliptin	50 mg daily		47.6	4.7	65.0	8.6	5.2	25.3	8.2	7.1						Metformin
Pavithra 2019						Liraglutide	1.8 mg daily		43.2	6.2	49.0	8.3	3.5	28.2	5.9	6.4						
Pavo 2003	Not applicable	206	2003	7.5	Multinational	Metformin	2550 mg daily		55.8	8.4	56	8.6		31.1	4.4	0.47						None
Pavo 2003						Pioglitazone	45 mg daily		54.2	9.1	43.8	8.6		31.3	4.2	0.53						
Perez 2009	NCT00727857	399	2009	5.5	Multinational	Metformin	1500 mg daily		53.7	12	46.7	8.65	1	30.8	5.7							None
Perez 2009						Pioglitazone	30 mg daily		54	12	40.7	8.69	1	31.2	5.5							
PERISCOPE	NCT00225277	547	2008	18	Multinational	Glimepiride	1-4 mg daily	Coronary artery disease	59.7	9.1	65.9	7.4	1	32	5.2		100					1-2 oral drugs excluding thiazolidinedione
PERISCOPE						Pioglitazone	15-45 mg daily		60	9.4	68.9	7.4	1	32.1	5.3		100					
Periello 2006	Not provided	283	2006	12	Italy	Gliclazide	320 mg daily		59	7	64.2	8.7	0.9	28.8	2.8	8.5						None
Periello 2006						Pioglitazone	45 mg daily		58	8	66.4	8.8	0.9	29.2	3.1	9.8						
Petrica 2009	Not provided	44	2009	6	Romania	Glimepiride	4 mg daily		63.2	7.19	41.2	7.58	1.01	33.58	4.93	10.4						Metformin
Petrica 2009						Rosiglitazone	4 mg daily		63	8.07	41.2	7.72	1.2	33.55	4.84	10.53						
Petrica 2011	Not provided	78	2011	12	Romania	Glimepiride	4 mg daily		58.82	7.78		7.49	1.03	32.1	5.95	10.17						Oral antidiabetic drugs
Petrica 2011						Pioglitazone	30 mg daily		56.88	6.44		7.7	0.81	33.71	6.37	10						
Philis-Tsimikas 2013	NCT01046110	458	2013	6	Multinational	Sitagliptin	100 mg daily		54.9	11.4	54.5	9	1	30.8	5.2	7.7						1-2 oral drugs including metformin, sulfonylureas, glinide or pioglitazone
Philis-Tsimikas 2013						Insulin degludev	Titrated		56.4	10.2	62.7	8.8	1	30	5.1	7.8						
Phillips 2001	Not applicable	908	2001	5.5	USA	Rosiglitazone	8 mg daily		56.5	9.7	65.2	9	1.5	29.9	4.3	5.9						None
Phillips 2001						Rosiglitazone	8 mg daily		58.9	9.9	65.7	8.9	1.5	30	4.3	6.1						
Phillips 2001						Rosiglitazone	4 mg daily		56.8	9.4	59.1	8.9	1.5	30	4.2	5.5						
Phillips 2001						Rosiglitazone	4 mg daily		57.5	9.9	58.6	8.9	1.6	29.9	4.1	5.4						
Phillips 2001						Placebo			57.7	9.2	68.8	8.9	1.5	29.1	4.2	6.6						
Phillips 2003	Not applicable	83	2003	5.5	Multinational	Acarbose	300 mg daily		58.37	10.7	65	8.05	0.89	30.75	2.96	5.32						Metformin
Phillips 2003						Placebo			62.39	8.02	77	7.82	0.83	30.09	2.85	6.06						
Phrommintikul 2019	NCT03178591	49	2019	6	Thailand	Vildagliptin	100 mg daily	Coronary artery disease	63.88	7.65	50	8.25	1.13	24.9	3.16		75		70.45			Metformin and or sulfonylurea and or thiazoledinedione
Phrommintikul 2019						Dapagliflozin	10 mg daily		62.6	8.27	56	8.17	1.41	25.6	3		60		74.32			
PIOCOMB	Not provided	82	2011	6	Germany	Metformin	1700 mg daily		64.2	7.3	54.8	7.35	0.53	31.8	5	12.3			114.2	11.4		Insulin glargine
PIOCOMB						Pioglitazone	30 mg daily		61.5	7.1	62.5	7.33	0.53	31.7	4.3	9.8			115.8	34.7		
PIOfix	NCT00770653	305	2011	5.5	Germany	Glimepiride	4 mg daily		59	10	64.1	7.4	0.7	32.5	5.3	5.9						Metformin
PIOfix						Pioglitazone	30 mg daily		59	10	65.8	7.1	0.6	32.6	4.9	6.2						
Pioglitazone 001	Not applicable	399	2000	6	USA	Pioglitazone	45 mg daily															None
Pioglitazone 001						Pioglitazone	30 mg daily															
Pioglitazone 001						Pioglitazone	15 mg daily															
Pioglitazone 001						Pioglitazone	7.5 mg daily															
Pioglitazone 001						Placebo																
PIONEER	Not applicable	173	2005	6	Germany	Glimepiride	1-6 mg daily		63	7.4	62	7.44	0.89	31.8	4.3	6.9						Excluding thiazolidinedione treatment
PIONEER						Pioglitazone	45 mg daily		62.2	8.4	62	7.52	0.85	31.7	5	7.4						
PIONEER 1	NCT02906930	703	2019	5.5	Multinational	Semaglutide	14 mg daily		54	11	49.1	8	0.7	31.7	6.6	3.4			97			None
PIONEER 1						Semaglutide	7 mg daily		56	11	53.1	8	0.6	31.6	6.4	3.6			95			
PIONEER 1						Semaglutide	3 mg daily		55	11	50.9	7.9	0.7	31.8	6.3	3.8			99			
PIONEER 1						Placebo			55	11	50	7.9	0.7	32.2	6.9	3.4			100			
PIONEER 2	NCT02863328	822	2019	12	Multinational	Semaglutide	14 mg daily		58	10	51	8.1	0.9	32.8	5.9	7.7			95			Metformin
PIONEER 2						Empagliflozin	25 mg daily		57	10	50.1	8.1	0.9	32.9	6.3	7.2			96			
PIONEER 3	NCT02607865	1864	2019	18	Multinational	Sitagliptin	100 mg daily		58	10	51	8.3	0.9	32.5	6.2	8.8	17.3		96			Metformin with or without sulfonylurea
PIONEER 3						Semaglutide	14 mg daily		57	10	53.1	8.3	0.9	32.3	6.3	8.7	16.6		95			
PIONEER 3						Semaglutide	7 mg daily		58	10	52.7	8.4	1	32.6	6.4	8.3	16.3		96			
PIONEER 3						Semaglutide	3-14 mg daily															
PIONEER 4	NCT02863419	711	2019	12	Multinational	Semaglutide	14 mg daily		56	10	52	8	0.7	32.5	5.9	7.8			96			Metformin with or without SGLT-2 inhibitor
PIONEER 4						Liraglutide	1.8 mg daily		56	10	52	8	0.7	33.4	6.7	7.3			96			
PIONEER 4						Placebo			57	10	52	7.9	0.7	32.9	6.1	7.8			95			
PIONEER 5	NCT02827708	324	2019	6	Multinational	Semaglutide	14 mg daily		71	8	51	8	0.7	32.2	5.4	14.1			47	19.2		Metformin, a sulfonylurea, or both; or basal insulin with or without metformin
PIONEER 5						Placebo			70	8	45	7.9	0.7	32.6	5.5	13.9			48	14.1		
PIONEER 6	NCT02692716	3183	2019	15.9	Multinational	Semaglutide	14 mg daily		66	7	68.1	8.2	1.6	32.3	6.6	14.7	35.3		74			Standard of care
PIONEER 6						Placebo			66	7	68.6	8.2	1.6	32.3	6.4	15.1	37		74			
PIONEER 7	NCT02849080	504	2019	12	Multinational	Sitagliptin	100 mg daily		56.9	9.7	57	8.3	0.6	31.5	6.5	8.6			97			One or two glucose-lowering drugs (metformin, sulphonylureas, sodium glucose co-transporter-2 [SGLT2] inhibitors, or thiazolidinediones)
PIONEER 7						Semaglutide	14 mg daily		57.9	10.1	56	8.3	0.6	31.5	6.1	9			95.3			
PIONEER 8	NCT03021187	731	2019	12	Multinational	Semaglutide	14 mg daily		61	10	47	8.2	0.7	30.8	6.3	14.1			91			Insulin with or without metformin
PIONEER 8						Semaglutide	7 mg daily		60	10	56.6	8.2	0.7	31.1	7	16.2			92			
PIONEER 8						Semaglutide	3 mg daily		61	9	55.4	8.2	0.7	31	6.8	15.1			92			
PIONEER 8						Placebo			61	10	57.1	8.2	0.7	31	6.7	14.8			91			
PIONEER 9	NCT03018028	243	2020	6.0	Japan	Semaglutide	14 mg daily		58.0	9.0	73.5	8.1	0.8	26.5	4.6	7.4						Oral drug monotherapy or no therapy
PIONEER 9						Semaglutide	7 mg daily		60.0	10.0	73.5	8.3	1.0	26.3	3.5	7.4						
PIONEER 9						Semaglutide	3 mg daily		61.0	9.0	83.3	8.0	0.9	24.7	4.1	7.9						
PIONEER 9						Liraglutide	0.9 mg daily		59.0	10.0	81.3	8.3	0.8	26.9	4.8	6.7						
PIONEER 9						Placebo			59.0	9.0	81.6	8.3	1.1	25.1	3.9	8.4						

PioRAGE	UMIN000002055	63	2014	6	Japan	Glimepiride	0.5-2 mg daily		65.2	9.3	66.7	8	0.8	24.4	18.1	6	16.7			Sulfonylurea or glinide or no treatment
PioRAGE						Pioglitazone	15-30 mg daily		64.6	10.4	74.1	7.9	0.7	25.8	5.7	8	11.1			
PIRAMID 2009	ISRCTN53177482	78	2009	5.5	Netherlands	Metformin	500-1000 mg daily		56.4	5.6	100	7	0.6	29.3	3.7	3				Glimepiride
PIRAMID 2009						Pioglitazone	15-30 mg daily		56.8	6.2	100	7.1	1.2	28.2	3.1	4 (median)				
Pistrosch 2012	NCT00324675	28	2012	12	Germany	Rosiglitazone	8 mg daily	Chronic kidney disease	65.4	9.6	85.7	7	3	33.5	4.8	15		41.8	130	Insulin ± sulfonylurea ± glinide ± α-glucosidase inhibitor therapy
Pistrosch 2012						Placebo			66.5	8.5	85.7	7.3	3	30.1	5.4	14.7		39.7	180	
Pistrosch 2013	NCT00857870	75	2013	8.4	Germany	Metformin	2000 mg daily		62.03	9.4	50	6.9	0.4	29.9	5.3	2.6				None
Pistrosch 2013						Insulin glargine	Titrated		60	9.3	66.6	7.2	0.7	29.2	4.6	2.8				
Pi-Sunyer 2007	NCT00120536	354	2007	5.5	Multinational	Vildagliptin	100 mg daily		52	11.7	53.8	8.3	0.8	31.9	5	2.1				None
Pi-Sunyer 2007						Vildagliptin	100 mg daily		50.2	12.7	56.6	8.4	0.9	32.2	6	2.4				
Pi-Sunyer 2007						Vildagliptin	50 mg daily		50.6	10.4	55.7	8.4	0.9	31.9	5.4	1.8				
Pi-Sunyer 2007						Placebo			52	12	54.3	8.5	0.8	32.7	6.4	2.5				
Pop-Busui 2009	NCT00549874	27	2009	6	USA	Glyburide	10 mg daily					7.5	1.9				23			Sulfonylurea
Pop-Busui 2009						Rosiglitazone	8 mg daily					6.5	1				18			
POPPS	Not provided	97	2009	6	Japan	Pioglitazone	15 mg daily	Coronary artery disease	64	8.8	83	7.5	1.8				100			Excluding pioglitazone
POPPS						Control			62.4	9.8	86	7	1.5				100			
Pratley 2014	NCT01023581	559	2014	6	Multinational	Metformin	2000 mg daily		52.6	11.3	56.6	8.39		30.51	5.043	4.08				None
Pratley 2014						Metformin	1000 mg daily		54.6	10.2	53.6	8.5		30.19	4.84	3.78				
Pratley 2014						Alogliptin	25 mg daily		52.6	9.38	53.8	8.3		30.81	5.22	3.65				
Pratley 2014						Alogliptin	25 mg daily		53.7	9.7	71.2	8.44		30.36	5.16	3.97				
Pratley 2014						Placebo			53.1	9.6	60	8.49		31.15	5.27	4.25				
PRESERVE-beta	Not applicable	428	2005	24	USA	Glyburide	1.25-10 mg daily		53.5	11.6	48	8.3	1.1	33.5	5.6	2				Metformin
PRESERVE-beta						Nateglinide	360 mg daily		52.6	11.6	51	8.4	1.2	33.3	6	1.5				
PREVENT-J	UMIN000021552	278	2018	18	Japan	Sulfonylurea (Gliclazide, glimepiride, tolbutamide)			58.8	8	49.5	6.91	0.6	24.7	4	4.3			37.8	None, metformin or alpha glucosidase inhibitor
PREVENT-J						Pioglitazone	30-45 mg daily		58.5	9	53.9	6.98	0.5	24.4	4	3.6			60.7	
PREVENT-J						Control			58.9	7.5	52.8	6.93	0.5	24.2	3.8	3.6			28.9	
PRIDE	Not provided	94	2018	6	Japan	Pioglitazone	30 mg daily	Coronary artery disease	67	57-74	83.3	6.5	6.0-7.8	24.8	22.6-26.7		87.5			Oral hypoglycemic agents
PRIDE						Control			69	64-76	63.2	6.5	6.0-7.2	24.9	22.1-25.9		82.6			
PRIME-V	UMIN000015170	98	2019	5.5	Japan	Metformin	1000-1500 mg daily		55.7	12.2	56	8.12	0.9	28.83	5.32	5.3	0			Sitagliptin
PRIME-V						Ipragliflozin	50 mg daily		56.6	11.9	64.6	7.95	0.73	27.55	4.24	5.4	0			
PRISMA	NCT00772174	213	2013	5.5	Italy	Pioglitazone	45 mg daily		57	8.6	59.2	6.92	0.42	32.4	5.4	5.8			41.3	Metformin
PRISMA						Placebo			57.8	8.2	60.2	7.02	0.46	32.6	5.3	5.7			50	
PROactive	NCT00174993	5238	2005	34.5	Multinational	Pioglitazone	15-45 mg daily	Cardiovascular disease	61.9	7.6	67			30.7	4.7		100			Oral agents ± insulin
PROactive						Placebo			61.6	7.8	66			31	4.8		100			
PROLOGUE	UMIN000004490	463	2016	24	Japan	Sitagliptin	100 mg daily		69.2	9.3	65.8	6.96	0.64	25.3	4.1		20.7	66.5		Antidiabetic drugs
PROLOGUE						Placebo			69.5	9.2	68.6	6.96	0.55	24.9	4		25	66.8		
QUARTER	Not applicable	1194	2004	12	Europe	Metformin	2550 mg daily		56	9.3	57.8	8.7	1	31.4	5.2	3.1				None
QUARTER						Pioglitazone	45 mg daily		57	9.4	52.6	8.7	1	31.2	4.9	3.4				
Quatraro 1986	Not applicable	30	1986	12	Italy	Glicazide	40-240 mg daily		56	7.4		12	2.3	28.6	3.1	12.1				Insulin
Quatraro 1986						Control			57	7.4		11.8	1.5	28.9	2.7	11.8				
Raghuveer 2020	Not provided	100	2020	12	India	Teneligliptin	20 mg daily													Metformin
Raghuveer 2020						Control														
Rahman 2010	NCT00489229	22	2010	12	Malaysia	Rosiglitazone	4 mg daily					7.5	1.7	26.6	1.4					None
Rahman 2010						Placebo						8.3	2.3	27	3.2					
Rahman 2011	Not provided	204	2011	12	Pakistan	Metformin	2000 mg daily		51.9	14.1	49	10.5	2.5	26.6	6.2					None
Rahman 2011						Glimepiride	8 mg daily		52	15.4	47	10.6	2.9	26	5.2					
Raji 2018	Not provided	613	2018	5.5	USA	Sitagliptin	100 mg daily	Chronic kidney disease				7.7						79		Metformin ± sulfonylurea
Raji 2018						Dapagliflozin	10 mg daily					7.8						77		
Raskin 2001	Not applicable	318	2001	6	USA	Rosiglitazone	8 mg daily		57.7	10.2	54.4	9	1.3	32.3	4.9	12.5				Insulin
Raskin 2001						Rosiglitazone	4 mg daily		57.1	10	56.6	9.1	1.3	32.1	4.8	12.7				
Raskin 2001						Placebo			55.6	10.3	55.8	8.9	1.1	32.7	4.5	11.7				
Raskin 2004	Not applicable	125	2004	5.5	USA	Rosiglitazone	8 mg daily		56.6	10.8	53.2				9	7.4				None
Raskin 2004						Repaglinide	12 mg daily		58.5	10.1	61.9				9.3	7.2				
Raskin 2009	Not provided	657	2009	6	USA	Rosiglitazone	4 mg daily		55.5	10.3	50.8	8.46	1.097	32.3	5.28	7.1				Oral agents
Raskin 2009						Repaglinide	10 mg daily		54.8	11.5	57.8	8.45	1.125	32.9	5.51	7.4				
Raskin 2009						Repaglinide	8 mg daily		54.5	10.5	58.8	8.29	0.973	32.5	5.47	7.3				
Raz 2008	NCT00337610	190	2008	6.9	Multinational	Sitagliptin	100 mg daily		53.6	9.5	51	9.3	0.9	30.1	4.4	8.4				Metformin ± oral monotherapy
Raz 2008						Placebo			56.1	9.5	41.5	9.1	0.8	30.4	5.3	7.3				
RECORD	NCT00379769	4447	2009	66	Multinational	Rosiglitazone	8 mg daily				51.5						17.3			Metformin
RECORD						Standard care					51.7						17.4			
REFORM	NCT02397421	56	2020	12	United Kingdom	Dapagliflozin	10 mg daily	Heart failure	66.9	7.0	64.3			33.0	5.5		100.0	68		Stable therapy
REFORM						Placebo			67.4	6.8	67.9			32.0	5.2		100.0	76		
REGO-F	UMIN000018321	72	2020	11.0	Japan	Glimepiride	1 mg daily		62.4	11.3	63.0	7.4	0.6	25.1	2.7	10.3				Antidiabetic agents
REGO-F						Repaglinide	0.75 mg daily		63.5	9.4	61.0	7.6	0.8	25.5	3.0	8.1				
RELEASE	NCT02015299	44	2017	6	The Netherlands	Linagliptin	5 mg daily		63	52-66	59	6.3	0.4	32.3	27.8-38.2	1.5		88		None
RELEASE						Placebo			62	56-69	64	6.2	0.5	29	27.4-34.2	1		81		
RESULT	Not provided	227	2006	24	USA, Canada	Rosiglitazone	4-8 mg daily		68.7	6.1	74.8	7.72	1.03	30.2	4.5	6.8				Sulfonylurea
RESULT						Placebo			68.2	6.3	71.8	7.65	0.99	30.5	4.9	6.8				
REWIND	NCT01394952	9901	2019	64.8	Multinational	Dulaglutide	1.5 mg weekly		66.2	6.5	53.4	7.3	1.1	32.3	5.7	10.5	31.5	75.3	1.8	Antihyperglycemic therapy except DPP-4 inhibitor or GLP-1 receptor agonist
REWIND						Placebo			66.2	6.5	53.9	7.4	1.1	32.3	5.8	10.6	31.4	74.7	1.88	
Reynolds 2002	Not applicable	18	2002	5.5	USA	Rosiglitazone	4 mg daily					8	0.8	36.4	5.1					None
Reynolds 2002						Placebo						9.8	1.6	36.3	5.7					
Reynolds 2007	Not provided	40	2007	5.5	USA	Rosiglitazone	4 mg daily					9.1	0.94							Metformin + sulfonylurea
Reynolds 2007						Insulin glargine	Titrated					8.86	0.87							
Ristic 2006	Not provided	262	2006	5.5	Multinational	Gliclazide	240 mg daily		61.6	10.1	50.4	7.6	0.58	29.5	3.6	6.7				Metformin
Ristic 2006						Nateglinide	540 mg daily		62	11	54.1	7.67	0.59	28.5	3.5	7.16				
Robbins 2007	NCT00191464	317	2007	5.5	Multinational	Insulin glargine	Titrated		57.4	9.2	50.3	7.8	0.9	32.1	6.3	11.3				Metformin ± sulfonylurea
Robbins 2007						Insulin protamine/	Titrated		58.1	8.9	49.4	7.8	1	32	6	12.5				
Roberts 2005	Not applicable	168	2005	7	USA, Canada	Glimepiride	2-8 mg daily		56.5	9.8	61	8.15	0.65	33.98	5.15	7.9				Metformin + thiazolidinedione
Roberts 2005						Placebo			56.4	10	62.3	8.15	0.76	32.76	5.11	8.7				
Rodbard 2016	Not provided	216	2016	6	Multinational	Canagliflozin	300 mg daily		57.4	9.3	61.7	8.5	0.9	32.3	5.8	9.8		91.4		Metformin and sitagliptin
Rodbard 2016						Placebo			57.5	10.1	51.9	8.4	0.8	31.7	5.5	10.1		89.6		
Rosenstock 1998	Not applicable	148	1998	5.5	USA	Acarbose	150-300 mg daily		57.2		61	8.46		32.4		7.2				Metformin
Rosenstock 1998						Placebo			55.9		49	8.17		32.3		7.8				
Rosenstock 2006	Not provided	313	2006	7.4	Multinational	Metformin	500-2000 mg daily		51.5	10.4	56	8.8	1	32.5	7	2.9				None
Rosenstock 2006						Rosiglitazone	4-8 mg daily		50.6	10.26	58	8.8	1	32.8	7.1	2.7				
Rosenstock 2007	NCT00099918	786	2007	5.5	Multinational	Rosiglitazone	8 mg daily		54.2	11.6	57.6	8.7	1.1	32.9	6	2.7				None
Rosenstock 2007						Vildagliptin	100 mg daily		54.5	11.7	57.5	8.7	1.1	32.2	5.7	2.3				
Rosenstock 2007a	NCT00101803	315	2007	5.5	Multinational	Pioglitazone	30 mg daily		52.4	10.3	64	8.7	1	28.9	5.5	2.2				None
Rosenstock 2007a						Vildagliptin	100 mg daily		51.4	10.8	63.6	8.6	1	29.4	5.8	1.9				
Rosenstock 2009	NCT00286429	390	2009	6	Multinational	Alogliptin	25 mg daily		55.9	10.2	34	9.3	1.1	32.3	5.6	13.4				Insulin ± metformin
Rosenstock 2009						Alogliptin	12.5 mg daily		55.4	9.8	42	9.3	1.1	32.7	5.5	12.1				
Rosenstock 2009						Placebo			55	10.6	48	9.3	1.1	32.4	5.6	12.2				
Rosenstock 2010	NCT00395512	327	2010	6	Multinational	Pioglitazone	30 mg daily													None
Rosenstock 2010						Alogliptin	25 mg daily													
Rosenstock 2012	NCT00683878	420	2012	11	Argentina,	Dapagliflozin	10 mg daily		53.8	10.4	42.1	8.37	0.96			5.75				None or metformin or sulfonylurea or thiazolidinedione
Rosenstock 2012						Dapagliflozin	5 mg daily		53.2	10.9	55.3	8.4	1.03			5.64				
Rosenstock 2012						Placebo			53.5	11.4	51.1	8.34	1			5.07				
Rosenstock 2013	NCT00707993	441	2013	12	Mutlinational	Glipizide	5-10 mg daily		69.8	4.07	43.8	7.45	0.634	30.02	4.459	5.94		72.9		None
Rosenstock 2013						Alogliptin	25 mg daily		70.1	4.42	45.9	7.5	0.703	29.58	4.348	6.25		73.6		
Rosenstock 2015	NCT01606007	355	2015	5.5	USA	Saxagliptin	5 mg daily		54	10	50	8.87	1.16	31.5	5.3	7.4		92.5		Metformin
Rosenstock 2015						Dapagliflozin	10 mg daily		55	10	53	9.03	1.05	31.8	5.1	8.2		93.9		
Rosenstock 2016	NCT01809327	712	2016	5.5	Multinational	Metformin	500-2000 mg daily		55.2	9.8	48.9	8.8	1.2	33	6	3.3		87		None
Rosenstock 2016						Canagliflozin	300 mg daily		55.8	9.6	52.5	8.8	1.2	32.6	5.8	3.3		85		
Rosenstock 2016						Canagliflozin	100 mg daily		54	10.7	44.3	8.8	1.2	32.4	5.4	3.5		90		
Rosenstock 2019	NCT02681094	590	2019	5.5	Multinational	Saxagliptin	5 mg daily		32.4	5.5	54	8.3	1	32.4	5.5	7.8				Metformin
Rosenstock 2019						Dapagliflozin	5 mg daily		31.8	5.2	52.6	8.2	0.9	31.8	5.2	7.6				
Ross 2015	NCT01512979	316	2015	5.5	Multinational	Metformin	1500-2000 mg daily		49	10.9	43.4	9.79	1.19	29.84	5.82		42.1			Linagliptin
Ross 2015						Standard care			48.6	11.2	49	9.88	1.1	29.63	5.43		45.9			

SAIS1	UMIN000004955	103	2016	6	Japan	Glimepiride	0.5-2.0 mg daily		60	36-60	52.7	7.4	7.5-8.6	25.2	3.5					Metformin
SAIS1						Sitagliptin	50-100 mg daily		62	35-80	68.8	7.4	6.7-8.4	25.7	3.9					
Saleem 2011	Not provided	100	2011	12	Pakistan	Glibenclamide	8.8 mg daily		45.8	8.8	20	10.2	1.6	30.4	5.6					None
Saleem 2011						Repaglinide	4.27 mg daily		46.6	10.5	32	9.9	1.6	27.1	3.5					
Salman 2001	Not applicable	57	2001	5.5	Turkey	Gliclazide	80-160 mg daily		56.1	8.7	53.3	8.7	0.6	29.2	2.8	4.7				None
Salman 2001						Acarbose	200-300 mg daily		52.6	9.1	63	8.9	0.7	30.2	3.8	4.2				
Saloranta 2002	Not applicable	675	2002	5.5	Multinational	Nateglinide	360 mg daily		59.6	9.9	65.5	6.57	0.69	29.12	3.67	3.7				None
Saloranta 2002						Nateglinide	180 mg daily		61.1	9.3	61.1	6.53	0.6	28.92	3.7	3.6				
Saloranta 2002						Nateglinide	60 mg daily		61	10.1	63.3	6.55	0.63	28.95	3.59	3.8				
Saloranta 2002						Placebo			59.1	10.6	60.1	6.45	0.6	28.78	3.54	3.2				
Samson 2011	NCT01432405	21	2011	12	USA	Exenatide	20 µg daily													Pioglitazone
Samson 2011						Placebo														
Sato 2019	UMIN000004985	41	2019	5.5	Japan	Glimepiride	6 mg daily		62.1	9		7.8	0.5	24.6	3.5	11.9			43.7	Oral hypoglycemic agents except sulfonylurea, glinide or DPP-4 inhibitor
Sato 2019						Sitagliptin	50 mg daily		63.4	5.9		8	0.6	24	2.4	12.9			33.8	
SAVOR -TIMI 53	NCT01107886	16492	2013	25.2	Multinational	Saxagliptin	2.5-5 mg daily	High cardiovascular risk	65.1	8.5	66.6	8	1.4	31.1	5.5		78.4	72.5	1.8	Excluded incretin-based therapy
SAVOR -TIMI 53						Placebo			65	8.6	67.3	8	1.4	31.2	5.7		78.7	72.7	1.9	
Saxagliptin 014	NCT00121667	743	2009	5.5	Multinational	Saxagliptin	10 mg daily		54.2	10.1	52.5	8	1	31.1	4.8	6.4				Metformin
Saxagliptin 014						Saxagliptin	5 mg daily		54.7	9.6	53.9	8.1	0.8	31.2	4.7	6.4				
Saxagliptin 014						Saxagliptin	2.5 mg daily		54.7	10.1	42.2	8.1	1	31.7	5.2	6.7				
Saxagliptin 014						Placebo			54.8	10.2	53.6	8.1	0.9	31.6	4.8	6.7				
SCALE Diabetes	NCT01272232	855	2015	13	Multinational	Liraglutide	3 mg daily		55	10.8	52	7.9	0.8	37.1	6.5	7.5	16.4			1 to 3 drugs (metformin, thiazolidinedione, sulfonylurea)
SCALE Diabetes						Liraglutide	1.8 mg daily		54.9	10.7	51.2	8	0.8	37	6.9	7.4	14.8			
SCALE Diabetes						Placebo			54.7	9.8	45.8	7.9	0.8	37.4	7.1	6.7	12.3			
Scherbaum 2002	Not applicable	233	2002	6	Germany	Pioglitazone	30 mg daily		59.6		41	9.06		29.3		4.6				None
Scherbaum 2002						Pioglitazone	15 mg daily		58		62.9	9.33		29.9		5.4				
Scherbaum 2002						Placebo			59.1		56	8.75		29.2		5.6				
Scherbaum 2008	NCT00101712	306	2008	12	Multinational	Vildagliptin	50 mg daily		63.3	10.2	59.6	6.7	0.4	30.4	4.9	2.5				None
Scherbaum 2008						Placebo			62.8	11	59.3	6.8	0.4	30	4.9	2.7				
Schweizer 2007	NCT00099866	780	2007	12	Multinational	Metformin	2000 mg daily		53.6	10.2	57.5	8.7	1.1	32.5	5.7					None
Schweizer 2007						Vildagliptin	100 mg daily		52.8	11.7	52.9	8.7	1.1	32.4	5.7					
Schweizer 2009	NCT00246619	335	2009	5.5	Multinational	Metformin	500-1500 mg daily		70.2	5.1	53	7.7	0.6	29.4	4.6	3				None
Schweizer 2009						Vildagliptin	100 mg daily		71.6	5.2	44.4	7.8	0.6	29.8	4.4	2.9				
Segal 1997	Not applicable	119	1997	5.5	Multinational	Glibenclamide	3.5 mg daily		56		62.2	7.96		29.2						None
Segal 1997						Miglitol	300 mg daily		61		55	7.95		28.6						
Segal 1997						Placebo			59		57	8.25		29.1						
Segal 2005	Not applicable	139	2005	18	Israel	Acarbose	150-900 mg daily		53.7	8	53.6	11	2.3	28.1	4.2	10				Mainly sulfonylureas
Segal 2005						Placebo			55.7	8.1	53.2	11.4	2.9	28	4.1	11				
Seino 2011	NCT00395746	264	2011	12	Japan	Liraglutide	0.9 mg daily		66.8	13.7	67	8.61	0.78	24.4	3.8	11.6				Sulfonylurea
Seino 2011						Liraglutide	0.6 mg daily		64.5	12	60.2	9	0.91	25.3	3.6	9.3				
Seino 2011						Placebo			59.1	10.3	64.8	8.85	0.99	24.9	4	10.1				
Seino 2014	JapicCTI-111661	158	2014	5.5	Japan	Luseogliflozin	2.5 mg daily		58.9	10.1	75.9	8.1	0.9	26.0	4.9	6.5				None
Seino 2014						Placebo			59.6	9.3	70.9	8.2	0.8	25.3	4.2	6.1				
Seino 2015	JapicCTI-111507	221	2015	5.5	Japan	Luseogliflozin	2.5 mg daily		61.2	8.4	74.7	8.07	0.85	24.78	3.63	7.4		81.5		Sulfonylurea
Seino 2015						Placebo			59.9	10.5	67.6	8.01	0.73	24.66	3.31	7.9		84.3		
Seino 2016	NCT01572740	257	2016	8.4	Japan	Liraglutide	0.9 mg daily		61.3	11	54.3	8.8	0.9	26.2	4.9	14.32				Insulin
Seino 2016						Placebo			59.8	11.3	57.7	8.8	0.9	25.2	4	14.69				
Seino 2018	NCT02254291	308	2018	7	Japan	Sitagliptin	100 mg daily		57.9	10.1	78.6	8.2	0.9	25.1	3.6	8.1				None
Seino 2018						Semaglutide	1.0 mg weekly		58.1	11.6	73.5	8	0.9	26.1	5.2	7.8				
Seino 2018						Semaglutide	0.5 mg weekly		58.8	10.4	76.7	8.2	1	25.1	3.8	8				
Shaddinger 2019	NCT02683746	308	2019	6	USA	Albiglutide	50 mg weekly		57.6	9.3	54.2	8.14	0.88	31.9	5	9.2				Metformin
Shaddinger 2019						Placebo			56.6	10.1	48.7	7.99	0.81	32.5	4.6	9.4				
Shah 2011	Not provided	200	2011	12	Pakistan	Glibenclamide	5-15 mg daily		45.2	8.2	31			30.2	5.5					None
Shah 2011						Repaglinide	0.5-2 mg three times daily		46	10.1	20			27.2	3.2					
Shankar 2017	NCT01590797	467	2017	5.5	China	Sitagliptin	100 mg daily		58.6	8.4	55.6	8.7	0.9	25.9	3	11				Insulin
Shankar 2017						Placebo			56.7	9.1	49.8	8.8	0.9	26.1	2.9	11.3				
Shankar 2017a	NCT01755156	402	2017	5.5	Multinational	Omarigliptin	25 mg daily		57.5	8.1	50.2	8.1	0.9	32.4	5.8	8.2				Metformin
Shankar 2017a						Placebo			56.8	9.1	50.7	8	0.9	32.6	6.1	7.4				
Shestakova 2018	NCT02794792	165	2018	5.5	Russia	Ipragliflozin	50 mg daily		58.9	9.3	43.6	8.39	0.93	32.8	4.76	6.65				Metformin
Shestakova 2018						Placebo			58	9.5	40	8.46	0.96	31.95	4.18	6.6				
Shibuya 2018	UMIN000016090	32	2018	6	Japan	Metformin	1500 mg daily		60	53-66	50	7.4	6.9-7.7	27.2	24.9-32.0	0.75				Oral agents
Shibuya 2018						Luseogliflozin	2.5 mg daily		51	47-62	62.5	7.8	7.2-7.9	27.9	26.2-28.7	0.4				
SIMPLE	NCT01966978	120	2019	6	USA	Liraglutide	1.8 mg daily		46.7	9	32.2	12.1	1.4	36.1	9.5	10				Any treatment plus insulin detemir
SIMPLE						Insulin aspart			48.1	10	26.2	12	1.5	38.3	11	10				
Sit2Mix	Not provided	389	2015	5.5	Multinational	Sitagliptin	100 mg daily		56.3	10.2	48.2	8.4	0.8	29.4	4.5					Metformin ± oral antidiabetic drugs
Sit2Mix						Standard care			54.8	9.5	57.2	8.4	0.8	29.3	4.3					
Sitagliptin 019	NCT00086502	353	2006	5.5	Multinational	Sitagliptin	100 mg daily		55.6	10.4	53.1	8.1	0.8	32	5.2	6.1				Pioglitazone
Sitagliptin 019						Placebo			56.9	11.1	57.9	8	0.8	31	5	6.1				
Sitagliptin 020	NCT00865515	701	2006	5.5	Multinational	Sitagliptin	100 mg daily		54.4	10.4	55.8	8	0.8	30.9	5.3	6				Metformin
Sitagliptin 020						Placebo			54.7	9.7	59.5	8	0.8	31.5	4.9	6.6				
Sitagliptin 021	NCT00087516	726	2006	5.5	Multinational	Sitagliptin	200 mg daily													None
Sitagliptin 021						Sitagliptin	100 mg daily													
Sitagliptin 021						Placebo														
Sitagliptin 024	NCT00094770	1172	2007	12	Multinational	Glipizide	5-20 mg daily		56.5	9.8	61.3	7.6	0.9	31.3	5.2	6.2				None, monotherapy or metformin + monotherapy
Sitagliptin 024						Sitagliptin	100 mg daily		56.8	9.3	57.1	7.7	0.9	31.5	5	6.5				
Sitagliptin 035	Not provided	441	2007	5.5	Multinational	Sitagliptin	100 mg daily		55.6	9.6	52.7	8.34	0.76	31.2	6.3	8.3				None, sulfonylurea ± metformin, or mono-, dual, or triple therapy
Sitagliptin 035						Placebo			56.5	9.6	53.4	8.34	0.74	30.7	6.3	9.3				
Sitagliptin 036	NCT00103857	355	2007	5.5	Multinational	Sitagliptin	100 mg daily		53.3	10.2	52	8.9	1	31.2	5.9	4.4				None
Sitagliptin 036						Placebo			53.6	10	52.8	8.7	1	32.5	6.7	4.6				
Sitagliptin 049	NCT00449930	1050	2010	6	Multinational	Metformin	2000 mg daily		55.7	10.3	44	7.2	0.7	30.9	4.9	2.1				None
Sitagliptin 049						Sitagliptin	100 mg daily		56.3	10.7	48	7.2	0.7	30.7	4.7	2.6				
Sitagliptin 051	NCT00395343	641	2010	5.5	Multinational	Sitagliptin	100 mg daily		58.3	9.1	49	8.7	0.9	31	5	13				Insulin ± metformin
Sitagliptin 051						Placebo			57.2	9.3	53	8.6	0.9	31	5	12				
SMART	NCT02243176	485	2017	5.5	China	Saxagliptin	5 mg daily		54.7	10.51	61.8	8.23	0.85	26.4	3.47	5.1				Metformin
SMART						Acarbose	300 mg daily		56.5	10.8	56.8	8.16	0.81	26.3	3.49	5.3				
Smith 2005	Not applicable	48	2005	6	USA	Pioglitazone	30-45 mg/day		56.2	9.7	47.6	6.88	1.4	32.1	5.6					Metformin; sulfonylurea
Smith 2005						Placebo			53.1	9.3	71.4	6.46	0.7	31.9	5					
Søfteland 2017	NCT01734785	333	2017	5.5	Multinational	Empagliflozin	25 mg daily		55.4	9.9	64.5	7.97	0.82	29.9	5.3			93		Meformin + linagliptin
Søfteland 2017						Empagliflozin	10 mg daily		54.3	9.6	60.6	7.97	0.84	31.2	5.9			91		
Søfteland 2017						Placebo			55.9	9.7	55.6	7.97	0.85	29.6	5.7			93		
Sohn 2008	Not provided	19	2006	7.5	Republic of Korea	Metformin	2000 mg daily		52	10.7	50	8.96	1.25	22.8	1.99	1.05				None
Sohn 2008						Rosiglitazone	8 mg daily		48.1	9.85	63.6	8.78	1.03	24.6	2.98	1.81				
Sone 2019	NCT02589639	266	2019	12.0	Japan	Empagliflozin	25 mg daily		58.6	9.5	67.8	8.7	0.7	26.8	3.3	14.6		84		Insulin
Sone 2019						Empagliflozin	10 mg daily		58.3	10.0	73.3	8.8	0.7	27.0	3.0	14.4		85		
Sone 2019						Placebo			59.1	10.7	76.7	8.7	0.7	26.9	3.4	12.4		83		
South Danish Diabete	Not provided	140	2011	24	Denmark	Metformin	1000-2000 mg daily		56.1	8.2	62.2	8.5	1.2	33.7	6.1	8.7				Oral agents ± insulin
South Danish Diabetes	Study					Rosiglitazone	4-8 mg daily		56.1	8.3	57.4	8.3	1	32.7	4.7	9.4				
South Danish Diabetes	Study					Placebo			57.1	8.5	47.9	8.5	1.2	33.7	5	9.1				
SPEAD-A	UMIN000005311	341	2016	24	Japan	Alogliptin	25 mg daily		64.4	9.8	63	7.3	0.8	24.6	4.3	9				Treatment excluding DPP-4 inhibitors
SPEAD-A						Standard care			64.8	9.1	61	7.2	0.8	24.9	3.7	8.2				
SPECIFY	NCT02280486	388	2019	11	China	Glimepiride	6 mg daily		52.8	9.5	58.6	8	0.7	25.6	2.9	4.9			9.8	Metformin
SPECIFY						Saxagliptin	5 mg daily		54.2	9.4	63.6	8	0.7	25.3	2.3	5.2			9.85	
Spengler 1989	Not applicable	55	1989	6	Not reported	Glibenclamide	3.5 mg one to 3 times daily		60	7	38	11	9.6 -12.5			0.7				None
Spengler 1989						Acarbose	50-100 mg three times daily		59	5	42	10.8	9.6-12.3			1				
SPIKE	UMIN000007396	282	2016	24	Japan	Sitagliptin	25-100 mg daily		63.8	9.7	61	8.1	1.1	25	4.3	17.2	0	77.7	20.3	Treatment excluding DPP-4 inhibitors
SPIKE						Standard care			63.6	10	60	8	1	25	3.8	17.3	0	79.7	19	
SPOTLIGHT	NCT01225081	152	2015	12	Japan	Ipragliflozin	50 mg daily		56.2	10.22	77.3	8.24	0.67	27.1	3.85	6.3				Pioglitazone
SPOTLIGHT						Placebo			56.1	11.91	68.5	8.39	0.64	27.1	4.31	7.7				
SPREAD-DIMCAD	NCT00513630	304	2013	36	China	Metformin	750-1500 mg daily	Coronary artery disease	62.8	8.5	78.2	7.6	1.7	25.2	3	5.6	100			Excluding insulin
SPREAD-DIMCAD						Glipizide	15-30 mg daily		63.8	9.4	77	7.6	1.7	25.1	2.9	5.6	100			

Sridhar 2013	NCT01206400	50	2013	6	India	Pioglitazone	30 mg daily		47.9	5.8	100	6.8	0.4	25.3	2.7	2.2						Glimepiride and metformin
Sridhar 2013						Placebo			44	7.2	100	6.8	0.4	25.1	3.2	2.9						
St. John Sutton 2002	Not applicable	203	2002	12	USA	Glyburide	20 mg daily		56.1	8.9	72	9.5	1.6			6.2						None
St. John Sutton 2002						Rosiglitazone	8 mg daily		55.1	9	72.1	9.1	1.7			5.3						
Standl 1999	Not applicable	48	1999	5.5	Germany	Acarbose	50 mg twice daily-200 mg three times daily		59.3	8.5	58.3	10.9	1	25.2	2.2	11.5						Sulphonylurea, Insulin
Standl 1999						Placebo			62.9	9.4	41.7	11	1.2	24.1	2	12.2						
Standl 2001	Not applicable	133	2001	5.5	Multinational	Miglitol	300 mg daily		62	8	50.8	8.83	0.85	27.7	3.7	8						Metformin + glibenclamide
Standl 2001						Placebo			61	8	54.4	8.84	0.66	27.9	3.5	9						
START	NCT02273050	424	2018	5.5	China	Metformin	2000 mg daily		50.1	11	63.8	9.5	1	26.5	3.6	0.72						None
START						Saxagliptin	5 mg daily		49.5	10.9	70.9	9.4	1	26.5	3.2	0.73						
START-J	NCT01183104;	305	2016	12	Japan	Glimepiride	0.25-3 mg daily		70.8	5.5	61.2	7.5	0.7	24.2	3.6	3.1						None
START-J						Sitagliptin	25-100 mg daily		70.2	5.4	51.7	7.5	0.7	24.1	3.3	4.2						
Stewart 2006	Not provided	526	2006	7.4	Europe	Rosiglitazone	4-8 mg daily		58.9	8.4	55	7.2	0.6	30.9	5.4	3.7						None or monotherapy excluding insulin
Stewart 2006						Control			59	7.9	56	7.2	0.6	30.6	5.5	3.7						
Stocker 2007	Not provided	92	2007	5.5	USA	Metformin	1500 mg daily		65	10	53.2	8.48	1.8	29.7	5.1							None
Stocker 2007						Rosiglitazone	4 mg daily		64	11	71.1	8.5	1.9	29.4	4.5							
STOP-OB	UMIN000026161	64	2020	5.5	Japan	Glimepiride	0.5 mg daily		57.6	9.3	61.3	7.5	0.4	25.4	3.8	7.7		89				Metformin + DPP-4 inhibitor
STOP-OB						Tofogliflozin	20 mg daily		57.3	11.4	54.5	7.4	0.5	25.3	3.9	11.3		92				
Strojek 2009	NCT00469092	480	2009	6	Multinational	Insulin glargine	Titrated		56.1	10	41.2	8.5	1.1	29.2	4.5	9.5						Metformin + secretagogue (no more than 3 oral drugs)
Strojek 2009						Insulin Aspart	Titrated		55.9	9.7	46.8	8.5	1	29	4.6	9.1						
Strojek 2011	NCT00680745	596	2011	5.5	Multinational	Dapagliflozin	10 mg daily		58.9	8.32	43.7	8.07	0.79	29.75	5.6	7.2	30.5					Sulfonylurea
Strojek 2011						Dapagliflozin	5 mg daily		60.2	9.73	50	8.12	0.78	29.84	5.2	7.4	38.7					
Strojek 2011						Dapagliflozin	2.5 mg daily		59.9	10.14	50	8.11	0.75	30	5.15	7.7	36.4					
Strojek 2011						Placebo			60.3	10.16	49	8.15	0.74	29.74	4.6	7.4	37.9					
Strøm Halden 2019	NCT03157414	44	2019	5.5	Norway	Empagliflozin	10 mg daily	Chronic kidney disease	63	31-72	77.3	6.9	6.5-8.2	28.8	24.7-39.3			66				None
Strøm Halden 2019						Placebo			59	21-75	77.3	6.8	6.1-7.2	27.5	22.4-45.8			59				
Su 2014	Not provided	600	2014	5.5	China	Vildagliptin	100 mg daily		47.6	14.4		8.76	1.72									Metformin + alpha glucosidase inhibitor
Su 2014						Placebo			48.7	11.5		8.42	1.37									
SUCCESS	UMIN000004675	119	2015	5.5	Japan	Sitagliptin	50 mg daily		57.6	12.9	65.5	7.6	0.7	25.9	4.3	6.7						Metformin or pioglitazone
SUCCESS						Alpha glucosidase	0.2 mg voglibose or 150 mg miglitol daily		59.3	11.3	62.1	7.6	0.74	26.3	4.6	6.8						
SUMER	Not provided	400	2015	5.5	México	Glimepiride	6 mg daily		49.5	10.5		9.6	0.9	24.5	4.4							None
SUMER						Sitagliptin	100 mg daily		48.6	11.7		9.6	0.8	24.5	5							
Sun 2006	Not provided	60	2006	6	China	Glipizide	5 mg daily					8.9	3	26.09	1.57					64.05		None
Sun 2006						Pioglitazone	30 mg daily					8.8	3.1	26.07	1.06					64.01		
Sun 2016	ChiCTR-TRC-	108	2016	5.5	China	Metformin	1500 mg daily		52	6	55.6	8.47	0.9	27.02	1.85							None
Sun 2016						Acarbose	300 mg daily		53	8	50	8.2	0.83	27.07	1.97							
SUPER	NCT02104804	462	2018	5.5	China	Saxagliptin	5 mg daily		59.3	7.9	47	8.52	0.69	26.1	3.3	13.4						Insulin with or without metformin
SUPER						Placebo			58.9	8.2	43.5	8.53	0.69	26.3	3.1	13.3						
SUSTAIN 1	NCT02054897	387	2014	6	Multinational	Semaglutide	1.0 mg weekly		52.7	11.9	62	8.12	0.81	33.92	8.43	3.62		100.9				None
SUSTAIN 1						Semaglutide	0.5 mg weekly		54.6	11.1	47	8.09	0.89	32.46	7.62	4.81		95.91				
SUSTAIN 1						Placebo			53.9	11	54	7.95	0.85	32.4	6.86	4.06		100.2				
SUSTAIN 2	NCT01930188	1225	2017	12	Multinational	Sitagliptin	100 mg daily		54.6	10.4	51	8.2	0.9	32.5	5.8	6.6		98				Metformin ± thiazolidinedione
SUSTAIN 2						Semaglutide	1.0 mg weekly		56	9.4	50	8	0.9	32.5	6.6	6.7		97				
SUSTAIN 2						Semaglutide	0.5 mg weekly		54.8	10.2	51	8	0.9	32.4	6.2	6.4		97				
SUSTAIN 4	NCT02128932	1082	2017	6	Multinational	Semaglutide	1.0 mg weekly		56.2	10.6	51	8.3	0.9	33	6.5	9.3		98				Metformin ± sulfonylurea
SUSTAIN 4						Semaglutide	0.5 mg weekly		56.7	10.4	54	8.1	0.8	33.1	6.5	7.8		97.9				
SUSTAIN 4						Insulin glargine	Titrated		56.2	10.6	54	8.1	0.9	33	6.5	8.6		99.7				
SUSTAIN 5	NCT02305381	396	2018	6	Multinational	Semaglutide	1.0 mg weekly		58.5	33-80	58.8	8.3	6.9-10.8	32	19.5-51.6	13.7						Insulin alone or in combination with metformin
SUSTAIN 5						Semaglutide	0.5 mg weekly		59.1	28-84	56.1	8.4	7.0-10.3	32.8	21.1-51.4	12.9						
SUSTAIN 5						Placebo			58.8	19-86	53.4	8.4	6.8-11.1	31.8	21.0-48.8	13.3						
SUSTAIN 6	NCT01720446	3297	2016	24	Multinational	Semaglutide	0.5-1.0 mg weekly										60					No more than two oral hypoglycemic drugs ± basal or premixed insulin
SUSTAIN 6						Placebo											61					
SUSTAIN 8	NCT03136484	788	2019	12.0	Multinational	Canagliflozin	300 mg daily		57.5	10.7	51.0	8.2	1.0									Metformin
SUSTAIN 8						Semaglutide	1.0 mg weekly		55.7	11.1	56.6	8.3	1.0									
SUSTAIN 9	NCT03086330	302	2019	6	Multinational	Semaglutide	1.0 mg weekly		57.5	8.9	58.9	8	0.8	31.1	6.2	9.8	5.3	94.5				SGLT-2 inhibitor as monotherapy or with a sulfonylurea or metformin
SUSTAIN 9						Placebo											5.3	96				
SUSTAIN CHINA	NCT03061214	868	2020	7.3	Multinational	Sitagliptin	100 mg daily		53.1	10.4	63.8											Metformin
SUSTAIN CHINA						Semaglutide	0.5 mg weekly		53.0	11.4	53.1											
SUSTAIN CHINA						Semaglutide	1 mg weekly		53.0	10.6	55.6											
Suzuki 2014	Not provided	40	2014	6	Japan	Sitagliptin	50 mg daily	Coronary artery disease	56.1	15.3	56	9.1	1.6	26.3	7.2	1.9		73.7	14			None
Suzuki 2014						Liraglutide	0.9 mg daily		58.6	15.9	62.5	9.8	2.2	28.2	7.2	2.4		73.2	19			
SWIM	NCT01341717	440	2017	5.5	India	Glimepiride	3 mg daily		50.11	7.83	51.13	7.91		25.15	3.69	15.67						Metformin and insulin
SWIM						Sitagliptin	100 mg daily		51.1	6.58	47.03	7.96		26.02	3.32	14.96						
Takagi 2003	Not applicable	44	2003	6	Japan	Pioglitazone	30 mg daily		64	10	86.9	6.8	0.6	25.6	2.8		100					Oral hypoglycemic agents or insulin
Takagi 2003						Control			65	9	66.7	6.7	1.2	24.5	2.9		100					
Takase 2007	Not provided	39	2007	6	Japan	Pioglitazone	15 mg daily		67.8	8.9	55	7	1.3	24.7	1.3							None
Takase 2007						Voglibose	0.6 mg daily		68.2	7.4	63.2	6.9	1.3	24.2	2.6							
Takashima 2018	UMIN000031454	40	2018	12	Japan	Canagliflozin	100 mg daily	Chronic kidney disease	64.7	9.8	55	7.5	0.9	24.9	3.1		20	57.1	139			Oral hypoglycemic agents with or without insulin
Takashima 2018						Control			65.4	10.4	60	7.3	0.7	25.5	3.2		15	55.4	159			
Tao 2018	ChiCTR-IPR-	42	2018	5.5	China	Metformin	2000 mg daily		28	3	100	7.3	0.2	26.4	24.6-28.2							None
Tao 2018						Saxagliptin	5 mg daily		30	5	100	7.4	0.3	27.2	24.94-29.46							
Taskinen 2011	NCT00601250	700	2011	5.5	Multinational	Linagliptin	5 mg daily		56.5	10.1	53	8.09	0.86	29.85	4.84							Metformin + maximum one other drug
Taskinen 2011						Placebo			56.6	10.9	57	8.02	0.88	30.05	5.01							
TECOS	NCT00790205	14671	2015	36	Multinational	Sitagliptin	50-100 mg daily		65.4	7.9	70.9	7.2	0.5	30.2	5.6	11.6	100	74.9	10.3			1-2 oral drugs (metformin, pioglitazone, or sulfonylurea) or insulin (± metformin)
TECOS						Placebo			65.5	8	70.5	7.2	0.5	30.2	5.7	11.6	100	74.9	11.4			
T-Emerge 1	NCT00744926	373	2012	6	Multinational	Taspoglutide	20 mg weekly		55	10.4	36	7.7	1	31.7	4.9	2.1						None
T-Emerge 1						Taspoglutide	10 mg weekly		53.4	9.6	37	7.5	1	33.2	5	2.8						
T-Emerge 1						Placebo			55.8	8.5	37	7.6	1	32.1	5.3	2.3						
T-Emerge 3	NCT00744367	326	2012	6	Multinational	Taspoglutide	20 mg weekly		55.5	10.1	53	8.1	0.9	33	5	8.3						Metformin + pioglitazone
T-Emerge 3						Taspoglutide	10 mg weekly		52.5	10.3	59	8.2	1	32.8	5.3	7.3						
T-Emerge 3						Placebo			54.3	9.6	50	8.1	0.9	32	5.3	7.5						
T-Emerge 4	NCT00754988	666	2012	5.5	Multinational	Sitagliptin	100 mg daily		55.5	9.9	59	7.94	0.85	32.4	5	6						Metformin
T-Emerge 4						Taspoglutide	20 mg weekly		56.8	8.8	52	7.97	0.86	32.3	5	5.7						
T-Emerge 4						Taspoglutide	10 mg weekly		55.3	9.5	56	7.95	0.93	32.7	5.2	6.1						
T-Emerge 4						Placebo			56.1	10.1	52	8.03	0.83	32.5	5.5	5.5						
T-Emerge 5	NCT00755287	1049	2013	6	Multinational	Taspoglutide	20 mg daily		57	9	57	8.3	0.9	32.4	5.3	9						Metformin
T-Emerge 5						Taspoglutide	10 mg daily		58	10	56	8.2	0.9	32.1	5.3	9						
T-Emerge 5						Insulin glargine	Titrated		58	9	46	8.4	0.9	32.7	5.2	10						
T-Emerge 6	NCT00909597	760	2013	5.5	Multinational	Pioglitazone	45 mg daily		65.4	9.8	51	8.3	0.8	32.7	5.1	8.6						Sulfonylurea ± metformin
T-Emerge 6						Taspoglutide	20 mg daily		55.8	9.8	50	8.3	0.9	32.4	5.2	8.5						
T-Emerge 6						Taspoglutide	10 mg daily		57.1	9.7	45	8.3	0.9	33.1	5.2	9.4						
T-Emerge 7	NCT00823992	305	2013	5.5	USA	Taspoglutide	10-20 mg daily		53	10	42	7.54	0.84	36.9	5	5.2						Metformin
T-Emerge 7						Placebo			54	10	39	7.55	0.84	36.5	4.8	4.9						
Teramoto 2007	Not provided	92	2007	5.5	Japan	Glibenclamide	2.5 mg daily		56.4	10.5	76.1	8.36	1.29	25.2	4.8							None
Teramoto 2007						Pioglitazone	30 mg daily		57	10.7	71.7	8.01	1.29	24.7	3.4							
Teupe 1991	Not applicable	100	1991	24	Germany	Metformin	1700 mg daily		51.5	10.1	40	9	1.3			8.1						None
Teupe 1991						Control			56	7.6	40	8.7	0.8			6.4						
Thrasher 2014	NCT01194830	226	2014	5.5	USA	Linagliptin	5 mg daily		53.7	10.1	56.6	8.68	1.05	32	6.1							None or 1 oral drug
Thrasher 2014						Placebo			54.1	9.9	50.8	8.78	1.18	33.4	5.4							
TIDE	NCT00879970	1332	2012	5.4	Multinational	Rosiglitazone	8 mg daily		66.5	6.4	59.6	7.4	0.9	30.7	5.3	9.1	36					Two or fewer glucose-lowering drugs
TIDE						Pioglitazone	45 mg daily		66.3	6.6	57.4	7.4	0.8	30.6	5.4	8.5	33					
TIDE						Placebo			66.4	6.8	59.3	7.3	0.9	30.4	5.2	8.7	35					
Tinahones 2017	NCT01778049	478	2017	5.5	Multinational	Linagliptin	5 mg daily		56.6	9.5	56.6	8.04	0.96	31.3	5.4							Metformin and emplagliflozin
Tinahones 2017						Placebo			56.8	9.4	56	8.03	0.85	30.8	4.8							
Tinahones 2017						Linagliptin	5 mg daily		56.6	9.8	47.3	7.81	0.71	30.8	4.6							
Tinahones 2017						Placebo			56.1	10.6	57.3	7.88	0.9	32	5.3							
Tofogliflozin 003	Japic CTI-101349	220	2014	5.5	Japan	Tofogliflozin	40 mg daily		57	9.1	67.2	8.37	0.77	25.78	4.1	6.7						None
Tofogliflozin 003						Tofogliflozin	20 mg daily		56.6	10.2	67.2	8.34	0.81	24.99	4.55	6.4						
Tofogliflozin 003						Tofogliflozin	10 mg daily		58.6	9.8	66.7	8.45	0.75	25.07	3.53	6.3						

Tofogliflozin 003						Placebo			56.8	9.9	66.1	8.41	0.78	26	4.11	6					
Tolman 2009	NCT00494312	2120	2009	36	USA	Glibenclamide	5-15 mg daily				55.5	9.5	2	32.5	6	6					Metformin ± sulfonylurea
Tolman 2009						Pioglitazone	15-45 mg daily				57.2	9.5	2	32.5	6.1	6					
TOPSCORE	UMIN000017861	75	2017	8.9	Japan	Sitagliptin	50 mg daily	Coronary artery disease	70	9	79	7.2	1	24.8	4.1		100				Insulin, biguanide, and/or thiazolidine
TOPSCORE						Control			72	10	83	7.3	1.2	25.1	4.1		100				
TOSCA.IT	NCT00700856	3028	2017	57.3	Italy	Sulfonylurea			62.2	6.5	58	7.69	0.51	30.4	4.5	8.5	10				Metformin
TOSCA.IT						Pioglitazone	15-45 mg daily		62.4	6.4	59	7.67	0.5	30.2	4.4	8.4	12				
Tripathy 2013	NCT01223196	29	2013	6	USA	Pioglitazone	15 mg daily		56	9.29	63.6	7	0.66	33.6	6.3						Metformin and or sulfonylurea
Tripathy 2013						Placebo			57	6.6	77.8	8	1.5	33.4	5.7						
TROICA	NCT01990469	218	2017	5.5	Republic of Korea	Gemgliptin	50 mg daily		61.4	9.2	37.4	8.2	0.8	25.1	3.1	13					Metformin + glimepiride
TROICA						Placebo			60.4	8.8	42.2	8.2	0.9	24.7	2.7	12.8					
Truitt 2010	NCT00143520	532	2010	6	USA	Pioglitazone	45 mg daily		56.6	10.1	58.2	7.98	0.83	32.9	5.7	6.6					Antidiabetes monotherapy or combinations of sulfonylureas, meglitinides, metformin and/or alpha-glucosidase inhibitors
Truitt 2010						Rivoglitazone	3 mg daily		56.4	10.8	52.3	8.23	1.02	33	6.5	6.7					
Truitt 2010						Rivoglitazone	2 mg daily		55	10.8	56.5	8.05	0.87	33.1	6.4	5.2					
Truitt 2010						Rivoglitazone	1 mg daily		55.4	10.9	52.9	8	0.81	32.9	6	6.2					
Truitt 2010						Placebo			55.3	9.3	51.1	8.21	0.98	32.2	5.8	6.7					
Türkmen Kemal 2007	Not provided	46	2007	6	Turkey	Metformin	1700 mg daily		56.8	8.8	25	6.3	1.2	34.5	7.9	1.5					None
Türkmen Kemal 2007						Rosiglitazone	8 mg daily		55.92	8.26	23.1	6.2	0.7	30.8	6.9	2.75					
Türkmen Kemal 2007						Control			54.59	10.76	23.5	5.7	0.6	31.4	5.4	1.2					
UKPDS 44	Not applicable	1946	1999	36	UK	Acarbose	50 mg daily to 100 mg thrice daily		60	9		8.7	6.8-11	29.8	5.6	7.9					Insulin;Metformin, Sulfonylurea - monotherapy or combination
UKPDS 44						Placebo			60	9		8.7	6.8-11.1	29.6	5.7	8					
Umpierrez 2006	Not provided	203	2006	6	USA	Glimepiride	8 mg daily		51.6	11.8	55.2	8.4	0.72	34.54	6.68	4.9					Metformin
Umpierrez 2006						Pioglitazone	45 mg daily		55.7	9.7	52.3	8.31	0.77	33.8	6.62	5.9					
Vähätalo 2007	Not provided	41	2007	12	Finland	Metformin	2500 mg daily					10.1									Insulin
Vähätalo 2007						Glipizide	10 mg daily					9.4									
Van Eyk 2019	NCT02660047	47	2019	5.5	The Netherlands	Liraglutide	1.8 mg daily		55	11	36	8.1	0.9	30.4	3.8	19					Concomitant treatment with metformin, sulfonylurea derivatives and insulin was optional
Van Eyk 2019						Placebo			55	9	44	8.6	1.1	28.6	4	17					
Van Gaal 2014	NCT00976937	319	2014	5.5	Belgium	Sitagliptin	100 mg daily		43.4	4.7	45.3	8.1	1	36.8	6.3	4.4					Metformin
Van Gaal 2014						Lixisenatide	20 µg daily		42.7	5.2	34.8	8.16	0.89	36.8	7.3	4.4					
Vanderheiden 2016	NCT01505673	71	2016	6	USA	Liraglutide	1.8 mg daily		52.8	8.1	34	9	1.2	40.7	6.7	16					Oral drugs and insulin
Vanderheiden 2016						Placebo			55.5	6.6	39	8.9	1	41.6	10.4	18					
Varghese 2009	Not provided	57	2009	12	UK	Pioglitazone	15 mg daily	Coronary artery disease	62.2	8.2	78			27.9	4.1						Metformin or sulfonylurea
Varghese 2009						Placebo			65.6	6.1	79			28.6	4.3						
Veleba 2015	EudraCT number	69	2015	5.5	Czech Republic	Pioglitazone	15 mg daily		62	60.0-65.0											Metformin
Veleba 2015						Placebo			62	58.0-65.0											
Veleba 2015						Pioglitazone	15 mg daily		60.5	55.3-65.5											
Veleba 2015						Placebo			59.5	55.8-63.8											
VERTIS Asia	NCT02630706	506	2019	6	Multinational	Ertugliflozin	15 mg daily		56.3	9.3	58	8.1	0.9	25.7	3.2	7.5					Metformin
VERTIS Asia						Ertugliflozin	5 mg daily		56.1	9	55.9	8.1	0.9	26	2.8	7					
VERTIS Asia						Placebo			56.9	9	52.7	8.1	1	26.1	3.4	6.4			92.6		
VERTIS CV	NCT01986881	8246	2020	60	Multinational	Ertugliflozin	5-15 mg daily	Atherosclerotic vascular dise	64.4	8.1	70.3	8.2	1.0	31.9	5.4	12.9	100.0	76			Metformin, insulin, sulfonylurea, DPP-4 inhibitor or GLP-1 receptor agonist
VERTIS CV						Placebo			64.4	8.0	69.3	8.2	0.9	32.0	5.5	13.1	100.0	76			
VERTIS FACTORIAL	NCT02099110	745	2017	6	Multinational	Sitagliptin	100 mg daily		54.8	10.7	62.3	8.6	1	31.5	5.8	7.3			92.8		Metformin
VERTIS FACTORIAL						Ertugliflozin	15 mg daily		55.3	9.5	54	8.6	1	31.5	5.8	7.3			91.9		
VERTIS FACTORIAL						Ertugliflozin	5 mg daily		55.1	10.1	50.8	8.6	1	31.8	6.2	7.1					
VERTIS-MET	NCT02033889	621	2018	6	Multinational	Ertugliflozin	15 mg daily		56.9	9.4	45.4	8.1	0.9	31.1	4.5	8.1			91		Metformin
VERTIS-MET						Ertugliflozin	5 mg daily		56.6	8.1	46.9	8.1	0.9	30.8	4.8	7.9			88.9		
VERTIS-MET						Placebo			56.5	8.7	46.9	8.2	0.9	30.7	4.7	8			91.6		
VERTIS MONO	NCT01958671	461	2017	6	Multinational	Ertugliflozin	15 mg daily		56.2	10.8	59.2	8.35	1.12	32.5	5.7	5.22			88.3		None
VERTIS MONO						Ertugliflozin	5 mg daily		56.8	11.4	57.1	8.16	0.88	33.2	7.4	5.11			88.5		
VERTIS MONO						Placebo			56.1	10.9	53.6	8.11	0.92	33.3	6.8	4.63			86.2		
VERTIS RENAL	NCT01986855	467	2018	12	Multinational	Ertugliflozin	15 mg daily	Chronic kidney disease	67.5	8.5	48.4	8.2	0.9	31.7	5.3	14.5	49.7	46.9			Antihyperglycemic therapy (monotherapy or combination therapy including sulfonylureas or insulin)
VERTIS RENAL						Ertugliflozin	5 mg daily		66.7	8.3	53.2	8.2	1	32.6	6.8	14.9	50	46.8			
VERTIS RENAL						Placebo			67.5	8.9	46.8	8.1	0.9	33.2	6.1	13.1	49.4	46			
VERTIS SITA2	NCT02036515	464	2018	12	Multinational	Ertugliflozin	15 mg daily		59.7	8.6	53.6	8	0.8	30.9	6.1	9.2			86.9		Metformin and sitagliptin
VERTIS SITA2						Ertugliflozin	5 mg daily		59.2	9.3	51.9	8.1	0.9	31.2	5.5	9.9			87		
VERTIS SITA2						Placebo			58.3	9.2	65.4	8	0.9	30.3	6.4	9.4			89.9		
VERTIS SU	NCT01999218	1326	2018	12	Multinational	Glimepiride	8 mg daily		57.8	9.2	51.3	7.8	0.6	31.2	6.4	7.5			86.6		Metformin and sitagliptin
VERTIS SU						Ertugliflozin	15 mg daily		58	9.9	43.3	7.8	0.6	31.3	6.2	7.5			86.7		
VERTIS SU						Ertugliflozin	5 mg daily		58.8	9.7	50.7	7.8	0.6	31.7	5.5	7.4			88.3		
Vianna 2017	NCT01679899	42	2017	12	Brazil	Gliclazide	120 mg daily		61	5.3	0	7.32	0.6	33.8	6.7						Metformin
Vianna 2017						Vildagliptin	100 mg daily		62.8	6.4	0	7.35	0.54	31.7	5.8						
VICTORY	NCT00169832	193	2010	12	Multinational	Rosiglitazone	8 mg daily		64.2	7.3	92	6.9	1.3	30.2	4.2	7.8	100				Oral drugs
VICTORY						Placebo			65.1	6.9	92	6.9	0.8	29.5	4.6	8.4	100				
VISION	NCT01541956	2985	2016	5.5	China	Vildagliptin	100 mg daily		56.5	10.6	54.4	7.2	0.9	25.1	3.2	4.3					Metformin
VISION						Standard care			56.2	10.8	49.6	7.2	0.8	25.1	3.2	4.1					
VIVIDD	NCT00894868	254	2018	12	Multinational	Vildagliptin	100 mg daily	Heart failure	62.9	8.5	77.3	7.8	0.95	29.6	4.6	9.5	64.1				Drug therapy, if any
VIVIDD						Placebo			63.4	10.2	76.2	7.8	1.1	29.3	4.7	9.1	63.5				
Vongthavaravat 2002	Not applicable	348	2002	6	Multinational	Rosiglitazone	4 mg daily		54.6		45.7	9.1		27.1		5					Sulfonylurea
Vongthavaravat 2002						Control			57.3		42.4	8.9		27.1		6					
Wajcberg 2007	Not provided	31	2007	5.5	USA	Pioglitazone	15-45 mg daily		51	8	43.8	8.1	1.6	32	4	7.1					None
Wajcberg 2007						Placebo			49	11.6	46.7	7.9	1.5	31	3.9	6.9					
Wang 2005	Not applicable	70	2005	6	China	Rosiglitazone	4 mg daily	Coronary artery disease	60.1	8.5	83.3	7.29	0.17	26.1	2.5		100				Other antidiabetic drugs
Wang 2005						Control			62.2	8.6	80	7.33	0.17	25.6	2.7		100				
Wang 2013	Not provided	90	2013	6	China	Metformin	1700 mg daily		54	10.3	62.1	8.07	0.77								None
Wang 2013						Gliclazide	120 mg daily		55.89	10.5	70	8.4	0.93								
Wang 2013						Acarbose	300 mg daily		54.7	8.9	66.7	8.06	0.82								
Wang 2015	Not provided	90	2015	12	China	Saxagliptin	5 mg daily		64.3	2.6	43.9	8.26	0.49			12.3					Metformin
Wang 2015						Acarbose	150 mg daily		65.1	3.1	47.5	8.3	0.37			14.2					
Wang 2016	NCT01215097	306	2016	5.5	Multinational	Linagliptin	5 mg daily		55.1	10.7	49.8	7.99	0.83	25.5	3.9						Metformin
Wang 2016						Placebo			56.5	8.7	50	8	0.8	25.8	4						
Wang 2016a	Not provided	28	2016	5.5	China	Dapagliflozin			60.7	10.1	61	7.96	0.33								None
Wang 2016a						Placebo			59.3	9	20	9.48	0.44								
Wang 2017	NCT01177384	381	2017	5.5	Multinational	Sitagliptin	100 mg daily		56.5	8.9	50.8	8.1	0.8	25.9	4.6	7.4					Acarbose
Wang 2017						Placebo			57.8	9.5	51.3	8.1	0.9	26	4.4	8.2					
Wang 2019	NCT01648582	744	2018	6	Multinational	Dulaglutide	1.5 mg weekly		55	9.6	53.4	8.5	1.2	26.6	3.7	7.9					Metformin and/or sulfonylurea
Wang 2019						Dulaglutide	0.75 mg weekly		54.5	10	56.7	8.3	1.1	27	3.8	8.1					
Wang 2019						Insulin glargine	Titrated		55.4	9.2	55.6	8.3	1.1	26.7	3.5	8.4					
Wang 2020	Not provided	60	2020	6	China	Sitagliptin	100 mg daily	Stroke	67.2	7.1	56.7	8.6	3.3	25.8	3.8	8.2	100.0				Metformin, sulfonylurea or insulin
Wang 2020						Liraglutide	1.2 mg daily		66.1	5.9	46.7	8.9	3.2	25.7	4.3	9.0	100.0				
Watanabe 2005	Not applicable	27	2005	6	Japan	Glibenclamide			65.1	8.1	85.7	7.2	0.5	24.7	3.7						None
Watanabe 2005						Pioglitazone			62.9	10.3	84.6	6.9	0.2	24.4	4.4						
Wolever 2000	Not applicable	152	2000	8.4	Canada	Metformin	1500 mg daily		58.7	8.7	72.6	8.2	0.79	30.5	4.7	7.3					None
Wolever 2000						Placebo			58.5	10.7	60	7.8	0.67	30.8	4	4.5					
Wolever 2000						Miglitol	300 mg daily		56.8	8.1	86.7	7.9	0.67	30.7	4.7	4.7					
Wolffenbuttel 1999	Not applicable	310	1999	12	Multinational	Glyburide	1.75-10.5 mg daily		61	9	68	7	1.2	28	3.4	6					None
Wolffenbuttel 1999						Repaglinide	1.5-12 mg daily		61	9	62	7.1	1.4	28.4	3.6	6					
Wolffenbuttel 2000	Not applicable	584	2000	6	Multinational	Rosiglitazone	4 mg daily		60.6	8.7	55.2	9.23	1.18	28.3	3.9	7					Sulfonylurea
Wolffenbuttel 2000						Rosiglitazone	2 mg daily		61	9.4	62.8	9.2	1.19	28	3.9	7					
Wolffenbuttel 2000						Placebo			61.9	9.1	57.3	9.21	1.3	28.1	4.1	8					
Wong 2005	Not applicable	52	2005	5.5	Hong Kong	Rosiglitazone	4 mg daily		62.92	7.3		7.33	1.3	24.5	6.2						Insulin
Wong 2005						Control			61.58	9.7		7.2	1.3	24.9	8.5						
Wu 2014	Not applicable	93	2014	12	China	Metformin	1500 mg daily		60.1	9.6	50	7.2	2.4	24.9	5.8	73					None
Wu 2014						Pioglitzone	15 mg daily		60.3	9.7	51.5	7.1	2.5	24.6	5.6	7.2					
Wu 2015	Not provided	57	2015	5.5	China	Linagliptin	5 mg daily		52.5	11	65.7	7.97	1.52	24.37	2.09						None
Wu 2015						Placebo			51.2	7.5	50	8	0.69	24.11	2.28						
Xiao 2015	Not provided	80	2015	5.5	China	Glipizide	5-10 mg daily		53.56	3.61	58.3	8.65	0.75	26.59	1.23						Metformin
Xiao 2015						Pioglitazone	15-45 mg daily		54.15	4.91	58.8	8.73	0.8	26.52	1.29						
Xiao 2016	Not provided	41	2016	5.5	China	Glimepiride	4 mg daily		69.1	6.5	55.6	7.27	1.15	27.92	3.87						Metformin

Xiao 2016						Sitaglipitin	100 mg daily		68.7	6.3	56.5	7.32	1.01	28.34	3.81					
Xu 2017	NCT01790930	2195	2017	5.5	China	Glimepiride	6 mg daily		53.5	9.8	53.9	7.68	0.74	25.9	3.3	5.8				Metformin + sitagliptin
Xu 2017						Gliclazide	120 mg daily		53.3	9.9	55.1	7.78	0.8	25.8	3.5	5.5				
Xu 2017						Acarbose	300 mg daily		52.6	10.2	56.6	7.7	0.72	25.7	3.4	5.9				
Xu 2017						Repaglinide	16 mg daily		52.1	9.9	54.1	7.74	0.73	25.9	3.3	5.7				
Yakibu 2017	ISCTRN33414972	366	2017	6	Japan	Metformin	1000 mg daily													None
Yakibu 2017						Pioglitazone	30 mg daily													
Yakibu 2017						Sitagliptin	100 mg daily													
Yakibu 2017						Control														
Yale 2013	Not provided	269	2013	6	Multinational	Canagliflozin	300 mg daily	Chronic kidney disease	67.9	8.2	53.9	8	0.8	33.4	6.5	17	51.7	38.5	30.1	None, monotherapy or combination therapy
Yale 2013						Canagliflozin	100 mg daily		69.5	8.2	64.4	7.9	0.9	32.4	5.5	15.6	55.6	39.7	23.7	
Yale 2013						Placebo			68.2	8.4	63.3	8	0.9	33.1	6.5	16.4	56.7	40.1	31.3	
Yamakage 2019	UMIN000021479	54	2019	5.5	Japan	Dapagliflozin	5 mg daily		58.4	13.0	40.7	7.5	0.8	31.3	7.6			76.2		Background glucose lowering therapy
Yamakage 2019						Control			60.7	11.9	51.9	7.4	0.9	30.7	6.2			73		
Yamamoto 2018	UMIN000028313	25	2018	5.5	Japan	Liraglutide	0.9 mg daily		60	7.8	66.7	7.3	1.2	27.8	3.1	10.8	0			Basal insulin with or without oral hypoglycemic agents
Yamamoto 2018						Insulin lispro/Aspa	Titrated		61.5	10.6	61.5	6.9	0.8	25.9	4.2	9.6	23			
Yamanouchi 2005	Not applicable	114	2005	12	Japan	Metformin	750 mg daily		54.7	9.8	51.3	9.9	0.7	26.2	3.8	3				None
Yamanouchi 2005						Glimepiride	1-2 mg daily		55.6	9.3	51.4	9.8	0.7	25.6	3.5	3.3				
Yamanouchi 2005						Pioglitazone	30-45 mg daily		55.2	9.2	47.4	10.2	0.8	25.8	4.2	3.2				
Yamasaki 2005	Not applicable	103	2005	39.6	Japan	Voglibose	0.4-0.6 mg daily		58.6	7.5	51	8.2	1.3	23	3.67	13.1				Diet; Sulphonylurea; Insulin
Yamasaki 2005						Control			60.4	9.6	60	8.4	1.4	22.7	2.92	12.7				
Yan 2019	NCT02147925	75	2019	6	China	Sitagliptin	100 mg daily		45.7	9.2	77.8	7.6	0.9	29.7	2.8	4.3				Metformin
Yan 2019						Liraglutide	1.8 mg daily		43.1	9.7	70.8	7.8	1.4	30.1	3.3	3.3				
Yan 2019						Insulin glargine	Titrated		45.6	7.6	58.3	7.7	0.9	29.6	3.5	5.8				
Yang 2002	Not applicable	64	2002	6	Unclear	Rosiglitazone	2 mg twice daily		58.9	9.4	43.3	9.5	1.1	25.76	2.87					Sulphonylurea
Yang 2002						Placebo			57.8	8.9	38.2	9.7	1.4	25.84	3.5					
Yang 2011	NCT00661362	570	2011	5.5	Multinational	Saxagliptin	5 mg daily		53.8	10.4	48.1	7.9	0.8	26.3	3.6	5.1				Metformin
Yang 2011						Placebo			54.4	10.1	48.4	7.9	0.8	26.1	3.5	5.1				
Yang 2012	NCT00813995	395	2012	5.5	China	Sitagliptin	100 mg daily		54.1	9	47	8.5	0.9	25.3	3.1	6.4				Metformin
Yang 2012						Placebo			55.1	9.8	55	8.5	0.9	25.3	3.6	7.3				
Yang 2013	Not provided	182	2013	5.5	Republic of Korea	Gemgliptin	50 mg daily		54	49-60	65.5	8.2	1	25.4	22.8-28.1	3.24				None
Yang 2013						Placebo			52	45-60	50.6	8.3	1.1	26.7	23.6-29.1	2.86				
Yang 2015	Not provided	109	2015	5.5	Korea	Anagliptin	200 mg daily		54.43	9.86	40.54	7.13	0.72	24.6	3.01	3.17				None
Yang 2015						Anagliptin	100 mg daily		57.7	9.71	60	7.19	0.73	24.97	2.64	3.43				
Yang 2015						Placebo			56.74	9.72	63.16	7.11	0.63	25.44	3.19	4.14				
Yang 2015a	NCT01357252	279	2015	5.5	China	Vildagliptin	50 mg daily		58.3	9.8	55.2	8.6	0.9	24.8	3	6.9				Sulfonylurea
Yang 2015a						Placebo			58.7	9.3	58.1	8.7	1	25	2.8	6.9				
Yang 2016	NCT01095666	444	2016	5.5	Multinational	Dapagliflozin	10 mg daily		54.6	9.5	57.9	8.17	0.84	26.2	3.5	5.3				Metformin
Yang 2016						Dapagliflozin	5 mg daily		53.1	9.1	45.6	8.09	0.72	26.4	3.5	4.2				
Yang 2016						Placebo			53.5	9.2	59.3	8.13	0.85	25.7	2.9	5.3				
Yang 2018	NCT02096705	272	2018	5.5	Multinational	Dapagliflozin	10 mg daily		56.5	8.4	47.5	8.52	0.76	26.4	3.8	12.7				Insulin with or without oral antidiabetic drugs
Yang 2018						Placebo			58.6	8.9	48.1	8.58	0.81	26.7	3.3	12.2				
Yee 2010	NCT00231387	57	2010	12	England	Rosiglitazone	4-8 mg daily	High cardiovascular risk	62.6	8.2	78.6	7.65	1.09	28	26.2-30.0	7.5	46.4			1-2 drug therapy excluding thiazolidinedione or insulin
Yee 2010						Placebo			66.1	6	79.3	7.55	1.38	28.4	26.7-30.1	10	48.3			
Yki-Järvinen 1999	Not applicable	31	1999	12	Finland	Metformin	2000 mg daily		57	8.7	58	9.8	1.7	28.9	4.8					Sulfonylurea
Yki-Järvinen 1999						Glyburide	10.5 mg daily		61	9.4	59	9.8	1.4	29.7	4.7					
Yki-Järvinen 2013	NCT00954447	1261	2013	12	Multinational	Linagliptin	5 mg daily		59.7	9.9	52.1	8.31	0.85	30.8	5.4					Insulin ± metformin and/or thiazolidinedione
Yki-Järvinen 2013						Placebo			60.4	10	52.2	8.29	0.85	31.2	4.9					
Yoon 2011	NCT00397631	520	2011	5.5	Multinational	Sitagliptin	100 mg daily		50.2	10.2	52.5	9.5	1.2	29.7	5.1	2.6				None
Yoon 2011						Placebo			51.7	11.2	56	9.5	1.2	29.6	5.2	2.1				
Yoon 2011a	Not provided	349	2011	11	Republic of Korea	Metformin	2000 mg daily		51.8	8.5	57.9	7.9	0.8	25.7	3.2					None
Yoon 2011a						Glimepiride	8 mg daily		50.8	8.9	55.9	7.8	0.8	25.5	3.1					
Yoon 2011a						Rosiglitazone	8 mg daily		50.1	8.2	52.14	7.8	0.8	25.8	3.3					
Yuan 2012	Not provided	59	2012	6	China	Metformin	1500 mg daily		56.8	7.6	46.2	8.11	1.92	29.3	2.6					None
Yuan 2012						Exenatide	20 µg daily		58.5	10.6	51.5	8.27	1.58	30.6	2.8					
Zang 2016	NCT02008682	368	2016	6	China	Sitagliptin	100 mg daily		51.4	11	63.6	8.11	0.78	27.2	4	5.2				Metformin
Zang 2016						Liraglutide	1.8 mg daily		51.7	10.7	55.7	8.14	0.83	27.3	3.4	5.3				
ZEUS II	NCT02831361	283	2020	5.5	Korea and	Gemgliptin	50 mg daily		61.1	8.6	32.4	8.4	1	26.7	4.1	16.3				Insulin with or without metformin
ZEUS II						Placebo			59	10.3	30.5	8.4	1	26.8	4.2	16.5				
Zhang 2020	Not provided	60	2020	5.5	China	Piolglitazone	30 mg daily		51.5	12.1	50.0	8.1	1.7	27.1	3.8					Metformin
Zhang 2020						Liraglutide	1.2 mg daily		50.2	11.5	43.3	8.1	2.0	27.6	5.2					
Zheng 2019	Not provided	91	2019	6	China	Liraglutide														Metformin and insulin
Zheng 2019						Control														
Zhu 2003	Not applicable	554	2003	5.5	China	Rosiglitazone	8 mg daily		58.9	6.9	48	9.9	1.6	24.9	3.1	7.9				Sulfonylurea
Zhu 2003						Rosiglitazone	4 mg daily		59	7.5	41	9.8	1.5	24.8	3.4	7.2				
Zhu 2003						Placebo			58.8	7.7	46	9.8	1.3	25.1	2.8	7.6				
Zib 2007	Not provided	32	2007	6	USA	Piogltazone	15-30 mg daily		51	9	43.8	11	2.8	32	8	5.6				Insulin
Zib 2007						Control			47	11	50	10.6	1.4	33	7	6.6				

Appendix 2
Reference list for included studies

3D
Oe H, Nakamura K, Kihara H, et al. Comparison of effects of sitagliptin and voglibose on left ventricular diastolic dysfunction in patients with type 2 diabetes: Results of the 3D trial. Cardiovasc Diabetol 2015;**14**(1):83

4B
Diamant M, Nauck MA, Shaginian R, et al. Glucagon-like peptide 1 receptor agonist or bolus insulin with optimized basal insulin in type 2 diabetes. Diabetes Care 2014;**37**(10):2763-73

4T
Holman RR, Thorne KI, Farmer AJ, et al. Addition of biphasic, prandial, or basal insulin to oral therapy in type 2 diabetes. N Engl J Med 2007;**357**(17):1716-30

1860-LIRA-DPP-4
Pratley RE, Nauck M, Bailey T, et al. Liraglutide versus sitagliptin for patients with type 2 diabetes who did not have adequate glycaemic control with metformin: a 26-week, randomised, parallel-group, open-label trial. Lancet 2010;**375**(9724):1447-56

Abe 2008
Abe M, Okada K, Maruyama T, et al. Clinical effectiveness and safety evaluation of long-term pioglitazone treatment for erythropoietin responsiveness and insulin resistance in type 2 diabetic patients on hemodialysis. Expert Opin Pharmacother 2010;**11**(10):1611-20

Abe 2016
Abe M, Higuchi T, Moriuchi M, et al. Efficacy and safety of saxagliptin, a dipeptidyl peptidase-4 inhibitor, in hemodialysis patients with diabetic nephropathy: A randomized open-label prospective trial. Diabetes Res Clin Pract 2016;**116**:244-52

ACTION-J
Yasunari E, Takeno K, Funayama H, et al. Efficacy of pioglitazone on glycemic control and carotid intima-media thickness in type 2 diabetes patients with inadequate insulin therapy. J Diabetes Invest 2011;**2**(1):56-62

ADOPT
Kahn SE, Haffner SM, Heise MA, et al. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. N Engl J Med 2006;**355**(23):2427-43

Ahmann 2015
Ahmann A, Rodbard HW, Rosenstock J, et al. Efficacy and safety of liraglutide versus placebo added to basal insulin analogues (with or without metformin) in patients with type 2 diabetes: A randomized, placebo-controlled trial. Diab Obes Metab 2015;**17**(11):1056-64

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Ahrén B, Gomis R, Standl E, et al. Twelve- and 52-week efficacy of the dipeptidyl peptidase IV inhibitor LAF237 in metformin-treated patients with type 2 diabetes. Diabetes Care 2004;**27**(12):2874-80

Allegretti 2019

Allegretti AS, Zhang W, Zhou W, et al. Safety and effectiveness of bexagliflozin in patients with type 2 diabetes mellitus and stage 3a/3b CKD. American Journal of Kidney Diseases 2019;**74**(3):328-37

Alogliptin Study 007
Pratley RE, Kipnes MS, Fleck PR, et al. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes inadequately controlled by glyburide monotherapy. Diabetes Obes Metab 2009;**11**(2):167-76

Alogliptin Study 009
Pratley RE, Reusch JE, Fleck PR, et al. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin added to pioglitazone in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. Curr Med Res Opin 2009;**25**(10):2361-71

Alogliptin Study 010
DeFronzo RA, Fleck PR, Wilson CA, et al. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes and inadequate glycemic control: a randomized, double-blind, placebo-controlled study. Diabetes Care 2008;**31**(12):2315-7

Alvarsson 2003
Alvarsson M, Sundkvist G, Lager I, et al. Beneficial effects of insulin versus sulphonylurea on insulin secretion and metabolic control in recently diagnosed type 2 diabetic patients. Diabetes Care 2003;**26**(8):2231-7

APOLLO
Bretzel RG, Nuber U, Landgraf W, et al. Once-daily basal insulin glargine versus thrice-daily prandial insulin lispro in people with type 2 diabetes on oral hypoglycaemic agents (APOLLO): an open randomised controlled trial. Lancet 2008;**371**(9618):1073-84

Apovian 2010
Apovian CM, Bergenstal RM, Cuddihy RM, et al. Effects of exenatide combined with lifestyle modification in patients with type 2 diabetes. Am J Med 2010;**123**(5):468.e9-17

APPROACH
Gerstein HC, Ratner RE, Cannon CP, et al. Effect of rosiglitazone on progression of coronary atherosclerosis in patients with type 2 diabetes mellitus and coronary artery disease: the assessment on the prevention of progression by rosiglitazone on atherosclerosis in diabetes patients with cardiovascular history trial. Circulation 2010;**121**(10):1176-87

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Morikawa A, Ishizeki K, Iwashima Y, et al. Pioglitazone reduces urinary albumin excretion in renin-angiotensin system inhibitor-treated type 2 diabetic patients with hypertension and microalbuminuria: the APRIME study. Clin Exp Nephrol 2011;**15**(6):848-53

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Araki E, Tanizawa Y, Tanaka Y, et al. Long-term treatment with empagliflozin as add-on to oral antidiabetes therapy in Japanese patients with type 2 diabetes mellitus. Diabetes Obes Metab 2015;**17**(7):665-74

Araki 2015a

Araki E, Inagaki N, Tanizawa Y, et al. Efficacy and safety of once-weekly dulaglutide in combination with sulphonylurea and/or biguanide compared with once-daily insulin glargine in Japanese patients with type 2 diabetes: a randomized, open-label, phase III, non-inferiority study. Diabetes Obes Metab 2015;**17**(10):994-1002

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Arechavaleta R, Seck T, Chen Y, et al. Efficacy and safety of treatment with sitagliptin or glimepiride in patients with type 2 diabetes inadequately controlled on metformin monotherapy: a randomized, double-blind, non-inferiority trial. Diabetes Obes Metab 2011;**13**(2):160-8

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Arjona Ferreira 2013a

Arjona Ferreira JC, Marre M, Barzilai N, et al. Efficacy and safety of sitagliptin versus glipizide in patients with type 2 diabetes and moderate-to-severe chronic renal insufficiency. Diabetes Care 2013;**36**(5):1067-73

Arturi 2017

Arturi F, Succurro E, Miceli S, et al. Liraglutide improves cardiac function in patients with type 2 diabetes and chronic heart failure. Endocrine 2017;**57**(3):464-73

Asian Acarbose Study

Chan JC, Chan KW, Ho LL, et al. An Asian multicenter clinical trial to assess the efficacy and tolerability of acarbose compared with placebo in type 2 diabetic patients previously treated with diet. Asian Acarbose Study Group. Diabetes Care 1998;**21**(7):1058-61

Aso 2019

Aso Y, Kato K, Sakurai S, et al. Impact of dapagliflozin, an SGLT2 inhibitor, on serum levels of soluble dipeptidyl peptidase-4 in patients with type 2 diabetes and non-alcoholic fatty liver disease. International Journal of Clinical Practice 2019;**73**(5):e13335

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Avilés-Santa L, Sinding J, Raskin P. Effects of metformin in patients with poorly controlled, insulin-treated type 2 diabetes mellitus. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 1999;**131**(3):182-8

AWARD-1

Wysham C, Blevins T, Arakaki R, et al. Efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in type 2 diabetes in a randomized controlled trial (AWARD-1). Diabetes Care 2014;**37**(8):2159-67

AWARD-2

Giorgino F, Benroubi M, Sun JH, et al. Efficacy and safety of once-weekly dulaglutide versus insulin glargine in patients with type 2 diabetes on metformin and glimepiride (AWARD-2). Diabetes Care 2015;**38**(12):2241-9

AWARD-3

Umpierrez G, Povedano ST, Manghi FP, et al. Efficacy and safety of dulaglutide monotherapy versus metformin in type 2 diabetes in a randomized controlled trial (AWARD-3). Diabetes Care 2014;**37**(8):2168-76

AWARD-4

Blonde L, Jendle J, Gross J, et al. Once-weekly dulaglutide versus bedtime insulin glargine, both in combination with prandial insulin lispro, in patients with type 2 diabetes (AWARD-4): a randomised, open-label, phase 3, non-inferiority study. Lancet 2015;**385**(9982):2057-66

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AWARD-7

Tuttle KR, Lakshmanan MC, Rayner B, et al. Dulaglutide versus insulin glargine in patients with type 2 diabetes and moderate-to-severe chronic kidney disease (AWARD-7): a multicentre, open-label, randomised trial. The Lancet Diabetes and Endocrinology 2018;**6**(8):605-17

AWARD-8

Dungan KM, Weitgasser R, Perez Manghi F, et al. A 24-week study to evaluate the efficacy and safety of once-weekly dulaglutide added on to glimepiride in type 2 diabetes (AWARD-8). Diabetes Obes Metab 2016;**18**(5):475-82

AWARD-9

Pozzilli P, Norwood P, Jodar E, et al. Placebo-controlled, randomized trial of the addition of once-weekly glucagon-like peptide-1 receptor agonist dulaglutide to titrated daily insulin glargine in patients with type 2 diabetes (AWARD-9). Diabetes Obes Metab 2017;**19**(7):1024-31

AWARD-9

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AWARD-CHN1

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Appendix 3 Risk of bias in included studies

Study	Trial registration	Number of participants	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and investigators (performance and detection bias)	Blinding of outcome assessment (performance and detection bias)	Incomplete data (attrition bias)	Selective reporting (reporting bias)
3D	UMIN000003784	80	Low	Low	High	Unclear	Low	High
4B	NCT00960661	627	Low	Unclear	High	Unclear	Low	Low
4T	ISCRTN51125379	473	Low	Low	High	Unclear	Low	Low
1860-LIRA-DPP-4	NCT00700817	665	Low	Low	High	Unclear	High	Low
Abe 2008	Not provided	63	Unclear	Unclear	High	Unclear	Low	High
Abe 2016	UMIN000018445	82	Unclear	Unclear	High	Unclear	Low	High
ACTION-J	UMIN000002333	54	Low	Unclear	High	Unclear	Low	High
ADOPT	NCT00279045	4360	Unclear	Low	Low	Low	High	Low
Ahmann 2015	NCT01617434	450	Unclear	Low	Low	Unclear	Low	High
Ahrén 2004	Not applicable	71	Unclear	Low	Low	Unclear	Low	High
Allegretti 2019	NCT02836873	312	Low	Low	Low	Low	Low	High
Alogliptin Study 007	NCT00286468	500	Unclear	Low	Low	Unclear	High	Low
Alogliptin Study 009	NCT00286494	493	Low	Low	Low	Unclear	Low	Low
Alogliptin Study 010	NCT00286455	328	Unclear	Unclear	High	Unclear	Unclear	High
Alvarsson 2003	Not applicable	51	Unclear	Unclear	High	Unclear	High	Low
APOLLO	NCT00311818	415	Low	Low	High	Unclear	Low	High
Apovian 2010	Not provided	194	Unclear	Low	Low	Unclear	High	High
APPROACH	NCT00116831	672	Low	Low	Low	Low	High	Low
APRIME	UMIN000004367	63	Unclear	Unclear	High	Unclear	High	Low
Araki 2015	NCT01368081	336	Low	Low	High	Unclear	Low	Low
Araki 2015a	NCT01584232	361	Low	Low	High	Low	Low	Low
Arechavaleta 2011	NCT00701090	1035	Low	Low	Low	Unclear	High	Low
Arjona Ferreira 2013	NCT00509236	129	Low	Low	Low	Unclear	High	Low
Arjona Ferreira 2013a	NCT00509262	423	Low	Low	Low	Unclear	High	Low
Arturi 2017	Not provided	32	Unclear	Unclear	High	Unclear	Low	High
Asian Acarbose Study	Not provided	121	Unclear	Low	Low	Unclear	Low	High
Aso 2019	Not provided	57	Unclear	Unclear	High	Unclear	Unclear	High
Avilés-Santa 1999	Not provided	43	Unclear	Low	Low	Unclear	Low	High
AWARD-1	NCT01064687	976	Low	Low	Low	Unclear	High	Low
AWARD-2	NCT01075282	807	Low	Low	High	Low	Low	Low
AWARD-3	NCT01126580	807	Low	Low	Low	Unclear	High	Low
AWARD-4	NCT01191268	884	Low	Low	High	Low	High	Low
AWARD-5	NCT00734474	1098	Unclear	Low	Low	Unclear	Low	Low
AWARD-7	NCT01621178	577	Low	Low	High	Low	Low	Low
AWARD-8	NCT01769378	299	Unclear	Low	Low	Unclear	Low	Low
AWARD-9	NCT02152371	300	Low	Low	Low	Low	Low	Low
AWARD-10	NCT02597049	424	Low	Low	Low	Low	Low	Low
AWARD-CHN1	NCT01644500	737	Low	Low	Low	Low	Low	Low
Ba 2017	NCT01590771	498	Low	Low	Low	Low	Low	Low
Bachmann 2003	Not applicable	373	Unclear	Low	Low	Unclear	Unclear	Low
Bailey 2010	NCT00528879	546	Low	Low	Low	Unclear	Low	Low
Bailey 2012	Not provided	282	Low	Low	Low	Unclear	Low	High
Bajaj 2014	NCT00996658	272	Low	Low	Low	Low	High	Low
Bakris 2006	Not provided	389	Unclear	Low	Low	Unclear	High	High
BALANCE	NCT02126358	193	Unclear	Unclear	High	Unclear	Unclear	High
Banerji 1995	Not applicable	20	Unclear	Low	Low	Unclear	High	High
Barnett 2003	Not applicable	171	Unclear	Low	Low	Unclear	Low	High
Barnett 2012	NCT00757588	455	Low	Low	Low	Unclear	High	Low
Barnett 2013	NCT01084005	241	Low	Low	Low	Low	Low	Low

Barzilai 2011	NCT00305604	206	Unclear	Low	Low	Unclear	High	High
Bayrasheva 2020	Not provided	44	Low	Low	High	Unclear	Unclear	High
BEGIN: ADD TO GLP-1	NCT01664247	346	Unclear	Low	Low	Unclear	High	Low
BEGIN: VICTOZA ADD-ON	NCT01388361	177	Unclear	Unclear	High	Unclear	Low	Low
Berberoglu 2010	Not provided	49	Unclear	Unclear	High	Unclear	High	High
Bergenstal 2009	NCT00097877	372	Low	Low	High	Unclear	High	Low
Berndt-Zipfel 2013	Not provided	44	Unclear	Unclear	High	Unclear	Unclear	High
BEST	NCT00420511	21	Unclear	Low	Low	Unclear	High	High
BETA	NCT00562172	75	Unclear	Unclear	High	Unclear	High	High
Bi 2013	ChiCTR-TRC-	160	Low	Unclear	High	Unclear	Unclear	High
Bilezikian 2013	NCT00679939	225	Low	Low	Low	Unclear	High	Low
Birkeland 1994a	Not applicable	36	Unclear	Unclear	High	Unclear	Low	High
Bode 2013	NCT01106651	714	Low	Low	Low	Unclear	High	Low
Bolinder 2012	NCT00855166	182	Low	Low	Low	Unclear	High	Low
Bolli 2009	Not provided	576	Unclear	Low	Low	Unclear	Unclear	Low
Borges 2011	NCT00386100	688	Unclear	Low	Low	Unclear	High	Low
Bosi 2007	NCT00099892	544	Unclear	Low	Low	Unclear	High	Low
Bosi 2009	NCT00382096 and	589	Unclear	Low	Low	Unclear	Low	Low
Bosi 2011	NCT00432276	803	Unclear	Low	Low	Unclear	Low	Low
Bouchi 2017	UMIN000015867	19	Unclear	Unclear	High	Unclear	Low	High
Braun 1996	Not applicable	152	Unclear	Low	Low	Unclear	High	High
BRL-049653/334	Not provided	200	Unclear	Low	Low	Unclear	High	High
Bryson 2016	Not provided	447	Unclear	Low	Low	Unclear	Unclear	Low
Bunck 2009	NCT00097500	69	Unclear	Unclear	High	Unclear	High	High
Buse 2011	NCT00765817	260	Low	Low	Low	Unclear	Low	Low
Camerini-Davalos 1988	Not applicable	147	Low	Low	Low	Low	High	High
Camerini-Davalos 1984	Not applicable	70	Low	Low	Low	Unclear	Low	High
Campbell 1994	Not applicable	48	Unclear	Unclear	High	Unclear	Low	High
CANDLE	UMIN000017669	245	Unclear	Unclear	High	Unclear	High	Low
CANATATA-D	NCT01106677	1284	Low	Low	Low	Unclear	Low	Low
CANTATA-D2	NCT01137812	756	Low	Low	Low	Unclear	High	Low
CANTATA-M	NCT01081834	584	Unclear	Low	Low	Unclear	High	Low
CANTATA-MSU	NCT01106625	469	Low	Low	Low	Unclear	High	Low
CANTATA-SU	NCT00968812	1450	Low	Low	Low	Unclear	Low	High
CANVAS/CANVAS-R	NCT01032629/NCT0	10142	Low	Low	Low	Unclear	Low	Low
Carlson 2019	Not provided	33	Unclear	Unclear	High	Unclear	High	High
CARMELINA	NCT01897532	6991	Low	Low	Low	Low	Low	Low
CAROLINA	NCT01243424	6042	Low	Low	Low	Low	Low	Low
Casner 1988	Not applicable	64	Unclear	Unclear	High	Unclear	High	High
Cefalu 2015	NCT01031680	922	Low	Low	Low	Unclear	Low	Low
Chacra 2017	NCT01698775	213	Unclear	Low	Low	Unclear	Low	Low
Chakraborty 2011	Not provided	208	Unclear	Unclear	High	Unclear	High	High
Charbonnel 2013	NCT01296412	653	Low	Low	High	Unclear	High	High
Charpentier 2009	Not provided	299	Unclear	Low	Low	Unclear	High	Low
Charpentier 2017	Not provided	359						
Chavez 2015	Not provided	21	Unclear	Unclear	High	Unclear	Unclear	High
Chen 2015	NCT01214239	299	High	Low	Low	Unclear	High	High
Chen 2016	NCT01175486	60	Unclear	Unclear	High	Unclear	Low	High
Chiasson 1994	Not applicable	354	Unclear	Unclear	High	Unclear	High	High
Chiasson 2001	Not applicable	248	Unclear	Low	Low	Unclear	Low	Low
CHICAGO	NCT00225264	462	Unclear	Low	Low	Unclear	Low	Low
Chien 2011	Not provided	97	Unclear	Unclear	High	Unclear	Unclear	High
Cho 2019	UMIN000022804	71	Unclear	Unclear	High	Unclear	Low	High
Choi 2004	Not applicable	55	Unclear	Unclear	High	Unclear	High	High
Chou 2008	SB-797620/004	457	Unclear	Low	Low	Unclear	Low	Low
Chou 2012	NCT00484198	1912	Unclear	Low	Low	Low	High	Low
CIMT	NCT00657943	412	Low	Low	Low	Unclear	High	High
Civera 2008	Not provided	24	Unclear	Unclear	High	Unclear	Low	Low

COMPASS	UMIN000004716	130	Low	Unclear	High	Unclear	High	High
CompoSIT-I	NCT02738879	746	Low	Low	Low	Unclear	High	Low
CompoSIT-R	NCT02532855	614	Low	Low	Low	Unclear	Low	Low
CONFIDENCE	NCT01147627	416	Low	Low	High	Unclear	High	High
Coniff 1994	Not applicable	189	Unclear	Low	Low	Unclear	High	High
Coniff 1995	Not applicable	129	Unclear	Low	Low	Unclear	High	Low
Coniff 1995a	Not applicable	207	Unclear	Low	Low	Unclear	Low	High
Costa 1997	Not applicable	65	Unclear	Low	Low	Unclear	High	High
CREDENCE	NCT02065791	4401	Low	Low	Low	Low	Low	Low
Cusi 2019	NCT02009488	56	Low	Low	Low	Unclear	High	High
CV181-011	NCT00121641	401	Unclear	Low	Low	Unclear	High	Low
CV181-013	NCT00295633	565	Low	Low	Low	Unclear	High	Low
CV181-039	NCT00327015	971	Low	Low	Low	Unclear	High	Low
da Silva 2016	NCT02607410	35	Unclear	Unclear	High	Unclear	Low	High
Dailey 2004	Not applicable	365	Unclear	Low	Low	Unclear	High	Low
Dapagliflozin 006	NCT00673231	807	Low	Low	Low	Low	Low	Low
DAPA-HF	NCT03036124	2139	Low	Low	Low	Low	Low	Low
Dargie 2007	GSK 49653/211	224	Low	Low	Low	Unclear	High	Low
Davidson 2007	Not provided	245	Unclear	Low	Low	Unclear	High	High
Davies 2013	NCT01003184	216	Low	Low	High	Unclear	High	High
Davies 2017	NCT01923181	421	Low	Low	High	Unclear	Low	Low
DECLARE-TIMI 58	NCT01730534	17160	Low	Low	Low	Low	Low	Low
DeFronzo 1995	Not applicable	419	Unclear	Low	Low	Unclear	High	Low
DeFronzo 2005	Not applicable	336	Unclear	Low	Low	Low	High	High
DeFronzo 2012	NCT00328627	386	Unclear	Low	Low	Unclear	High	Low
DeFronzo 2015	NCT01422876	405	Low	Low	Low	Unclear	High	Low
Dei Cas 2017	NCT01822548	64	Low	Unclear	High	Unclear	High	High
Dejager 2007	NCT00099905	632	Unclear	Low	Low	Unclear	Low	High
Del Prato 2003	Not applicable	428	Unclear	Low	Low	Unclear	High	High
Del Prato 2011	Not provided	503	Unclear	Low	Low	Unclear	Low	High
Del Prato 2014	NCT00856284	2639	Unclear	Low	Low	Low	High	Low
DELIGHT	NCT02547935	293	Low	Low	Low	Low	Low	High
Deng 2017	Not provided	72	Unclear	Low	High	Unclear	Low	High
DERIVE	NCT02413398	321	Low	Low	Low	Unclear	Low	Low
Derosa 2003	Not applicable	124	Unclear	Unclear	High	Unclear	Low	High
Derosa 2003a	Not applicable	112	Unclear	Unclear	High	Unclear	Low	High
Derosa 2004	Not applicable	164	Unclear	Unclear	High	Unclear	Low	High
Derosa 2005	Not applicable	95	Low	Low	Low	Unclear	Low	High
Derosa 2007	Not provided	248	Low	Low	Low	Unclear	Low	High
Derosa 2009	Not provided	350	Low	Low	Low	Unclear	High	High
Derosa 2009a	Not provided	271	Low	Low	Low	Unclear	Low	High
Derosa 2010	Not provided	151	Unclear	Unclear	High	Unclear	Low	High
Derosa 2010a	Not provided	128	Unclear	Unclear	High	Unclear	Low	High
Derosa 2011	Not provided	188	Unclear	Unclear	High	Unclear	High	High
Derosa 2011a	Not provided	111	Unclear	Unclear	High	Unclear	High	High
Derosa 2012	Not provided	178	Unclear	Unclear	High	Unclear	High	High
Derosa 2012a	Not provided	167	Unclear	Unclear	High	Unclear	High	High
Derosa 2013	Not provided	171	Unclear	Low	Low	Unclear	Low	High
Derosa 2014	Not provided	167	Unclear	Low	Low	Unclear	High	High
Derosa 2014a	Not provided	205	Unclear	Low	Low	Unclear	Low	High
DIA3004	NCT01064414	269	Low	Low	Low	Unclear	High	Low
Distiller 2014	Not provided	28	Unclear	Unclear	High	Unclear	Low	High
DIVERSITY-CVR	UMIN000028014	340	Low	Low	High	Low	High	High
Dobs 2013	NCT00350779	278	Low	Low	Low	Unclear	High	Low
Dorkhan 2009	Not provided	30	Unclear	Unclear	High	Unclear	Low	High
Douek 2005	Not provided	183	Unclear	Low	Low	Unclear	High	High
Drent 2002	Not applicable	465	Unclear	Low	Low	Unclear	High	Low
DUAL-I	NCT01336023	829	Low	Low	High	Low	Low	High

DUAL-I CHINA	NCT03172494	359	Low	Low	Low	Low	Low	Low
DUAL-I JAPAN	NCT02607306	544	Low	Low	High	Low	Low	Low
DUAL-II	NCT01392573	398	Low	Low	High	Unclear	Low	Low
DUAL-II CHINA	NCT03175120	453	Low	Low	Low	Low	Low	Low
DUAL-III	NCT01676116	438	Unclear	Unclear	High	Unclear	High	High
DUAL-VIII	NCT02501161	1012	Low	Low	High	Low	High	Low
DUAL-IX	NCT02773368	420	Low	Low	High	Low	High	Low
DUET-Beta	Not provided	48	Unclear	Unclear	High	Unclear	Unclear	High
DURATION-2	NCT00637273	491	Low	Low	Low	Unclear	High	Low
DURATION-3	NCT00641056	456	Low	Low	High	Low	High	Low
DURATION-4	NCT00676338	820	Low	Low	Low	Unclear	High	Low
DURATION-7	NCT02229383	461	Low	Low	Low	Low	High	Low
DURATION-8	NCT02229396	464	Low	Low	Low	Low	Low	Low
DURATION-NEO-2	NCT01652729	364	Low	Low	Low	Low	Low	Low
EAGLE	Not provided	978	Unclear	Unclear	High	Unclear	High	High
EASIE	NCT00751114	515	Low	Low	High	Unclear	High	Low
Ebato 2009	Not provided	26	Unclear	Unclear	High	Unclear	Low	High
EDIT	UMIN000004678	50	Low	Unclear	High	Unclear	Low	High
Efstathiou 2015	Not provided	66	Unclear	Unclear	High	Unclear	Unclear	High
ELEGANT	NCT01392898	50	Low	Unclear	High	Unclear	Low	High
ELIXA	NCT01147250	6068	Low	Low	Low	Low	Low	Low
ELLENA-IT	UMIN000027614	61	Low	Low	High	Unclear	Low	Low
EMBLEM	UMIN000024502	117	Low	Low	Low	Unclear	High	High
EMIT	NCT01242215	243	Unclear	Low	Low	Unclear	High	High
EMLIFA001	NCT02637973	84	Low	Low	Low	Unclear	High	High
EMPA-HEART CardioLink-6	NCT01011868	97	Low	Low	Low	Low	Low	Low
EMPA-REG BASAL	NCT01011868	494	Low	Low	Low	Unclear	High	Low
EMPA-REG H2H-SU	NCT02998970	1549	Low	Low	Low	Unclear	High	Low
EMPA-REG MDI	NCT01306214	563	Unclear	Low	Low	Unclear	Low	Low
EMPA-REG MET	NCT01159600	637	Low	Low	Low	Unclear	Low	Low
EMPA-REG METSU	NCT01159600	669	Low	Low	Low	Unclear	Low	Low
EMPA-REG MONO	NCT01177813	899	Low	Low	Low	Unclear	Low	Low
EMPA-REG OUTCOME	NCT01131676	7020	Low	Low	Low	Unclear	Low	Low
EMPA-REG PIO	NCT01210001	498	Low	Low	Low	Unclear	Low	Low
EMPA-REG RENAL	NCT01164501	741	Low	Low	Low	Unclear	Low	High
Engelbrechtsen 2016	NCT02094183	42	Unclear	Unclear	High	Unclear	High	High
Erem 2014	Not provided	57	Unclear	Unclear	High	Unclear	Low	Low
ESPECIAL-ACS	UMIN000007900	41	Unclear	Unclear	High	Unclear	High	Low
Esposito 2004	Not applicable	175	Low	Unclear	High	Unclear	Low	High
Esposito 2011	Not provided	110	Low	Unclear	High	Unclear	Low	Low
Essen Study	Not applicable	85	Low	Unclear	High	Unclear	Low	High
EUREXA	NCT00359762	1029	Low	Unclear	High	Unclear	High	Low
EUREXA extension	NCT00359762	154	Low	Unclear	High	Unclear	High	Low
EXAMINE	NCT00968708	5380	Unclear	Low	Low	Unclear	Low	Low
Exenatide-113	Not applicable	377	Unclear	Low	Low	Unclear	High	High
EXSCEL	NCT01144338	14752	Low	Low	Low	Low	Low	Low
Feng 2017	NCT03068065	93	Unclear	Unclear	High	Unclear	Low	High
Ferdinand 2019	NCT02182830	150	Unclear	Low	Low	Unclear	High	Low
Fernandez 2008	Not provided	20	Unclear	Unclear	High	Unclear	Low	High
Ferrannini 2010	NCT00528372	485	Unclear	Low	Low	Unclear	Low	Low
FIGHT	NCT01800968	178	Low	Low	Low	Low	Low	Low
Filozof 2010	Not provided	1007	Unclear	Low	Low	Low	High	High
Finn 2009	NCT00116792	65	Low	Low	Low	Unclear	Low	High
Fischer 1998	Not applicable	495	Unclear	Low	Low	Unclear	High	High
Foley 2009	NCT00102388	1092	Unclear	Low	Low	Unclear	High	High
Foley 2011	NCT00260156	59	Unclear	Low	Low	Unclear	Low	High
Fonseca 2000	Not applicable	348	Low	Low	Low	Low	Low	Low
Fonseca 2003	Not applicable	402	Unclear	Low	Low	Unclear	High	High

Fonseca 2007	NCT00099931	296	Unclear	Low	Low	Unclear	Low	Low
Fonseca 2013	NCT00885352	313	Unclear	Low	Low	Unclear	Low	Low
Forst 2003	Not applicable	143	Unclear	Unclear	High	Unclear	Unclear	High
Forst 2005	Not applicable	173	Unclear	Unclear	High	Unclear	High	High
Forst 2014	NCT01106690	342	Low	Low	Low	Unclear	Low	Low
Forst 2015	NCT01649466	161	Unclear	Unclear	High	Unclear	High	Low
Frederich 2012	NCT00316082	365	Unclear	Unclear	Unclear	Unclear	High	Low
FREEDOM-1	NCT01455857	460	Low	Low	Low	Low	High	High
Frias 2018	NCT03131687	105	Low	Low	Low	Low	High	Low
Gaal 2001	Not applicable	152	Unclear	Low	Low	Unclear	High	High
Gallwitz 2011	NCT00434954	494	Unclear	Unclear	Unclear	Unclear	High	High
Gallwitz 2012	NCT00622284	1552	Low	Low	Low	Unclear	High	Low
Gantz 2017	NCT01703208	4202	Low	Low	Low	Low	High	Low
Gantz 2017a	NCT01814748	303	Low	Low	Low	Low	High	Low
Garber 2006	Not provided	318	Unclear	Low	Low	Unclear	High	High
Garber 2007	NCT00099853	463	Unclear	Low	Low	Unclear	High	High
Garber 2008	NCT00099944	515	Unclear	Low	Low	Unclear	High	Low
Gastaldelli 2014	NCT00381342	79	Unclear	Low	Low	Unclear	High	High
GENERATION	NCT01006603	720	Low	Low	Low	Unclear	High	Low
Gentile 2001	Not applicable	100	Unclear	Low	Low	Unclear	Low	High
GetGoal-Duo-1	NCT00975286	446	Low	Low	Low	Low	Low	Low
GetGoal-Duo-2	NCT01768559	894	Low	Low	High	Unclear	High	Low
GetGoal-F1	NCT00763451	482	Unclear	Low	Low	Unclear	Low	High
GetGoal-L	NCT00715624	496	Low	Low	Low	Unclear	High	Low
GetGoal-L-C	NCT01632163	448	Low	Low	Low	Unclear	High	High
GetGoal-L Asia	NCT00866658	311	Unclear	Low	Low	Unclear	High	Low
GetGoal-M	NCT00712673	680	Unclear	Low	Low	Unclear	High	Low
GetGoal-M-Asia	NCT01169779	390	Low	Low	Low	Unclear	High	Low
GetGoal-O	NCT01798706	350	Unclear	Low	Low	Unclear	Low	Low
GetGoal-P	NCT00763815	484	Unclear	Low	Low	Unclear	Low	Low
GetGoal-S	NCT00713830	859	Unclear	Low	Low	Unclear	High	Low
Giles 2008	NCT00521820	518	Unclear	Low	Low	Unclear	High	Low
Giugliano 1993	Not applicable	50	Unclear	Low	Low	Unclear	Unclear	High
GLAC	Not applicable	200	Unclear	Unclear	High	Unclear	High	High
GLAD	Not applicable	244	Low	Low	Low	Unclear	High	High
GLAL	Not applicable	567	Unclear	Unclear	High	Unclear	High	High
Glimepiride Combination Group	Not applicable	145	Unclear	Low	Low	Unclear	High	Low
Göke 2002	Not applicable	265	Unclear	Low	High	Unclear	High	High
Göke 2010	Not provided	858	Low	Low	Low	Unclear	High	Low
Gómez-Perez 2002	Not applicable	105	Unclear	Low	Low	Unclear	Low	High
Gomis 2011	NCT00641043	389	Low	Low	Low	Unclear	High	High
Goodman 2009	Not provided	370	Unclear	Low	Low	Unclear	High	High
Grant 1996	Not applicable	75	Unclear	Unclear	High	Unclear	High	High
GRAVITAS	ISCTRN13643081	80	Unclear	Low	Low	Unclear	High	Low
Grey 2014	ACTRN12607000610	86	Low	Low	Low	Unclear	High	High
Gudipaty 2014	NCT00775684	47	Unclear	Unclear	High	Unclear	High	High
Gurkan 2014	Not provided	34	Unclear	Unclear	High	Unclear	Unclear	High
Gutniak 1987	Not applicable	20	Unclear	Unclear	High	Unclear	Unclear	High
Güvener 1999	Not applicable	40	Unclear	Low	Low	Unclear	Unclear	High
Guzman 2017	NCT02111096	174	Low	Low	Low	Low	High	High
Haak 2012	NCT00798161	791	Unclear	Low	Low	Unclear	High	Low
Hadjadj 2016	NCT01719003	665	Low	Low	Low	Unclear	Low	High
Halimi 2000	Not applicable	152	Unclear	Low	Low	Unclear	Low	High
Hällsten 2002	Not applicable	31	Unclear	Low	Low	Unclear	Low	High
Halvorsen 2019	NCT01377844	286	Unclear	Low	Low	Low	High	Low
Halvorsen 2019a	NCT03115112	384	Low	Low	Low	Low	Unclear	Low
Han 2016	Not provided	219	Unclear	Unclear	Low	Unclear	Unclear	High
Han 2018	NCT02452632	143	Low	Low	Low	Unclear	High	High

Handelsman 2017	NCT01682759	751	Low	Low	Low	Low	High	Low
Handelsman 2019	NCT02284893	461	Low	Low	Low	Unclear	High	Low
Haneda 2016	JapicCTI-111507	145	Unclear	Low	Low	Unclear	High	High
Hanefeld 1991	Not applicable	100	Unclear	Low	Low	Unclear	Low	High
Hanefeld 2004	Not applicable	639	Unclear	Low	Low	Unclear	High	High
Hanefeld 2007	Not provided	598	Unclear	Low	Low	Unclear	High	Low
HARMONY 1	NCT00849056	310	Low	Low	Low	Low	High	Low
HARMONY 2	NCT00849017	301	Low	Low	Low	Unclear	High	Low
HARMONY 3	NCT00838903	1012	Unclear	Low	Low	Unclear	High	Low
HARMONY 4	NCT00838916	745	Low	Low	High	Low	High	High
HARMONY 5	NCT00839527	685	Low	Low	Low	Low	High	Low
HARMONY 6	NCT00976391	566	Unclear	Low	Low	Unclear	Low	High
HARMONY OUTCOMES	NCT02465515	9463	Low	Low	Low	Low	Low	Low
Hartemann-Heurtier 2009	NCT00159211	27	Unclear	Low	Low	Unclear	Low	High
Hartley 2015	NCT01189890	480	Low	Low	Low	Unclear	High	Low
Hasche 1999	Not applicable	74	Unclear	Low	Low	Unclear	Low	High
Hattori 2017	UMIN000004674	74	Unclear	Unclear	High	Unclear	Low	High
Hattori 2018	UMIN000021552	102	Unclear	Unclear	High	Unclear	Unclear	High
HEELA	Not provided	235	Unclear	Unclear	High	Unclear	High	High
Hegele 1995	Not applicable	141	Unclear	Unclear	Unclear	Unclear	High	High
Heine 2005	NCT00082381	549	Low	Low	High	Unclear	High	High
Heliövaara 2007	Not provided	59	Unclear	Low	Low	Unclear	Unclear	High
Henry 2012	NCT00643851	831	Low	Low	Low	Unclear	High	Low
Henry 2014	NCT00722371	751	Unclear	Unclear	Unclear	Unclear	High	Low
Hermann 1999	Not applicable	35	Unclear	Low	Low	Unclear	High	High
Hiramatsu 2018	Not provided	139	Unclear	Unclear	High	Unclear	High	High
Hirano 2009	Not provided	61	Low	Low	Unclear	Unclear	Low	High
Hirano 2012	Not provided	44	Low	Unclear	Unclear	Unclear	Low	High
Hollander 2007	NCT00054782	670	Unclear	Low	Low	Low	High	High
HOME	NCT00375388	390	Low	Low	Low	Unclear	Low	Low
Home 2018	NCT01717313	329	Unclear	Low	Low	Unclear	High	Low
Hong 2013	Not provided	50	Unclear	Unclear	Unclear	Unclear	High	High
Hong 2015	Not provided	72	Unclear	Unclear	High	Unclear	High	Low
Hong 2016	Not provided	142	Unclear	Low	Low	Unclear	High	High
Horton 2000	Not applicable	529	Low	Low	Low	Unclear	High	Low
Hotta 1993	Not applicable	37	Unclear	Low	Low	Unclear	High	High
Hsieh 2011	Not provided	105	Unclear	Unclear	Unclear	Unclear	High	High
Hu 2007	Not provided	78	Unclear	Low	Low	Unclear	Unclear	High
Hwang 2008	Not provided	90	Unclear	Unclear	High	Unclear	High	High
Hygum 2020	NCT02473809	60	Unclear	Low	Low	Low	Low	High
Iacobellis 2017	NCT02014740	95	Unclear	Unclear	High	Unclear	High	High
ILLUMINATE	Not provided	60	Unclear	Low	Low	Unclear	Low	Low
Ikonomidis 2018	NCT03878706	80	Unclear	Unclear	High	Unclear	Unclear	High
Ikonomidis 2020	NCT01135433	168	Unclear	Unclear	High	Unclear	Unclear	High
Inagaki 2012	NCT00935532	427	Low	Low	High	Unclear	High	Low
Inagaki 2013	NCT01204294	206	Unclear	Unclear	High	Unclear	Low	Low
Inagaki 2014	NCT01413204	272	Unclear	Low	Low	Unclear	Low	Low
Inagaki 2015	NCT01632007	245	Low	Low	Low	Unclear	Low	High
INICOM	NCT01787396	292	Unclear	Low	Low	Unclear	High	High
Inoue 2019	UMIN000018839	49	Low	Low	High	Unclear	High	High
Insulin Glargine 4014	Not provided	216	Unclear	Unclear	High	Unclear	Low	High
INTERVAL	NCT01257451	278	Low	Low	Low	Unclear	Low	Low
Ito 2011	Not provided	60	Unclear	Unclear	High	Unclear	High	High
Ito 2017	UMIN000022651	66	Low	Unclear	High	Unclear	Low	High
Jabbour 2014	NCT00984867	451	Unclear	Low	Low	Unclear	High	Low
Jacob 2007	Not provided	57	Unclear	Unclear	High	Unclear	High	High
Jain 2006	Not provided	502	Unclear	Low	Low	Unclear	High	Low
JEDIS-1	Not provided	49	Unclear	Unclear	High	Unclear	High	High

Jeon 2011	Not provided	102	Unclear	Unclear	High	Unclear	Low	High
Jeon 2018	Not provided	310	Unclear	Unclear	High	Unclear	Unclear	High
Jerums 1987	Not applicable	40	Unclear	Low	Low	Unclear	High	High
Ji 2014	NCT01095653	393	Low	Low	Low	Unclear	High	High
Ji 2016	Not provided	497	Low	Low	Low	Unclear	High	Low
Ji 2017	Not provided	484	Unclear	Low	Low	Unclear	High	High
Jian 2018	Not provided	126	Unclear	Unclear	High	Unclear	Unclear	High
Jibran 2006	Not provided	100	Unclear	Unclear	Unclear	Unclear	Unclear	High
Johnston 1998	Not applicable	385	Unclear	Low	Low	Unclear	High	High
Johnston 1998a	Not applicable	340	Unclear	Low	Low	Unclear	Low	High
Johnston 1998b	Not applicable	364	Unclear	Low	Low	Unclear	Low	Low
Josse 2003	Not applicable	192	Unclear	Low	Low	Unclear	Low	High
Jovanovic 2000	Not applicable	361	Unclear	Low	Low	Unclear	High	High
Jovanovic 2004	Not applicable	123	Unclear	Unclear	High	Unclear	Low	High
Jung 2005	Not applicable	30	Unclear	Unclear	Unclear	Unclear	Low	High
Juurinen 2009	Not provided	81	Unclear	Low	Low	Unclear	Low	High
Kadoglou 2007	NCT00306176	50	Unclear	Unclear	Unclear	Unclear	Low	High
Kadoglou 2008	Not provided	70	Unclear	Unclear	High	Unclear	Low	High
Kadoglou 2011	Not provided	140	Unclear	Unclear	High	Unclear	Low	High
Kadowaki 2011	NCT00577824	179	Unclear	Low	Low	Unclear	High	Low
Kadowaki 2017	NCT02354235	138	Unclear	Low	Low	Unclear	High	Low
Kadowaki 2018	NCT02354222	154	Unclear	Low	Low	Unclear	High	Low
Kaku 2009	UMIN000001110	169	Unclear	Low	Low	Unclear	High	High
Kaku 2009a	UMIN000001363	587	Unclear	Unclear	Unclear	Low	High	Low
Kaku 2011	NCT00393718	400	Unclear	Unclear	High	Unclear	High	Low
Kaku 2014	Not provided	261	Unclear	Low	Low	Unclear	High	High
Kaku 2017	Not provided	374	Unclear	Low	Low	Unclear	Low	Low
Kaku 2019	NCT02489968	447	Low	Low	High	Unclear	Low	Low
Kanazawa 2010	UMIN000001997	55	Unclear	Unclear	High	Unclear	Low	High
Kanazawa 2011	UMIN000002099	66	Unclear	Unclear	High	Unclear	Low	Low
Kato 2015	UMIN000013356	20	Unclear	Unclear	High	Unclear	Low	High
Kawamori 2018	NCT02453555	275	Low	Low	Low	Low	Low	Low
Kelly 2007	NCT00123643	36	Unclear	Low	Low	Unclear	Low	Low
Kendall 2005	Not applicable	733	Unclear	Low	Low	Unclear	High	High
Khaloo 2019	NCT03125694	250	Unclear	Unclear	High	Unclear	Low	High
Khanolkar 2008	Not provided	50	Unclear	Unclear	High	Unclear	Low	High
Kikuchi 2012	NCT00297063	372	Unclear	Low	Low	Unclear	High	Low
Kim 2014	NCT01001611	173	Unclear	Low	Low	Unclear	Low	High
Kim 2019	NCT02426294	135	Unclear	Unclear	High	Unclear	High	High
Kim 2020	Not provided	243	Unclear	Low	Low	Unclear	High	Low
KIND-LM	UMIN000004243	46	Unclear	Unclear	High	Unclear	Low	High
Kinoshita 2020	UMIN000021291	98	Low	Low	High	Unclear	High	High
Kiyici 2009	Not provided	50	Unclear	Unclear	High	Unclear	Low	High
Ko 2006	Not provided	112	Unclear	Unclear	High	Unclear	High	High
Koffert 2017	NCT02526615	41	Unclear	Unclear	High	Unclear	Unclear	High
Kohan 2014	NCT00663260	252	Low	Low	Low	Low	Low	Low
Kondo 2016	UMIN00004791	171	Unclear	Unclear	High	Unclear	High	High
Kothny 2013	Not provided	449	Low	Low	Low	Unclear	High	Low
Krawczyk 2005	Not applicable	40	Unclear	Unclear	High	High	High	High
Kudo-Fujimaki 2014	UMIN000004010	40	Unclear	Unclear	High	Unclear	Low	High
Kumashiro 2018	Not provided	34	Unclear	Unclear	High	Unclear	High	High
Laberge 2016	Not provided	116	Unclear	Unclear	Unclear	Unclear	Unclear	High
Lam 1998	Not applicable	89	Unclear	Low	Low	Unclear	Low	High
Lambadiari 2018	NCT03010683	60	Unclear	Unclear	High	Unclear	Unclear	High
Langenfeld 2005	Not applicable	179	Unclear	Unclear	High	Unclear	High	High
LANTERN	NCT01316094	165	Unclear	Low	Low	Unclear	High	High
Lawrence 2004	Not applicable	65	Unclear	Unclear	High	Low	Unclear	High
LEAD-1	Not provided	809	Unclear	Low	Low	Unclear	High	Low

LEAD-2	NCT00318461	1091	Low	Low	Low	Unclear	High	Low
LEAD-3	NCT00294723	745	Low	Low	Low	Unclear	High	Low
LEAD-4	NCT00333151	533	Low	Low	Low	Unclear	High	Low
LEAD-5	NCT00331851	581	Low	Low	High	Unclear	Low	High
LEADER	NCT01179048	9340	Low	Low	Low	Low	Low	Low
Lebovitz 2001	Not applicable	493	Unclear	Low	Low	Unclear	Low	High
Ledesma 2019	NCT02240680	302	Unclear	Low	Low	Unclear	High	Low
Lee 2013	Not provided	121	Unclear	Low	Low	Unclear	Unclear	Low
Lee 2017	NCT01704261	307	Low	Low	Low	Low	High	Low
Leiter 2014	NCT01098539	495	Low	Low	Low	Low	Low	Low
Leiter 2014a	NCT01042977	965	Low	Low	Low	Unclear	Low	Low
Leonhardt 1991	Not applicable	94	Unclear	Low	Low	Unclear	Low	High
Lewin 2007	Not provided	575	Unclear	Low	Low	Unclear	High	High
Lewin 2015	NCT01422876	398	Low	Low	Low	Unclear	Low	Low
Li 2014	Not provided	203	Low	Unclear	High	Unclear	High	High
Li 2014b	Not provided	42	Unclear	Unclear	High	Unclear	Unclear	High
Li 2017	Not provided	33	Unclear	Low	Low	Unclear	Low	High
Li 2019	Not provided	64	Unclear	Unclear	High	Unclear	Low	High
Li 2019a	NCT01644500	23	Unclear	Unclear	High	Unclear	Unclear	High
Li 2020	NCT02655757	149	Low	Unclear	High	Low	High	Low
LIBRA	NCT01270789	51	Low	Low	Low	Unclear	Low	High
Lim 2017	Not applicable	170	Unclear	Low	Low	Unclear	Low	High
Lin 2003	Not applicable	65	Unclear	Low	Low	Unclear	High	Low
Linagliptin-LTC Trial	NCT02061969	140	Low	Low	High	Unclear	Low	Low
Lindström 1999	Not applicable	107	Unclear	Low	Low	Unclear	High	High
Lingvay 2018	NCT02461589	641	Low	Low	Low	Unclear	Low	Low
LIPER2	EudraCT number	24	Unclear	Low	Low	Unclear	High	High
Liraglutide-Detemir Study	NCT00856986	323	Unclear	Low	Low	Unclear	High	Low
LIRA-ADD2SGLT2i	NCT02964247	303	Low	Low	Low	Unclear	Low	Low
LIRA-RENAL	NCT01620489	277	Low	Low	Low	Unclear	High	Low
LIRA-SWITCH	NCT01907854	406	Low	Low	Low	Unclear	High	High
Liu 2013	NCT01195090	119	Unclear	Unclear	High	Unclear	Low	High
Liu 2014	Not provided	146	Low	Low	Low	Unclear	Low	High
Liu 2020	NCT02303730	71	Low	Low	High	Unclear	High	Low
Liutkus 2010	Not provided	165	Unclear	Low	Low	Unclear	High	Low
LixiLan-G	NCT02787551	514	Low	Low	High	Low	Low	Low
LixiLan JP-L	NCT02752412	512	Low	Low	High	Unclear	Low	Low
LixiLan JP-O1	NCT02749890	321	Low	Low	High	Unclear	High	Low
LixiLan JP-O2	NCT02752828	521	Low	Low	High	Unclear	Low	Low
LixiLan-L	NCT02058160	736	Low	Low	High	Low	Low	Low
Lou 2020	Not reported	86	Unclear	Unclear	High	Unclear	Unclear	High
Lu 2016	NCT01505426	170	Low	Low	Low	Unclear	High	High
Lukashevich 2011	Not provided	515	Unclear	Low	Low	Unclear	Low	High
Lund 2009	NCT00118963	101	Low	Low	Low	Unclear	Low	High
LYDIA	NCT02043054	76	Low	Low	High	Unclear	High	Low
Ma 2015	Not provided	60	Unclear	Unclear	High	Unclear	Low	High
Macauley 2015	NCT01356381	44	Unclear	Low	Low	Unclear	Low	High
Madsbad 2001	Not applicable	256	Unclear	Low	Low	Unclear	High	High
Maffioli 2013	Not provided	170	Unclear	Low	Low	Unclear	Low	High
MAGNA VICTORIA	NCT01761318	49	Unclear	Low	Low	Unclear	Low	High
Marbury 1999	Not applicable	576	Unclear	Low	Low	Unclear	High	Low
MARCH	ChiCTR-TRC-	784	Low	Low	Low	Unclear	High	Low
Marena 1993	Not applicable	20	Unclear	Low	Low	Unclear	Unclear	High
Mari 2008	NCT00101712	306	Unclear	Low	Low	Unclear	High	High
MARLINA-T2D	NCT01792518	360	Unclear	Low	Low	Unclear	Unclear	High
Marre 2002	Not applicable	468	Low	Low	Low	Unclear	Low	High
Maruyama 2019	Not provided	44	Unclear	Unclear	High	Unclear	Unclear	High
MASTER	UMIN000001671	28	Unclear	Unclear	High	Unclear	Low	High

Mathieu 2015	NCT01462266	658	Unclear	Low	Low	Unclear	Low	Low
Mathieu 2016	NCT01646320	320	Unclear	Low	Low	Unclear	Low	Low
Matthaei 2015	NCT01619059	322	Unclear	Low	Low	Unclear	Low	Low
Matthaei 2015a	NCT01392677	218	Low	Low	Low	Unclear	Low	High
Matthews 2005	Not applicable	630	Unclear	Low	Low	Unclear	High	Low
Matthews 2010	EudraCT 2004-	3118	Unclear	Low	Low	Unclear	High	Low
Mattoo 2005	Not applicable	289	Low	Low	Low	Unclear	Low	High
McCluskey 2004	Not applicable	40	Unclear	Low	Low	Unclear	Low	High
McGill 2013	Not provided	133	Unclear	Low	Low	Low	High	Low
McGuire 2010	NCT00424762	150	Unclear	Low	Low	Unclear	High	High
MDI Liraglutide	EudraCT 2012-	124	Unclear	Low	Low	Unclear	Low	High
Meneghini 2010	Not provided	247	Unclear	Unclear	High	Unclear	High	High
Meneilly 2000	Not applicable	45	Unclear	Low	Low	Unclear	Unclear	High
Milovanova 2019	Not provided	42	Unclear	Unclear	High	Unclear	Unclear	High
Mita 2007	Not provided	70	Low	Unclear	High	Unclear	Low	High
Mita 2019	UMIN000022953	43	Unclear	Unclear	High	Unclear	Low	High
Mitrakou 1998	Not applicable	120	Unclear	Low	Low	Unclear	Low	High
Miyagawa 2015	NCT01558271	492	Low	Low	Low	Low	Low	Low
Miyazaki 2002	Not applicable	58	Low	Low	High	Unclear	Unclear	High
Mokta 2018	Not provided	217	Unclear	Unclear	High	Unclear	Low	High
Moretto 2008	NCT00381342	233	Low	Low	Low	Unclear	Low	Low
Morino 2018	Not provided	46	Unclear	Unclear	High	Unclear	Unclear	High
Moriwaki 2018	UMIN000012562	28	Unclear	Unclear	High	Unclear	Low	High
Moses 2014	Not provided	257	Unclear	Low	Low	Unclear	Low	Low
Moses 2016	NCT01076075	427	Unclear	Low	Low	Unclear	High	Low
Mu 2017	NCT01708902	436	Unclear	Low	Low	Unclear	Low	Low
Müller-Wieland 2018	NCT02471404	939	Low	Low	Low	Unclear	High	Low
Nakamura 2001	Not applicable	28	Unclear	Low	Low	Unclear	Low	High
Nakamura 2004	Not applicable	45	Unclear	Unclear	High	Unclear	Low	High
Nakamura 2006	Not provided	68	Unclear	Unclear	High	Unclear	Low	High
Nar 2009	Not provided	34	Unclear	Unclear	High	Unclear	Unclear	High
Nathan 1988	Not applicable	31	Low	Low	Low	Unclear	Unclear	High
Nauck 2007a	Not provided	501	Low	Low	High	Unclear	High	High
Nauck 2007b	NCT00094770	1172	Unclear	Low	Low	Unclear	High	Low
Nauck 2009	NCT00286442	527	Low	Low	Low	Unclear	High	Low
Nauck 2011	NCT00660907	814	Low	Low	Low	Unclear	High	Low
Nauck 2016	NCT01183013	544	Low	Low	Low	Unclear	High	High
Neff 2016	NCT01847313	20	Unclear	Unclear	Unclear	Unclear	High	High
Negro 2005	Not applicable	38	Unclear	Unclear	High	Unclear	Unclear	High
Ning 2016	NCT01582230	293	Low	Low	Low	Unclear	Low	High
Nino 2017	NCT01733758	387	Low	Low	Low	Unclear	High	Low
Nishimura 2016	UMIN000011420	40	Unclear	Unclear	High	Unclear	Low	High
Nishio 2006	Not provided	54	Unclear	Unclear	High	Unclear	Unclear	High
Nogueira 2014	Not provided	35	Unclear	Unclear	High	Unclear	High	High
Nowicki 2011	NCT00614939	170	Low	Low	Low	Unclear	High	Low
Ogasawara 2009	Not provided	54	Unclear	Unclear	High	Unclear	Low	High
Oh 2019	NCT01370707	187	Unclear	Low	Low	Unclear	High	High
Ohira 2014	Not provided	70	Unclear	Unclear	High	Unclear	Unclear	High
Ohira 2014a	Not provided	60	Unclear	Low	High	Unclear	Low	High
Omariglitin Study 015	NCT01697592	585	Low	Low	Low	Unclear	Low	Low
Omarigliptin Protocol 2010	NCT01703221	394	Low	Low	Low	Unclear	Low	Low
Onoue 2020	UMIN000014531	24	Low	Low	High	Unclear	Low	High
Onuchin 2010	None	184	Unclear	Unclear	High	High	Low	High
Osman 2004	Not applicable	16	Unclear	Low	Low	Unclear	Low	Low
Ovalle 2004	Not applicable	17	Unclear	Unclear	High	Unclear	Low	High
Owens 2011	NCT00602472	1058	Unclear	Low	Low	Unclear	Low	High
Oyama 2008	Not provided	84	Unclear	Low	High	Unclear	Unclear	High
Pagano 1995	Not applicable	96	Unclear	Unclear	High	Unclear	Low	High

Pan 2008	NCT00110240	661	Unclear	Low	Low	Unclear	High	Low
Pan 2012	Not provided	438	Unclear	Low	Low	Unclear	Low	Low
Pan 2012a	NCT00698932	568	Low	Low	Low	Unclear	High	Low
Pan 2015	Not provided	461	Unclear	Low	Low	Unclear	Unclear	High
Park 2011	Not provided	68	Unclear	Unclear	High	Unclear	Unclear	High
Park 2014	NCT00708578	67	Unclear	Unclear	High	Unclear	Low	High
Park 2017	NCT02946541	160	Unclear	Low	Low	Unclear	High	High
Parmar Vinendra 2019	Not provided	130	Unclear	Unclear	High	Unclear	Low	Low
Parthan 2018	NCT02097342	30	Low	Low	High	Unclear	High	High
Patel 2013	Not provided	219	Unclear	Low	Low	Unclear	High	High
Pavithra 2019	Not provided	80	Unclear	Unclear	High	Unclear	Unclear	High
Pavo 2003	Not applicable	206	Unclear	Low	Low	Unclear	Low	High
Perez 2009	NCT00727857	399	Unclear	Low	Low	Unclear	High	Low
PERISCOPE	NCT00225277	547	Low	Low	Low	Low	High	Low
Periello 2006	Not provided	283	Unclear	Low	Low	Unclear	Unclear	High
Petrica 2009	Not provided	44	Unclear	Unclear	High	High	Low	High
Petrica 2011	Not provided	78	Unclear	Unclear	High	Unclear	Low	High
Philis-Tsimikas 2013	NCT01046110	458	Low	Low	High	Low	High	Low
Phillips 2001	Not applicable	908	Unclear	Low	Low	Unclear	High	High
Phillips 2003	Not applicable	83	Unclear	Low	Low	Unclear	High	High
Phrommintikul 2019	NCT03178591	49	Low	Low	Low	Unclear	High	Low
PIOCOMB	Not provided	82	Unclear	Low	Low	Unclear	Unclear	High
PIOfix	NCT00770653	305	Unclear	Low	Low	Unclear	High	High
Pioglitazone 001	Not applicable	399	Unclear	Low	Low	Unclear	High	High
PIONEER	Not applicable	173	Unclear	Unclear	High	Unclear	High	High
PIONEER 1	NCT02906930	703	Low	Low	Low	Low	Low	Low
PIONEER 2	NCT02863328	822	Low	Low	High	Low	High	Low
PIONEER 3	NCT02607865	1864	Low	Low	Low	Low	Low	Low
PIONEER 4	NCT02863419	711	Low	Low	Low	Low	Low	Low
PIONEER 5	NCT02827708	324	Low	Low	Low	Low	Low	Low
PIONEER 6	NCT02692716	3183	Low	Low	Low	Low	Low	Low
PIONEER 7	NCT02849080	504	Low	Low	Low	Low	High	Low
PIONEER 8	NCT03021187	731	Low	Low	Low	Low	Low	Low
PIONEER 9	NCT03018028	243	Low	Low	Low	Low	Low	Low
PioRAGE	UMIN000002055	63	Low	Unclear	High	Unclear	Low	High
PIRAMID 2009	ISRCTN53177482	78	Unclear	Low	Low	Unclear	Low	High
Pistrosch 2012	NCT00324675	28	Unclear	Low	Low	Unclear	Unclear	High
Pistrosch 2013	NCT00857870	75	Unclear	Unclear	High	Unclear	High	High
Pi-Sunyer 2007	NCT00120536	354	Unclear	Low	Low	Unclear	High	High
Pop-Busui 2009	NCT00549874	27	Unclear	Unclear	High	Unclear	High	High
POPPS	Not provided	97	Unclear	Unclear	High	Unclear	Unclear	High
Pratley 2014	NCT01023581	559	Unclear	Low	Low	Low	High	Low
PRESERVE-beta	Not applicable	428	Unclear	Low	Low	Unclear	High	High
PREVENT-J	UMIN000021552	278	Unclear	Unclear	High	Unclear	High	High
PRIDE	Not provided	94	Low	Unclear	High	Unclear	High	Low
PRIME-V study	UMIN000015170	98	Unclear	Unclear	High	Unclear	Low	High
PRISMA	NCT00772174	213	Unclear	Low	Low	Unclear	Low	Low
PROactive	NCT00174993	5238	Low	Low	Low	Low	Low	Low
PROLOGUE	UMIN000004490	463	Low	Low	High	Low	Low	Low
QUARTER	Not applicable	1194	Low	Low	Low	Unclear	Low	High
Quatraro 1986	Not applicable	30	Unclear	Unclear	High	Unclear	Unclear	High
Raghuveer 2020	Not provided	100	Unclear	Unclear	High	Unclear	Unclear	High
Rahman 2010	NCT00489229	22	Unclear	Low	Low	Unclear	Low	Low
Rahman 2011	Not provided	204	Unclear	Unclear	High	Unclear	Unclear	High
Raji 2018	Not provided	613	Unclear	Unclear	high	Unclear	Unclear	High
Raskin 2001	Not applicable	318	Low	Low	Low	Unclear	High	High
Raskin 2004	Not applicable	125	Unclear	Unclear	High	Unclear	High	High
Raskin 2009	Not provided	657	Unclear	Unclear	High	Unclear	High	Low

Raz 2008	NCT00337610	190	Low	Low	Low	Unclear	Low	Low
RECORD	NCT00379769	4447	Unclear	Unclear	High	Low	Low	Low
REGO-F	NCT02397421	56	Unclear	Unclear	High	Unclear	High	High
REFORM	UMIN000018321	72	Low	Low	Low	Unclear	Unclear	Low
RELEASE	NCT02015299	44	Unclear	Low	Low	Unclear	High	High
RESULT	Not provided	227	Unclear	Low	Low	Unclear	High	Low
REWIND	NCT01394952	9901	Low	Low	Low	Low	Low	Low
Reynolds 2002	Not applicable	18	Unclear	Unclear	High	Unclear	High	High
Reynolds 2007	Not provided	40	Unclear	Unclear	High	Unclear	Low	High
Ristic 2006	Not provided	262	Low	Low	Low	Unclear	High	Low
Robbins 2007	NCT00191464	317	Unclear	Low	High	Unclear	High	High
Roberts 2005	Not applicable	168	Unclear	Low	Low	Unclear	High	Low
Rodbard 2016	Not provided	216	Low	Low	Low	Unclear	High	High
Rosenstock 1998	Not applicable	148	Unclear	Low	Low	Unclear	High	High
Rosenstock 2006	Not provided	313	Unclear	Low	Low	Unclear	High	Low
Rosenstock 2007	NCT00099918	786	Unclear	Low	Low	Unclear	Low	Low
Rosenstock 2007a	NCT00101803	315	Unclear	Low	Low	Unclear	High	High
Rosenstock 2009	NCT00286429	390	Low	Low	Low	Unclear	High	Low
Rosenstock 2010	NCT00395512	327	Unclear	Low	Low	Unclear	High	High
Rosenstock 2012	NCT00683878	420	Unclear	Low	Low	Unclear	High	Low
Rosenstock 2013	NCT00707993	441	Unclear	Low	Low	Unclear	High	Low
Rosenstock 2015	NCT01606007	355	Unclear	Low	Low	Unclear	High	Low
Rosenstock 2016	NCT01809327	712	Low	Low	Low	Unclear	Low	Low
Rosenstock 2019	NCT02681094	590	Low	Low	Low	Unclear	Low	Low
Ross 2015	NCT01512979	316	Low	Low	Low	Unclear	High	Low
SAIS1	UMIN000004955	103	Unclear	Unclear	High	Unclear	High	Low
Saleem 2011	Not provided	100	Unclear	Unclear	High	Unclear	Unclear	High
Salman 2001	Not applicable	57	Unclear	Unclear	High	Unclear	Low	High
Saloranta 2002	Not applicable	675	Unclear	Low	Low	Unclear	Unclear	Low
Samson 2011	NCT01432405	21	Low	Low	High	High	Unclear	High
Sato 2019	UMIN000004985	41	Unclear	Unclear	High	Unclear	Unclear	High
SAVOR -TIMI 53	NCT01107886	16492	Low	Low	Low	Low	Low	Low
Saxagliptin 014	NCT00121667	743	Low	Low	Low	Unclear	High	Low
SCALE Diabetes	NCT01272232	855	Low	Low	Low	Unclear	Low	Low
Scherbaum 2002	Not applicable	233	Unclear	Low	Low	Unclear	High	High
Scherbaum 2008	NCT00101712	306	Unclear	Low	Low	Unclear	Low	Low
Schweizer 2007	NCT00099866	780	Unclear	Low	Low	Unclear	High	Low
Schweizer 2009	NCT00246619	335	Unclear	Low	Low	Unclear	High	Low
Segal 1997	Not applicable	119	Unclear	Low	Low	Unclear	High	High
Segal 2005	Not applicable	139	Unclear	Low	Low	Unclear	High	Low
Seino 2011	NCT00395746	264	Unclear	Low	Low	Unclear	High	Low
Seino 2014	JapicCTI-111661	158	Unclear	Low	Low	Unclear	Low	Low
Seino 2015	JapicCTI-111507	221	Unclear	Low	Low	Unclear	Low	High
Seino 2016	NCT01572740	257	Low	Low	Low	Unclear	Low	Low
Seino 2018	NCT02254291	308	Low	Low	High	Low	Low	Low
Shaddinger 2019	NCT02683746	308	Low	Low	Low	Low	High	Low
Shah 2011	Not provided	200	Unclear	Unclear	Unclear	Unclear	Unclear	High
Shankar 2017	NCT01590797	467	Unclear	Low	Low	Unclear	Low	Low
Shankar 2017a	NCT01755156	402	Unclear	Low	Low	Unclear	Low	High
Shestakova 2018	NCT02794792	165	Low	Low	Low	Unclear	Low	Low
Shibuya 2018	UMIN000016090	32	Unclear	Unclear	High	Unclear	Low	High
SIMPLE	NCT01966978	120	Unclear	Unclear	High	Unclear	High	Low
Sit2Mix	Not provided	389	Unclear	Unclear	High	Unclear	High	High
Sitagliptin 019	NCT00086502	353	Unclear	Low	Low	Unclear	High	High
Sitagliptin 020	NCT0086515	701	Unclear	Low	Low	Unclear	High	High
Sitagliptin 021	NCT00087516	726	Unclear	Low	Low	Unclear	Low	High
Sitagliptin 024	NCT00094770	1172	Unclear	Low	Low	Unclear	High	Low
Sitagliptin 035	Not provided	441	Low	Low	Low	Unclear	High	High

Sitagliptin 036	NCT00103857	355	Unclear	Low	Low	Unclear	Low	Low
Sitagliptin 049	NCT00449930	1050	Low	Low	Low	Unclear	High	Low
Sitagliptin 051	NCT00395343	641	Low	Unclear	Unclear	Unclear	Low	Low
SMART	NCT02243176	485	Low	Low	High	Unclear	Low	Low
Smith 2005	Not applicable	48	Unclear	Low	Low	Unclear	Unclear	High
Søfteland 2017	NCT01734785	333	Low	Low	Low	Unclear	Low	Low
Sohn 2008	Not provided	19	Unclear	Unclear	High	Unclear	High	High
Sone 2019	NCT02589639	266	Low	Low	Low	Unclear	Low	Low
South Danish Diabetes Study	Not provided	140	Low	Unclear	High	High	High	High
SPEAD-A	UMIN000005311	341	Unclear	Unclear	High	Unclear	Low	Low
SPECIFY	NCT02280486	388	Low	Low	High	Unclear	High	High
Spengler 1989	Not applicable	55	Unclear	Unclear	High risk	Unclear	Unclear	High
SPIKE	UMIN000007396	282	Unclear	Unclear	High	Unclear	Low	Low
SPOTLIGHT	NCT01225081	152	Unclear	Unclear	High	Unclear	High	High
SPREAD-DIMCAD	NCT00513630	304	Low	Low	Low	Low	Unclear	Low
Sridhar 2013	NCT01206400	50	Unclear	Low	Low	Unclear	Low	High
St. John Sutton 2002	Not applicable	203	Unclear	Unclear	High	Unclear	Unclear	High
Standl 1999	Not applicable	48	Unclear	Low	Low	Unclear	High	High
Standl 2001	Not applicable	133	Unclear	Low	Low	Unclear	High	High
START	NCT02273050	424	Low	Low	Low	Unclear	High	Low
START-J	NCT01183104;	305	Low	Unclear	High	Unclear	Low	Low
Stewart 2006	Not provided	526	Unclear	Low	Low	Unclear	High	High
Stocker 2007	Not provided	92	Low	Unclear	High	Unclear	High	High
STOP-OB	UMIN000026161	64	Unclear	Unclear	High	Unclear	Low	High
Strojek 2009	NCT00469092	480	Low	Low	High	Unclear	Low	Low
Strojek 2011	NCT00680745	596	Low	Low	Low	Unclear	Low	Low
Strøm Halden 2019	NCT03157414	44	Low	Low	Low	Unclear	High	Low
Su 2014	Not provided	600	Unclear	Low	Low	Unclear	High	High
SUCCESS	UMIN000004675	119	Unclear	Unclear	High	Unclear	Low	Low
SUMER	Not provided	400	Unclear	Unclear	High	Unclear	High	Low
Sun 2006	Not provided	60	Unclear	Unclear	Unclear	Unclear	Low	High
Sun 2016	ChiCTR-TRC-	108	Unclear	Unclear	High	Unclear	Low	Low
SUPER	NCT02104804	462	Unclear	Low	Low	Unclear	Low	Low
SUSTAIN 1	NCT02054897	387	Low	Low	Low	Low	Low	Low
SUSTAIN 2	NCT01930188	1225	Low	Low	Low	Unclear	High	High
SUSTAIN 4	NCT02128932	1082	Low	Low	Low	Low	Low	Low
SUSTAIN 5	NCT02305381	396	Low	Low	Low	Low	Low	Low
SUSTAIN 6	NCT01720446	3297	Low	Low	Low	Low	Low	Low
SUSTAIN 8	NCT03136484	788	Low	Low	Low	Low	Low	Low
SUSTAIN 9	NCT03086330	302	Low	Low	Low	Low	Low	Low
SUSTAIN CHINA MRCT	NCT03061214	868	Low	Low	Low	Low	High	Low
Suzuki 2014	Not provided	40	Unclear	Unclear	High	Unclear	High	High
SWIM	NCT01341717	440	Low	Low	High	Unclear	Low	High
Takagi 2003	Not applicable	44	Unclear	Unclear	High	Unclear	Unclear	High
Takase 2007	Not provided	39	Low	Low	High	Unclear	Low	High
Takashima 2018	UMIN000031454	40	Unclear	Unclear	High	Unclear	Unclear	High
Tao 2018	ChiCTR-IPR-	42	Low	Unclear	High	Unclear	High	High
Taskinen 2011	NCT00601250	700	Unclear	Low	Low	Unclear	Low	High
TECOS	NCT00790205	14671	Low	Low	Low	Low	Low	Low
T-Emerge 1	NCT00744926	373	Unclear	Low	Low	Unclear	High	Low
T-Emerge 3	NCT00744367	326	Unclear	Low	Low	Unclear	High	Low
T-Emerge 4	NCT00754988	666	Unclear	Low	Low	Unclear	Low	High
T-Emerge 5	NCT00755287	1049	Unclear	Unclear	High	Unclear	High	High
T-Emerge 6	NCT00909597	760	Unclear	Low	Low	Unclear	High	Low
T-Emerge 7	NCT00823992	305	Unclear	Unclear	Unclear	Low	High	Low
Teramoto 2007	Not provided	92	Unclear	Unclear	High	Unclear	Low	High
Teupe 1991	Not applicable	100	Unclear	Unclear	Unclear	Unclear	High	Low
Thrasher 2014	NCT01194830	226	Low	Low	Low	Unclear	Low	Low

TIDE	NCT00879970	1332	Unclear	Low	Low	Low	High	Low
Tinahones 2017	NCT01778049	478	Low	Low	Low	Unclear	Low	Low
Tofogliflozin 003	Japic CTI-101349	220	Unclear	Low	Low	Unclear	High	Low
Tolman 2009	NCT00494312	2120	Unclear	Low	Low	Unclear	High	Low
TOPSCORE	UMIN000017861	75	Unclear	Unclear	High	Unclear	High	High
TOSCA.IT	NCT00700856	3028	Low	Low	High	Low	High	Low
Tripathy 2013	NCT01223196	29	Unclear	Unclear	High	Unclear	High	High
TROICA	NCT01990469	218	Unclear	Low	Low	Unclear	High	Low
Truitt 2010	NCT00143520	532	Unclear	Low	Low	Unclear	High	Low
Türkmen Kemal 2007	Not provided	46	Unclear	Unclear	Unclear	Unclear	Low	High
UKPDS 44	Not applicable	1946	Unclear	Low	Low	Unclear	High	High
Umpierrez 2006	Not provided	203	Unclear	Unclear	High	Unclear	High	High
Vähätalo 2007	Not provided	41	Unclear	Unclear	Unclear	Unclear	Unclear	High
Van Eyk 2019	NCT02660047	47	Unclear	Low	Low	Low	Low	High
Van Gaal 2014	NCT00976937	319	Unclear	Low	Low	Unclear	High	Low
Vanderheiden 2016	NCT01505673	71	Low	Low	Low	Unclear	Low	High
Varghese 2009	Not provided	57	Unclear	Low	Low	Unclear	High	High
Veleba 2015	EudraCT number	69	Low	Unclear	High	Unclear	High	High
VERTIS Asia	NCT02630706	506	Low	Low	Low	Low	Low	Low
VERTIS CV	NCT01986881	8246	Low	Low	Low	Low	Low	Low
VERTIS FACTORIAL	NCT02099110	745	Low	Low	Low	Unclear	Low	Low
VERTIS-MET	NCT02033889	621	Low	Low	Low	Unclear	Low	Low
VERTIS MONO	NCT01958671	461	Low	Low	Low	Unclear	Low	Low
VERTIS RENAL	NCT01986855	467	Low	Low	Low	Unclear	High	Low
VERTIS SITA2	NCT02036515	464	Low	Low	Low	Unclear	Low	Low
VERTIS SU	NCT01999218	1326	Low	Low	Low	Unclear	High	Low
Vianna 2017	NCT01679899	42	Low	Unclear	High	Low	Low	High
VICTORY	NCT00169832	193	Unclear	Low	Low	Unclear	Low	Low
VISION	NCT01541956	2985	Unclear	Unclear	High	Unclear	Low	Low
VIVIDD	NCT00894868	254	Low	Low	Low	Low	High	Low
Vongthavaravat 2002	Not applicable	348	Unclear	Unclear	High	Unclear	High	High
Wajcberg 2007	Not provided	31	Unclear	Low	Low	Unclear	Unclear	High
Wang 2005	Not applicable	70	Unclear	Unclear	High	Unclear	Low	Low
Wang 2013	Not provided	90	Low	Unclear	High	Unclear	Low	High
Wang 2015	Not provided	90	Unclear	Unclear	High	Unclear	High	High
Wang 2016	NCT01215097	306	Low	Low	Low	Unclear	Low	Low
Wang 2016a	Not provided	28	Unclear	Unclear	Unclear	Unclear	Unclear	High
Wang 2017	NCT01177384	381	Low	Low	Low	Unclear	High	Low
Wang 2019	NCT01648582	744	Low	Low	High	Low	Low	Low
Wang 2020	Not provided	60	Low	Unclear	high	Unclear	Unclear	High
Watanabe 2005	Not applicable	27	Unclear	Unclear	High	Unclear	Low	High
Wolever 2000	Not applicable	152	Unclear	Unclear	High	Unclear	High	High
Wolffenbuttel 1999	Not applicable	310	Unclear	Low	Low	Unclear	High	High
Wolffenbuttel 2000	Not applicable	584	Unclear	Low	Low	Unclear	High	High
Wong 2005	Not applicable	52	Low	Unclear	High	Unclear	Low	Low
Wu 2014	Not applicable	93	Unclear	Unclear	High	Unclear	Unclear	High
Wu 2015	Not provided	57	Low	Low	Low	Unclear	Low	High
Xiao 2015	Not provided	80	Low	Low	High	Unclear	Low	High
Xiao 2016	Not provided	41	Low	Low	High	Unclear	Low	Low
Xu 2017	NCT017909305	2195	Low	Low	High	Unclear	Low	Low
Yakibu 2017	ISCTRN33414972	366	Low	Unclear	High	Unclear	Low	High
Yale 2013	Not provided	269	Low	Low	Low	Unclear	High	High
Yamakage 2019	UMIN000021479	54	Low	Low	High	Unclear	Low	High
Yamamoto 2018	UMIN000028313	25	Unclear	Unclear	High	Unclear	High	High
Yamanouchi 2005	Not applicable	114	Low	Low	High	Unclear	Low	High
Yamasaki 2005	Not applicable	103	Unclear	Unclear	High	Unclear	Unclear	High
Yan 2019	NCT02147925	75	Low	Unclear	High	Unclear	Low	High
Yang 2002	Not applicable	64	Unclear	Low	Low	Unclear	Unclear	High

Yang 2011	NCT00661362	570	Low	Low	Low	Unclear	High	Low
Yang 2012	NCT00813995	395	Low	Low	Low	Unclear	Low	Low
Yang 2013	Not provided	182	Unclear	Low	Low	Unclear	Low	High
Yang 2015	Not provided	109	Unclear	Low	Low	Unclear	High	High
Yang 2015a	NCT01357252	279	Unclear	Low	Low	Unclear	Low	Low
Yang 2016	NCT01095666	444	Low	Low	Low	Unclear	High	Low
Yang 2018	NCT02096705	272	Low	Low	Low	Unclear	Low	Low
Yee 2010	NCT00231387	57	Unclear	Low	Low	Unclear	Low	Low
Yki-Järvinen 1999	Not applicable	31	Low	Unclear	High	Unclear	Low	High
Yki-Järvinen 2013	NCT00954447	1261	Low	Low	Low	Unclear	Low	Low
Yoon 2011	NCT00397631	520	Unclear	Low	Low	High	High	Low
Yoon 2011a	Not provided	349	Unclear	Low	Low	Unclear	High	High
Yuan 2012	Not provided	59	Low	Unclear	High	Unclear	Low	High
Zang 2016	NCT02008682	368	Low	Low	Low	Unclear	Low	Low
ZEUS II	NCT02831361	283	Low	Low	Low	Unclear	Low	Low
Zhang 2020	Not provided	60	Low	Low	High	Unclear	Unclear	High
Zheng 2019	Not provided	91	Unclear	Unclear	Unclear	Unclear	Unclear	High
Zhu 2003	Not applicable	554	Unclear	Unclear	Unclear	Unclear	High	Low
Zib 2007	Not provided	32	Unclear	Unclear	High	Unclear	Low	High

Appendix 4 Network plots for each outcome

The size of the circle in each network is proportional to the number of participants randomly assigned to the treatment comparison. The width of each line is proportional to the number of trials comparing the two connected treatments. When a line is absent, this indicates that there were no head-to-head trials of the corresponding treatments reporting the outcome of interest. The number provided for each treatment class indicates the number of patients assigned to the treatment in the network.

Figure 1 Network plot for all-cause mortality

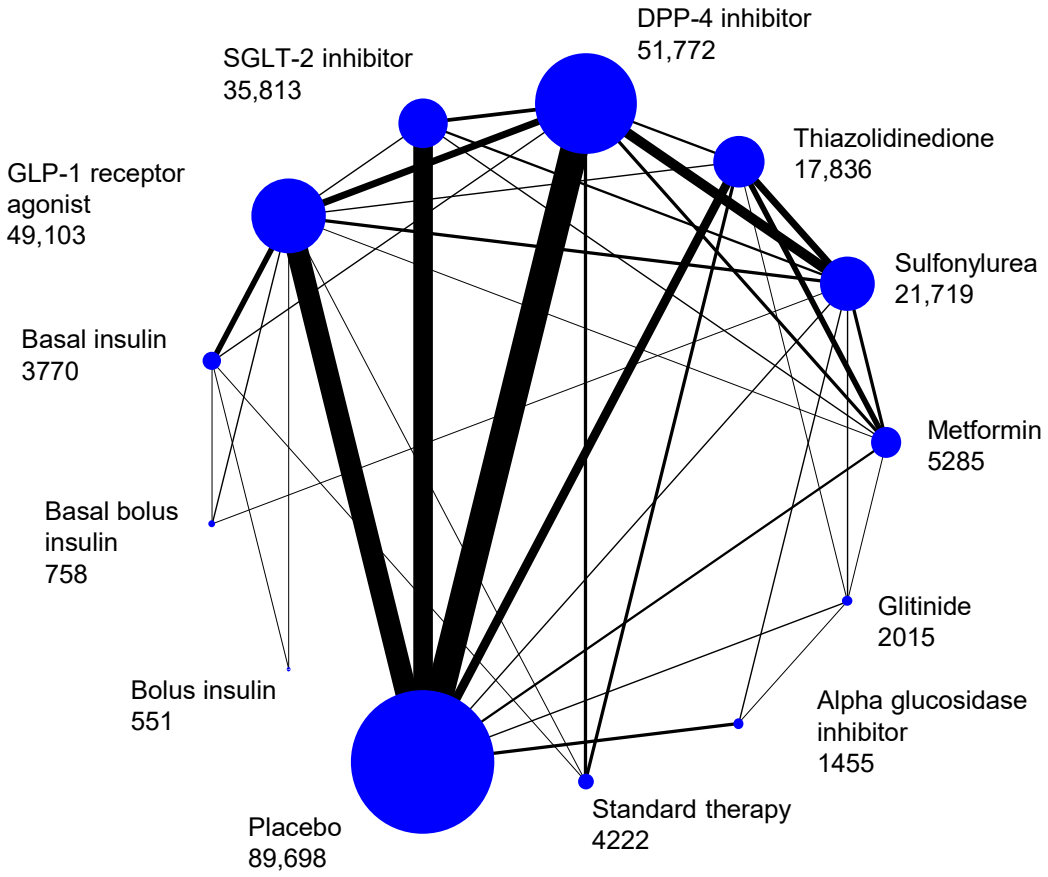


Figure 2 Network plot for cardiovascular mortality

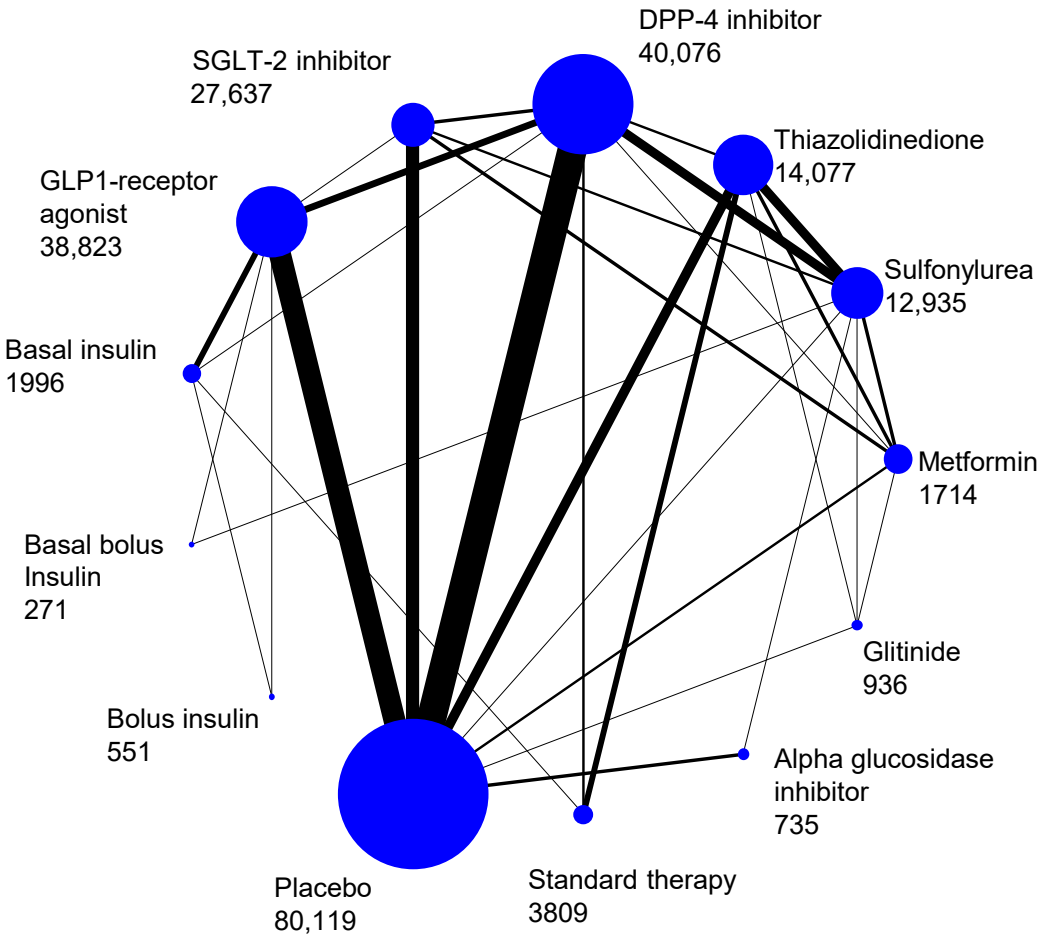


Figure 3 Network plot for nonfatal myocardial infarction

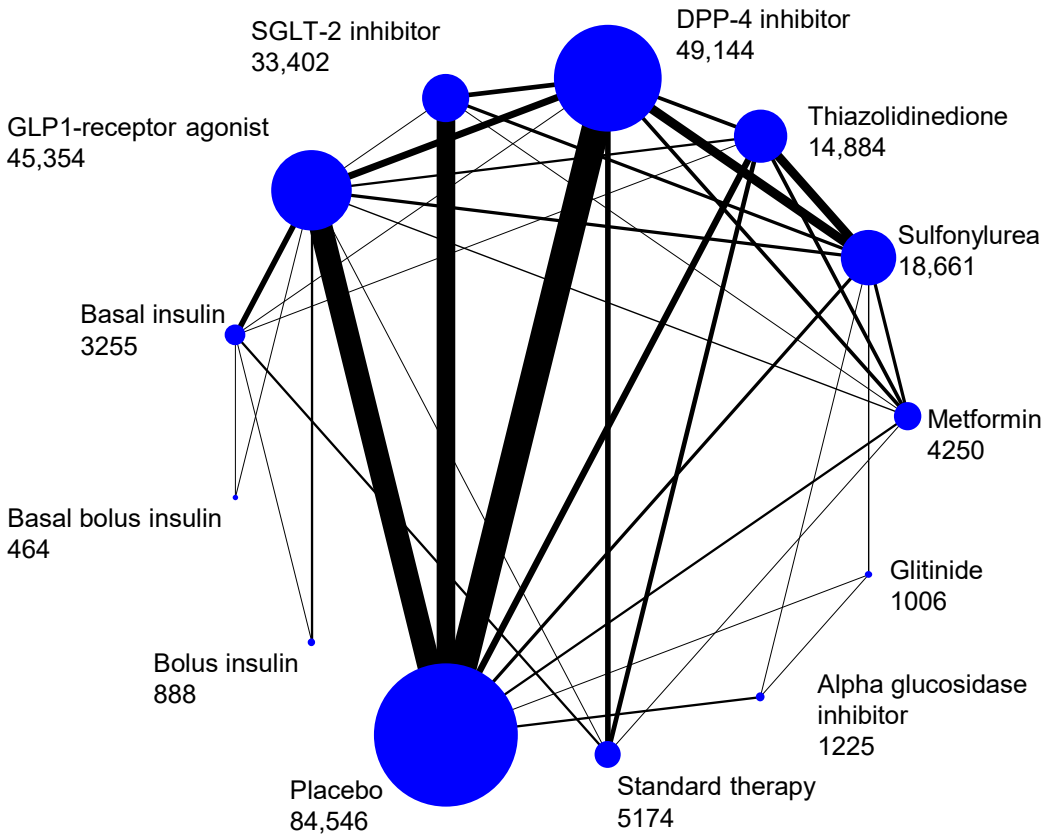


Figure 4 Network plot for nonfatal stroke

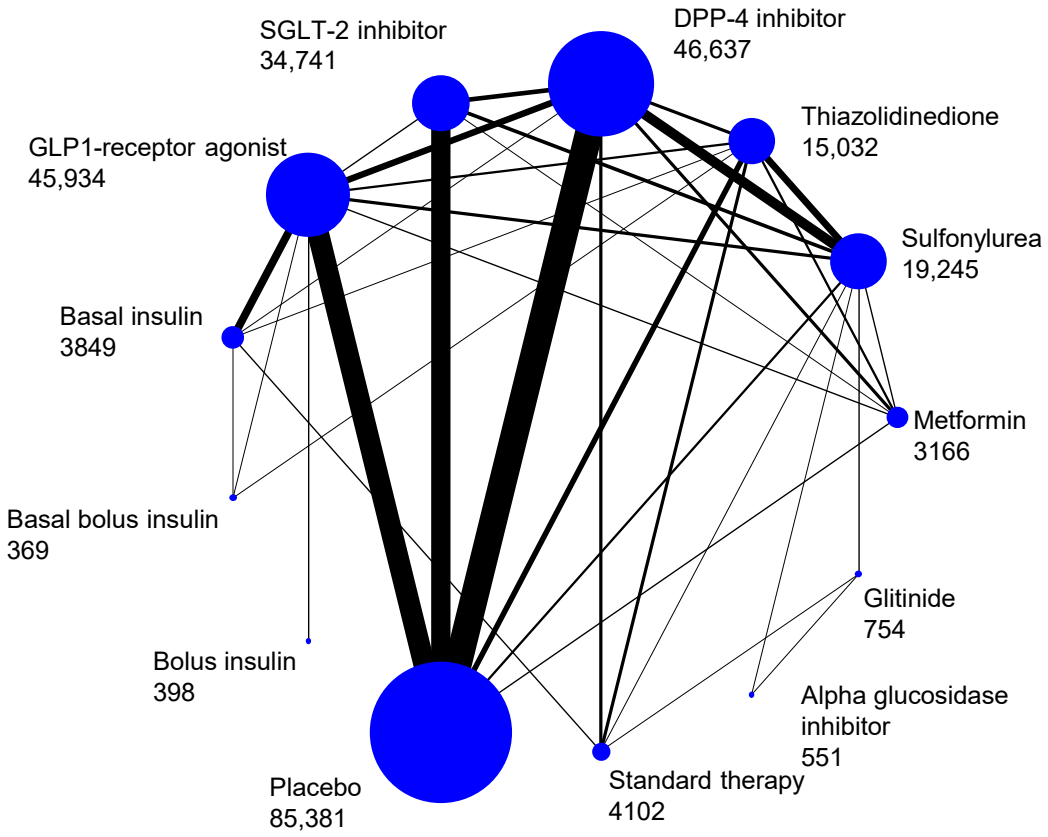


Figure 5 Network plot for kidney failure

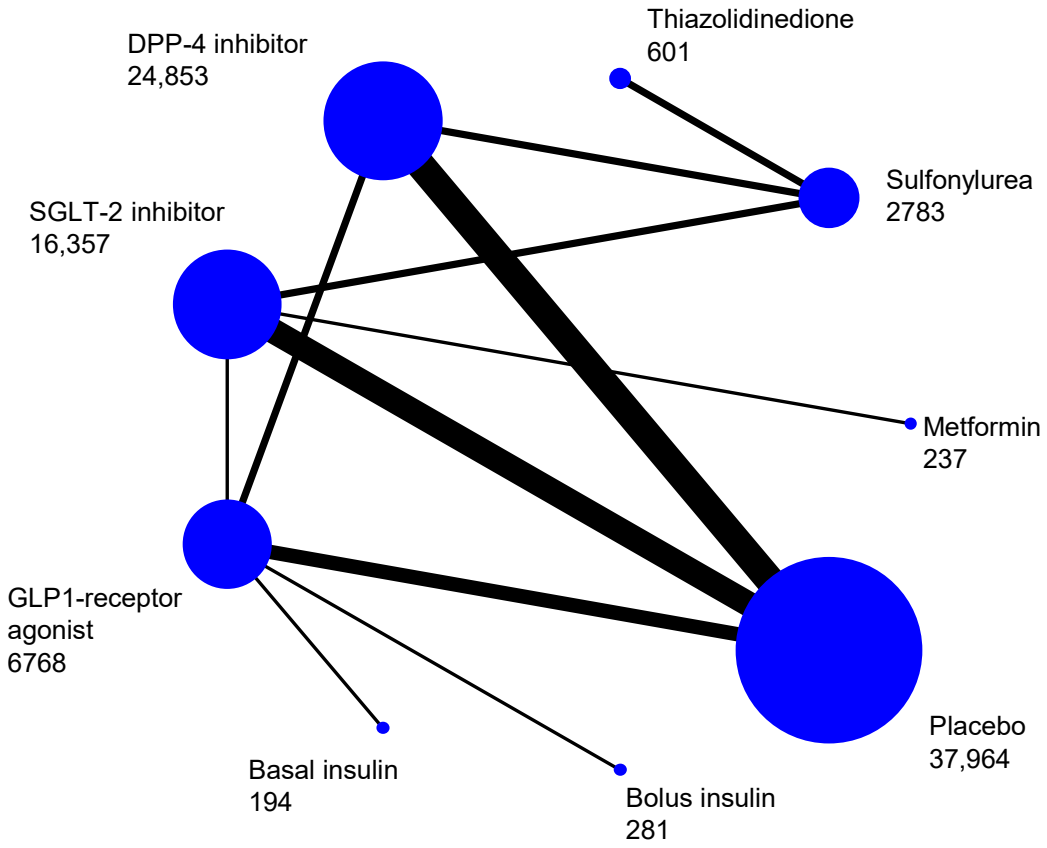


Figure 6 Network plot for hospitalisation for heart failure

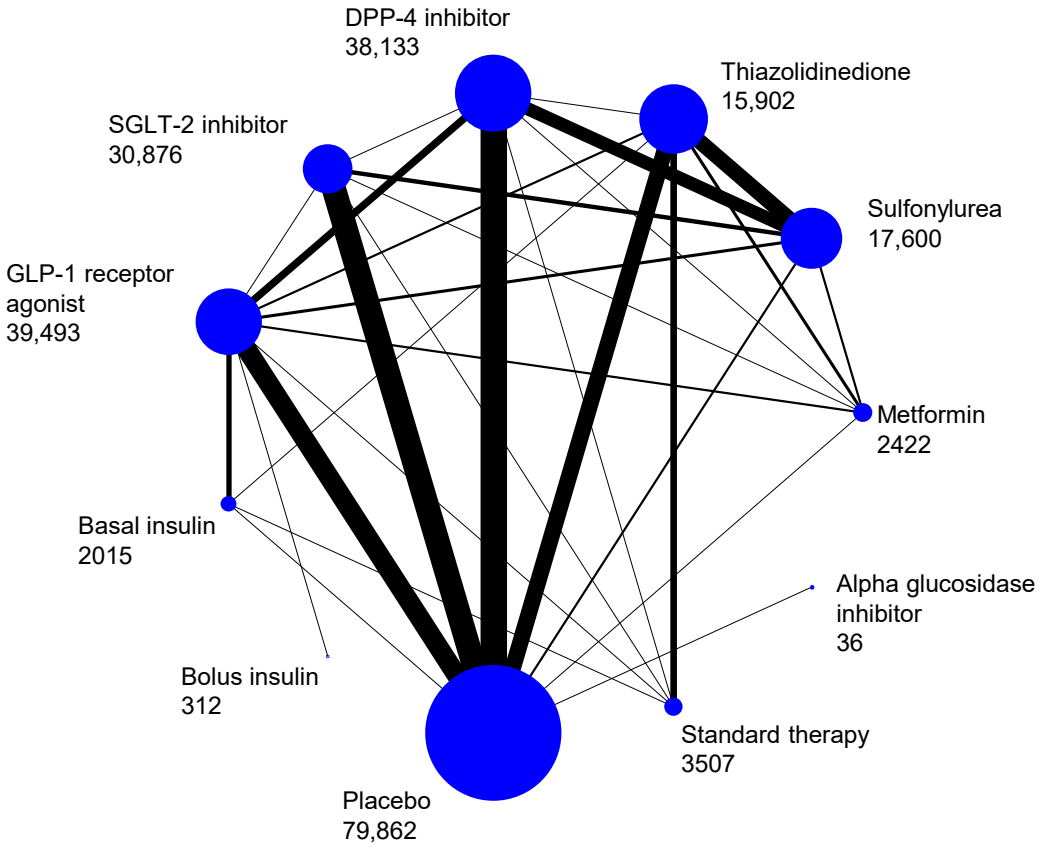


Figure 7 Network plot for severe hypoglycaemia

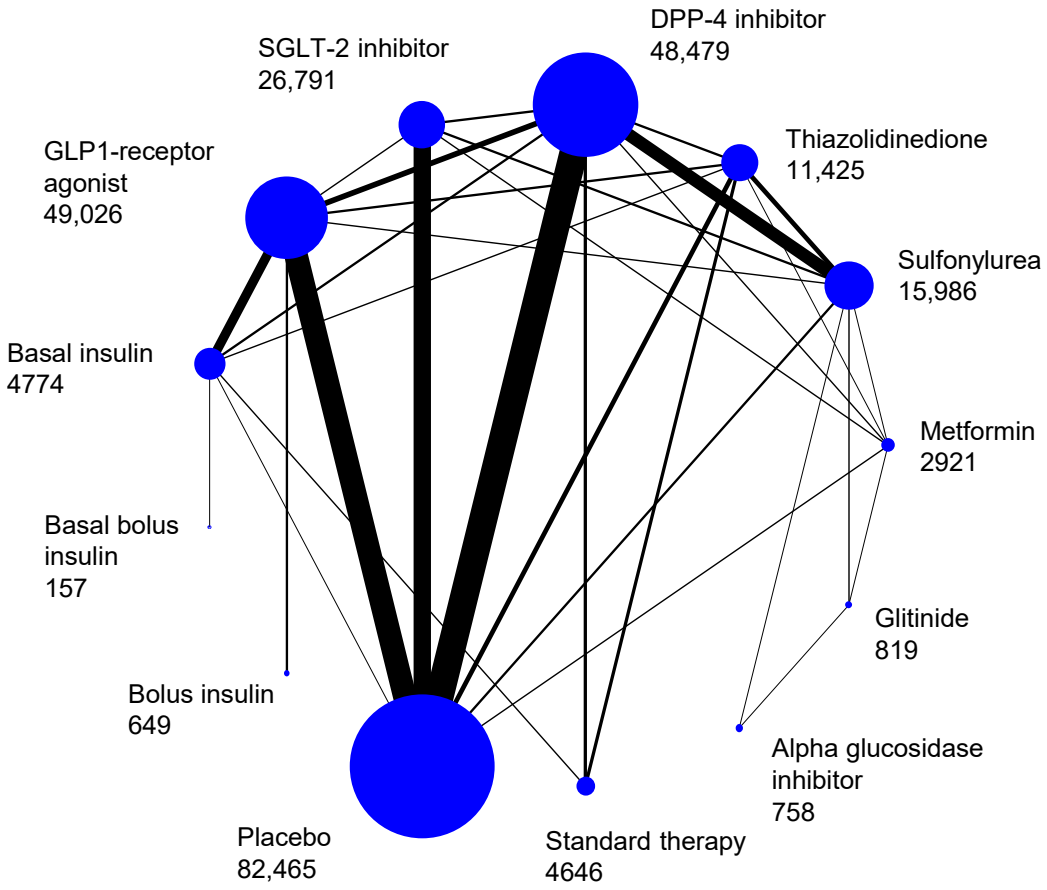


Figure 8 Network plot for blindness

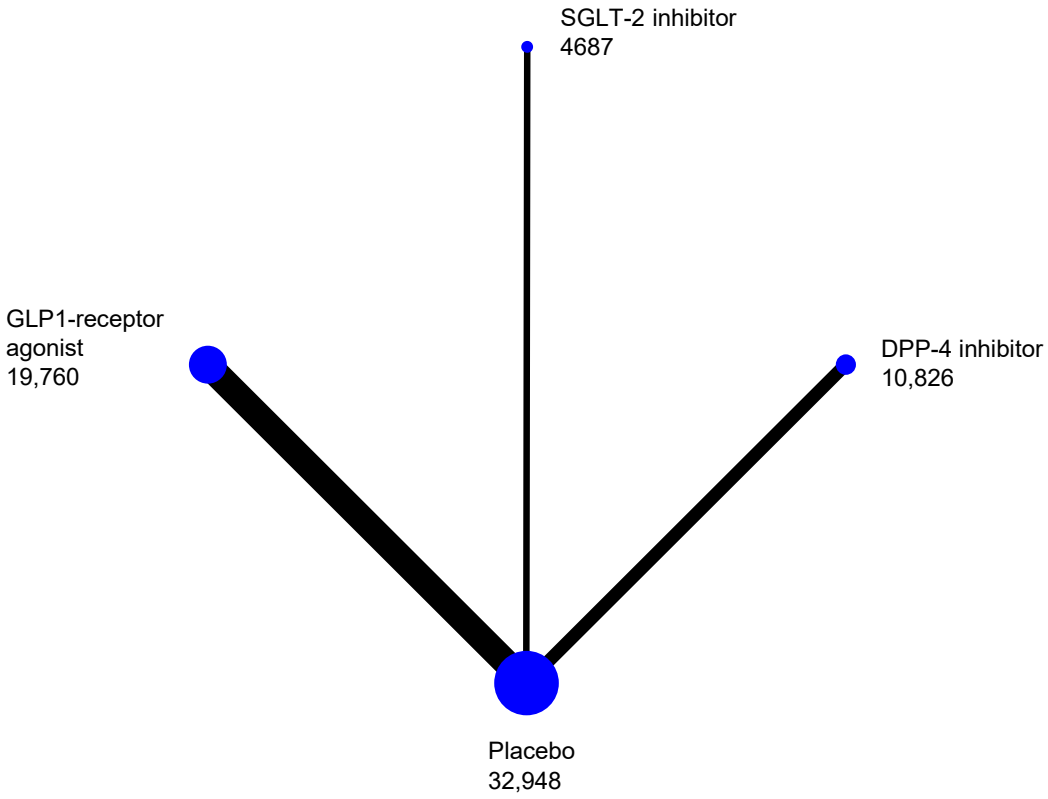


Figure 9 Network plot for health-related quality of life

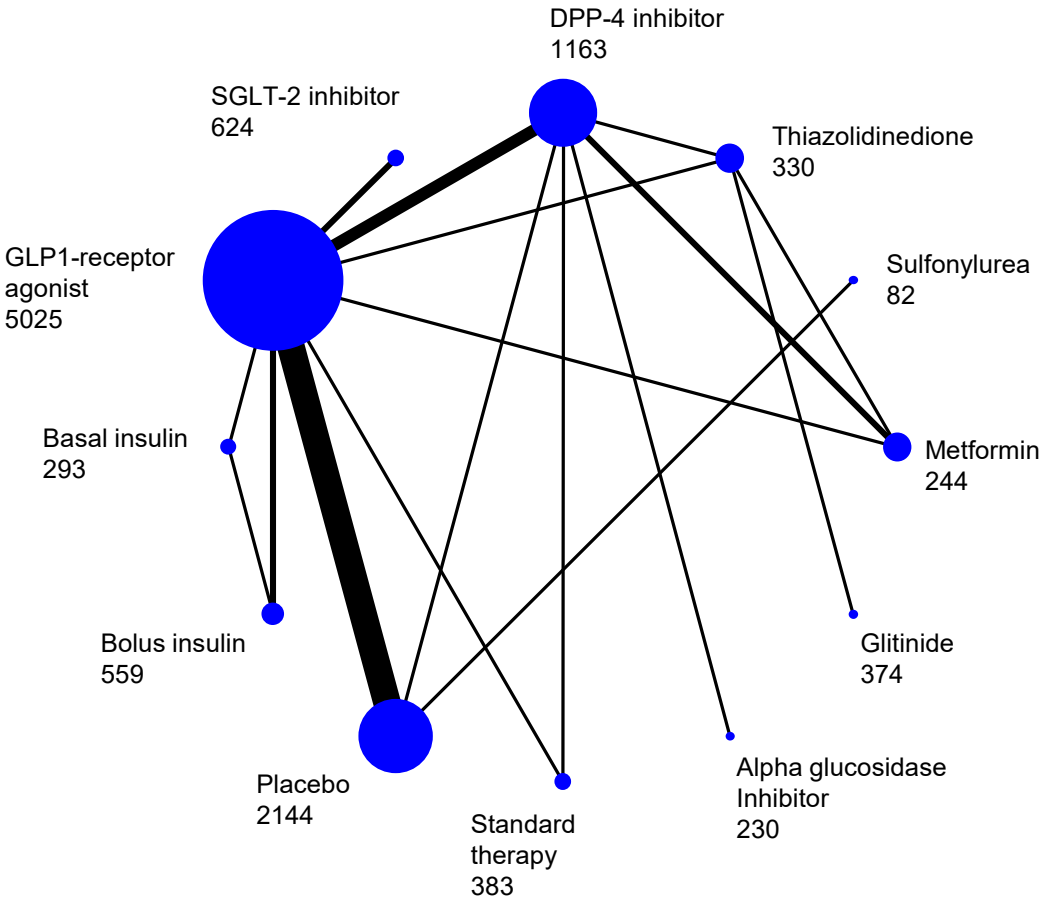


Figure 10 Network plot for body weight

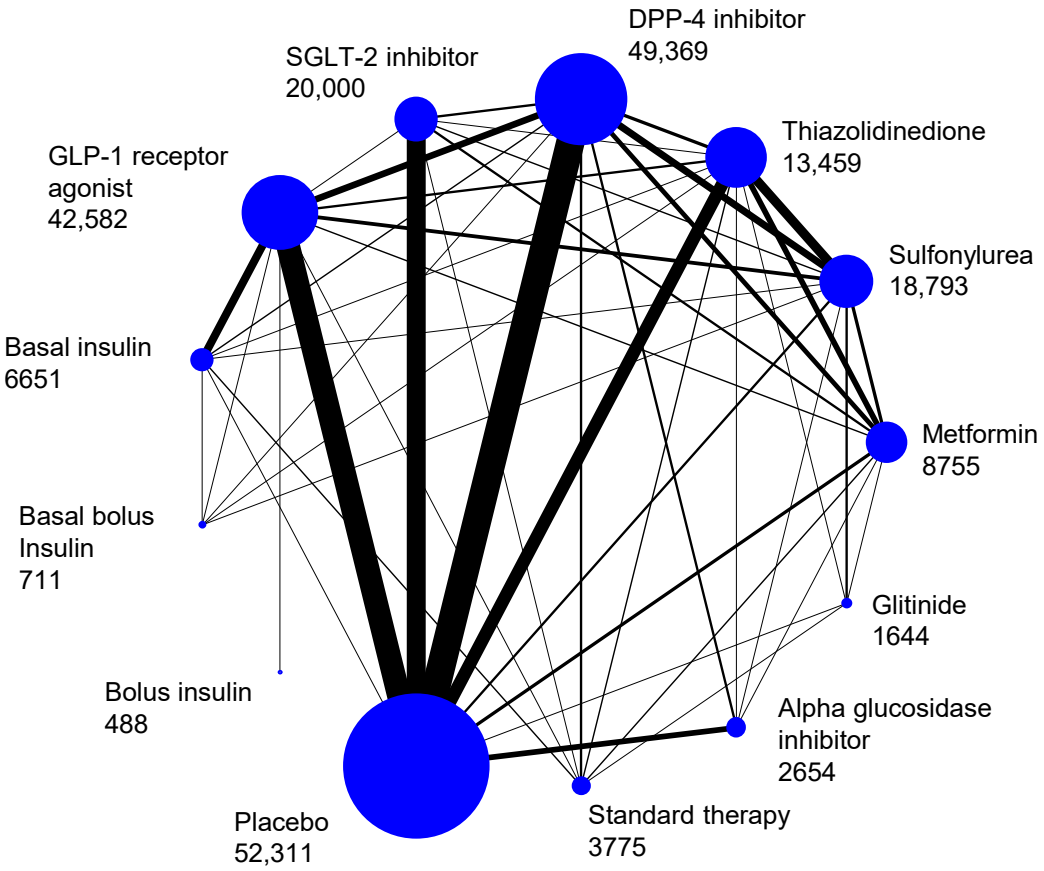


Figure 11 Network plot for amputation

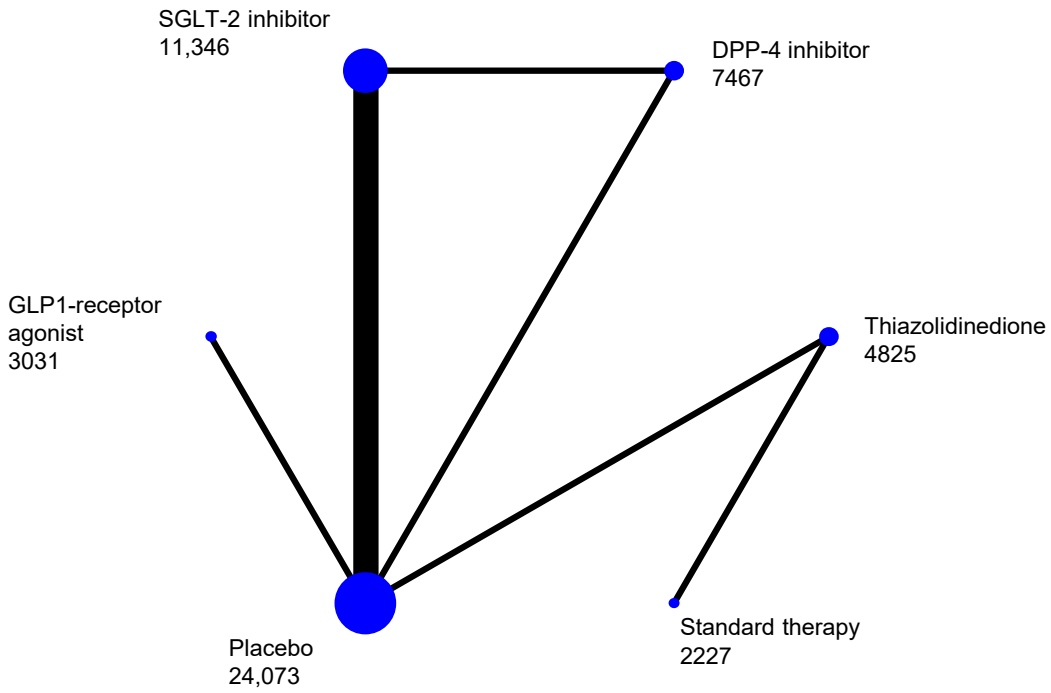


Figure 12 Network plot for neuropathic pain

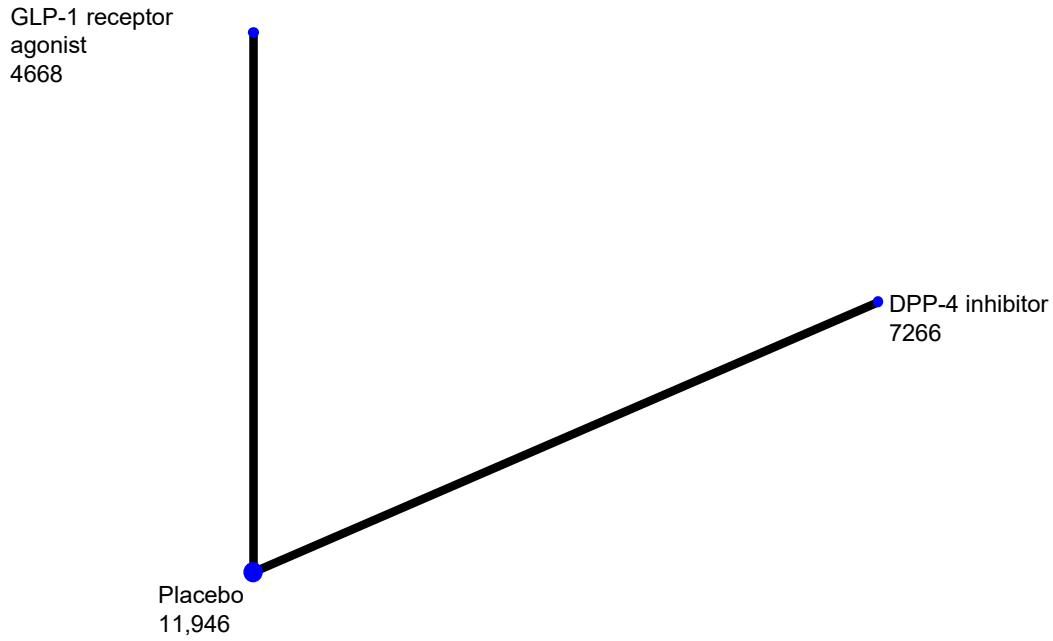


Figure 13 Network plot for diabetic ketoacidosis

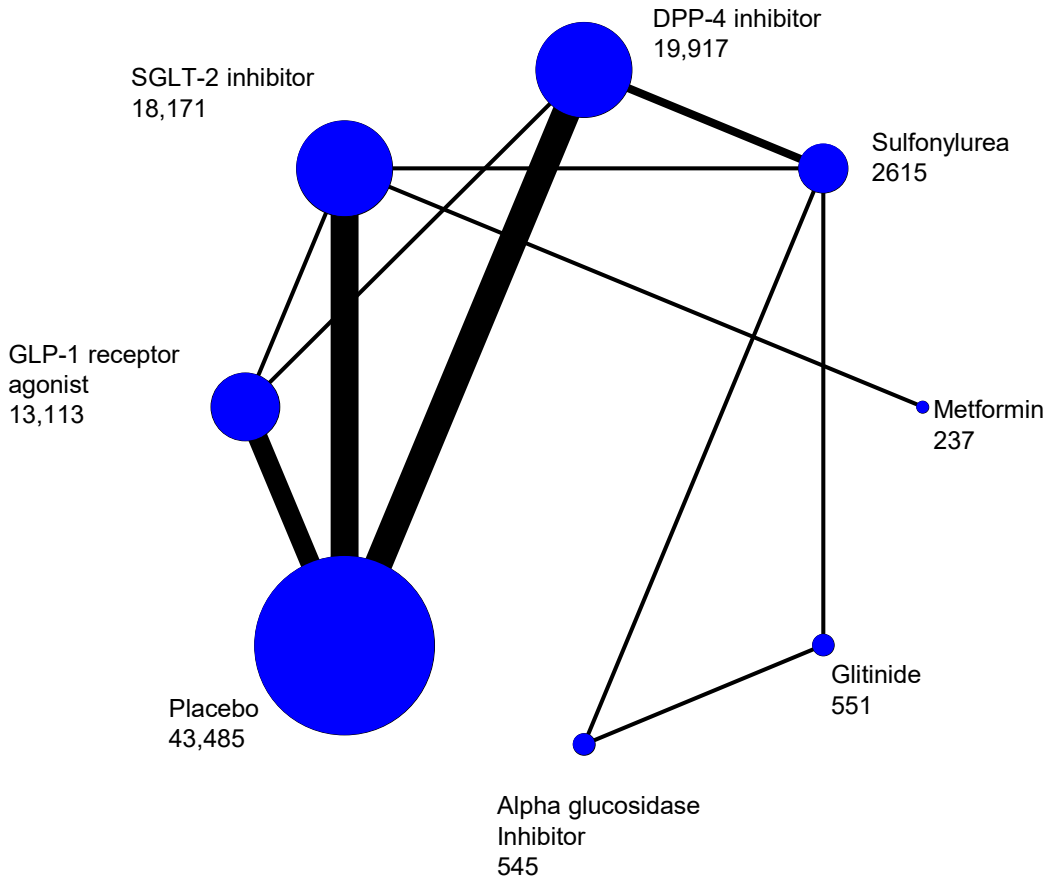


Figure 14 Network plot for serious hyperglycaemia

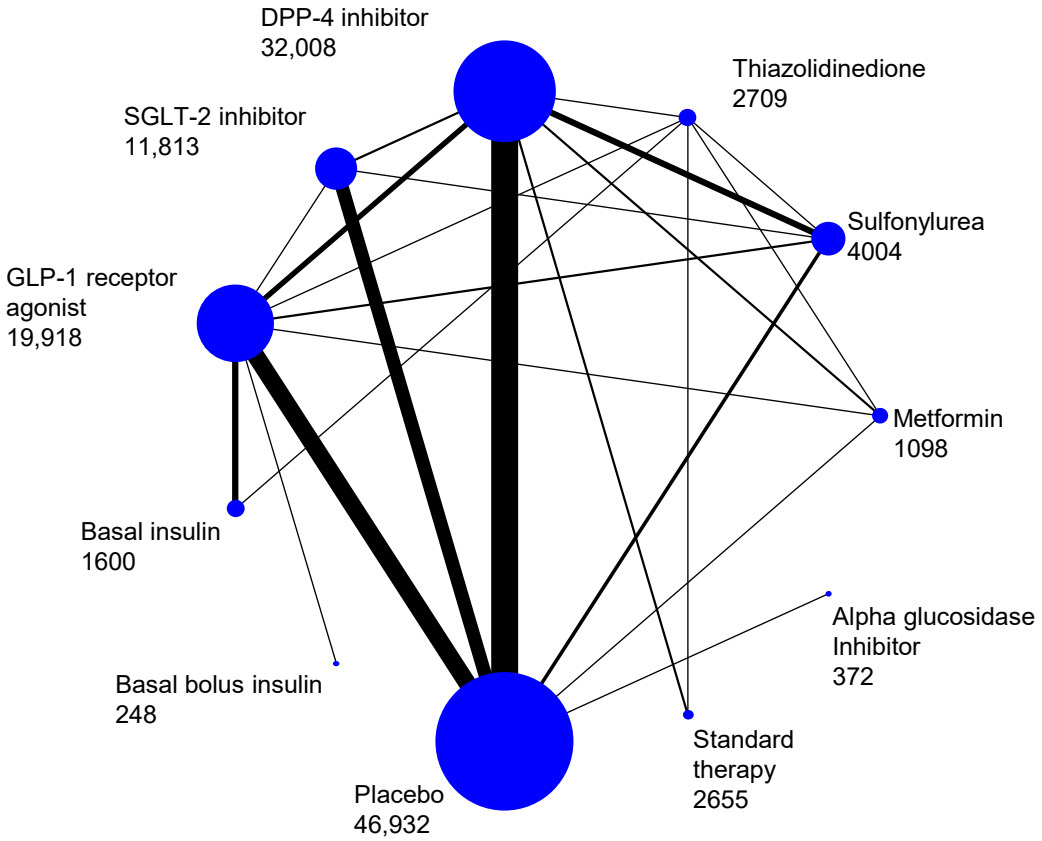


Figure 15 Network plot for genital infection

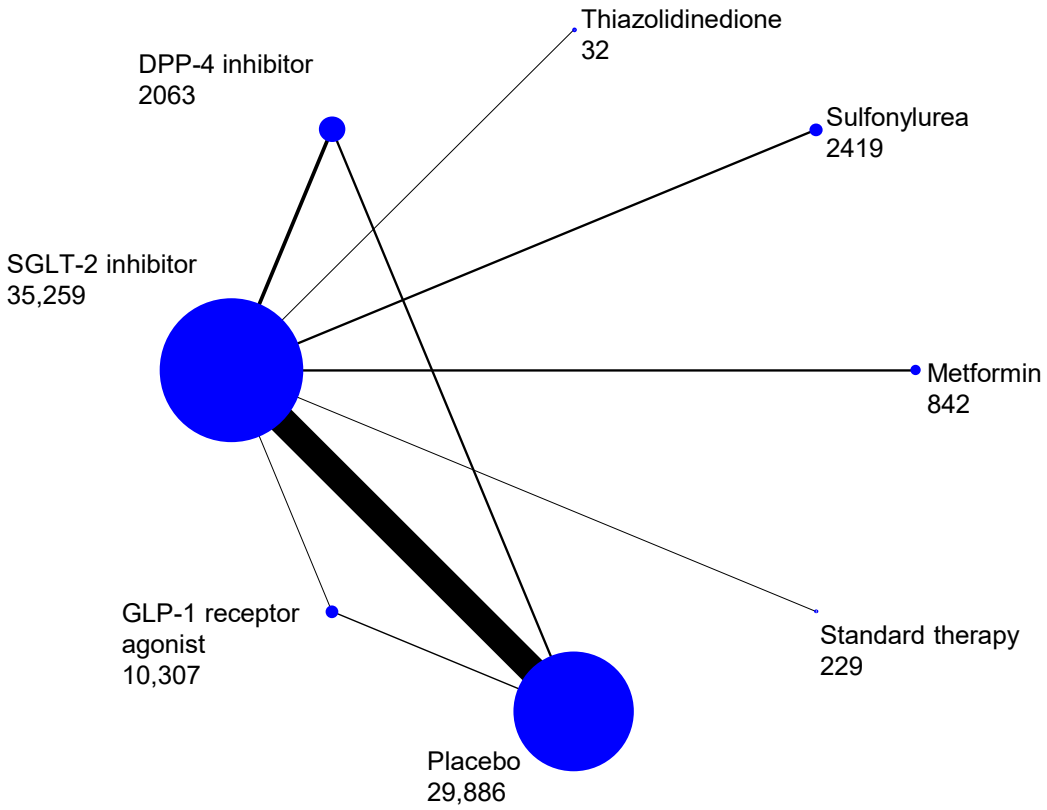


Figure 16 Network plot for Fournier gangrene

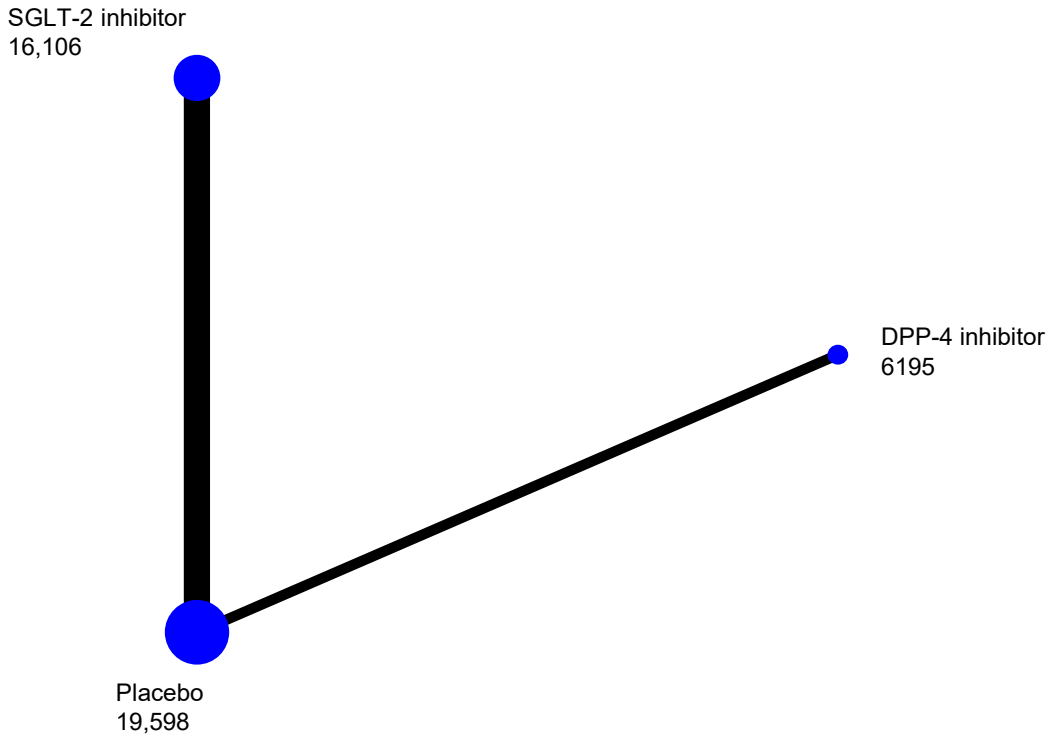


Figure 17 Network plot for severe gastrointestinal events

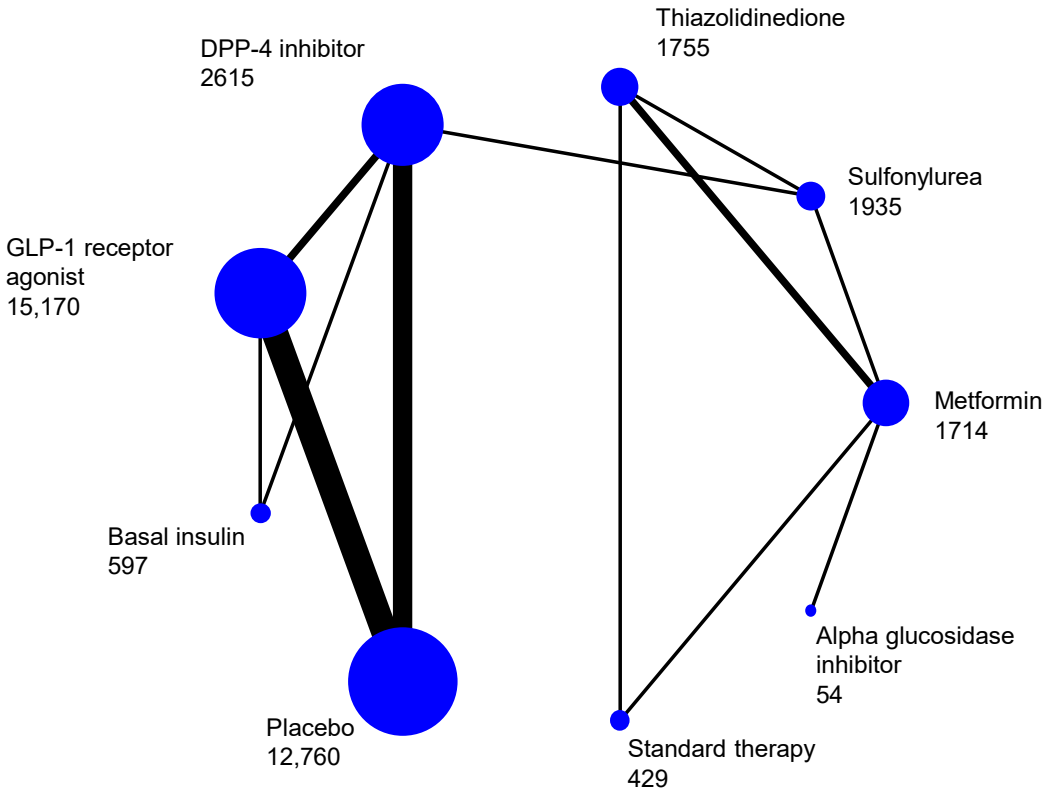


Figure 18 Network plot for pancreatic cancer

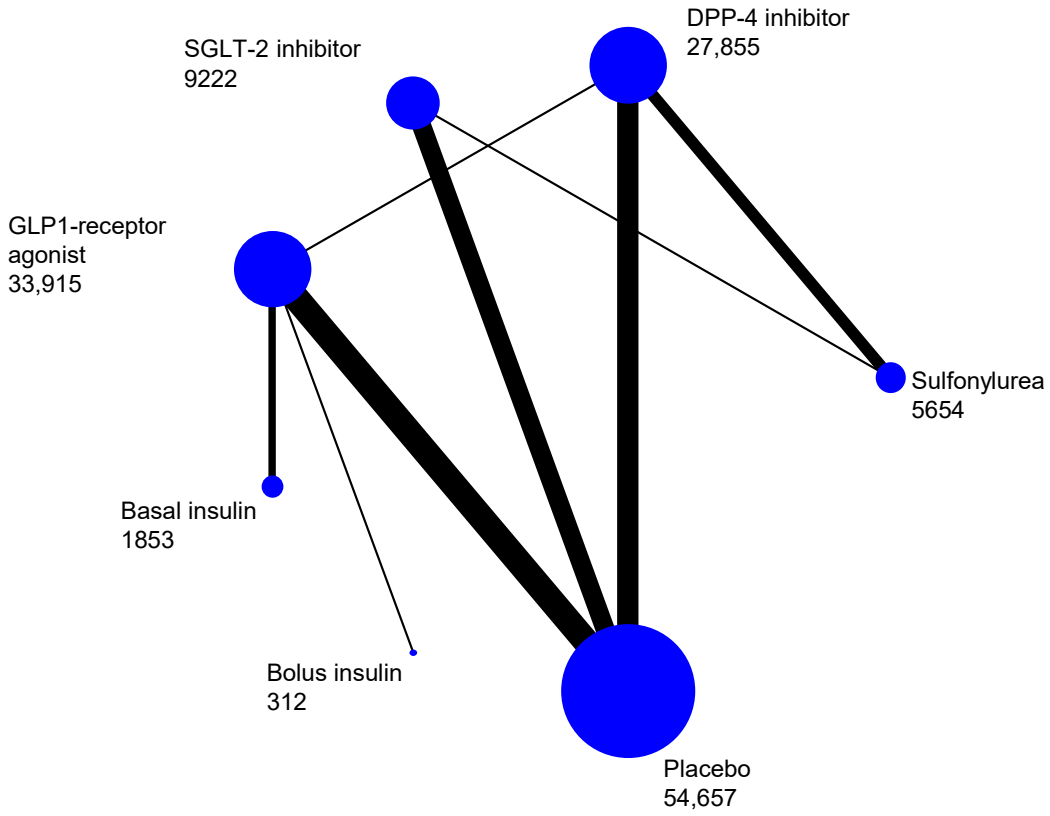


Figure 19 Network plot for pancreatitis

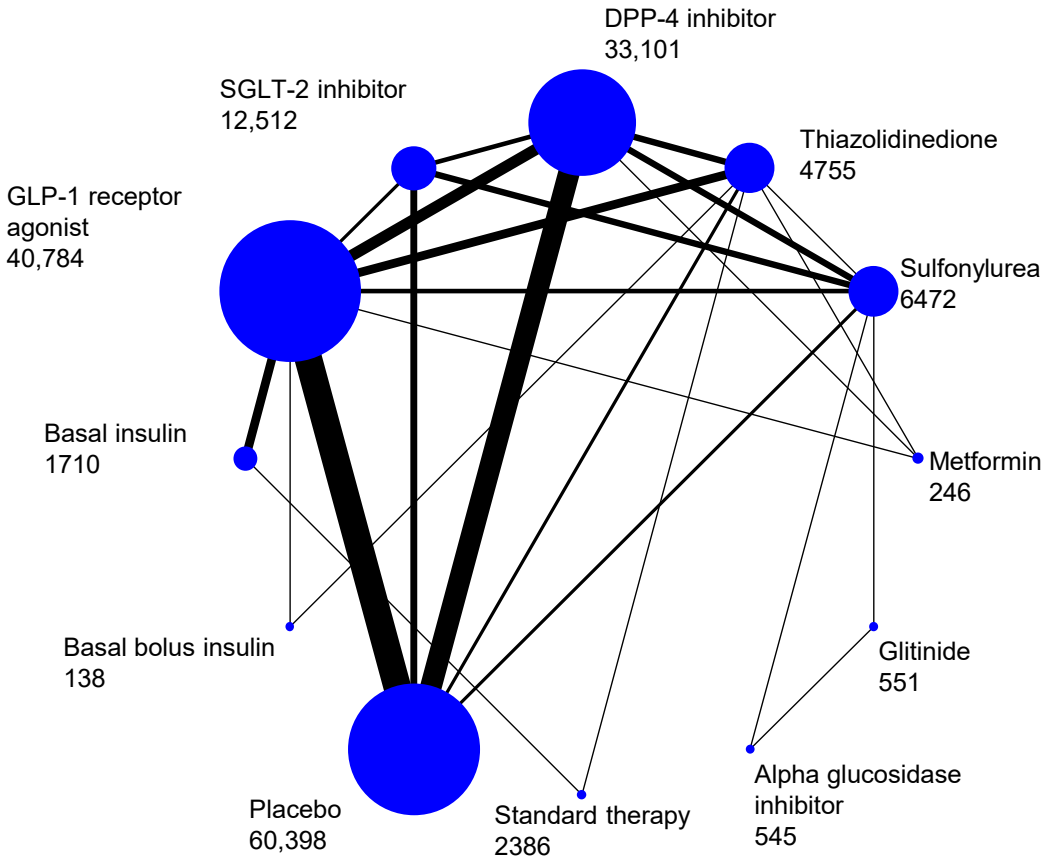
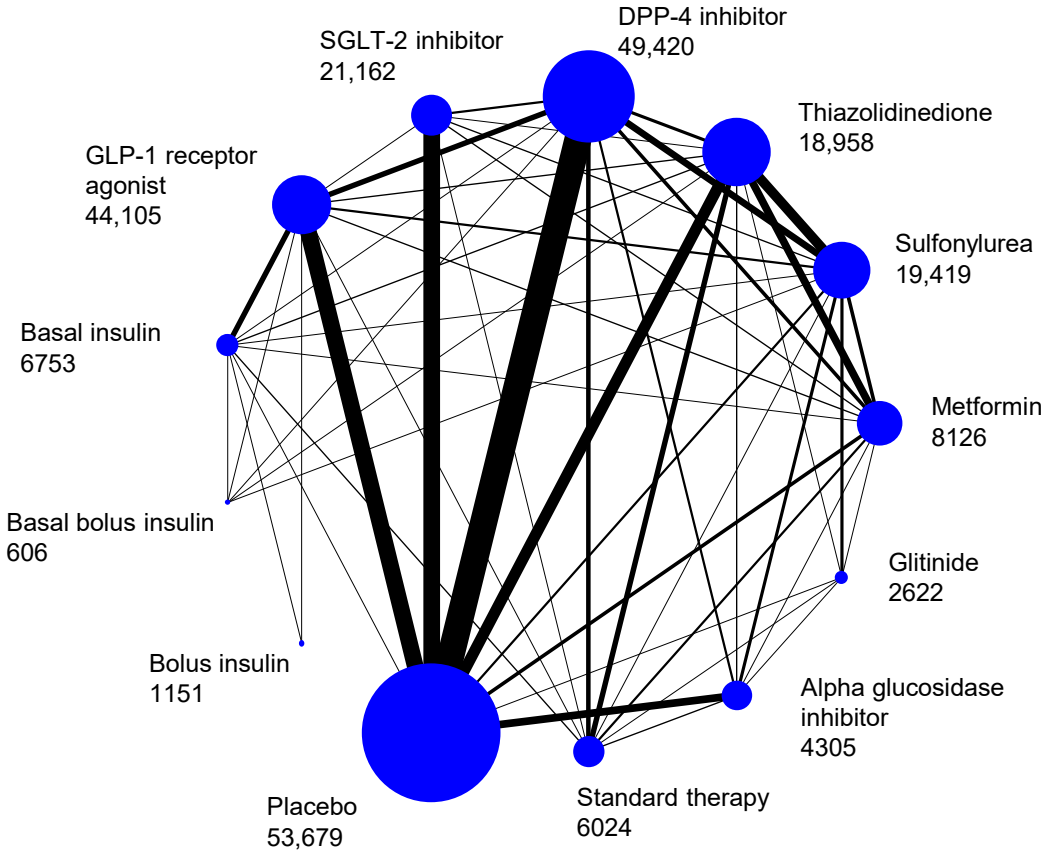


Figure 20 Network plot for glycated haemoglobin A1C



Appendix 5 Evaluations of network inconsistency and heterogeneity

	Global consistency		Network heterogeneity
Clinical outcome	**Chi square**	**P value**	**Tau squared**
All-cause mortality	21.1	0.999	0.08
Cardiovascular mortality	13.1	0.983	0.11
Nonfatal myocardial infarction	22.0	0.997	0.03
Nonfatal stroke	15.7	0.999	<0.001
Kidney failure	0.15	0.985	<0.001
Hospitalisation for heart failure	10.3	0.998	<0.001
Severe hypoglycaemia	24.6	0.743	0.15
Blindness	0.00	0.999	Fixed model
Eye disease requiring intervention	…	…	…
Health-related quality of life	13.5	0.04	0.065
Body weight	82.4	0.129	<0.001
Amputation	0.02	0.897	<0.001
Neuropathic pain*	…	…	Fixed model
Diabetic ketoacidosis	1.66	0.645	<0.001
Serious hyperglycaemia	14.6	0.798	0.61
Genital infection	4.17	0.384	0.09
Fournier gangrene*	…	…	<0.001
Severe gastrointestinal events	3.00	0.558	0.69
Pancreatic cancer	3.05	0.549	<0.001
Pancreatitis	11.1	0.973	0.07
HbA1C	86.6	0.522	0.32

*No source of inconsistency

Appendix 6 Direct, indirect and network treatment estimates

Table 1 All-cause mortality

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence between direct and indirect estimate (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.85 (0.79-0.92)	1.04 (0.55-1.97)	0.50	0.85 (0.79-0.92)
GLP-1 receptor agonist	*v*	Placebo	0.88 (0.83-0.94)	0.81 (0.51-1.28)	0.71	0.88 (0.83-0.94)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.51 (0.09-2.96)	0.95 (0.86-1.06)	0.49	0.95 (0.86-1.06)
Metformin	*v*	Placebo	1.51 (0.64-3.57)	0.97 (0.68-1.39)	0.35	1.03 (0.74-1.44)
Sulfonylurea	*v*	Placebo	1.83 (0.34-9.76)	1.11 (0.96-1.28)	0.56	1.11 (0.96-1.29)
Thiazolidinedione	*v*	Placebo	0.94 (0.77-1.16)	1.19 (0.9-1.58)	0.19	1.02 (0.87-1.20)
DPP-4 inhibitor	*v*	Placebo	1.02 (0.95-1.09)	0.92 (0.7-1.21)	0.50	1.01 (0.94-1.08)
Alpha glucosidase inhibitor	*v*	Placebo	1.21 (0.31-4.68)	0.41 (0.04-4.39)	0.47	0.89 (0.30-2.63)
Glitinide	*v*	Placebo	1.72 (0.15-19.01)	1.62 (0.45-5.86)	0.97	1.64 (0.53-5.10)
Metformin	*v*	Sulfonylurea	0.90 (0.58-1.38)	0.98 (0.59-1.63)	0.80	0.93 (0.67-1.29)
Metformin	*v*	Thiazolidinedione	0.94 (0.6-1.46)	1.12 (0.67-1.87)	0.60	1.01 (0.73-1.41)
Metformin	*v*	DPP-4 inhibitor	0.95 (0.28-3.25)	1.03 (0.73-1.45)	0.90	1.02 (0.73-1.43)
Metformin	*v*	SGLT-2 inhibitor	1.86 (0.29-11.83)	1.24 (0.88--1.4)	0.66	1.24 (0.88-1.74)
Metformin	*v*	GLP-1 receptor agonist	3.3 (0.16-69.1)	1.16 (0.82-1.63)	0.50	1.17 (0.84-1.65)
Metformin	*v*	Glitinide	3.15 (0.14-70.73)	0.50 (0.15-1.73)	0.27	0.63 (0.20-2.03)
Sulfonylurea	*v*	Thiazolidinedione	0.97 (0.74-1.28)	1.2 (0.94-1.54)	0.26	1.09 (0.91-1.31)
Sulfonylurea	*v*	DPP-4 inhibitor	1.14 (0.98-1.33)	0.97 (0.73-1.3)	0.34	1.10 (0.96-1.26)
Sulfonylurea	*v*	SGLT-2 inhibitor	1.28 (0.54-3.05)	1.33 (1.13-1.58)	0.93	1.33 (1.13-1.57)
Sulfonylurea	*v*	GLP-1 receptor agonist	1.07 (0.45-2.56)	1.27 (1.08-1.49)	0.71	1.26 (1.08-1.48)
Sulfonylurea	*v*	Basal bolus insulin	0.15 (0.01-3.31)	2.60 (0.51-13.3)	0.11	1.40 (0.33-5.91)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence between direct and indirect estimate (p value)	Network estimate
Sulfonylurea	*v*	Alpha glucosidase inhibitor	1.56 (0.31-7.85)	1.04 (0.24-4.43)	0.71	1.25 (0.42-3.66)
Sulfonylurea	*v*	Glitinide	0.54 (0.12-2.52)	0.90 (0.16-5.17)	0.67	0.68 (0.22-2.11)
Thiazolidinedione	*v*	DPP-4 inhibitor	0.46 (0.09-2.23)	1.02 (0.86-1.21)	0.32	1.01 (0.85-1.20)
Thiazolidinedione	*v*	GLP-1 receptor agonist	2.20 (0.33-14.4)	1.15 (0.97-1.37)	0.50	1.16 (0.97-1.38)
Thiazolidinedione	*v*	Standard therapy	0.87 (0.69-1.1)	0.66 (0.28-1.59)	0.55	0.85 (0.68-1.07)
Thiazolidinedione	*v*	Glitinide	0.66 (0.03-16.38)	0.62 (0.18-2.09)	0.97	0.62 (0.20-1.95)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.41 (0.12-1.36)	1.20 (1.08-1.34)	0.08	1.20 (1.08-1.34)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.15 (0.61-2.17)	1.15 (1.04-1.26)	0.99	1.15 (1.05-1.26)
DPP-4 inhibitor	*v*	Basal insulin	1.83 (0.3-11.29)	0.86 (0.49-1.49)	0.44	0.91 (0.54-1.55)
DPP-4 inhibitor	*v*	Standard therapy	1.21 (0.29-5.10)	0.83 (0.63-1.11)	0.62	0.85 (0.64-1.12)
GLP-1 receptor agonist	*v*	Basal insulin	0.7 (0.39-1.29)	1.17 (0.4-3.38)	0.42	0.80 (0.47-1.34)
GLP-1 receptor agonist	*v*	Basal bolus insulin	1.33 (0.19-9.12)	0.88 (0.1-7.60)	0.78	1.11 (0.26-4.65)
GLP-1 receptor agonist	*v*	Bolus insulin	2.98 (0.12-73.46)	0.26 (0.01-6.73)	0.30	0.90 (0.09-8.78)
GLP-1 receptor agonist	*v*	Standard therapy	0.38 (0.09-1.64)	0.76 (0.57-1.00)	0.36	0.74 (0.56-0.97)
Basal insulin	*v*	Basal bolus insulin	7.03 (0.36-136.8)	0.81 (0.15-4.50)	0.22	1.39 (0.31-6.15)
Basal insulin	*v*	Bolus insulin	0.34 (0.01-8.36)	3.87 (0.15-99.6)	0.30	1.13 (0.12-11.0)
Basal insulin	*v*	Standard therapy	0.61 (0.14-2.64)	1.00 (0.53-1.87)	0.54	0.93 (0.52-1.65)
Alpha glucosidase inhibitor	*v*	Glitinide	0.24 (0.01-5.48)	0.69 (0.13-3.79)	0.57	0.55 (0.12-2.41)

Table 2 Cardiovascular mortality

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.84 (0.76-0.92)	1.27 (0.45-3.62)	0.44	0.84 (0.76-0.92)
GLP-1 receptor agonist	*v*	Placebo	0.88 (0.8-0.96)	0.63 (0.27-1.48)	0.44	0.88 (0.80-0.96)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.99 (0.06-15.9)	0.96 (0.84-1.09)	0.98	0.96 (0.84-1.09)
Metformin	*v*	Placebo	3.05 (0.48-19.3)	0.78 (0.37-1.64)	0.18	0.95 (0.48-1.89)
Sulfonylurea	*v*	Placebo	3.47 (0.15-78.26)	1.00 (0.79-1.25)	0.43	1.00 (0.80-1.26)
Thiazolidinedione	*v*	Placebo	0.94 (0.73-1.22)	1.16 (0.66-2.03)	0.51	0.97 (0.77-1.23)
DPP-4 inhibitor	*v*	Placebo	0.98 (0.89-1.09)	0.99 (0.6-1.63)	0.98	0.98 (0.89-1.09)
Alpha glucosidase inhibitor	*v*	Placebo	1.54 (0.24-9.80)	0.17 (0.00-13.4)	0.39	0.99 (0.21-4.70)
Glitinide	*v*	Placebo	0.96 (0.02-48.8)	0.59 (0.08-4.18)	0.83	0.65 (0.11-3.75)
Metformin	*v*	Sulfonylurea	1.30 (0.53-3.19)	1.25 (0.43-3.61)	0.5	0.95 (0.48-1.87)
Metformin	*v*	Thiazolidinedione	0.76 (0.12-4.85)	1.02 (0.47-2.20)	0.78	0.97 (0.48-1.98)
Metformin	*v*	DPP-4 inhibitor	0.34 (0.01-8.30)	1.01 (0.5-2.05)	0.51	0.96 (0.48-1.92)
Metformin	*v*	SGLT-2 inhibitor	1.86 (0.29-11.84)	1.04 (0.49-2.2)	0.57	1.13 (0.56-2.26)
Metformin	*v*	Glitinide	3.54 (0.16-80.0)	0.99 (0.12-8.35)	0.49	1.46 (0.24-8.97)
Sulfonylurea	*v*	Thiazolidinedione	0.85 (0.45-1.60)	1.09 (0.77-1.54)	0.5	1.04 (0.76-1.42)
Sulfonylurea	*v*	DPP-4 inhibitor	1.02 (0.81-1.29)	0.98 (0.55-1.75)	0.89	1.02 (0.82-1.27)
Sulfonylurea	*v*	SGLT-2 inhibitor	0.84 (0.10-6.86)	1.20 (0.94-1.54)	0.74	1.21 (0.93-1.57)
Sulfonylurea	*v*	Basal bolus insulin	0.26 (0.01-6.78)	0.76 (0.03-19.0)	0.65	0.45 (0.05-4.42)
Sulfonylurea	*v*	Alpha glucosidase inhibitor	1.96 (0.2-19.15)	0.57 (0.07-4.80)	0.44	1.01 (0.21-4.81)
Sulfonylurea	*v*	Glitinide	1.99 (0.12-32.0)	1.31 (0.14-12.5)	0.82	1.55 (0.27-8.93)
Thiazolidinedione	*v*	DPP-4 inhibitor	0.18 (0.02-1.72)	1.01 (0.78-1.30)	0.14	0.98 (0.76-1.27)
Thiazolidinedione	*v*	GLP-1 receptor agonist	0.97 (0.02-49.2)	1.11 (0.87-1.43)	0.95	1.11 (0.87-1.43)
Thiazolidinedione	*v*	Standard therapy	0.87 (0.61-1.23)	0.49 (0.14-1.74)	0.40	0.86 (0.61-1.21)
Thiazolidinedione	*v*	Glitinide	0.66 (0.03-16.4)	2.13 (0.26-17.4)	0.55	1.49 (0.26-8.64)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.29 (0.05-1.72)	1.18 (1.03-1.36)	0.12	1.19 (1.02-1.39)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.55 (0.5-4.8)	1.12 (0.98-1.28)	0.57	1.12 (0.97-1.29)
DPP-4 inhibitor	*v*	Basal insulin	0.33 (0.01-8.2)	0.92 (0.42-2.01)	0.54	0.87 (0.39-1.94)
DPP-4 inhibitor	*v*	Standard therapy	1.00 (0.1-9.67)	0.84 (0.55-1.27)	0.88	0.88 (0.57-1.34)
GLP-1 receptor agonist	*v*	Basal insulin	0.71 (0.3-1.67)	1.03 (0.22-4.81)	0.67	0.78 (0.35-1.72)
GLP-1 receptor agonist	*v*	Basal bolus insulin	0.66 (0.03-16.41)	0.23 (0.01-5.96)	0.65	0.39 (0.04-3.88)
GLP-1 receptor agonist	*v*	Bolus insulin	2.98 (0.12-73.6)	0.25 (0.01-6.62)	0.29	1.13 (0.11-11.25)
GLP-1 receptor agonist	*v*	Standard therapy	0.21 (0.02-1.85)	0.78 (0.52-1.18)	0.25	0.75 (0.50-1.12)
Basal insulin	*v*	Bolus insulin	0.34 (0.01-8.38)	4.12 (0.15-111)	0.29	0.50 (0.04-5.68)
Basal insulin	*v*	Standard therapy	0.69 (0.11-4.40)	1.05 (0.42-2.61)	0.69	1.00 (0.41-2.43)

Table 3 Nonfatal myocardial infarction

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.88 (0.79-0.97)	0.72 (0.31-1.69)	0.66	0.87 (0.79-0.97)
GLP-1 receptor agonist	*v*	Placebo	0.92 (0.85-0.99)	1.00 (0.56-1.79)	0.78	0.92 (0.85-0.99)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	1.98 (0.18-22.0)	0.95 (0.84-1.08)	0.55	0.95 (0.84-1.08)
Metformin	*v*	Placebo	1.16 (0.66-2.04)	1.13 (0.71-1.81)	0.95	1.16 (0.81-1.66)
Sulfonylurea	*v*	Placebo	0.49 (0.13-1.82)	1.10 (0.89-1.37)	0.23	1.09 (0.88-1.35)
Thiazolidinedione	*v*	Placebo	1.19 (0.45-3.14)	1.14 (0.82-1.58)	0.94	1.19 (0.87-1.64)
DPP-4 inhibitor	*v*	Placebo	1.01 (0.92-1.12)	1.01 (0.68-1.52)	1.00	1.01 (0.92-1.11)
Alpha glucosidase inhibitor	*v*	Placebo	0.15 (0.03-0.86)	0.40 (0.02-8.25)	0.58	0.19 (0.04-0.88)
Glitinide	*v*	Placebo	1.33 (0.06-27.9)	0.14 (0.02-1.13)	0.23	0.29 (0.05-1.63)
Metformin	*v*	Sulfonylurea	1.16 (0.68-1.97)	0.98 (0.59-1.62)	0.66	1.06 (0.74-1.53)
Metformin	*v*	Thiazolidinedione	0.79 (0.46-1.34)	1.30 (0.74-2.28)	0.21	0.97 (0.66-1.44)
Metformin	*v*	DPP-4 inhibitor	2.04 (0.48-8.75)	1.08 (0.75-1.57)	0.41	1.14 (0.79-1.64)
Metformin	*v*	SGLT-2 inhibitor	1.43 (0.06-35.5)	1.30 (0.89-1.9)	0.96	1.32 (0.91-1.93)
Metformin	*v*	GLP-1 receptor agonist	0.79 (0.07-9.43)	1.26 (0.86-1.82)	0.72	1.26 (0.87-1.83)
Metformin	*v*	Standard therapy	3.06 (0.12-76.9)	1.17 (0.72-1.89)	0.56	1.12 (0.69-1.82)
Sulfonylurea	*v*	Thiazolidinedione	0.97 (0.69-1.35)	0.86 (0.5-1.49)	0.72	0.91 (0.69-1.22)
Sulfonylurea	*v*	DPP-4 inhibitor	1.05 (0.83-1.31)	1.12 (0.73-1.71)	0.79	1.07 (0.88-1.31)
Sulfonylurea	*v*	SGLT-2 inhibitor	1.70 (0.48-5.98)	1.22 (0.96-1.55)	0.61	1.25 (0.98-1.58)
Sulfonylurea	*v*	GLP-1 receptor agonist	0.94 (0.33-2.68)	1.19 (0.94-1.5)	0.67	1.19 (0.94-1.49)
Sulfonylurea	*v*	Alpha glucosidase inhibitor	2.50 (0.13-47.0)	7.20 (1.30-40.0)	0.53	5.63 (1.23-25.7)
Sulfonylurea	*v*	Glitinide	6.07 (0.76-48.3)	1.49 (0.09-24.7)	0.41	3.77 (0.67-21.3)
Thiazolidinedione	*v*	DPP-4 inhibitor	1.17 (0.31-4.43)	1.13 (0.82-1.55)	0.96	1.17 (0.86-1.61)
Thiazolidinedione	*v*	GLP-1 receptor agonist	3.10 (0.54-17.9)	1.21 (0.87-1.67)	0.30	1.30 (0.94-1.80)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
Thiazolidinedione	*v*	Basal insulin	3.05 (0.12-76.6)	0.99 (0.45-2.15)	0.5	1.18 (0.57-2.45)
Thiazolidinedione	*v*	Standard therapy	1.17 (0.84-1.65)	1.36 (0.62-2.99)	0.74	1.15 (0.84-1.58)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	1.51 (0.47-4.87)	1.16 (1.01-1.33)	0.66	1.16 (1.01-1.33)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.06 (0.47-2.36)	1.11 (0.98-1.25)	0.91	1.11 (0.98-1.25)
DPP-4 inhibitor	*v*	Basal insulin	2.70 (0.11-66.7)	0.88 (0.42-1.83)	0.5	1.00 (0.50-2.00)
DPP-4 inhibitor	*v*	Standard therapy	0.65 (0.23-1.86)	1.15 (0.75-1.77)	0.32	0.98 (0.65-1.49)
GLP-1 receptor agonist	*v*	Basal insulin	0.83 (0.35-1.95)	0.88 (0.25-3.03)	0.94	0.91 (0.46-1.80)
GLP-1 receptor agonist	*v*	Basal bolus insulin	2.84 (0.12-70.1)	2.45 (0.09-65.5)	0.95	2.75 (0.28-27.2)
GLP-1 receptor agonist	*v*	Bolus insulin	0.88 (0.18-4.2)	0.62 (0.11-3.33)	0.77	0.78 (0.25-2.43)
GLP-1 receptor agonist	*v*	Standard therapy	1.42 (0.45-4.46)	0.91 (0.59-1.4)	0.48	0.89 (0.58-1.36)
Basal insulin	*v*	Basal bolus insulin	2.92 (0.12-72.2)	3.39 (0.13-90.6)	0.95	3.03 (0.31-29.9)
Basal insulin	*v*	Bolus insulin	0.76 (0.17-3.45)	1.08 (0.19-6.14)	0.77	0.86 (0.27-2.66)
Basal insulin	*v*	Standard therapy	3.94 (0.43-35.8)	0.95 (0.41-2.22)	0.24	0.98 (0.46-2.10)
Alpha glucosidase inhibitor	*v*	Glitinide	0.99 (0.02-50.0)	0.56 (0.04-8.58)	0.82	0.67 (0.07-6.31)

Table 4 Nonfatal stroke

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	1.01 (0.89-1.14)	1.15 (0.54-2.47)	0.73	1.01 (0.89-1.14)
GLP-1 receptor agonist	*v*	Placebo	0.83 (0.75-0.92)	1.20 (0.6-2.37)	0.31	0.84 (0.76-0.93)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.40 (0.09-1.82)	1.22 (1.04-1.43)	0.15	1.20 (1.03-1.41)
Metformin	*v*	Placebo	0.95 (0.38-2.39)	1.02 (0.63-1.65)	0.90	1.01 (0.66-1.54)
Sulfonylurea	*v*	Placebo	0.63 (0.12-3.37)	1.11 (0.87-1.42)	0.51	1.09 (0.86-1.40)
Thiazolidinedione	*v*	Placebo	0.90 (0.59-1.37)	0.97 (0.65-1.45)	0.78	0.94 (0.70-1.25)
DPP-4 inhibitor	*v*	Placebo	0.94 (0.83-1.08)	0.75 (0.49-1.15)	0.32	0.93 (0.82-1.05)
Metformin	*v*	Sulfonylurea	0.88 (0.52-1.48)	0.99 (0.50-1.96)	0.79	0.92 (0.61-1.38)
Metformin	*v*	Thiazolidinedione	1.29 (0.68-2.44)	0.90 (0.49-1.67)	0.43	1.07 (0.69-1.66)
Metformin	*v*	DPP-4 inhibitor	1.21 (0.27-5.31)	1.08 (0.69-1.67)	0.88	1.09 (0.71-1.66)
Metformin	*v*	SGLT-2 inhibitor	0.67 (0.03-16.4)	1.00 (0.64-1.56)	0.80	0.99 (0.64-1.55)
Metformin	*v*	GLP-1 receptor agonist	1.53 (0.17-13.9)	1.18 (0.76-1.84)	0.82	1.20 (0.77-1.85)
Sulfonylurea	*v*	Thiazolidinedione	1.10 (0.74-1.63)	1.26 (0.81-1.96)	0.66	1.17 (0.87-1.57)
Sulfonylurea	*v*	DPP-4 inhibitor	1.26 (0.97-1.63)	1.00 (0.64-1.55)	0.38	1.18 (0.94-1.48)
Sulfonylurea	*v*	SGLT-2 inhibitor	0.43 (0.13-1.4)	1.14 (0.86-1.5)	0.12	1.08 (0.83-1.42)
Sulfonylurea	*v*	GLP-1 receptor agonist	1.19 (0.3-4.8)	1.31 (1.00-1.70)	0.90	1.30 (1.01-1.69)
Sulfonylurea	*v*	Standard therapy	3.04 (0.14-68.4)	0.9 (0.58-1.4)	0.45	0.92 (0.59-1.43)
Thiazolidinedione	*v*	DPP-4 inhibitor	1.43 (0.41-4.99)	0.99 (0.73-1.34)	0.58	1.01 (0.76-1.36)
Thiazolidinedione	*v*	GLP-1 receptor agonist	1.51 (0.25-9.22)	1.11 (0.81-1.51)	0.74	1.12 (0.82-1.51)
Thiazolidinedione	*v*	Basal insulin	3.15 (0.12-82.2)	1.04 (0.45-2.42)	0.52	1.12 (0.49-2.52)
Thiazolidinedione	*v*	Basal-bolus insulin	1.01 (0.06-16.4)	1.97 (0.2-19.05)	0.72	1.51 (0.26-8.77)
Thiazolidinedione	*v*	Standard therapy	0.77 (0.54-1.11)	0.93 (0.32-2.68)	0.76	0.79 (0.56-1.11)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.92 (0.28-3.01)	0.92 (0.77-1.09)	0.99	0.92 (0.77-1.09)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.03 (0.37-2.88)	1.1 (0.94-1.3)	0.89	1.10 (0.94-1.29)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
DPP-4 inhibitor	*v*	Basal insulin	0.30 (0.01-7.35)	1.20 (0.53-2.69)	0.41	1.10 (0.50-2.42)
DPP-4 inhibitor	*v*	Standard therapy	0.90 (0.21-3.92)	0.77 (0.49-1.21)	0.84	0.78 (0.51-1.20)
GLP-1 receptor agonist	*v*	Basal insulin	1.20 (0.5-2.87)	0.53 (0.1-2.76)	0.39	1.00 (0.46-2.17)
GLP-1 receptor agonist	*v*	Basal bolus insulin	0.97 (0.06-15.7)	1.68 (0.18-15.9)	0.76	1.35 (0.24-7.78)
GLP-1 receptor agonist	*v*	Standard therapy	0.70 (0.11-4.32)	0.71 (0.45-1.11)	0.99	0.71 (0.46-1.10)
Basal insulin	*v*	Basal bolus insulin	1.95 (0.18-21.6)	0.90 (0.07-11.4)	0.67	1.35 (0.24-7.77)
Basal insulin	*v*	Standard therapy	3.00 (0.12-74.0)	0.63 (0.26-1.55)	0.36	0.71 (0.30-1.68)
Glitinide	*v*	Standard therapy	2.92 (0.11-74.1)	0.28 (0.03-3.04)	0.25	1.56 (0.23-10.6)

Table 5 Kidney failure

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.71 (0.57-0.89)	0.85 (0.11-6.48)	0.87	0.71 (0.57-0.89)
GLP-1 receptor agonist	*v*	Placebo	0.79 (0.67-0.93)	0.64 (0.2-2.11)	0.74	0.78 (0.67-0.92)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.99 (0.06-15.9)	0.91 (0.69-1.20)	0.95	0.91 (0.69-1.20)
DPP-4 inhibitor	*v*	Placebo	0.95 (0.72-1.26)	1.11 (0.34-3.63)	0.81	0.96 (0.73-1.26)
Sulfonylurea	*v*	DPP-4 inhibitor	0.96 (0.14-6.57)	0.73 (0.07-7.23)	0.86	0.86 (0.20-3.74)
Sulfonylurea	*v*	SGLT-2 inhibitor	0.99 (0.1-9.51)	1.30 (0.18-9.18)	0.86	1.15 (0.26-5.08)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.52 (0.42-5.49)	1.21 (0.88-1.67)	0.73	1.23 (0.90-1.68)

Table 6 Hospitalisation for heart failure

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.70 (0.63-0.77)	0.91 (0.34-2.47)	0.6	0.70 (0.63-0.77)
GLP-1 receptor agonist	*v*	Placebo	0.95 (0.86-1.04)	0.62 (0.33-1.15)	0.18	0.94 (0.85-1.03)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	2.00 (0.18-22.2)	0.74 (0.65-0.85)	0.42	0.74 (0.65-0.85)
Metformin	*v*	Placebo	0.74 (0.16-3.35)	1.26 (0.77-2.05)	0.51	1.19 (0.75-1.90)
Sulfonylurea	*v*	Placebo	0.68 (0.07-7.00)	0.89 (0.71-1.12)	0.82	0.89 (0.71-1.11)
Thiazolidinedione	*v*	Placebo	1.53 (1.26-1.85)	1.67 (1.13-2.46)	0.68	1.55 (1.31-1.84)
DPP-4 inhibitor	*v*	Placebo	1.05 (0.94-1.18)	1.05 (0.71-1.54)	0.98	1.05 (0.95-1.17)
Basal insulin	*v*	Placebo	0.33 (0.01-8.05)	0.84 (0.38-1.86)	0.57	0.79 (0.37-1.72)
Metformin	*v*	Sulfonylurea	1.43 (0.79-2.61)	1.18 (0.51-2.77)	0.73	1.34 (0.84-2.13)
Metformin	*v*	Thiazolidinedione	0.81 (0.44-1.48)	0.72 (0.36-1.44)	0.80	0.77 (0.49-1.22)
Metformin	*v*	DPP-4 inhibitor	0.66 (0.01-33.6)	1.14 (0.71-1.83)	0.79	1.13 (0.71-1.81)
Metformin	*v*	SGLT-2 inhibitor	1.43 (0.06-35.5)	1.72 (1.06-2.78)	0.91	1.71 (1.06-2.75)
Metformin	*v*	GLP-1 receptor agonist	2.77 (0.36-21.5)	1.22 (0.75-1.98)	0.45	1.27 (0.79-2.05)
Sulfonylurea	*v*	Thiazolidinedione	0.57 (0.4-0.79)	0.58 (0.42-0.81)	0.92	0.57 (0.45-0.73)
Sulfonylurea	*v*	DPP-4 inhibitor	0.86 (0.65-1.12)	0.83 (0.57-1.20)	0.90	0.85 (0.68-1.05)
Sulfonylurea	*v*	SGLT-2 inhibitor	1.18 (0.32-4.43)	1.28 (1.00-1.64)	0.91	1.28 (1.00-1.63)
Sulfonylurea	*v*	GLP-1 receptor agonist	0.59 (0.13-2.61)	0.96 (0.75-1.23)	0.52	0.95 (0.75-1.21)
Thiazolidinedione	*v*	DPP-4 inhibitor	4.12 (0.20-86.7)	1.47 (1.21-1.78)	0.51	1.47 (1.21-1.79)
Thiazolidinedione	*v*	GLP-1 receptor agonist	7.33 (0.85-63.1)	1.64 (1.35-1.99)	0.17	1.66 (1.36-2.01)
Thiazolidinedione	*v*	Basal insulin	2.9 (0.12-72.0)	1.9 (0.86-4.24)	0.80	1.95 (0.90-4.24)
Thiazolidinedione	*v*	Standard therapy	1.93 (1.26-2.96)	1.32 (0.45-3.85)	0.51	1.83 (1.23-2.73)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.40 (0.02-9.88)	1.51 (1.31-1.75)	0.42	1.51 (1.31-1.74)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.19 (0.54-2.65)	1.12 (0.97-1.3)	0.88	1.12 (0.98-1.29)
DPP-4 inhibitor	*v*	Standard therapy	1.98 (0.18-21.9)	1.23 (0.79-1.91)	0.7	1.25 (0.81-1.92)

SGLT-2 inhibitor	*v*	Standard therapy	0.33 (0.01-8.09)	0.84 (0.54-1.3)	0.57	0.83 (0.53-1.28)
GLP-1 receptor agonist	*v*	Basal insulin	0.96 (0.32-2.89)	1.44 (0.48-4.27)	0.61	1.18 (0.54-2.55)
GLP-1 receptor agonist	*v*	Standard therapy	0.32 (0.03-3.17)	1.16 (0.75-1.8)	0.28	1.11 (0.72-1.71)
Basal insulin	*v*	Standard therapy	0.89 (0.28-2.8)	0.99 (0.33-2.92)	0.90	0.94 (0.43-2.07)

Table 7 Severe hypoglycaemia

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.87 (0.65-1.17)	1.01 (0.60-1.68)	0.64	0.90 (0.70-1.16)
GLP-1 receptor agonist	*v*	Placebo	0.96 (0.81-1.14)	0.77 (0.54-1.09)	0.26	0.94 (0.63-1.41)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.92 (0.42-2.03)	0.99 (0.72-1.35)	0.86	0.98 (0.73-1.31)
Metformin	*v*	Placebo	1.70 (0.63-4.59)	1.58 (0.59-4.26)	0.92	1.64 (0.81-3.30)
Sulfonylurea	*v*	Placebo	0.93 (0.11-7.7)	6.64 (4.39-10.1)	0.07	6.18 (4.11-9.29)
Thiazolidinedione	*v*	Placebo	1.52 (0.83-2.78)	1.2 (0.67-2.17)	0.59	1.35 (0.89-2.05)
DPP-4 inhibitor	*v*	Placebo	1.06 (0.89-1.27)	1.2 (0.84-1.72)	0.54	1.09 (0.93-1.27)
Basal insulin	*v*	Placebo	0.49 (0.01-25.3)	2.34 (1.63-3.35)	0.44	2.31 (1.62-3.30)
Alpha glucosidase inhibitor	*v*	Placebo	0.72 (0.11-4.68)	3.99 (0.17-93.3)	0.36	1.12 (0.22-5.63)
Metformin	*v*	Sulfonylurea	0.12 (0.02-0.84)	0.3 (0.13-0.69)	0.38	0.27 (0.12-0.57)
Metformin	*v*	Thiazolidinedione	1 (0.06-16.4)	1.24 (0.53-2.88)	0.89	1.21 (0.54-2.73)
Metformin	*v*	DPP-4 inhibitor	0.98 (0.11-8.55)	1.59 (0.75-3.37)	0.68	1.51 (0.74-3.07)
Metformin	*v*	SGLT-2 inhibitor	3.67 (0.84-16.0)	1.45 (0.63-3.33)	0.28	1.82 (0.88-3.74)
Metformin	*v*	Glitinide	0.43 (0.11-1.6)	0.96 (0.09-9.9)	0.55	0.52 (0.16-1.64)
Sulfonylurea	*v*	Thiazolidinedione	7.48 (2.6-21.5)	3.87 (2.09-7.17)	0.29	4.58 (2.68-7.81)
Sulfonylurea	*v*	DPP-4 inhibitor	5.60 (3.44-9.13)	5.82 (2.96-11.5)	0.93	5.68 (3.82-8.44)
Sulfonylurea	*v*	SGLT-2 inhibitor	6.01 (2.29-15.8)	7.09 (4.23-11.9)	0.77	6.84 (4.34-10.8)
Sulfonylurea	*v*	GLP-1 receptor agonist	1.25 (0.11-14.5)	7.03 (4.57-10.8)	0.17	6.70 (4.38-10.3)
Sulfonylurea	*v*	Alpha glucosidase inhibitor	1.68 (0.07-39.0)	8.11 (1.26-52.2)	0.39	5.50 (1.07-28.4)
Sulfonylurea	*v*	Glitinide	2.47 (0.27-22.2)	1.76 (0.38-8.05)	0.80	1.96 (0.55-6.95)
Thiazolidinedione	*v*	DPP-4 inhibitor	0.37 (0.08-1.69)	1.38 (0.88-2.15)	0.10	1.24 (0.81-1.90)
Thiazolidinedione	*v*	GLP-1 receptor agonist	0.83 (0.23-3.08)	1.56 (1-2.44)	0.37	1.46 (0.96-2.23)
Thiazolidinedione	*v*	Basal insulin	0.81 (0.24-2.72)	0.54 (0.31-0.95)	0.55	0.58 (0.35-0.97)

Thiazolidinedione	*v*	Standard therapy	2.48 (1.01-6.09)	1.05 (0.57-1.92)	0.12	1.38 (0.83-2.30)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.65 (0.25-1.66)	1.29 (0.95-1.74)	0.17	1.21 (0.90-1.61)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.43 (0.93-2.2)	1.11 (0.88-1.41)	0.31	1.18 (0.97-1.44)
DPP-4 inhibitor	*v*	Basal insulin	0.24 (0.03-2.19)	0.48 (0.33-0.71)	0.54	0.47 (0.32-0.69)
DPP-4 inhibitor	*v*	Standard therapy	1.36 (0.35-5.23)	1.09 (0.7-1.71)	0.76	1.11 (0.72-1.71)
GLP-1 receptor agonist	*v*	Basal insulin	0.4 (0.29-0.57)	0.36 (0.13-0.97)	0.83	0.40 (0.29-0.55)
Basal insulin	*v*	Standard therapy	4.03 (0.44-37.3)	2.3 (1.37-3.86)	0.63	2.36 (1.42-3.94)
Alpha glucosidase inhibitor	*v*	Glitinide	1.01 (0.02-51.9)	0.25 (0.03-2.48)	0.55	0.36 (0.05-2.58)

Table 8 Health-related quality of life

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
GLP-1 receptor agonist	*v*	Placebo	0.13 (0.03-0.22)	0.71 (0.09-1.32)	0.06	0.13 (0.0-0.23)
DPP-4 inhibitor	*v*	Placebo	0.26 (-0.11-0.63)	-0.04 (-0.21-0.14)	0.26	0.02 (-0.14-0.19)
Metformin	*v*	Thiazolidinedione	-0.16 (-0.47-0.15)	-0.30 (-1.69-1.09)	0.86	-0.16 (-0.46-0.14)
Metformin	*v*	DPP-4 inhibitor	-0.02 (-0.31-0.27)	0.01 (-0.63-0.65)	0.92	-0.02 (-0.26-0.23)
Metformin	*v*	GLP-1 receptor agonist	-0.11 (-0.42-0.19)	-0.16 (-0.66-0.34)	0.87	-0.12 (-0.37-0.12)
Thiazolidinedione	*v*	DPP-4 inhibitor	0.15 (-0.21-0.50)	0.14 (-0.50-0.78)	0.99	0.15 (-0.14-0.43)
Thiazolidinedione	*v*	GLP-1 receptor agonist	0.05 (-0.28-0.37)	0.01 (-0.64-0.66)	0.92	0.04 (-0.24-0.32)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	-0.14 (-0.291-0.02)	0.05 (-0.30-0.40)	0.34	-0.11 (-0.25-0.03)
DPP-4 inhibitor	*v*	Standard therapy	0.41 (0.12-0.71)	0.25 (-0.10-0.591)	0.46	0.34 (0.13-0.56)
GLP-1 receptor agonist	*v*	Basal insulin	0.20 (-0.11-0.52)	-0.31 (-0.64-0.02)	0.03	-0.03 (-0.29-0.23)
GLP-1 receptor agonist	*v*	Bolus insulin	0.24 (0.04-0.44)	0.75 (0.34-1.16)	0.03	0.34 (0.13-0.55)
Basal insulin	*v*	Bolus insulin	0.55 (0.28-0.81)	0.04 (-0.33-0.41)	0.03	0.37 (0.13-0.62)

Table 9 Body weight

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	-1.89 (-2.26--1.53)	-1.98 (-2.52--1.44)	0.80	-1.92 (-2.23--1.62)
GLP-1 receptor agonist	*v*	Placebo	-1.50 (-1.83--1.17)	-1.36 (-1.81--0.90)	0.62	-1.45 (-1.72--1.18)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.06 (-1.21-1.34)	-0.52 (-0.92--0.13)	0.39	-0.47 (-0.85--0.09)
Metformin	*v*	Placebo	-0.88 (-1.94-0.19)	-0.72 (-1.19--0.25)	0.8	-0.75 (-1.18--0.32)
Sulfonylurea	*v*	Placebo	2.85 (1.59-4.10)	1.60 (1.21-1.99)	0.06	1.71 (1.33-2.08)
Thiazolidinedione	*v*	Placebo	2.92 (2.39-3.45)	2.37 (1.93-2.82)	0.12	2.60 (2.26-2.94)
DPP-4 inhibitor	*v*	Placebo	0.23 (-0.08-0.55)	0.48 (0.09-0.87)	0.34	0.33 (0.08-0.57)
Basal insulin	*v*	Placebo	2.67 (0.79-4.56)	1.95 (1.42-2.48)	0.47	2.00 (1.50-2.51)
Alpha glucosidase inhibitor	*v*	Placebo	-0.38 (-1.14-0.38)	-0.24 (-1.01-0.54)	0.80	-0.31 (-0.85-0.23)
Glitinide	*v*	Placebo	1.11 (-0.79-3.02)	1.07 (0.12-2.02)	0.97	1.08 (0.23-1.93)
Metformin	*v*	Sulfonylurea	-1.52 (-2.61--0.44)	-2.69 (-3.24--2.15)	0.06	-2.46 (-2.95--1.97)
Metformin	*v*	Thiazolidinedione	-3.79 (-4.63--2.95)	-3.15 (-3.72--2.59)	0.22	-3.35 (-3.82--2.88)
Metformin	*v*	DPP-4 inhibitor	-1.29 (-2.04--0.54)	-0.97 (-1.5--0.44)	0.50	-1.08 (-1.51--0.64)
Metformin	*v*	SGLT-2 inhibitor	1.72 (0.55-2.89)	1.06 (0.53-1.59)	0.32	1.17 (0.69-1.66)
Metformin	*v*	GLP-1 receptor agonist	-0.27 (-1.55-1.01)	0.85 (0.35-1.35)	0.11	0.70 (0.24-1.17)
Metformin	*v*	Standard therapy	-0.35 (-2.01-1.31)	-1.59 (-2.23--0.94)	0.17	-1.42 (-2.02--0.82)
Metformin	*v*	Alpha glucosidase inhibitor	-0.54 (-2.08-1.00)	-0.42 (-1.12-0.29)	0.88	-0.44 (-1.08-0.20)
Metformin	*v*	Glitinide	-2.51 (-5.45-0.43)	-1.76 (-2.71--0.81)	0.63	-1.83 (-2.73--0.93)
Sulfonylurea	*v*	Thiazolidinedione	-0.87 (-1.44--0.29)	-0.92 (-1.46--0.38)	0.90	-0.89 (-1.29--0.50)
Sulfonylurea	*v*	DPP-4 inhibitor	1.42 (0.79-2.05)	1.36 (0.89-1.83)	0.89	1.38 (1.00-1.75)
Sulfonylurea	*v*	SGLT-2 inhibitor	4.25 (3.30-5.19)	3.46 (2.98-3.95)	0.15	3.63 (3.20-4.06)
Sulfonylurea	*v*	GLP-1 receptor agonist	2.15 (1.19-3.11)	3.38 (2.93-3.82)	0.02	3.16 (2.75-3.57)
Sulfonylurea	*v*	Basal insulin	-0.97 (-4.02-2.25)	-0.27 (-0.86-0.32)	0.67	-0.29 (-0.88-0.29)
Sulfonylurea	*v*	Basal bolus insulin	4.42 (1.57-7.27)	-1.59 (-2.89--0.29)	0.00	-0.55 (-1.75-0.65)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
Sulfonylurea	*v*	Bolus insulin	-2.10 (-6.98-2.78)	1.22 (-0.4-2.84)	0.21	0.89 (-0.65-2.43)
Sulfonylurea	*v*	Alpha glucosidase inhibitor	1.01 (-1.23-3.24)	2.10 (1.46-2.75)	0.36	2.02 (1.40-2.64)
Sulfonylurea	*v*	Glitinide	0.99 (-0.22-2.20)	0.29 (-0.87-1.46)	0.42	0.63 (-0.21-1.47)
Thiazolidinedione	*v*	DPP-4 inhibitor	1.84 (0.97-2.72)	2.36 (1.96-2.77)	0.29	2.27 (1.91-2.64)
Thiazolidinedione	*v*	SGLT-2 inhibitor	4.27 (2.40-6.14)	4.54 (4.1-4.98)	0.78	4.52 (4.10-4.95)
Thiazolidinedione	*v*	GLP-1 receptor agonist	3.95 (2.09-5.00)	4.07 (3.65-4.49)	0.83	4.05 (3.66-4.44)
Thiazolidinedione	*v*	Basal insulin	1.30 (-0.79-3.39)	0.54 (-0.04-1.13)	0.50	0.60 (0.03-1.17)
Thiazolidinedione	*v*	Basal bolus insulin	-1.01 (-3.69-1.67)	0.68 (-0.66-2.02)	0.27	0.34 (-0.85-1.54)
Thiazolidinedione	*v*	Standard therapy	0.63 (-0.91-2.17)	2.12 (1.53-2.72)	0.08	1.93 (1.37-2.49)
Thiazolidinedione	*v*	Alpha glucosidase inhibitor	2.37 (0.79-3.96)	3.00 (2.35-3.65)	0.47	2.91 (2.31-3.51)
Thiazolidinedione	*v*	Glitinide	1.22 (-1.03-3.47)	1.57 (0.64-2.51)	0.78	1.52 (0.66-2.38)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	2.10 (1.24-2.96)	2.28 (1.89-2.67)	0.7	2.25 (1.90-2.61)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.74 (1.12-2.37)	1.79 (1.43-2.15)	0.90	1.78 (1.47-2.09)
DPP-4 inhibitor	*v*	Basal insulin	-2.07 (-3.62--0.53)	-1.62 (-2.18--1.07)	0.59	-1.67 (-2.19--1.15)
DPP-4 inhibitor	*v*	Standard therapy	-0.42 (-1.34-0.5)	-0.31 (-0.92-0.3)	0.85	-0.34 (-0.85-0.16)
DPP-4 inhibitor	*v*	Alpha glucosidase inhibitor	1.11 (-0.06-2.27)	0.50 (-0.14-1.14)	0.37	0.64 (0.08-1.20)
SGLT-2 inhibitor	*v*	Standard therapy	-1.92 (-3.78--0.05)	-2.66 (-3.25--2.07)	0.46	-2.59 (-3.16--2.03)
GLP-1 receptor agonist	*v*	Basal insulin	-3.56 (-4.14--2.99)	-3.23 (-4.04--2.43)	0.51	-3.45 (-3.92--2.98)
GLP-1 receptor agonist	*v*	Basal bolus insulin	-4.83 (-6.68--2.97)	-2.97 (-4.48--1.47)	0.13	-3.71 (-4.88--2.54)
GLP-1 receptor agonist	*v*	Bolus insulin	-1.96 (-3.53--0.39)	-5.27 (-10.2--0.38)	0.21	-2.27 (-3.76--0.77)
GLP-1 receptor agonist	*v*	Standard therapy	-1.79 (-2.72--0.87)	-2.27 (-2.87--1.66)	0.4	-2.12 (-2.63--1.62)
Basal insulin	*v*	Basal bolus insulin	-0.88 (-2.7-0.94)	0.19 (-1.36-1.75)	0.38	-0.26 (-1.44-0.92)
Basal insulin	*v*	Standard therapy	0.70 (-0.45-1.85)	1.58 (0.85-2.31)	0.21	1.33 (0.71-1.94)
Alpha glucosidase inhibitor	*v*	Standard therapy	-0.77 (-3.35-1.81)	-1.00 (-1.74-0.26)	0.87	-0.98 (-1.69--0.27)
Glitinide	*v*	Standard therapy	0.84 (-1.25-2.93)	0.30 (-0.73-1.33)	0.65	0.41 (-0.52-1.33)

Table 10 Amputation

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	1.11 (0.90-1.36)	1.37 (0.05-34.5)	0.90	1.14 (0.96-1.35)

Table 11 Neuropathic pain

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
GLP-1 receptor agonist	*v*	Placebo	0.33 (0.07-1.65)	1.50 (0.62-3.64)	0.002	0.33 (0.01-8.19)

Table 12 Diabetic ketoacidosis

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	1.16 (0.66-2.05)	0.41 (0.03-5.17)	0.27	1.04 (0.61-1.78)
GLP-1 receptor agonist	*v*	Placebo	0.50 (0.26-0.97)	1.59 (0.38-6.70)	0.15	0.61 (0.33-1.11)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.66 (0.09-4.64)	2.04 (0.88,4.73)	0.30	1.71 (0.79-3.69)
DPP-4 inhibitor	*v*	Placebo	0.94 (0.23-1.67)	0.66 (0.13,3.27)	0.68	0.91 (0.53-1.54)
Sulfonylurea	*v*	DPP-4 inhibitor	0.94 (0.23-3.78)	1.64 (0.20-13.6)	0.67	1.11 (0.35-3.52)
Sulfonylurea	*v*	SGLT-2 inhibitor	1.35 (0.19-9.64)	0.78 (0.16-3.83)	0.67	0.97 (0.28-3.30)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	0.66 (0.09-4.71)	1.73 (0.74-4.00)	0.38	1.49 (0.69-3.20)

Table 13 Serious hyperglycaemia

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.64 (0.36-1.16)	0.41 (0.12-1.42)	0.52	0.59 (0.35-1.01)
GLP-1 receptor agonist	*v*	Placebo	0.42 (0.24-0.72)	0.34 (0.13-0.92)	0.71	0.40 (0.25-0.64)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	1.49 (0.17-12.86)	1.48 (0.72-3.04)	1.00	1.48 (0.75-2.93)
Metformin	*v*	Placebo	0.31 (0.04-2.64)	0.49 (0.09-2.78)	0.73	0.41 (0.10-1.60)
Sulfonylurea	*v*	Placebo	0.28 (0.09-0.92)	0.58 (0.24-1.40)	0.35	0.45 (0.22-0.91)
DPP-4 inhibitor	*v*	Placebo	0.62 (0.43-0.91)	0.63 (0.25-1.56)	0.98	0.62 (0.44-0.88)
Metformin	*v*	Thiazolidinedione	0.66 (0.07-6.57)	0.28 (0.03-2.64)	0.61	0.43 (0.09-2.11)
Metformin	*v*	DPP-4 inhibitor	0.81 (0.16-4.13)	0.39 (0.03-4.92)	0.63	0.66 (0.17-2.57)
Metformin	*v*	GLP-1 receptor agonist	0.64 (0.07-5.51)	1.40 (0.24-8.29)	0.58	1.02 (0.25-4.11)
Sulfonylurea	*v*	Thiazolidinedione	0.66 (0.08-5.66)	0.41 (0.10-1.61)	0.71	0.47 (0.15-1.48)
Sulfonylurea	*v*	DPP-4 inhibitor	0.92 (0.35-2.40)	0.53 (0.19-1.51)	0.45	0.72 (0.36-1.45)
Sulfonylurea	*v*	SGLT-2 inhibitor	1.47 (0.17-12.60)	0.67 (0.27-1.67)	0.51	0.75 (0.32-1.75)
Sulfonylurea	*v*	GLP-1 receptor agonist	0.44 (0.10-1.82)	1.61 (0.65-4.00)	0.12	0.89 (0.41-1.96)
Thiazolidinedione	*v*	DPP-4 inhibitor	1.00 (0.10-9.99)	1.72 (0.52-5.70)	0.68	1.54 (0.53-4.43)
Thiazolidinedione	*v*	GLP-1 receptor agonist	1.02 (0.12-8.77)	3.13 (0.92-10.7)	0.37	2.39 (0.82-7.00)
Thiazolidinedione	*v*	Basal insulin	5.87 (0.82-41.78)	1.82 (0.40-8.25)	0.35	2.81 (0.85-9.31)
Thiazolidinedione	*v*	Standard therapy	0.65 (0.16-2.67)	0.47 (0.07-3.17)	0.79	0.58 (0.19-1.79)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	1.62 (0.34-7.80)	0.97 (0.50-1.88)	0.56	1.05 (0.57-1.93)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.21 (0.46-3.18)	1.75 (0.92.3.35)	0.54	1.56 (0.92-2.65)
DPP-4 inhibitor	*v*	Standard therapy	0.64 (0.36-1.16)	0.41 (0.12-1.42)	0.70	0.38 (0.12-1.18)
GLP-1 receptor agonist	*v*	Basal insulin	1.02 (0.43-2.41)	3.30 (0.32-33.6)	0.35	1.18 (0.52-2.64)

Table 14 Genital infection

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	3.54 (3.04-4.12)	2.24 (0.90-5.62)	0.34	3.50 (3.01-4.07)
GLP-1 receptor agonist	*v*	Placebo	1.14 (0.18-7.26)	0.64 (0.29-1.40)	0.57	0.70 (0.34-1.44)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	5.45 (2.52-11.8)	3.05 (0.48-19.5)	0.57	5.00 (2.45-10.2)
DPP-4 inhibitor	*v*	Placebo	0.49 (0.21-1.15)	0.89 (0.52-1.52)	0.26	0.75 (0.48-1.17)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.25 (0.15-0.41)	0.12 (0.05-0.30)	0.18	0.21 (0.14-0.33)

Table 15 Severe gastrointestinal events

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
GLP-1 receptor agonist	*v*	Placebo	2.43 (1.29-4.60)	2.48 (0.40-15.4)	0.99	2.46 (1.22-4.97)
DPP-4 inhibitor	*v*	Placebo	1.73 (0.66,4.56)	1.83 (0.43,7.69)	0.99	1.76 (0.42-7.34)
Metformin	*v*	Sulfonylurea	2.16 (0.32-14.6)	6.12 (0.14-271)	0.63	2.64 (0.48-14.5)
Metformin	*v*	Thiazolidinedione	1.62 (0.35-7.50)	1.33 (0.05-32.3)	0.91	1.54 (0.40-5.91)
Metformin	*v*	Standard therapy	1.99 (0.12-31.7)	3.30 (0.41-26.6)	0.77	2.73 (0.53-13.9)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	0.63 (0.18-2.23)	0.82 (0.21-3.17)	0.78	0.71 (0.29-1.77)
DPP-4 inhibitor	*v*	Basal insulin	0.90 (0.04-19.5)	0.17 (0.03-1.08)	0.36	0.26 (0.05-1.29)
GLP-1 receptor agonist	*v*	Basal insulin	0.26 (0.05-1.31)	1.42 (0.06-35.4)	0.36	0.37 (0.09-1.55)

Table 16 Pancreatic cancer

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	1.60 (0.45-5.63)	3.63 (0.13-100.4)	0.65	1.77 (0.55-5.75)
GLP-1 receptor agonist	*v*	Placebo	1.23 (0.81-1.86)	0.52 (0.06-4.57)	0.45	1.19 (0.78-1.81)
DPP-4 inhibitor	*v*	Placebo	0.84 (0.49-1.44)	1.24 (0.20-7.77)	0.69	0.86 (0.51-1.45)
Sulfonylurea	*v*	DPP-4 inhibitor	1.35 (0.69-2.62)	0.59 (0.02-19.52)	0.65	1.32 (0.68-2.55)
Sulfonylurea	*v*	SGLT-2 inhibitor	0.33 (0.01-8.14)	0.74 (0.16-3.34)	0.45	0.64 (0.16-2.51)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	1.57 (0.19-12.9)	0.67 (0.34-1.32)	0.45	0.73 (0.37-1.42)

Table 17 Pancreatitis

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	0.64 (0.23-1.11)	0.63 (0.20-1.98)	0.97	0.64 (0.39-1.05)
GLP-1 receptor agonist	*v*	Placebo	1.14 (0.85-1.52)	1.88 (0.70-5.00)	0.34	1.18 (0.90-1.56)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.62 (0.08-5.05)	0.54 (0.30-0.95)	0.90	0.54 (0.31-0.94)
Sulfonylurea	*v*	Placebo	0.85 (0.08-9.19)	1.55 (0.55-4.35)	0.66	1.40 (0.56-3.49)
Thiazolidinedione	*v*	Placebo	0.45 (0.03-7.27)	1.32 (0.45-3.84)	0.48	1.15 (0.42-3.10)
DPP-4 inhibitor	*v*	Placebo	1.54 (1.05-2.26)	1.12 (0.46-2.72)	0.52	1.46 (1.03-2.08)
Metformin	*v*	Thiazolidinedione	0.66 (0.01-33.6)	0.20 (0.00-38.5)	0.72	0.43 (0.02-9.95)
Metformin	*v*	DPP-4 inhibitor	0.22 (0.01-5.42)	2.17 (0.01-398)	0.39	0.34 (0.02-7.11)
Metformin	*v*	GLP-1 receptor agonist	1.01 (0.02-51.0)	0.11 (0.00-14.4)	0.49	0.42 (0.02-8.91)
Sulfonylurea	*v*	Thiazolidinedione	2.96 (0.12,72.8)	1.03 (0.26,4.14)	0.56	1.22 (0.34-4.33)
Sulfonylurea	*v*	DPP-4 inhibitor	0.89 (0.20-4.04)	1.00 (0.29-3.45)	0.91	0.95 (0.37-2.42)
Sulfonylurea	*v*	SGLT-2 inhibitor	2.83 (0.58-13.7)	1.87 (0.56-6.25)	0.68	2.17 (0.83-5.66)
Sulfonylurea	*v*	GLP-1 receptor agonist	0.95 (0.19-4.68)	1.31 (0.42-4.07)	0.75	1.18 (0.47-2.99)
Thiazolidinedione	*v*	DPP-4 inhibitor	1.20 (0.26-5.64)	0.57 (0.15-2.16)	0.47	0.78 (0.29-2.14)
Thiazolidinedione	*v*	GLP-1 receptor agonist	0.96 (0.26-3.55)	0.98 (0.22-4.36)	0.99	0.97 (0.36-2.61)
Thiazolidinedione	*v*	Basal bolus insulin	1.01 (0.02-51.5)	9.93 (0.04,2401)	0.51	2.19 (0.09-52.7)
Thiazolidinedione	*v*	Standard therapy	2.51 (0.79-8.03)	0.60 (0.02-21.4)	0.45	2.19 (0.73-6.58)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	1.87 (0.27-11.9)	2.34 (1.26-4.32)	0.82	2.28 (1.27-4.08)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	0.81 (0.27-2.41)	1.34 (0.84-2.13)	0.41	1.24 (0.81-1.90)
GLP-1 receptor agonist	*v*	Basal insulin	2.12 (0.63-7.13)	8.94 (0.25-315.5)	0.45	2.45 (0.78-7.66)
GLP-1 receptor agonist	*v*	Basal bolus insulin	2.94 (0.12-72.7)	0.30 (0.00-254.7)	0.51	2.26 (0.10-50.2)
Basal insulin	*v*	Standard therapy	0.32 (0.01-7.99)	1.36 (0.19-9.77)	0.45	0.92 (0.17-4.90)

Table 18 Glycated haemoglobin A1C

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
SGLT-2 inhibitor	*v*	Placebo	-0.59 (-0.68--0.51)	-0.63 (-0.75--0.51)	0.62	-0.60 (-0.67--0.54)
GLP-1 receptor agonist	*v*	Placebo	-0.87 (-0.95--0.78)	-0.92 (-1.02--0.81)	0.44	-0.89 (-0.95--0.82)
SGLT-2 inhibitor	*v*	GLP-1 receptor agonist	0.40 (0.11-0.69)	0.27 (0.18-0.36)	0.39	0.28 (0.19-0.37)
Metformin	*v*	Placebo	-0.91 (-1.10--0.71)	-0.77 (-0.87--0.67)	0.23	-0.80 (-0.89--0.71)
Sulfonylurea	*v*	Placebo	-0.87 (-1.14--0.60)	-0.63 (-0.72--0.55)	0.10	-0.65 (-0.74--0.57)
Thiazolidinedione	*v*	Placebo	-0.74 (-0.86--0.63)	-0.68 (-0.77--0.59)	0.40	-0.71 (-0.78--0.63)
DPP-4 inhibitor	*v*	Placebo	-0.55 (-0.62--0.48)	-0.66 (-0.75--0.57)	0.06	-0.60 (-0.65--0.54)
Basal insulin	*v*	Placebo	-0.88 (-1.35--0.42)	-0.74 (-0.85--0.62)	0.54	-0.74 (-0.86--0.63)
Alpha glucosidase inhibitor	*v*	Placebo	-0.63 (-0.76--0.49)	-0.4 (-0.56--0.25)	0.03	-0.53 (-0.63--0.43)
Glitinide	*v*	Placebo	-0.74 (-1.13--0.35)	-0.74 (-0.92--0.56)	0.99	-0.74 (-0.90--0.58)
Metformin	*v*	Sulfonylurea	-0.15 (-0.38-0.08)	-0.14 (-0.26--0.03)	0.99	-0.15 (-0.25--0.04)
Metformin	*v*	Thiazolidinedione	-0.13 (-0.28-0.02)	-0.07 (-0.19-0.05)	0.53	-0.09 (-0.19-0.00)
Metformin	*v*	DPP-4 inhibitor	-0.2 (-0.39--0.01)	-0.21 (-0.31--0.10)	0.96	-0.20 (-0.30--0.11)
Metformin	*v*	SGLT-2 inhibitor	0.04 (-0.26-0.34)	-0.23 (-0.34--0.12)	0.11	-0.20 (-0.30--0.09)
Metformin	*v*	GLP-1 receptor agonist	0.15 (-0.18-0.47)	0.08 (-0.03-0.19)	0.70	0.09 (-0.02-0.19)
Metformin	*v*	Basal insulin	-0.38 (-0.85-0.10)	-0.03 (-0.17-0.11)	0.17	-0.06 (-0.19-0.08)
Metformin	*v*	Standard therapy	-0.29 (-0.58-0.01)	-0.66 (-0.79--0.53)	0.02	-0.60 (-0.72--0.48)
Metformin	*v*	Alpha glucosidase inhibitor	-0.32 (-0.69-0.06)	-0.26 (-0.4--0.13)	0.80	-0.27 (-0.40--0.14)
Metformin	*v*	Glitinide	-0.24 (-0.71-0.23)	-0.03 (-0.22-0.16)	0.43	-0.06 (-0.23-0.11)
Sulfonylurea	*v*	Thiazolidinedione	0.06 (-0.05-0.18)	0.04 (-0.08-0.15)	0.76	0.05 (-0.03-0.13)
Sulfonylurea	*v*	DPP-4 inhibitor	-0.03 (-0.17-0.11)	-0.08 (-0.18-0.02)	0.59	-0.06 (-0.14-0.02)
Sulfonylurea	*v*	SGLT-2 inhibitor	-0.06 (-0.28-0.17)	-0.05 (-0.15-0.06)	0.95	-0.05 (-0.15-0.05)
Sulfonylurea	*v*	GLP-1 receptor agonist	0.24 (-0.02-0.50)	0.23 (0.13-0.33)	0.94	0.23 (0.14-0.32)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
Sulfonylurea	*v*	Basal insulin	-0.03 (-0.5-0.45)	0.10 (-0.03-0.23)	0.62	0.09 (-0.04-0.22)
Sulfonylurea	*v*	Basal bolus insulin	1.60 (0.44-2.76)	0.07 (-0.29-0.44)	0.01	0.21 (-0.14-0.56)
Sulfonylurea	*v*	Bolus insulin	0.20 (-0.52-0.92)	0.27 (-0.02-0.56)	0.86	0.26 (-0.01-0.53)
Sulfonylurea	*v*	Standard therapy	-0.79 (-1.44--0.14)	-0.45 (-0.56--0.33)	0.31	-0.46 (-0.57--0.35)
Sulfonylurea	*v*	Alpha glucosidase inhibitor	-0.18 (-0.45-0.09)	-0.11 (-0.24-0.02)	0.65	-0.12 (-0.24--0.00)
Sulfonylurea	*v*	Glitinide	0.10 (-0.1-0.31)	0.06 (-0.19-0.31)	0.78	0.08 (-0.07-0.24)
Thiazolidinedione	*v*	DPP-4 inhibitor	-0.10 (-0.3-0.1)	-0.11 (-0.2--0.03)	0.90	-0.11 (-0.19--0.03)
Thiazolidinedione	*v*	SGLT-2 inhibitor	-0.10 (-0.55-0.35)	-0.10 (-0.19--0.01)	0.99	-0.10 (-0.19--0.01)
Thiazolidinedione	*v*	GLP-1 receptor agonist	0.04 (-0.24-0.32)	0.20 (0.1-0.29)	0.29	0.18 (0.09-0.27)
Thiazolidinedione	*v*	Basal insulin	0.35 (0-0.7)	0.00 (-0.13-0.13)	0.07	0.04 (-0.08-0.16)
Thiazolidinedione	*v*	Basal bolus insulin	0.00 (-1.3-1.3)	0.17 (-0.19-0.53)	0.80	0.16 (-0.19-0.51)
Thiazolidinedione	*v*	Standard therapy	-0.39 (-0.58--0.20)	-0.56 (-0.68--0.43)	0.14	-0.51 (-0.61--0.40)
Thiazolidinedione	*v*	Alpha glucosidase inhibitor	-0.21 (-0.57-0.14)	-0.17 (-0.29--0.05)	0.83	-0.17 (-0.29--0.06)
Thiazolidinedione	*v*	Glitinide	0.05 (-0.42-0.52)	0.03 (-0.14-0.21)	0.94	0.03 (-0.13-0.20)
DPP-4 inhibitor	*v*	SGLT-2 inhibitor	0.03 (-0.15-0.20)	0.01 (-0.08-0.09)	0.84	0.01 (-0.07-0.09)
DPP-4 inhibitor	*v*	GLP-1 receptor agonist	0.32 (0.18-0.46)	0.28 (0.20-0.36)	0.65	0.29 (0.22-0.36)
DPP-4 inhibitor	*v*	Basal insulin	-0.04 (-0.36-0.28)	0.18 (0.05-0.30)	0.21	0.15 (0.03-0.26)
DPP-4 inhibitor	*v*	Standard therapy	-0.47 (-0.62--0.31)	-0.36 (-0.48--0.24)	0.29	-0.40 (-0.49--0.30)
DPP-4 inhibitor	*v*	Alpha glucosidase inhibitor	-0.33 (-0.58--0.09)	0.00 (-0.12-0.11)	0.02	-0.06 (-0.17-0.04)
SGLT-2 inhibitor	*v*	Basal insulin	-0.02 (-0.7-0.66)	0.14 (0.02-0.27)	0.64	0.14 (0.01-0.26)
SGLT-2 inhibitor	*v*	Standard therapy	-0.44 (-0.81--0.07)	-0.4 (-0.52--0.29)	0.87	-0.41 (-0.52--0.30)
GLP-1 receptor agonist	*v*	Basal insulin	-0.16 (-0.31--0.02)	-0.12 (-0.28-0.04)	0.68	-0.14 (-0.25--0.04
GLP-1 receptor agonist	*v*	Basal bolus insulin	0.00 (-0.45-0.44)	-0.04 (-0.57-0.48)	0.91	-0.02 (-0.36-0.32)
GLP-1 receptor agonist	*v*	Bolus insulin	-0.08 (-0.43-0.27)	0.17 (-0.22-0.56)	0.35	0.03 (-0.23-0.29)

Intervention		Comparator	Direct estimate	Indirect estimate	Incoherence (p value)	Network estimate
GLP-1 receptor agonist	*v*	Standard therapy	-0.66 (-0.87--0.45)	-0.70 (-0.81--0.58)	0.75	-0.69 (-0.79--0.59)
Basal insulin	*v*	Basal bolus insulin	-0.3 (-0.94-0.34)	0.29 (-0.12-0.71)	0.13	0.12 (-0.22-0.47)
Basal insulin	*v*	Bolus insulin	0.38 (-0.07-0.83)	0.06 (-0.28-0.39)	0.26	0.17 (-0.10-0.44)
Basal insulin	*v*	Standard therapy	-0.68 (-0.96--0.40)	-0.51 (-0.66--0.36)	0.30	-0.55 (-0.68--0.42)
Alpha glucosidase inhibitor	*v*	Standard therapy	0.36 (-0.01-0.73)	0.33 (0.19-0.47)	0.89	-0.33 (-0.46--0.20)
Glitinide	*v*	Standard therapy	0.63 (0.09-1.18)	0.53 (0.34-0.72)	0.73	-0.54 (-0.72--0.36)
Alpha glucosidase inhibitor	*v*	Glitinide	0.12 (-0.43-0.66)	0.22 (0.03-0.42)	0.72	0.21 (0.02-0.39)

Appendix 7 Network meta-analysis treatment estimates

Table 1 All-cause mortality

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for death from any cause with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.88 (95% confidence interval 0.79 to 0.97). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of death is 1.05 (0.95 to 1.16) (95% confidence interval 1.03 to 1.26).

SGLT-2 inhibitor	1..05 (0.95, 1.16)	1.24 (0.88, 1.74)	1.33 (1.13, 1.57)	1.22 (1.01, 1.47)	1.20 (1.08, 1.34)	1.32(0.77, 2.25)	0.95 (0.22, 4.01)	1.17 (0.12, 11.48)	1.07 (0.36, 3.14)	1.96 (0.63, 6.10)	1.18 (1.09, 1.27)	1.43 (1.07, 1.90)
0.95 (0.86, 1.06)	GLP-1 receptor agonist	1.17 (0.84,1.65)	1.26 (1.08,1.48)	1.16 (0.97,1.38)	1.15 (1.05,1.26)	1.26 (0.74,2.12)	0.90 (0.21,3.80)	1.11 (0.11,10.91)	1.02 (0.35,2.99)	1.86 (0.60,5.80)	1.14 (1.07,1.21)	1.36 (1.03,1.79)
0.81 (0.57, 1.14)	0.85 (0.61,1.19)	Metformin	1.08 (0.77,1.50)	0.99 (0.71,1.38)	0.98 (0.70,1.36)	1.07 (0.58,1.99)	0.77 (0.18,3.36)	0.95 (0.09,9.52)	0.86 (0.28,2.65)	1.58 (0.49,5.09)	0.97 (0.69,1.35)	1.16 (0.77,1.72)
0.75 (0.64, 0.89)	0.79 (0.68,0.92)	0.93 (0.67,1.29)	Sulfonylurea	0.92 (0.76,1.10)	0.91 (0.79,1.04)	0.99 (0.58,1.71)	0.71 (0.17,3.02)	0.88 (0.09,8.67)	0.80 (0.27,2.36)	1.47 (0.47,4.57)	0.90 (0.78,1.04)	1.07 (0.81,1.43)
0.82 (0.68, 0.99)	0.86 (0.72,1.03)	1.01 (0.73,1.41)	1.09 (0.91,1.31)	Thiazol idinedione	0.99 (0.83,1.17)	1.08 (0.63,1.87)	0.78 (0.18,3.31)	0.96 (0.10,9.47)	0.88 (0.30,2.60)	1.61 (0.51,5.02)	0.98 (0.83,1.15)	1.17 (0.93,1.47)
0.83 (0.75, 0.92)	0.87 (0.79,0.96)	1.02 (0.73,1.43)	1.10 (0.96,1.26)	1.01 (0.85,1.20)	DPP-4 inhibitor	1.10 (0.65,1.86)	0.79 (0.19,3.32)	0.97 (0.10,9.52)	0.88 (0.30,2.60)	1.62 (0.52,5.05)	0.99 (0.92,1.06)	1.18 (0.90,1.56)
0.76 (0.45, 1.29)	0.80 (0.47,1.34)	0.93 (0.50,1.73)	1.01 (0.58,1.73)	0.92 (0.53,1.59)	0.91 (0.54,1.55)	Basal insulin	0.72 (0.16,3.18)	0.89 (0.09,8.68)	0.81 (0.24,2.68)	1.48 (0.42,5.17)	0.90 (0.53,1.53)	1.08 (0.61,1.92)
1.05 (0.25, 4.45)	1.11 (0.26,4.65)	1.30 (0.30,5.67)	1.40 (0.33,5.91)	1.28 (0.30,5.44)	1.27 (0.30,5.35)	1.39 (0.31,6.15)	Basal bolus insulin	1.23 (0.08,18.06)	1.12 (0.19,6.76)	2.06 (0.33,12.83)	1.26 (0.30,5.29)	1.50 (0.35,6.47)
0.85 (0.09, 8.39)	0.90 (0.09,8.78)	1.05 (0.11,10.57)	1.13 (0.12,11.16)	1.04 (0.11,10.24)	1.03 (0.11,10.10)	1.13 (0.12,11.04)	0.81 (0.06,11.88)	Bolus insulin	0.91 (0.07,11.36)	1.67 (0.13,21.35)	1.02 (0.10,9.98)	1.22 (0.12,12.09)
0.94 (0.32, 2.76)	0.99 (0.33,2.90)	1.16 (0.38,3.55)	1.25 (0.42,3.66)	1.14 (0.39,3.39)	1.13 (0.38,3.32)	1.24 (0.37,4.10)	0.89 (0.15,5.36)	1.10 (0.09,13.69)	Alpha glucosidase inhibitor	1.83 (0.41,8.10)	1.12 (0.38,3.28)	1.34 (0.44,4.05)
0.51 (0.16, 1.60)	0.54 (0.17,1.68)	0.63 (0.20,2.03)	0.68 (0.22,2.11)	0.62 (0.20,1.95)	0.62 (0.20,1.92)	0.68 (0.19,2.36)	0.49 (0.08,3.03)	0.60 (0.05,7.66)	0.55 (0.12,2.41)	Glitinide	0.61 (0.20,1.90)	0.73 (0.23,2.33)
0.85 (0.79, 0.92)	0.88 (0.83,0.94)	1.03 (0.74,1.44)	1.11 (0.96,1.29)	1.02 (0.87,1.20)	1.01 (0.94,1.08)	1.11 (0.65,1.87)	0.80 (0.19,3.35)	0.98 (0.10,9.62)	0.89 (0.30,2.63)	1.64 (0.53,5.10)	Placebo	1.20 (0.91,1.57)
0.70 (0.53, 0.93)	0.74 (0.56,0.97)	0.87 (0.58,1.29)	0.93 (0.70,1.24)	0.85 (0.68,1.07)	0.85 (0.64,1.12)	0.93 (0.52,1.65)	0.67 (0.15,2.87)	0.82 (0.08,8.16)	0.75 (0.25,2.27)	1.37 (0.43,4.38)	0.84 (0.64,1.10)	Standard therapy

Table 2 Cardiovascular mortality

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for death from a cardiovascular cause with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.96 (95% confidence interval 0.84 to 1.09). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of cardiovascular death is 1.04 (95% confidence interval 0.92 to 1.19).

SGLT-2 inhibitor	1.04 (0.92,1.19)	1.13 (0.56,2.26)	1.20 (0.93,1.53)	1.16 (0.90,1.49)	1.17 (1.02,1.34)	1.35 (0.63,2.87)	2.66 (0.27,26.20)	1.18 (0.12,11.78)	1.18 (0.25,5.61)	0.77 (0.13,4.48)	1.19 (1.08,1.31)	1.40 (0.93,2.11)
0.96 (0.84,1.09)	GLP-1 receptor agonist	1.08 (0.54,2.17)	1.14 (0.89,1.46)	1.11 (0.87,1.43)	1.12 (0.98,1.28)	1.29 (0.61,2.73)	2.55 (0.26,25.05)	1.13 (0.11,11.24)	1.13 (0.24,5.37)	0.74 (0.13,4.29)	1.14 (1.04,1.25)	1.34 (0.89,2.01)
0.89 (0.44,1.77)	0.92 (0.46,1.85)	Metformin	1.06 (0.54,2.09)	1.03 (0.51,2.09)	1.04 (0.52,2.07)	1.19 (0.43,3.30)	2.35 (0.22,25.46)	1.04 (0.09,11.51)	1.05 (0.19,5.69)	0.68 (0.11,4.21)	1.05 (0.53,2.10)	1.24 (0.57,2.70)
0.84 (0.65,1.07)	0.87 (0.68,1.12)	0.95 (0.48,1.87)	Sulfonylurea	0.97 (0.72,1.32)	0.98 (0.79,1.22)	1.13 (0.52,2.47)	2.22 (0.23,21.89)	0.99 (0.10,9.95)	0.99 (0.21,4.70)	0.65 (0.11,3.73)	1.00 (0.79,1.25)	1.17 (0.75,1.82)
0.86 (0.67,1.11)	0.90 (0.70,1.15)	0.97 (0.48,1.98)	1.03 (0.76,1.39)	Thiazol idinedione	1.01 (0.79,1.30)	1.16 (0.53,2.52)	2.29 (0.23,22.74)	1.02 (0.10,10.22)	1.02 (0.21,4.89)	0.67 (0.11,3.86)	1.03 (0.81,1.29)	1.20 (0.86,1.68)
0.85 (0.74,0.98)	0.89 (0.78,1.02)	0.96 (0.48,1.92)	1.02 (0.82,1.26)	0.99 (0.77,1.27)	DPP-4 inhibitor	1.15 (0.54,2.45)	2.26 (0.23,22.29)	1.00 (0.10,10.04)	1.01 (0.21,4.77)	0.66 (0.11,3.81)	1.02 (0.92,1.12)	1.19 (0.79,1.79)
0.74 (0.35,1.58)	0.77 (0.37,1.64)	0.84 (0.30,2.32)	0.89 (0.41,1.94)	0.86 (0.40,1.87)	0.87 (0.41,1.86)	Basal insulin	1.97 (0.18,21.85)	0.88 (0.09,8.71)	0.88 (0.16,4.93)	0.57 (0.09,3.86)	0.88 (0.42,1.87)	1.04 (0.46,2.35)
0.38 (0.04,3.71)	0.39 (0.04,3.87)	0.43 (0.04,4.60)	0.45 (0.05,4.43)	0.44 (0.04,4.35)	0.44 (0.04,4.35)	0.51 (0.05,5.62)	Basal bolus insulin	0.44 (0.02,11.35)	0.44 (0.03,7.03)	0.29 (0.02,5.17)	0.45 (0.05,4.41)	0.53 (0.05,5.35)
0.85 (0.08,8.47)	0.89 (0.09,8.81)	0.96 (0.09,10.56)	1.01 (0.10,10.21)	0.98 (0.10,9.92)	1.00 (0.10,9.94)	1.14 (0.11,11.38)	2.25 (0.09,57.62)	Bolus insulin	1.00 (0.06,16.08)	0.66 (0.04,11.82)	1.01 (0.10,10.07)	1.18 (0.12,12.15)
0.85 (0.18,4.02)	0.88 (0.19,4.20)	0.96 (0.18,5.21)	1.01 (0.21,4.81)	0.98 (0.20,4.73)	0.99 (0.21,4.72)	1.14 (0.20,6.42)	2.25 (0.14,35.62)	1.00 (0.06,16.04)	Alpha glucosidase inhibitor	0.66 (0.06,6.80)	1.01 (0.21,4.78)	1.18 (0.24,5.88)
1.29 (0.22,7.48)	1.35 (0.23,7.81)	1.46 (0.24,8.97)	1.54 (0.27,8.90)	1.50 (0.26,8.70)	1.52 (0.26,8.76)	1.74 (0.26,11.71)	3.43 (0.19,60.96)	1.52 (0.08,27.46)	1.53 (0.15,15.83)	Glitinide	1.54 (0.27,8.89)	1.81 (0.30,10.78)
0.84 (0.76,0.92)	0.88 (0.80,0.96)	0.95 (0.48,1.89)	1.00 (0.80,1.26)	0.97 (0.77,1.23)	0.98 (0.89,1.09)	1.13 (0.53,2.40)	2.23 (0.23,21.95)	0.99 (0.10,9.87)	0.99 (0.21,4.70)	0.65 (0.11,3.75)	Placebo	1.17 (0.79,1.75)
0.72 (0.47,1.08)	0.75 (0.50,1.12)	0.81 (0.37,1.77)	0.86 (0.55,1.33)	0.83 (0.59,1.16)	0.84 (0.56,1.26)	0.96 (0.43,2.19)	1.90 (0.19,19.35)	0.84 (0.08,8.66)	0.85 (0.17,4.21)	0.55 (0.09,3.31)	0.85 (0.57,1.27)	Standard therapy

Table 3 Nonfatal myocardial infarction

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for myocardial infarction with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.95 (95% confidence interval 0.84 to 1.09). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of myocardial infarction is 1.05 (95% confidence interval 0.93 to 1.19).

SGLT-2 inhibitor	1.05 (0.93,1.19)	1.30 (0.90,1.90)	1.23 (0.97,1.56)	1.31 (0.95,1.82)	1.16 (1.01,1.33)	1.25 (0.61,2.56)	0.40 (0.04,3.95)	1.41 (0.44,4.46)	0.22 (0.05,1.00)	0.33 (0.06,1.86)	1.14 (1.03,1.27)	1.09 (0.72,1.65)
0.95 (0.84,1.08)	GLP-1 receptor agonist	1.24 (0.86,1.80)	1.17 (0.94,1.47)	1.25 (0.91,1.72)	1.10 (0.98,1.25)	1.19 (0.59,2.41)	0.38 (0.04,3.75)	1.34 (0.43,4.22)	0.21 (0.05,0.95)	0.31 (0.05,1.77)	1.09 (1.01,1.17)	1.04 (0.69,1.56)
0.77 (0.53,1.11)	0.81 (0.56,1.16)	Metformin	0.94 (0.66,1.36)	1.01 (0.68,1.48)	0.89 (0.62,1.28)	0.96 (0.43,2.11)	0.30 (0.03,3.11)	1.08 (0.32,3.59)	0.17 (0.04,0.80)	0.25 (0.04,1.47)	0.88 (0.61,1.26)	0.84 (0.52,1.34)
0.81 (0.64,1.03)	0.85 (0.68,1.07)	1.06 (0.74,1.52)	Sulfonylurea	1.07 (0.80,1.41)	0.94 (0.77,1.15)	1.01 (0.49,2.12)	0.32 (0.03,3.23)	1.14 (0.36,3.67)	0.18 (0.04,0.82)	0.27 (0.05,1.50)	0.93 (0.75,1.15)	0.89 (0.60,1.31)
0.76 (0.55,1.06)	0.80 (0.58,1.10)	0.99 (0.67,1.47)	0.94 (0.71,1.25)	Thiazol-idinedione	0.88 (0.65,1.20)	0.95 (0.45,2.03)	0.30 (0.03,3.06)	1.07 (0.33,3.50)	0.17 (0.04,0.78)	0.25 (0.04,1.44)	0.87 (0.64,1.19)	0.83 (0.61,1.14)
0.86 (0.75,0.99)	0.91 (0.80,1.02)	1.12 (0.78,1.61)	1.06 (0.87,1.30)	1.13 (0.83,1.53)	DPP-4 inhibitor	1.08 (0.53,2.20)	0.34 (0.03,3.40)	1.21 (0.38,3.84)	0.19 (0.04,0.86)	0.28 (0.05,1.60)	0.99 (0.90,1.08)	0.94 (0.63,1.40)
0.80 (0.39,1.64)	0.84 (0.41,1.71)	1.04 (0.47,2.30)	0.99 (0.47,2.06)	1.05 (0.49,2.24)	0.93 (0.45,1.90)	Basal insulin	0.32 (0.03,3.16)	1.13 (0.36,3.52)	0.18 (0.03,0.94)	0.26 (0.04,1.71)	0.92 (0.45,1.86)	0.87 (0.40,1.93)
2.52 (0.25,25.05)	2.64 (0.27,26.22)	3.28 (0.32,33.50)	3.10 (0.31,31.06)	3.30 (0.33,33.38)	2.92 (0.29,29.05)	3.14 (0.32,31.18)	Basal bolus insulin	3.54 (0.29,43.75)	0.56 (0.04,8.67)	0.82 (0.05,14.65)	2.88 (0.29,28.60)	2.75 (0.27,28.13)
0.71 (0.22,2.25)	0.75 (0.24,2.35)	0.93 (0.28,3.08)	0.88 (0.27,2.81)	0.93 (0.29,3.04)	0.82 (0.26,2.61)	0.89 (0.28,2.77)	0.28 (0.02,3.49)	Bolus insulin	0.16 (0.02,1.05)	0.23 (0.03,1.86)	0.81 (0.26,2.56)	0.78 (0.23,2.59)
4.53 (1.00,20.60)	4.76 (1.05,21.61)	5.91 (1.25,27.86)	5.58 (1.22,25.49)	5.95 (1.28,27.67)	5.26 (1.16,23.87)	5.66 (1.07,30.03)	1.80 (0.12,28.11)	6.38 (0.96,42.54)	Alpha glucosidase inhibitor	1.49 (0.16,13.97)	5.19 (1.14,23.50)	4.95 (1.04,23.53)
3.05 (0.54,17.34)	3.20 (0.56,18.19)	3.98 (0.68,23.22)	3.76 (0.67,21.22)	4.00 (0.70,23.05)	3.54 (0.63,20.06)	3.81 (0.59,24.79)	1.21 (0.07,21.52)	4.29 (0.54,34.35)	0.67 (0.07,6.33)	Glitinide	3.49 (0.62,19.78)	3.33 (0.57,19.58)
0.87 (0.79,0.97)	0.92 (0.85,0.99)	1.14 (0.79,1.64)	1.08 (0.87,1.33)	1.15 (0.84,1.56)	1.01 (0.92,1.11)	1.09 (0.54,2.22)	0.35 (0.03,3.45)	1.23 (0.39,3.88)	0.19 (0.04,0.87)	0.29 (0.05,1.62)	Placebo	0.95 (0.64,1.42)
0.92 (0.61,1.38)	0.96 (0.64,1.44)	1.19 (0.74,1.92)	1.13 (0.76,1.67)	1.20 (0.88,1.64)	1.06 (0.71,1.58)	1.14 (0.52,2.52)	0.36 (0.04,3.72)	1.29 (0.39,4.30)	0.20 (0.04,0.96)	0.30 (0.05,1.76)	1.05 (0.70,1.56)	Standard therapy

Table 4 Nonfatal stroke

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for stroke with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 1.20 (95% confidence interval 1.03 to 1.41). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of stroke is 0.83 (95% confidence interval 0.71 to 0.98).

SGLT-2 inhibitor	0.83 (0.71,0.98)	0.99 (0.64,1.55)	1.08 (0.83,1.42)	0.93 (0.68,1.27)	0.92 (0.77,1.09)	0.83 (0.38,1.83)	0.61 (0.11,3.55)	0.84 (0.09,8.19)	9.95 (0.80,123.72)	1.84 (0.27,12.46)	0.99 (0.87,1.12)	1.18 (0.75,1.84)
1.20 (1.03,1.41)	GLP-1 receptor agonist	1.20 (0.77,1.85)	1.30 (1.01,1.69)	1.12 (0.82,1.51)	1.10 (0.94,1.29)	1.00 (0.46,2.17)	0.74 (0.13,4.25)	1.01 (0.10,9.78)	11.96 (0.96,148.53)	2.21 (0.33,14.95)	1.19 (1.08,1.31)	1.41 (0.91,2.19)
1.01 (0.65,1.56)	0.84 (0.54,1.29)	Metformin	1.09 (0.72,1.64)	0.93 (0.60,1.45)	0.92 (0.60,1.41)	0.84 (0.35,2.02)	0.62 (0.10,3.72)	0.85 (0.08,8.53)	10.01 (0.79,126.77)	1.85 (0.27,12.85)	1.00 (0.65,1.52)	1.18 (0.68,2.05)
0.92 (0.70,1.21)	0.77 (0.59,0.99)	0.92 (0.61,1.38)	Sulfonylurea	0.86 (0.64,1.15)	0.85 (0.67,1.06)	0.77 (0.34,1.72)	0.57 (0.10,3.30)	0.78 (0.08,7.62)	9.18 (0.75,112.72)	1.70 (0.25,11.34)	0.91 (0.72,1.16)	1.09 (0.70,1.68)
1.08 (0.79,1.47)	0.90 (0.66,1.21)	1.07 (0.69,1.66)	1.17 (0.87,1.57)	Thiazol-idinedione	0.99 (0.74,1.32)	0.90 (0.40,2.02)	0.66 (0.11,3.84)	0.91 (0.09,8.94)	10.72 (0.86,133.16)	1.98 (0.29,13.35)	1.07 (0.80,1.42)	1.27 (0.90,1.79)
1.09 (0.92,1.30)	0.91 (0.77,1.06)	1.09 (0.71,1.66)	1.18 (0.94,1.48)	1.01 (0.76,1.36)	DPP-4 inhibitor	0.91 (0.41,1.99)	0.67 (0.12,3.87)	0.92 (0.09,8.93)	10.86 (0.88,134.44)	2.01 (0.30,13.53)	1.08 (0.95,1.23)	1.28 (0.83,1.98)
1.20 (0.55,2.64)	1.00 (0.46,2.17)	1.20 (0.50,2.88)	1.30 (0.58,2.93)	1.12 (0.49,2.52)	1.10 (0.50,2.42)	Basal insulin	0.74 (0.13,4.24)	1.01 (0.09,11.13)	11.97 (0.86,166.34)	2.21 (0.28,17.30)	1.19 (0.55,2.59)	1.42 (0.59,3.37)
1.63 (0.28,9.41)	1.35 (0.24,7.78)	1.62 (0.27,9.74)	1.76 (0.30,10.27)	1.51 (0.26,8.77)	1.49 (0.26,8.61)	1.35 (0.24,7.77)	Basal bolus insulin	1.37 (0.08,24.04)	16.20 (0.76,346.03)	2.99 (0.23,39.66)	1.61 (0.28,9.27)	1.92 (0.32,11.43)
1.19 (0.12,11.56)	0.99 (0.10,9.56)	1.18 (0.12,11.92)	1.29 (0.13,12.65)	1.10 (0.11,10.90)	1.09 (0.11,10.60)	0.99 (0.09,10.87)	0.73 (0.04,12.82)	Bolus insulin	11.83 (0.40,351.07)	2.19 (0.11,42.49)	1.18 (0.12,11.41)	1.40 (0.14,14.11)
0.10 (0.01,1.25)	0.08 (0.01,1.04)	0.10 (0.01,1.27)	0.11 (0.01,1.34)	0.09 (0.01,1.16)	0.09 (0.01,1.14)	0.08 (0.01,1.16)	0.06 (0.00,1.32)	0.08 (0.00,2.51)	Alpha glucosidase inhibitor	0.18 (0.02,2.27)	0.10 (0.01,1.23)	0.12 (0.01,1.49)
0.54 (0.08,3.68)	0.45 (0.07,3.06)	0.54 (0.08,3.75)	0.59 (0.09,3.94)	0.50 (0.07,3.40)	0.50 (0.07,3.36)	0.45 (0.06,3.53)	0.33 (0.03,4.42)	0.46 (0.02,8.89)	5.41 (0.44,66.42)	Glitinide	0.54 (0.08,3.63)	0.64 (0.09,4.34)
1.01 (0.89,1.14)	0.84 (0.76,0.93)	1.00 (0.66,1.54)	1.09 (0.86,1.40)	0.94 (0.70,1.25)	0.93 (0.82,1.05)	0.84 (0.39,1.83)	0.62 (0.11,3.57)	0.85 (0.09,8.24)	10.05 (0.81,124.59)	1.86 (0.28,12.54)	Placebo	1.19 (0.77,1.83)
0.85 (0.54,1.33)	0.71 (0.46,1.10)	0.85 (0.49,1.46)	0.92 (0.59,1.43)	0.79 (0.56,1.11)	0.78 (0.51,1.20)	0.71 (0.30,1.68)	0.52 (0.09,3.12)	0.71 (0.07,7.21)	8.46 (0.67,106.45)	1.56 (0.23,10.61)	0.84 (0.55,1.29)	Standard therapy

Table 5 Kidney failure

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for kidney failure with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.91 (95% confidence interval 0.69 to 1.20). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of kidney failure is 1.10 (95% confidence interval 0.83 to 1.45).

SGLT-2 inhibitor	1.10 (0.83,1.45)	0.09 (0.01,1.60)	1.15 (0.26,5.08)	0.39 (0.03,5.83)	1.35 (0.95,1.92)	1.08 (0.19,6.09)	3.35 (0.13,83.65)	1.40 (1.12,1.75)
0.91 (0.69,1.20)	GLP-1 receptor agonist	0.09 (0.00,1.48)	1.05 (0.24,4.65)	0.35 (0.02,5.33)	1.23 (0.90,1.68)	0.98 (0.18,5.42)	3.05 (0.12,75.27)	1.27 (1.08,1.50)
10.69 (0.62,183.08)	11.74 (0.68,203.78)	Metformin	12.35 (0.50,303.82)	4.16 (0.08,210.50)	14.41 (0.82,252.10)	11.56 (0.42,321.33)	35.86 (0.49,2619.65)	14.97 (0.87,258.59)
0.87 (0.20,3.81)	0.95 (0.22,4.21)	0.08 (0.00,1.99)	Sulfonylurea	0.34 (0.03,3.25)	1.17 (0.27,5.10)	0.94 (0.10,9.00)	2.90 (0.08,99.39)	1.21 (0.28,5.32)
2.57 (0.17,38.50)	2.82 (0.19,42.41)	0.24 (0.00,12.15)	2.97 (0.31,28.60)	Thiazol-idinedione	3.46 (0.23,51.68)	2.78 (0.11,68.31)	8.62 (0.13,572.91)	3.60 (0.24,53.82)
0.74 (0.52,1.06)	0.82 (0.60,1.12)	0.07 (0.00,1.21)	0.86 (0.20,3.74)	0.29 (0.02,4.31)	DPP-4 inhibitor	0.80 (0.14,4.55)	2.49 (0.10,62.30)	1.04 (0.79,1.36)
0.93 (0.16,5.21)	1.02 (0.18,5.60)	0.09 (0.00,2.40)	1.07 (0.11,10.27)	0.36 (0.01,8.85)	1.25 (0.22,7.07)	Basal insulin	3.10 (0.08,117.07)	1.30 (0.23,7.19)
0.30 (0.01,7.44)	0.33 (0.01,8.07)	0.03 (0.00,2.04)	0.34 (0.01,11.78)	0.12 (0.00,7.72)	0.40 (0.02,10.06)	0.32 (0.01,12.17)	Bolus insulin	0.42 (0.02,10.34)
0.71 (0.57,0.89)	0.78 (0.67,0.92)	0.07 (0.00,1.15)	0.82 (0.19,3.62)	0.28 (0.02,4.16)	0.96 (0.73,1.26)	0.77 (0.14,4.29)	2.40 (0.10,59.29)	Placebo

Table 6 Hospitalisation for heart failure

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for heart failure with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.74 (95% confidence interval 0.65 to 0.85). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of heart failure is 1.10 (95% confidence interval 0.83 to 1.45).

SGLT-2 inhibitor	1.34 (1.17,1.54)	1.71 (1.06,2.75)	1.28 (1.00,1.63)	2.22 (1.82,2.71)	1.51 (1.31,1.74)	1.14 (0.52,2.48)	0.45 (0.02,11.13)	4.66 (0.18,118.31)	1.43 (1.30,1.58)	1.21 (0.78,1.87)
0.74 (0.65,0.85)	GLP-1 receptor agonist	1.27 (0.79,2.05)	0.95 (0.75,1.21)	1.66 (1.36,2.01)	1.12 (0.98,1.29)	0.85 (0.39,1.84)	0.34 (0.01,8.27)	3.47 (0.14,88.13)	1.07 (0.97,1.17)	0.90 (0.59,1.39)
0.58 (0.36,0.94)	0.78 (0.49,1.26)	Metformin	0.75 (0.47,1.19)	1.30 (0.82,2.05)	0.88 (0.55,1.41)	0.67 (0.27,1.63)	0.26 (0.01,6.72)	2.72 (0.10,71.40)	0.84 (0.53,1.33)	0.71 (0.39,1.29)
0.78 (0.62,1.00)	1.05 (0.83,1.34)	1.34 (0.84,2.13)	Sulfonylurea	1.74 (1.38,2.20)	1.18 (0.95,1.47)	0.89 (0.40,1.98)	0.35 (0.01,8.78)	3.65 (0.14,93.28)	1.12 (0.90,1.40)	0.95 (0.60,1.50)
0.45 (0.37,0.55)	0.60 (0.50,0.73)	0.77 (0.49,1.22)	0.57 (0.45,0.73)	Thiazol-idinedione	0.68 (0.56,0.82)	0.51 (0.24,1.11)	0.20 (0.01,5.02)	2.10 (0.08,53.41)	0.64 (0.54,0.77)	0.55 (0.37,0.81)
0.66 (0.57,0.77)	0.89 (0.77,1.03)	1.13 (0.71,1.81)	0.85 (0.68,1.05)	1.47 (1.21,1.79)	DPP-4 inhibitor	0.75 (0.35,1.65)	0.30 (0.01,7.38)	3.09 (0.12,78.45)	0.95 (0.85,1.05)	0.80 (0.52,1.24)
0.88 (0.40,1.92)	1.18 (0.54,2.55)	1.50 (0.62,3.67)	1.12 (0.50,2.49)	1.95 (0.90,4.24)	1.33 (0.61,2.89)	Basal insulin	0.40 (0.01,10.69)	4.09 (0.15,113.70)	1.26 (0.58,2.73)	1.06 (0.48,2.34)
2.22 (0.09,54.91)	2.98 (0.12,73.48)	3.80 (0.15,96.96)	2.83 (0.11,70.49)	4.93 (0.20,122.37)	3.35 (0.14,82.84)	2.53 (0.09,68.30)	Bolus insulin	10.34 (0.11,982.25)	3.18 (0.13,78.49)	2.69 (0.11,68.25)
0.21 (0.01,5.45)	0.29 (0.01,7.32)	0.37 (0.01,9.63)	0.27 (0.01,7.00)	0.48 (0.02,12.16)	0.32 (0.01,8.23)	0.24 (0.01,6.79)	0.10 (0.00,9.18)	Alpha glucosidase inhibitor	0.31 (0.01,7.80)	0.26 (0.01,6.78)
0.70 (0.63,0.77)	0.94 (0.85,1.03)	1.19 (0.75,1.90)	0.89 (0.71,1.11)	1.55 (1.31,1.84)	1.05 (0.95,1.17)	0.79 (0.37,1.72)	0.31 (0.01,7.76)	3.25 (0.13,82.52)	Placebo	0.85 (0.55,1.29)
0.83 (0.53,1.28)	1.11 (0.72,1.71)	1.41 (0.77,2.58)	1.05 (0.67,1.66)	1.83 (1.23,2.73)	1.25 (0.81,1.92)	0.94 (0.43,2.07)	0.37 (0.01,9.43)	3.85 (0.15,100.27)	1.18 (0.77,1.81)	Standard therapy

Table 7 Severe hypoglycaemia

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for severe hypoglycaemia with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.98 (95% confidence interval 0.73 to 1.31). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of severe hypoglycaemia is 1.02 (95% confidence interval 0.76 to 1.36).

SGLT-2 inhibitor	1.02 (0.76,1.36)	1.82 (0.88,3.74)	6.84 (4.34,10.79)	1.49 (0.92,2.44)	1.21 (0.90,1.61)	2.56 (1.66,3.94)	2.58 (0.15,43.94)	2.96 (0.56,15.78)	1.24 (0.24,6.35)	3.49 (0.99,12.37)	1.11 (0.86,1.43)	1.08 (0.66,1.79)
0.98 (0.73,1.31)	GLP-1 receptor agonist	1.78 (0.87,3.64)	6.70 (4.38,10.25)	1.46 (0.96,2.23)	1.18 (0.97,1.44)	2.51 (1.81,3.48)	2.52 (0.15,42.42)	2.90 (0.56,15.06)	1.22 (0.24,6.15)	3.42 (0.97,12.03)	1.08 (0.93,1.27)	1.06 (0.71,1.58)
0.55 (0.27,1.13)	0.56 (0.28,1.15)	Metformin	3.77 (1.74,8.15)	0.82 (0.37,1.85)	0.66 (0.33,1.35)	1.41 (0.64,3.09)	1.42 (0.08,26.08)	1.63 (0.27,9.84)	0.69 (0.12,3.91)	1.92 (0.61,6.07)	0.61 (0.30,1.23)	0.60 (0.26,1.35)
0.15 (0.09,0.23)	0.15 (0.10,0.23)	0.27 (0.12,0.57)	Sulfonylurea	0.22 (0.13,0.37)	0.18 (0.12,0.26)	0.37 (0.22,0.64)	0.38 (0.02,6.53)	0.43 (0.08,2.37)	0.18 (0.04,0.94)	0.51 (0.14,1.81)	0.16 (0.11,0.24)	0.16 (0.09,0.28)
0.67 (0.41,1.09)	0.68 (0.45,1.04)	1.21 (0.54,2.73)	4.58 (2.68,7.81)	Thiazol-idinedione	0.81 (0.53,1.24)	1.71 (1.03,2.85)	1.72 (0.10,29.77)	1.98 (0.36,10.86)	0.83 (0.16,4.39)	2.34 (0.63,8.65)	0.74 (0.49,1.13)	0.72 (0.43,1.21)
0.83 (0.62,1.11)	0.85 (0.69,1.04)	1.51 (0.74,3.07)	5.68 (3.82,8.44)	1.24 (0.81,1.90)	DPP-4 inhibitor	2.12 (1.45,3.10)	2.14 (0.13,36.18)	2.46 (0.47,12.92)	1.03 (0.20,5.20)	2.90 (0.83,10.15)	0.92 (0.79,1.07)	0.90 (0.58,1.38)
0.39 (0.25,0.60)	0.40 (0.29,0.55)	0.71 (0.32,1.55)	2.67 (1.57,4.54)	0.58 (0.35,0.97)	0.47 (0.32,0.69)	Basal insulin	1.01 (0.06,16.60)	1.16 (0.22,6.21)	0.49 (0.09,2.53)	1.36 (0.37,5.00)	0.43 (0.30,0.62)	0.42 (0.25,0.70)
0.39 (0.02,6.62)	0.40 (0.02,6.67)	0.70 (0.04,12.94)	2.66 (0.15,46.04)	0.58 (0.03,10.02)	0.47 (0.03,7.91)	0.99 (0.06,16.39)	Basal bolus insulin	1.15 (0.04,30.19)	0.48 (0.02,12.49)	1.36 (0.06,29.76)	0.43 (0.03,7.26)	0.42 (0.02,7.26)
0.34 (0.06,1.80)	0.34 (0.07,1.79)	0.61 (0.10,3.69)	2.31 (0.42,12.65)	0.50 (0.09,2.76)	0.41 (0.08,2.14)	0.86 (0.16,4.63)	0.87 (0.03,22.82)	Bolus insulin	0.42 (0.04,4.23)	1.18 (0.15,9.36)	0.37 (0.07,1.95)	0.37 (0.07,1.99)
0.80 (0.16,4.11)	0.82 (0.16,4.15)	1.46 (0.26,8.33)	5.50 (1.07,28.41)	1.20 (0.23,6.34)	0.97 (0.19,4.89)	2.06 (0.39,10.74)	2.07 (0.08,53.63)	2.38 (0.24,24.01)	Alpha glucosidase inhibitor	2.81 (0.39,20.39)	0.89 (0.18,4.47)	0.87 (0.16,4.61)
0.29 (0.08,1.01)	0.29 (0.08,1.03)	0.52 (0.16,1.64)	1.96 (0.55,6.95)	0.43 (0.12,1.58)	0.35 (0.10,1.21)	0.73 (0.20,2.69)	0.74 (0.03,16.20)	0.85 (0.11,6.74)	0.36 (0.05,2.58)	Glitinide	0.32 (0.09,1.11)	0.31 (0.08,1.16)
0.90 (0.70,1.16)	0.92 (0.79,1.08)	1.64 (0.81,3.30)	6.18 (4.11,9.29)	1.35 (0.89,2.05)	1.09 (0.93,1.27)	2.31 (1.62,3.30)	2.33 (0.14,39.25)	2.67 (0.51,13.99)	1.12 (0.22,5.63)	3.15 (0.90,11.01)	Placebo	0.98 (0.64,1.49)
0.92 (0.56,1.53)	0.94 (0.63,1.41)	1.68 (0.74,3.80)	6.32 (3.59,11.13)	1.38 (0.83,2.30)	1.11 (0.72,1.71)	2.36 (1.42,3.94)	2.38 (0.14,41.09)	2.74 (0.50,14.91)	1.15 (0.22,6.08)	3.22 (0.86,12.03)	1.02 (0.67,1.56)	Standard therapy

Table 8 Blindness

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for blindness with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.17 (95% confidence interval 0.00 to 5.64). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of blindness is 6.04 (95% confidence interval 0.18 to 205.45).

SGLT-2 inhibitor	6.04 (0.18,205.45)	5.99 (0.23,154.28)	6.03 (0.25,148.05)
0.17 (0.00,5.64)	GLP-1 receptor agonist	0.99 (0.20,4.83)	1.00 (0.23,4.39)
0.17 (0.01,4.30)	1.01 (0.21,4.90)	DPP-4 inhibitor	1.01 (0.58,1.75)
0.17 (0.01,4.07)	1.00 (0.23,4.41)	0.99 (0.57,1.73)	Placebo

Table 9 Health-related quality of life

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as standardised mean difference and 95% confidence interval. For example, the standardised mean difference in health-related quality of life for SGLT-2 inhibitor therapy compared to GLP-1 receptor agonist therapy is 0.01 (95% confidence interval -0.19 to 0.20). The standardised mean difference in health-related quality of life for GLP1 receptor agonist therapy is the inverse (0.01 (95% confidence interval -0.20 to 0.19)).

SGLT-2 inhibitor	-0.01 (-0.20,0.19)	-0.13 (-0.45,0.19)	0.11 (-0.35,0.57)	0.03 (-0.31,0.37)	-0.11 (-0.35,0.13)	0.03 (-0.30,0.35)	-0.35 (-0.63,-0.06)	-0.11 (-0.49,0.26)	-0.01 (-0.45,0.44)	-0.14 (-0.36,0.08)	-0.46 (-0.75,-0.16)
0.01 (-0.19,0.20)	GLP-1 receptor agonist	-0.12 (-0.37,0.12)	0.12 (-0.30,0.54)	0.04 (-0.24,0.32)	-0.11 (-0.25,0.03)	0.03 (-0.23,0.29)	-0.34 (-0.55,-0.13)	-0.11 (-0.43,0.21)	0.00 (-0.40,0.40)	-0.13 (-0.23,-0.03)	-0.45 (-0.67,-0.23)
0.13 (-0.19,0.45)	0.12 (-0.12,0.37)	Metformin	0.24 (-0.25,0.73)	0.16 (-0.14,0.46)	0.02 (-0.23,0.26)	0.16 (-0.20,0.52)	-0.21 (-0.54,0.11)	0.02 (-0.36,0.40)	0.13 (-0.29,0.54)	-0.01 (-0.28,0.26)	-0.33 (-0.64,-0.01)
-0.11 (-0.57,0.35)	-0.12 (-0.54,0.30)	-0.24 (-0.73,0.25)	Sulfonylurea	-0.08 (-0.58,0.43)	-0.22 (-0.67,0.22)	-0.08 (-0.58,0.41)	-0.46 (-0.92,0.01)	-0.22 (-0.75,0.30)	-0.12 (-0.69,0.46)	-0.25 (-0.66,0.16)	-0.57 (-1.04,-0.09)
-0.03 (-0.37,0.31)	-0.04 (-0.32,0.24)	-0.16 (-0.46,0.14)	0.08 (-0.43,0.58)	Thiazol-idinedione	-0.15 (-0.43,0.14)	-0.01 (-0.39,0.38)	-0.38 (-0.73,-0.03)	-0.15 (-0.55,0.26)	-0.04 (-0.32,0.25)	-0.17 (-0.47,0.13)	-0.49 (-0.83,-0.15)
0.11 (-0.13,0.35)	0.11 (-0.03,0.25)	-0.02 (-0.26,0.23)	0.22 (-0.22,0.67)	0.15 (-0.14,0.43)	DPP-4 inhibitor	0.14 (-0.16,0.44)	-0.23 (-0.48,0.02)	-0.00 (-0.29,0.29)	0.11 (-0.29,0.51)	-0.02 (-0.19,0.14)	-0.34 (-0.56,-0.13)
-0.03 (-0.35,0.30)	-0.03 (-0.29,0.23)	-0.16 (-0.52,0.20)	0.08 (-0.41,0.58)	0.01 (-0.38,0.39)	-0.14 (-0.44,0.16)	Basal insulin	-0.37 (-0.62,-0.13)	-0.14 (-0.55,0.27)	-0.03 (-0.51,0.45)	-0.16 (-0.44,0.11)	-0.48 (-0.82,-0.14)
0.35 (0.06,0.63)	0.34 (0.13,0.55)	0.21 (-0.11,0.54)	0.46 (-0.01,0.92)	0.38 (0.03,0.73)	0.23 (-0.02,0.48)	0.37 (0.13,0.62)	Bolus insulin	0.23 (-0.15,0.61)	0.34 (-0.11,0.79)	0.21 (-0.02,0.44)	-0.11 (-0.41,0.19)
0.11 (-0.26,0.49)	0.11 (-0.21,0.43)	-0.02 (-0.40,0.36)	0.22 (-0.30,0.75)	0.15 (-0.26,0.55)	0.00 (-0.29,0.29)	0.14 (-0.27,0.55)	-0.23 (-0.61,0.15)	Alpha glucosidase inhibitor	0.11 (-0.38,0.60)	-0.02 (-0.36,0.31)	-0.34 (-0.70,0.02)
0.01 (-0.44,0.45)	-0.00 (-0.40,0.40)	-0.13 (-0.54,0.29)	0.12 (-0.46,0.69)	0.04 (-0.25,0.32)	-0.11 (-0.51,0.29)	0.03 (-0.45,0.51)	-0.34 (-0.79,0.11)	-0.11 (-0.60,0.38)	Glitinide	-0.13 (-0.54,0.28)	-0.45 (-0.90,-0.01)
0.14 (-0.08,0.36)	0.13 (0.03,0.23)	0.01 (-0.26,0.28)	0.25 (-0.16,0.66)	0.17 (-0.13,0.47)	0.02 (-0.14,0.19)	0.16 (-0.11,0.44)	-0.21 (-0.44,0.02)	0.02 (-0.31,0.36)	0.13 (-0.28,0.54)	Placebo	-0.32 (-0.56,-0.08)
0.46 (0.16,0.75)	0.45 (0.23,0.67)	0.33 (0.01,0.64)	0.57 (0.09,1.04)	0.49 (0.15,0.83)	0.34 (0.13,0.56)	0.48 (0.14,0.82)	0.11 (-0.19,0.41)	0.34 (-0.02,0.70)	0.45 (0.01,0.90)	0.32 (0.08,0.56)	Standard therapy

Table 10 Body weight

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in body weight for SGLT-2 inhibitor therapy compared to GLP-1 receptor agonist therapy is 0.47 kg (95% confidence interval -0.85 kg to -0.09 kg). The standardised mean difference in body weight for GLP1 receptor agonist therapy compared to SGLT-2 inhibitor therapy is the inverse (0.47 kg (95% confidence interval 0.09 to 0.85 kg)).

SGLT-2 inhibitor	0.47 (0.09,0.85)	1.17 (0.69,1.66)	3.63 (3.20,4.06)	4.52 (4.10,4.95)	2.25 (1.90,2.61)	3.92 (3.35,4.49)	4.18 (2.97,5.39)	2.74 (1.20,4.27)	1.61 (1.00,2.22)	3.00 (2.12,3.89)	1.92 (1.62,2.23)	2.59 (2.03,3.16)
-0.47 (-0.85,-0.09)	GLP-1 receptor agonist	0.70 (0.24,1.17)	3.16 (2.75,3.57)	4.05 (3.66,4.44)	1.78 (1.47,2.09)	3.45 (2.98,3.92)	3.71 (2.54,4.88)	2.27 (0.77,3.76)	1.14 (0.55,1.73)	2.53 (1.66,3.40)	1.45 (1.18,1.72)	2.12 (1.62,2.63)
-1.17 (-1.66,-0.69)	-0.70 (-1.17,-0.24)	Metformin	2.46 (1.97,2.95)	3.35 (2.88,3.82)	1.08 (0.64,1.51)	2.75 (2.12,3.38)	3.01 (1.78,4.24)	1.56 (0.01,3.12)	0.44 (-0.20,1.08)	1.83 (0.93,2.73)	0.75 (0.32,1.18)	1.42 (0.82,2.02)
-3.63 (-4.06,-3.20)	-3.16 (-3.57,-2.75)	-2.46 (-2.95,-1.97)	Sulfonylurea	0.89 (0.50,1.29)	-1.38 (-1.75,-1.00)	0.29 (-0.29,0.88)	0.55 (-0.65,1.75)	-0.89 (-2.43,0.65)	-2.02 (-2.64,-1.40)	-0.63 (-1.47,0.21)	-1.71 (-2.08,-1.33)	-1.03 (-1.61,-0.46)
-4.52 (-4.95,-4.10)	-4.05 (-4.44,-3.66)	-3.35 (-3.82,-2.88)	-0.89 (-1.29,-0.50)	Thiazol-idinedione	-2.27 (-2.64,-1.91)	-0.60 (-1.17,-0.03)	-0.34 (-1.54,0.85)	-1.79 (-3.32,-0.25)	-2.91 (-3.51,-2.31)	-1.52 (-2.38,-0.66)	-2.60 (-2.94,-2.26)	-1.93 (-2.49,-1.37)
-2.25 (-2.61,-1.90)	-1.78 (-2.09,-1.47)	-1.08 (-1.51,-0.64)	1.38 (1.00,1.75)	2.27 (1.91,2.64)	DPP-4 inhibitor	1.67 (1.15,2.19)	1.93 (0.74,3.12)	0.49 (-1.03,2.01)	-0.64 (-1.20,-0.08)	0.75 (-0.11,1.61)	-0.33 (-0.57,-0.08)	0.34 (-0.16,0.85)
-3.92 (-4.49,-3.35)	-3.45 (-3.92,-2.98)	-2.75 (-3.38,-2.12)	-0.29 (-0.88,0.29)	0.60 (0.03,1.17)	-1.67 (-2.19,-1.15)	Basal insulin	0.26 (-0.92,1.44)	-1.19 (-2.75,0.38)	-2.31 (-3.03,-1.59)	-0.92 (-1.88,0.04)	-2.00 (-2.51,-1.50)	-1.33 (-1.94,-0.71)
-4.18 (-5.39,-2.97)	-3.71 (-4.88,-2.54)	-3.01 (-4.24,-1.78)	-0.55 (-1.75,0.65)	0.34 (-0.85,1.54)	-1.93 (-3.12,-0.74)	-0.26 (-1.44,0.92)	Basal bolus insulin	-1.44 (-3.34,0.45)	-2.57 (-3.85,-1.28)	-1.18 (-2.61,0.25)	-2.26 (-3.44,-1.08)	-1.59 (-2.83,-0.34)
-2.74 (-4.27,-1.20)	-2.27 (-3.76,-0.77)	-1.56 (-3.12,-0.01)	0.89 (-0.65,2.43)	1.79 (0.25,3.32)	-0.49 (-2.01,1.03)	1.19 (-0.38,2.75)	1.44 (-0.45,3.34)	Bolus insulin	-1.12 (-2.73,0.48)	0.26 (-1.46,1.98)	-0.82 (-2.33,0.70)	-0.14 (-1.72,1.43)
-1.61 (-2.22,-1.00)	-1.14 (-1.73,-0.55)	-0.44 (-1.08,0.20)	2.02 (1.40,2.64)	2.91 (2.31,3.51)	0.64 (0.08,1.20)	2.31 (1.59,3.03)	2.57 (1.28,3.85)	1.12 (-0.48,2.73)	Alpha glucosidase inhibitor	1.39 (0.40,2.38)	0.31 (-0.23,0.85)	0.98 (0.27,1.69)
-3.00 (-3.89,-2.12)	-2.53 (-3.40,-1.66)	-1.83 (-2.73,-0.93)	0.63 (-0.21,1.47)	1.52 (0.66,2.38)	-0.75 (-1.61,0.11)	0.92 (-0.04,1.88)	1.18 (-0.25,2.61)	-0.26 (-1.98,1.46)	-1.39 (-2.38,-0.40)	Glitinide	-1.08 (-1.93,-0.23)	-0.41 (-1.33,0.52)
-1.92 (-2.23,-1.62)	-1.45 (-1.72,-1.18)	-0.75 (-1.18,-0.32)	1.71 (1.33,2.08)	2.60 (2.26,2.94)	0.33 (0.08,0.57)	2.00 (1.50,2.51)	2.26 (1.08,3.44)	0.82 (-0.70,2.33)	-0.31 (-0.85,0.23)	1.08 (0.23,1.93)	Placebo	0.67 (0.16,1.18)
-2.59 (-3.16,-2.03)	-2.12 (-2.63,-1.62)	-1.42 (-2.02,-0.82)	1.03 (0.46,1.61)	1.93 (1.37,2.49)	-0.34 (-0.85,0.16)	1.33 (0.71,1.94)	1.59 (0.34,2.83)	0.14 (-1.43,1.72)	-0.98 (-1.69,-0.27)	0.41 (-0.52,1.33)	-0.67 (-1.18,-0.16)	Standard therapy

Table 11 Amputation

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for amputation with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 3.43 (95% confidence interval 0.14 to 84.49). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of amputation is 0.29 (95% confidence interval 0.01 to 7.19).

SGLT-2 inhibitor	0.29 (0.01,7.19)	0.88 (0.50,1.56)	0.79 (0.54,1.17)	0.87 (0.74,1.04)	2.64 (0.83,8.42)
3.43 (0.14,84.49)	GLP-1 receptor agonist	3.03 (0.12,77.83)	2.72 (0.11,68.08)	3.00 (0.12,73.59)	9.07 (0.30,271.42)
1.13 (0.64,1.99)	0.33 (0.01,8.47)	Thiazol-idinedione	0.90 (0.47,1.71)	0.99 (0.58,1.70)	2.99 (1.09,8.21)
1.26 (0.86,1.85)	0.37 (0.01,9.18)	1.11 (0.59,2.12)	DPP-4 inhibitor	1.10 (0.78,1.56)	3.33 (1.01,11.02)
1.14 (0.96,1.35)	0.33 (0.01,8.18)	1.01 (0.59,1.74)	0.91 (0.64,1.28)	Placebo	3.02 (0.96,9.51)
0.38 (0.12,1.20)	0.11 (0.00,3.30)	0.33 (0.12,0.92)	0.30 (0.09,0.99)	0.33 (0.11,1.04)	Standard therapy

Table 12 Neuropathic pain

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for amputation with GLP-1 receptor agonist therapy compared to placebo is 0.33 (95% confidence interval 0.01 to 0.819). For the reverse, the effect of placebo compared toGLP-1 receptor agonist therapy on the odds of amputation is 3.00 (95% confidence interval 0.12 to 73.61).

GLP-1 receptor agonist	9.01 (0.10,832.5)	3.00 (0.12,73.61)
0.11 (0.00,10.27)	DPP-4 inhibitor	0.33 (0.01,8.17)
0.33 (0.01,8.19)	3.00 (0.12,73.75)	Placebo

Table 13 Diabetic ketoacidosis

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for diabetic ketoacidosis with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 1.71 (95% confidence interval 0.79 to 3.69). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of diabetic ketoacidosis is 0.58 (95% confidence interval 0.27 to 1.26).

SGLT-2 inhibitor	0.58 (0.27,1.26)	1.34 (0.19,9.42)	0.97 (0.28,3.30)	0.87 (0.42,1.80)	1.30 (0.13,13.01)	1.29 (0.13,12.87)	0.96 (0.56,1.64)
1.71 (0.79,3.69)	GLP-1 receptor agonist	2.29 (0.28,18.64)	1.65 (0.44,6.18)	1.49 (0.69,3.20)	2.23 (0.21,23.39)	2.20 (0.21,23.13)	1.64 (0.90,2.99)
0.75 (0.11,5.26)	0.44 (0.05,3.56)	Metformin	0.72 (0.07,7.24)	0.65 (0.08,5.22)	0.97 (0.05,19.88)	0.96 (0.05,19.67)	0.72 (0.09,5.42)
1.03 (0.30,3.52)	0.60 (0.16,2.26)	1.38 (0.14,13.87)	Sulfonylurea	0.90 (0.28,2.85)	1.35 (0.19,9.44)	1.33 (0.19,9.34)	0.99 (0.30,3.28)
1.15 (0.55,2.38)	0.67 (0.31,1.44)	1.54 (0.19,12.36)	1.11 (0.35,3.52)	DPP-4 inhibitor	1.50 (0.16,14.39)	1.48 (0.15,14.23)	1.10 (0.65,1.87)
0.77 (0.08,7.68)	0.45 (0.04,4.72)	1.03 (0.05,21.03)	0.74 (0.11,5.21)	0.67 (0.07,6.42)	Alpha glucosidase inhibitor	0.99 (0.12,8.13)	0.74 (0.07,7.25)
0.78 (0.08,7.76)	0.45 (0.04,4.77)	1.04 (0.05,21.26)	0.75 (0.11,5.27)	0.68 (0.07,6.49)	1.01 (0.12,8.31)	Glitinide	0.75 (0.08,7.33)
1.04 (0.61,1.78)	0.61 (0.33,1.11)	1.39 (0.18,10.55)	1.01 (0.30,3.33)	0.91 (0.53,1.54)	1.36 (0.14,13.34)	1.34 (0.14,13.19)	Placebo

Table 14 Serious hyperglycaemia

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for serious hyperglycaemia with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 1.48 (95% confidence interval 0.75 to 2.93). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of serious hyperglycaemia is 0.67 (95% confidence interval 0.34 to 1.33).

SGLT-2 inhibitor	0.67 (0.34,1.33)	0.69 (0.16,2.95)	0.75 (0.32,1.75)	1.61 (0.50,5.22)	1.05 (0.57,1.93)	0.57 (0.20,1.62)	0.50 (0.05,4.81)	0.11 (0.02,0.53)	1.68 (0.99,2.86)	2.79 (0.78,9.95)
1.48 (0.75,2.93)	GLP-1 receptor agonist	1.02 (0.25,4.11)	1.12 (0.51,2.45)	2.39 (0.82,7.00)	1.56 (0.92,2.65)	0.85 (0.38,1.91)	0.75 (0.09,6.43)	0.17 (0.04,0.77)	2.50 (1.56,4.00)	4.14 (1.24,13.84)
1.45 (0.34,6.23)	0.98 (0.24,3.94)	Metformin	1.09 (0.24,4.91)	2.34 (0.47,11.58)	1.53 (0.39,5.98)	0.83 (0.17,4.05)	0.73 (0.06,9.50)	0.16 (0.02,1.20)	2.45 (0.62,9.59)	4.05 (0.73,22.56)
1.33 (0.57,3.08)	0.89 (0.41,1.96)	0.91 (0.20,4.09)	Sulfonylurea	2.14 (0.67,6.79)	1.39 (0.69,2.81)	0.76 (0.25,2.27)	0.67 (0.07,6.61)	0.15 (0.03,0.75)	2.23 (1.10,4.54)	3.70 (1.02,13.38)
0.62 (0.19,2.01)	0.42 (0.14,1.22)	0.43 (0.09,2.11)	0.47 (0.15,1.48)	Thiazol-idinedione	0.65 (0.23,1.88)	0.36 (0.11,1.18)	0.31 (0.03,3.46)	0.07 (0.01,0.42)	1.04 (0.36,3.04)	1.73 (0.56,5.35)
0.95 (0.52,1.75)	0.64 (0.38,1.09)	0.66 (0.17,2.57)	0.72 (0.36,1.45)	1.54 (0.53,4.43)	DPP-4 inhibitor	0.55 (0.21,1.39)	0.48 (0.05,4.40)	0.11 (0.02,0.48)	1.60 (1.13,2.27)	2.66 (0.85,8.32)
1.74 (0.62,4.92)	1.18 (0.52,2.64)	1.20 (0.25,5.84)	1.31 (0.44,3.93)	2.81 (0.85,9.31)	1.83 (0.72,4.68)	Basal insulin	0.88 (0.09,8.75)	0.20 (0.04,1.09)	2.94 (1.18,7.32)	4.87 (1.23,19.27)
1.99 (0.21,18.98)	1.34 (0.16,11.53)	1.37 (0.11,17.76)	1.50 (0.15,14.81)	3.20 (0.29,35.51)	2.09 (0.23,19.15)	1.14 (0.11,11.34)	Basal bolus insulin	0.22 (0.02,3.13)	3.34 (0.37,30.29)	5.54 (0.47,65.41)
8.88 (1.90,41.52)	5.99 (1.30,27.45)	6.11 (0.83,44.77)	6.69 (1.33,33.57)	14.32 (2.36,86.66)	9.32 (2.10,41.37)	5.09 (0.92,28.21)	4.47 (0.32,62.47)	Alpha glucosidase inhibitor	14.95 (3.51,63.66)	24.78 (3.84,159.69)
0.59 (0.35,1.01)	0.40 (0.25,0.64)	0.41 (0.10,1.60)	0.45 (0.22,0.91)	0.96 (0.33,2.79)	0.62 (0.44,0.88)	0.34 (0.14,0.85)	0.30 (0.03,2.71)	0.07 (0.02,0.28)	Placebo	1.66 (0.51,5.35)
0.36 (0.10,1.28)	0.24 (0.07,0.81)	0.25 (0.04,1.37)	0.27 (0.07,0.98)	0.58 (0.19,1.79)	0.38 (0.12,1.18)	0.21 (0.05,0.81)	0.18 (0.02,2.13)	0.04 (0.01,0.26)	0.60 (0.19,1.95)	Standard therapy

Table 15 Genital infection

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for genital infection with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 5.00 (95% confidence interval 2.45 to 10.20). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of genital infection is 0.20 (95% confidence interval 0.10 to 0.41).

SGLT-2 inhibitor	0.20 (0.10,0.41)	0.39 (0.21,0.73)	0.16 (0.11,0.22)	3.29 (0.13,83.62)	0.21 (0.14,0.33)	0.29 (0.25,0.33)	0.62 (0.20,1.94)
5.00 (2.45,10.20)	GLP-1 receptor agonist	1.97 (0.77,5.07)	0.79 (0.36,1.73)	16.43 (0.60,451.95)	1.07 (0.46,2.45)	1.43 (0.69,2.95)	3.13 (0.82,11.91)
2.53 (1.37,4.70)	0.51 (0.20,1.30)	Metformin	0.40 (0.20,0.80)	8.33 (0.31,224.71)	0.54 (0.25,1.15)	0.72 (0.38,1.37)	1.58 (0.44,5.76)
6.37 (4.56,8.90)	1.27 (0.58,2.80)	2.51 (1.24,5.08)	Sulfonylurea	20.92 (0.81,541.85)	1.36 (0.79,2.35)	1.82 (1.26,2.63)	3.98 (1.22,12.97)
0.30 (0.01,7.75)	0.06 (0.00,1.67)	0.12 (0.00,3.24)	0.05 (0.00,1.24)	Thiazol-idinedione	0.06 (0.00,1.70)	0.09 (0.00,2.22)	0.19 (0.01,5.87)
4.69 (3.04,7.23)	0.94 (0.41,2.16)	1.85 (0.87,3.94)	0.74 (0.43,1.27)	15.41 (0.59,403.76)	DPP-4 inhibitor	1.34 (0.86,2.10)	2.93 (0.87,9.86)
3.50 (3.01,4.07)	0.70 (0.34,1.44)	1.38 (0.73,2.61)	0.55 (0.38,0.79)	11.49 (0.45,293.51)	0.75 (0.48,1.17)	Placebo	2.19 (0.70,6.85)
1.60 (0.52,4.97)	0.32 (0.08,1.22)	0.63 (0.17,2.29)	0.25 (0.08,0.82)	5.26 (0.17,162.18)	0.34 (0.10,1.15)	0.46 (0.15,1.43)	Standard therapy

Table 16 Fournier gangrene

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for Fournier gangrene with SGLT-2 inhibitors compared to placebo is 0.56 (95% confidence interval 0.16 to 1.92). For the reverse, the effect of placebo compared to SGLT-2 inhibitor on the odds of Fournier gangrene is 1.80 (95% confidence interval 0.52 to 6.21).

SGLT-2 inhibitor	7.02 (0.56,87.98)	1.80 (0.52,6.21)
0.14 (0.01,1.78)	DPP-4 inhibitor	0.26 (0.03,2.32)
0.56 (0.16,1.92)	3.91 (0.43,35.37)	Placebo

Table 17 Severe gastrointestinal events

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for severe gastrointestinal events with a GLP-1 receptor agonist compared to a sulfonylurea is 1.27 (95% confidence interval 0.20 to 8.17). For the reverse, the effect of a sulfonylurea compared to a GLP-1 receptor on the odds of severe gastrointestinal events is 0.79 (95% confidence interval 0.12 to 5.11).

GLP-1 receptor agonist	2.08 (0.23,19.09)	0.79 (0.12,5.11)	1.36 (0.16,11.38)	0.71 (0.29,1.77)	2.73 (0.64,11.59)	3.19 (0.14,74.97)	0.41 (0.22,0.78)	0.76 (0.10,5.98)
0.48 (0.05,4.39)	Metformin	0.38 (0.07,2.09)	0.65 (0.17,2.51)	0.34 (0.04,3.02)	1.31 (0.10,17.77)	1.53 (0.16,14.52)	0.20 (0.02,1.91)	0.37 (0.07,1.87)
1.27 (0.20,8.17)	2.64 (0.48,14.50)	Sulfonylurea	1.72 (0.33,8.97)	0.90 (0.16,5.18)	3.45 (0.35,34.46)	4.03 (0.24,67.91)	0.52 (0.08,3.52)	0.97 (0.15,6.27)
0.74 (0.09,6.18)	1.54 (0.40,5.91)	0.58 (0.11,3.04)	Thiazol-idinedione	0.52 (0.06,4.27)	2.01 (0.16,25.03)	2.35 (0.17,32.38)	0.30 (0.03,2.65)	0.56 (0.14,2.22)
1.40 (0.57,3.48)	2.93 (0.33,25.87)	1.11 (0.19,6.37)	1.91 (0.23,15.51)	DPP-4 inhibitor	3.83 (0.78,18.95)	4.48 (0.20,102.70)	0.58 (0.22,1.52)	1.07 (0.13,8.53)
0.37 (0.09,1.55)	0.76 (0.06,10.36)	0.29 (0.03,2.89)	0.50 (0.04,6.19)	0.26 (0.05,1.29)	Basal insulin	1.17 (0.04,36.59)	0.15 (0.03,0.70)	0.28 (0.02,3.33)
0.31 (0.01,7.38)	0.65 (0.07,6.21)	0.25 (0.01,4.17)	0.43 (0.03,5.87)	0.22 (0.01,5.13)	0.86 (0.03,26.84)	Alpha glucosidase inhibitor	0.13 (0.01,3.15)	0.24 (0.01,3.86)
2.46 (1.22,4.97)	5.07 (0.52,49.20)	1.92 (0.28,13.02)	3.30 (0.38,28.90)	1.76 (0.42,7.34)	6.65 (1.43,30.98)	7.76 (0.32,190.02)	Placebo	1.86 (0.22,15.42)
1.31 (0.17,10.27)	2.73 (0.53,13.94)	1.04 (0.16,6.72)	1.78 (0.45,7.01)	0.93 (0.12,7.43)	3.58 (0.30,42.59)	4.18 (0.26,67.28)	0.54 (0.06,4.47)	Standard therapy

Table 18 Pancreatic cancer

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for pancreatic cancer with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 1.49 (95% confidence interval 0.43 to 5.19). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of pancreatic cancer is 0.67 (95% confidence interval 0.19 to 2.33).

SGLT-2 inhibitor	0.67 (0.19,2.33)	0.64 (0.16,2.51)	0.49 (0.14,1.72)	0.44 (0.06,3.07)	0.23 (0.01,7.08)	0.56 (0.17,1.83)
1.49 (0.43,5.19)	GLP-1 receptor agonist	0.96 (0.40,2.30)	0.73 (0.37,1.42)	0.65 (0.15,2.90)	0.34 (0.01,8.36)	0.84 (0.55,1.28)
1.56 (0.40,6.09)	1.05 (0.43,2.52)	Sulfonylurea	0.76 (0.39,1.47)	0.68 (0.12,3.86)	0.35 (0.01,9.84)	0.88 (0.39,1.96)
2.05 (0.58,7.25)	1.38 (0.70,2.70)	1.32 (0.68,2.55)	DPP-4 inhibitor	0.90 (0.18,4.63)	0.46 (0.02,12.35)	1.16 (0.69,1.95)
2.28 (0.33,15.90)	1.53 (0.34,6.77)	1.46 (0.26,8.23)	1.11 (0.22,5.69)	Basal insulin	0.51 (0.01,17.74)	1.28 (0.27,6.05)
4.44 (0.14,139.86)	2.98 (0.12,74.30)	2.85 (0.10,79.88)	2.16 (0.08,57.81)	1.95 (0.06,67.53)	Bolus insulin	2.51 (0.10,64.21)
1.77 (0.55,5.75)	1.19 (0.78,1.81)	1.14 (0.51,2.54)	0.86 (0.51,1.45)	0.78 (0.17,3.66)	0.40 (0.02,10.22)	Placebo

Table 19 Pancreatitis

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as odds ratios and 95% confidence intervals. For example, the odds ratio for pancreatitis with SGLT-2 inhibitors compared to GLP-1 receptor agonists is 0.54 (95% confidence interval 0.31 to 0.94). For the reverse, the effect of a GLP-1 receptor compared to SGLT-2 inhibitor on the odds of pancreatitis is 1.84 (95% confidence interval 1.06 to 3.19).

SGLT-2 inhibitor	1.84 (1.06,3.19)	0.78 (0.04,16.94)	2.17 (0.83,5.66)	1.79 (0.60,5.33)	2.28 (1.27,4.08)	0.75 (0.21,2.66)	0.81 (0.04,18.94)	4.38 (0.08,247.19)	12.99 (0.46,366.18)	1.56 (0.95,2.54)	0.82 (0.18,3.62)
0.54 (0.31,0.94)	GLP-1 receptor agonist	0.42 (0.02,8.91)	1.18 (0.47,2.99)	0.97 (0.36,2.61)	1.24 (0.81,1.90)	0.41 (0.13,1.28)	0.44 (0.02,9.84)	2.38 (0.04,133.48)	7.06 (0.25,197.45)	0.85 (0.64,1.11)	0.44 (0.11,1.82)
1.29 (0.06,28.16)	2.37 (0.11,50.14)	Metformin	2.80 (0.12,66.43)	2.30 (0.10,52.77)	2.94 (0.14,61.48)	0.97 (0.04,25.00)	1.05 (0.01,80.30)	5.64 (0.04,869.84)	16.75 (0.19,1508.73)	2.01 (0.10,42.31)	1.05 (0.04,28.46)
0.46 (0.18,1.20)	0.85 (0.33,2.14)	0.36 (0.02,8.47)	Sulfonylurea	0.82 (0.23,2.93)	1.05 (0.41,2.67)	0.35 (0.08,1.50)	0.37 (0.01,9.46)	2.01 (0.04,101.40)	5.98 (0.24,146.51)	0.72 (0.29,1.79)	0.38 (0.07,1.91)
0.56 (0.19,1.67)	1.03 (0.38,2.76)	0.43 (0.02,9.95)	1.22 (0.34,4.33)	Thiazol-idinedione	1.28 (0.47,3.48)	0.42 (0.10,1.77)	0.46 (0.02,10.96)	2.45 (0.04,150.74)	7.27 (0.23,227.21)	0.87 (0.32,2.35)	0.46 (0.15,1.38)
0.44 (0.25,0.78)	0.81 (0.53,1.23)	0.34 (0.02,7.11)	0.95 (0.37,2.42)	0.78 (0.29,2.14)	DPP-4 inhibitor	0.33 (0.10,1.11)	0.36 (0.02,8.13)	1.92 (0.03,107.82)	5.70 (0.20,159.53)	0.68 (0.48,0.97)	0.36 (0.09,1.49)
1.33 (0.38,4.71)	2.45 (0.78,7.66)	1.03 (0.04,26.59)	2.89 (0.67,12.48)	2.37 (0.57,9.98)	3.03 (0.90,10.18)	Basal insulin	1.08 (0.04,29.26)	5.82 (0.09,381.47)	17.27 (0.51,582.07)	2.07 (0.64,6.68)	1.09 (0.20,5.78)
1.23 (0.05,28.57)	2.26 (0.10,50.22)	0.95 (0.01,72.86)	2.67 (0.11,67.38)	2.19 (0.09,52.73)	2.80 (0.12,63.71)	0.92 (0.03,24.97)	Basal bolus insulin	5.38 (0.03,862.10)	15.95 (0.17,1502.35)	1.91 (0.09,42.91)	1.00 (0.04,28.37)
0.23 (0.00,12.90)	0.42 (0.01,23.57)	0.18 (0.00,27.31)	0.50 (0.01,24.98)	0.41 (0.01,25.11)	0.52 (0.01,29.25)	0.17 (0.00,11.26)	0.19 (0.00,29.83)	Alpha glucosidase inhibitor	2.97 (0.12,72.68)	0.36 (0.01,19.89)	0.19 (0.00,12.99)
0.08 (0.00,2.17)	0.14 (0.01,3.96)	0.06 (0.00,5.38)	0.17 (0.01,4.10)	0.14 (0.00,4.30)	0.18 (0.01,4.92)	0.06 (0.00,1.95)	0.06 (0.00,5.90)	0.34 (0.01,8.25)	Glitinide	0.12 (0.00,3.34)	0.06 (0.00,2.28)
0.64 (0.39,1.05)	1.18 (0.90,1.56)	0.50 (0.02,10.51)	1.40 (0.56,3.49)	1.15 (0.42,3.10)	1.46 (1.03,2.08)	0.48 (0.15,1.56)	0.52 (0.02,11.74)	2.81 (0.05,157.35)	8.35 (0.30,232.65)	Placebo	0.52 (0.13,2.16)
1.22 (0.28,5.43)	2.25 (0.55,9.22)	0.95 (0.04,25.66)	2.66 (0.52,13.54)	2.19 (0.73,6.58)	2.79 (0.67,11.62)	0.92 (0.17,4.90)	1.00 (0.04,28.20)	5.36 (0.08,373.11)	15.90 (0.44,575.71)	1.91 (0.46,7.86)	Standard therapy

Table 20 Glycated haemoglobin A1C

The columns present the row drug class compared to the column drug class. The rows present the row drug class compared to the column drug class. The effect estimates are expressed as a mean difference (%) and 95% confidence interval. For example, the glycated haemoglobin difference with an SGLT-2 inhibitor treatment compared to a GLP-1 receptor agonist is 0.28% (95% confidence interval 0.19% to 0.37%). The reverse is true for a GLP-1 receptor agonist compared to an SGLT-2 inhibitor (-0.28 kg, 95% confidence interval -0.37,-0.19).

SGLT-2 inhibitor	-0.28 (-0.37,-0.19)	-0.20 (-0.30,-0.09)	-0.05 (-0.15,0.05)	-0.10 (-0.19,-0.01)	0.01 (-0.07,0.09)	-0.14 (-0.26,-0.01)	-0.26 (-0.61,0.09)	-0.31 (-0.58,-0.04)	0.07 (-0.05,0.19)	-0.13 (-0.31,0.04)	0.60 (0.54,0.67)	0.41 (0.30,0.52)
0.28 (0.19,0.37)	GLP-1 receptor agonist	0.09 (-0.02,0.19)	0.23 (0.14,0.32)	0.18 (0.09,0.27)	0.29 (0.22,0.36)	0.14 (0.04,0.25)	0.02 (-0.32,0.36)	-0.03 (-0.29,0.23)	0.36 (0.24,0.47)	0.15 (-0.02,0.32)	0.89 (0.82,0.95)	0.69 (0.59,0.79)
0.20 (0.09,0.30)	-0.09 (-0.19,0.02)	Metformin	0.15 (0.04,0.25)	0.09 (-0.00,0.19)	0.20 (0.11,0.30)	0.06 (-0.08,0.19)	-0.07 (-0.42,0.29)	-0.12 (-0.39,0.16)	0.27 (0.14,0.40)	0.06 (-0.11,0.23)	0.80 (0.71,0.89)	0.60 (0.48,0.72)
0.05 (-0.05,0.15)	-0.23 (-0.32,-0.14)	-0.15 (-0.25,-0.04)	Sulfonylurea	-0.05 (-0.13,0.03)	0.06 (-0.02,0.14)	-0.09 (-0.22,0.04)	-0.21 (-0.56,0.14)	-0.26 (-0.53,0.01)	0.12 (0.00,0.24)	-0.08 (-0.24,0.07)	0.65 (0.57,0.74)	0.46 (0.35,0.57)
0.10 (0.01,0.19)	-0.18 (-0.27,-0.09)	-0.09 (-0.19,0.00)	0.05 (-0.03,0.13)	Thiazol-idinedione	0.11 (0.03,0.19)	-0.04 (-0.16,0.08)	-0.16 (-0.51,0.19)	-0.21 (-0.48,0.06)	0.17 (0.06,0.29)	-0.03 (-0.20,0.13)	0.71 (0.63,0.78)	0.51 (0.40,0.61)
-0.01 (-0.09,0.07)	-0.29 (-0.36,-0.22)	-0.20 (-0.30,-0.11)	-0.06 (-0.14,0.02)	-0.11 (-0.19,-0.03)	DPP-4 inhibitor	-0.15 (-0.26,-0.03)	-0.27 (-0.61,0.07)	-0.32 (-0.59,-0.05)	0.06 (-0.04,0.17)	-0.14 (-0.31,0.02)	0.60 (0.54,0.65)	0.40 (0.30,0.49)
0.14 (0.01,0.26)	-0.14 (-0.25,-0.04)	-0.06 (-0.19,0.08)	0.09 (-0.04,0.22)	0.04 (-0.08,0.16)	0.15 (0.03,0.26)	Basal insulin	-0.12 (-0.47,0.22)	-0.17 (-0.44,0.10)	0.21 (0.07,0.36)	0.00 (-0.19,0.19)	0.74 (0.63,0.86)	0.55 (0.42,0.68)
0.26 (-0.09,0.61)	-0.02 (-0.36,0.32)	0.07 (-0.29,0.42)	0.21 (-0.14,0.56)	0.16 (-0.19,0.51)	0.27 (-0.07,0.61)	0.12 (-0.22,0.47)	Basal bolus insulin	-0.05 (-0.48,0.38)	0.33 (-0.02,0.69)	0.13 (-0.25,0.50)	0.87 (0.52,1.21)	0.67 (0.32,1.02)
0.31 (0.04,0.58)	0.03 (-0.23,0.29)	0.12 (-0.16,0.39)	0.26 (-0.01,0.53)	0.21 (-0.06,0.48)	0.32 (0.05,0.59)	0.17 (-0.10,0.44)	0.05 (-0.38,0.48)	Bolus insulin	0.39 (0.10,0.67)	0.18 (-0.13,0.48)	0.92 (0.65,1.18)	0.72 (0.44,0.99)
-0.07 (-0.19,0.05)	-0.36 (-0.47,-0.24)	-0.27 (-0.40,-0.14)	-0.12 (-0.24,-0.00)	-0.17 (-0.29,-0.06)	-0.06 (-0.17,0.04)	-0.21 (-0.36,-0.07)	-0.33 (-0.69,0.02)	-0.39 (-0.67,-0.10)	Alpha glucosidase inhibitor	-0.21 (-0.39,-0.02)	0.53 (0.43,0.63)	0.33 (0.20,0.46)
0.13 (-0.04,0.31)	-0.15 (-0.32,0.02)	-0.06 (-0.23,0.11)	0.08 (-0.07,0.24)	0.03 (-0.13,0.20)	0.14 (-0.02,0.31)	-0.00 (-0.19,0.19)	-0.13 (-0.50,0.25)	-0.18 (-0.48,0.13)	0.21 (0.02,0.39)	Glitinide	0.74 (0.58,0.90)	0.54 (0.36,0.72)
-0.60 (-0.67,-0.54)	-0.89 (-0.95,-0.82)	-0.80 (-0.89,-0.71)	-0.65 (-0.74,-0.57)	-0.71 (-0.78,-0.63)	-0.60 (-0.65,-0.54)	-0.74 (-0.86,-0.63)	-0.87 (-1.21,-0.52)	-0.92 (-1.18,-0.65)	-0.53 (-0.63,-0.43)	-0.74 (-0.90,-0.58)	Placebo	-0.20 (-0.30,-0.10)
-0.41 (-0.52,-0.30)	-0.69 (-0.79,-0.59)	-0.60 (-0.72,-0.48)	-0.46 (-0.57,-0.35)	-0.51 (-0.61,-0.40)	-0.40 (-0.49,-0.30)	-0.55 (-0.68,-0.42)	-0.67 (-1.02,-0.32)	-0.72 (-0.99,-0.44)	-0.33 (-0.46,-0.20)	-0.54 (-0.72,-0.36)	0.20 (0.10,0.30)	Standard therapy

Appendix 8 GRADE summary of findings for SGLT-2 inhibitors and GLP-1 receptor agonists compared to placebo or each other

Table 1: Cardiovascular mortality

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT 2 inhibitor *v* placebo	OR 0.84 (0.76 to 0.92)	Very low	Placebo: 13 per 1000	SGLT-2 inhibitor: 11 per 1000	2 fewer per 1000 (from 1 to 3 fewer)	Moderate due to directness	SGLT-2 inhibitor therapy probably reduces cardiovascular mortality in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 46 per 1000	SGLT-2 inhibitor: 39 per 1000	7 fewer per 1000 (from 4 fewer to 11 fewer)	High	SGLT-2 inhibitor therapy reduces cardiovascular mortality in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 79 per 1000	SGLT-2 inhibitor: 67 per 1000	12 fewer per 1000 (from 6 fewer to 18 fewer)	High	SGLT-2 inhibitor therapy reduces cardiovascular mortality in people with diabetes and established cardiovascular disease.
		High	Placebo: 112 per 1000	SGLT-2 inhibitor: 96 per 1000	16 fewer per 1000 (from 3 fewer to 23 fewer)	High	SGLT-2 inhibitor therapy reduces cardiovascular mortality in people with diabetes and chronic kidney disease.
		Very high	Placebo: 175 per 1000	SGLT-2 inhibitor: 151 per 1000	24 fewer per 1000 (from 12 fewer to 36 fewer)	High	SGLT-2 inhibitor therapy reduces cardiovascular mortality in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 1: Cardiovascular mortality

Comparison	Relative effect	Anticipated absolute effects over 5 years			Anticipated absolute effects (95% CI) over 5 years	Certainty in treatment effects (GRADE)	Plain text summary
		Baseline risk	Risk with control	Risk with intervention			
GLP-1 receptor agonist *v* placebo	OR 0.88 (0.83 to 0.94)	Very low	Placebo: 13 per 1000	GLP-1 receptor agonist: 11 per 1000	2 fewer per 1000 (from 1 fewer to 3 fewer)	Moderate due to directness	GLP-1 receptor agonist therapy probably reduces cardiovascular mortality in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 46 per 1000	GLP-1 receptor agonist: 41 per 1000	5 fewer per 1000 (from 2 fewer to 9 fewer)	High	GLP-1 receptor agonist therapy reduces cardiovascular mortality in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 79 per 1000	GLP-1 receptor agonist: 67 per 1000	12 fewer per 1000 (from 6 fewer to 18 fewer)	High	reduces cardiovascular mortality in people with diabetes and established cardiovascular disease.
		High	Placebo: 112 per 1000	GLP-1 receptor agonist: 100per 1000	12 fewer per 1000 (from 4 fewer to 20 fewer)	High	GLP-1 receptor agonist therapy reduces cardiovascular mortality in people with diabetes and chronic kidney disease.
		Very high	Placebo: 175 per 1000	GLP-1 receptor agonist: 151 per 1000	24 fewer per 1000 (from 12 fewer to 36 fewer)	High	GLP-1 receptor agonist therapy reduces cardiovascular mortality in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 1: Cardiovascular mortality

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT 2 inhibitor *v* GLP-1 receptor agonist	OR 0.96 (0.84 to 1.09)	Very low	GLP-1 receptor agonist: 11 per 1000	SGLT-2 inhibitor: 11per 1000	0 fewer per 1000 (from 2 fewer to 1 more)	Moderate due to directness	There is probably no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on cardiovascular mortality in people with diabetes and few or no cardiovascular risk factors.
		Low	GLP-1 receptor agonist: 41 per 1000	SGLT-2 inhibitor: 39 per 1000	2 fewer per 1000 (from 6 fewer to 4 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on cardiovascular mortality in people with diabetes and cardiovascular risk factors.
		Moderate	GLP-1 receptor agonist: 70 per 1000	SGLT-2 inhibitor: 67 per 1000	3 fewer per 1000 (from 11 fewer to 6 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on cardiovascular mortality in people with diabetes and established cardiovascular disease.
		High	GLP-1 receptor agonist: 100 per 1000	SGLT-2 inhibitor: 96 per 1000	4 fewer per 1000 (from 15 fewer to 8 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on cardiovascular mortality in people with diabetes and chronic kidney disease.
		Very high	GLP-1 receptor agonist: 157 per 1000	SGLT-2 inhibitor: 152 per 1000	5 fewer per 1000 (22 fewer to 12 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on cardiovascular mortality in people with diabetes and established cardiovascular disease and chronic kidney disease.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonist therapy, obtained from GLP-1 receptor agonist therapy versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 2 Nonfatal myocardial infarction

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 0.87 (0.79 to 0.97)	Very low	Placebo: 30 per 1000	SGLT-2 inhibitor: 26 per 1000	4 fewer per 1000 (from 1 fewer to 6 fewer)	Moderate due to indirectness	SGLT-2 inhibitor therapy probably reduces nonfatal myocardial infarction in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 58 per 1000	SGLT-2 inhibitor: 51 per 1000	7 fewer per 1000 (from 2 fewer to 12 fewer)	High	SGLT-2 inhibitor therapy reduces nonfatal myocardial infarction in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 108 per 1000	SGLT-2 inhibitor: 95 per 1000	13 fewer per 1000 (from 3 fewer to 21 fewer)	High	SGLT-2 inhibitor therapy reduces nonfatal myocardial infarction in people with diabetes and established cardiovascular disease.
		High	Placebo: 120 per 1000	SGLT-2 inhibitor: 106 per 1000	14 fewer per 1000 (from 3 fewer to 23 fewer)	High	SGLT-2 inhibitor therapy reduces nonfatal myocardial infarction in people with diabetes and chronic kidney disease.
		Very high	Placebo: 190 per 1000	SGLT-2 inhibitor: 169 per 1000	21 fewer per 1000 (from 5 fewer to 34 fewer)	High	SGLT-2 inhibitor therapy reduces nonfatal myocardial infarction in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 2 Nonfatal myocardial infarction

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
GLP-1 receptor agonist versus placebo	OR 0.92 (0.85 to 0.99)	Very low	Placebo: 30 per 1000	GLP-1 receptor agonist: 28 per 1000	2 fewer per 1000 (from 0 fewer to 4 fewer)	Moderate due to indirectness	GLP-1 receptor agonist therapy probably reduces nonfatal myocardial infarction in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 58 per 1000	GLP-1 receptor agonist: 54 per 1000	4 fewer per 1000 (from 1 fewer to 8 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal myocardial infarction in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 108 per 1000	GLP-1 receptor agonist: 100 per 1000	8 fewer per 1000 (from 1 fewer to 15 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal myocardial infarction in people with diabetes and established cardiovascular disease.
		High	Placebo: 120 per 1000	GLP-1 receptor agonist: 111 per 1000	9 fewer per 1000 (from 1 fewer to 16 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal myocardial infarction in people with diabetes and chronic kidney disease.
		Very high	Placebo: 190 per 1000	GLP-1 receptor agonist: 177 per 1000	13 fewer per 1000 (from 2 fewer to 24 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal myocardial infarction in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 2 Nonfatal myocardial infarction

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 0.95 (0.84 to 1.08)	Very low	GLP-1 receptor agonist: 28 per 1000	SGLT-2 inhibitor: 27 per 1000	1 fewer per 1000 (from 4 fewer to 2 more)	Moderate due to indirectness	There is probably no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on nonfatal myocardial infarction in people with diabetes and few or no cardiovascular risk factors.
		Low	GLP-1 receptor agonist: 54 per 1000	SGLT-2 inhibitor: 51 per 1000	3 fewer per 1000 (from 8 fewer to 4 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on nonfatal myocardial infarction in people with diabetes and cardiovascular risk factors.
		Moderate	GLP-1 receptor agonist: 100 per 1000	SGLT-2 inhibitor: 95 per 1000	5 fewer per 1000 (from 15 fewer to 7 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on nonfatal myocardial infarction in people with diabetes and established cardiovascular disease.
		High	GLP-1 receptor agonist: 111 per 1000	SGLT-2 inhibitor: 106 per 1000	5 fewer per 1000 (from 16 fewer to 8 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on nonfatal myocardial infarction in people with diabetes and chronic kidney disease.
		Very high	GLP-1 receptor agonist: 177 per 1000	SGLT-2 inhibitor: 170 per 1000	7 fewer per 1000 (24 fewer to 11 more)	High	There is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on nonfatal myocardial infarction in people with diabetes and established cardiovascular disease and chronic kidney disease.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 3 Nonfatal stroke

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 1.01 (0.89 to 1.14)	Very low	Placebo: 30 per 1000	SGLT-2 inhibitor: 30 per 1000	0 fewer per 1000 (from 3 fewer to 4 more)	Moderate due to indirectness	SGLT-2 inhibitors probably do not reduce nonfatal stroke in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 58 per 1000	SGLT-2 inhibitor: 59 per 1000	1 more per 1000 (from 6 fewer to 8 more)	High	SGLT-2 inhibitors do not reduce nonfatal stroke in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 108 per 1000	SGLT-2 inhibitor: 109 per 1000	1 more per 1000 (from 11 fewer to 13 more)	High	SGLT-2 inhibitors do not reduce nonfatal stroke in people with diabetes and established cardiovascular disease.
		High	Placebo: 120 per 1000	SGLT-2 inhibitor: 121 per 1000	1 more per 1000 (from 12 fewer to 15 more)	High	SGLT-2 inhibitors do not reduce nonfatal stroke in people with diabetes and chronic kidney disease.
		Very high	Placebo: 190 per 1000	SGLT-2 inhibitor: 192 per 1000	2 more per 1000 (from 21 fewer to 17 more)	High	SGLT-2 inhibitors do not have an important effect on nonfatal stroke in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 3 Nonfatal stroke

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
GLP-1 receptor agonist versus placebo	OR 0.84 (0.76 to 0.93)	Very low	Placebo: 30 per 1000	GLP-1 receptor agonist: 25 per 1000	5 fewer per 1000 (from 2 fewer to 7 fewer)	Moderate due to indirectness	GLP-1 receptor agonist therapy probably reduces nonfatal stroke in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 58 per 1000	GLP-1 receptor agonist: 49 per 1000	9 fewer per 1000 (from 4 fewer to 13 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 108 per 1000	GLP-1 receptor agonist: 92 per 1000	16 fewer per 1000 (from 7 fewer to 24 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke in people with diabetes and established cardiovascular disease.
		High	Placebo: 120 per 1000	GLP-1 receptor agonist: 103 per 1000	17 fewer per 1000 (from 7 fewer to 26 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke in people with diabetes and chronic kidney disease.
		Very high	Placebo: 190 per 1000	GLP-1 receptor agonist: 165 per 1000	25 fewer per 1000 (from 11 fewer to 39 fewer)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 3 Nonfatal stroke

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 1.20 (1.03 to 1.41)	Very low	GLP-1 receptor agonist: 25 per 1000	SGLT-2 inhibitor: 30per 1000	5 more per 1000 (from 1 more to 10 more)	Moderate due to indirectness	GLP-1 receptor agonist therapy probably reduces nonfatal stroke compared to SGLT-2 inhibitor therapy in people with diabetes and few or no cardiovascular risk factors.
		Low	GLP-1 receptor agonist: 49 per 1000	SGLT-2 inhibitor: 59 per 1000	10 more per 1000 (from 1 more to 12 more)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke compared to SGLT-2 inhibitor therapy in people with diabetes and cardiovascular risk factors.
		Moderate	GLP-1 receptor agonist: 91 per 1000	SGLT-2 inhibitor: 109 per 1000	18 more per 1000 (from 3 more to 37 more)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke compared to SGLT-2 inhibitor therapy in people with diabetes and established cardiovascular disease.
		High	GLP-1 receptor agonist: 101 per 1000	SGLT-2 inhibitor: 121 per 1000	20 more per 1000 (from 3 more to 41 more)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke compared to SGLT-2 inhibitor therapy in people with diabetes and chronic kidney disease.
		Very high	GLP-1 receptor agonist: 160 per 1000	SGLT-2 inhibitor: 192 per 1000	32 more per 1000 (from 5 more to 66 more)	High	GLP-1 receptor agonist therapy reduces nonfatal stroke compared to SGLT-2 inhibitor therapy in people with diabetes and established cardiovascular disease and chronic kidney disease.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 4 Kidney failure

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 0.71 (0.57 to 0.89)	Very low	Placebo: 2 per 1000	SGLT-2 inhibitor: 1 per 1000	1 fewer per 1000 (from 0 fewer to 1 fewer)	Moderate due to indirectness	SGLT-2 inhibitor therapy probably reduces kidney failure in people with diabetes and few or no risk factors for cardiovascular disease.
		Low	Placebo: 10 per 1000	SGLT-2 inhibitor: 7 per 1000	3 fewer per 1000 (from 1 to 4 fewer)	High	SGLT-2 inhibitor therapy reduces kidney failure in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 20 per 1000	SGLT-2 inhibitor: 14 per 1000	6 fewer per 1000 (from 2 to 9 fewer)	High	SGLT-2 inhibitor therapy reduces kidney failure in people with diabetes and established cardiovascular disease.
		High	Placebo: 92 per 1000	SGLT-2 inhibitor: 67	25 fewer (from 9 fewer to 37 fewer)	High	SGLT-2 inhibitor therapy reduces kidney failure in people with diabetes and chronic kidney disease.
		Very high	Placebo: 148 per 1000	SGLT-2 inhibitor: 110	38 fewer per 1000 (from 14 fewer to 58 fewer)	High	SGLT-2 inhibitor therapy reduces kidney failure in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 4 Kidney failure

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
GLP-1 receptor agonist versus placebo	OR 0.78 (0.67 to 0.92)	Very low	Placebo: 2 per 1000	GLP-1 receptor agonist: 2 per 1000	0 fewer per 1000 (from 0 fewer to 1 fewer)	Moderate due to indirectness	GLP-1 receptor agonist therapy probably reduces kidney failure in people with diabetes and few or no risk factors for cardiovascular disease.
		Low	Placebo: 10 per 1000	GLP-1 receptor agonist: 8 per 1000	2 fewer per 1000 (from 1 fewer to 3 fewer)	High	GLP-1 receptor agonist therapy reduces kidney failure in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 20 per 1000	GLP-1 receptor agonist: 16 per 1000	4 fewer per 1000 (from 2 fewer to 7 fewer)	High	GLP-1 receptor agonist therapy reduces kidney failure in people with diabetes and established cardiovascular disease.
		High	Placebo: 92 per 1000	GLP-1 receptor agonist: 67 per 1000	25 fewer per 1000 (from 9 fewer to 37 fewer)	High	GLP-1 receptor agonist therapy reduces kidney failure in people with diabetes and chronic kidney disease.
		Very high	Placebo: 148 per 1000	GLP-1 receptor agonist: 110 per 1000	38 fewer per 1000 (from 14 fewer to 58 fewer)	High	GLP-1 receptor agonist therapy reduces kidney failure in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 4 Kidney failure

Comparison	Relative effect	Anticipated absolute effects over 5 years			Anticipated absolute effects (95% CI) over 5 years	Certainty in treatment effects (GRADE)	Plain text summary
		Baseline risk	Risk with control	Risk with intervention			
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 0.91 (0.69 to 1.20)	Very low	GLP-1 receptor agonist: 2 per 1000	SGLT-2 inhibitor: 1 per 1000	0 fewer per 1000 (from 0 fewer to 1 more)	Low due to serious imprecision and indirectness	There is may be no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on kidney failure in people with diabetes and few or no cardiovascular risk factors.
		Low	GLP-1 receptor agonist: 8 per 1000	SGLT-2 inhibitor: 7 per 1000	1 fewer per 1000 (from 2 fewer to 2 more)	Moderate due to serious imprecision	There is probably no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on kidney failure in people with diabetes and cardiovascular risk factors.
		Moderate	GLP-1 receptor agonist: 16 per 1000	SGLT-2 inhibitor: 15 per 1000	1 fewer per 1000 (from 5 fewer to 3 more)	Moderate due to serious imprecision	There is probably no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on kidney failure in people with diabetes and established cardiovascular disease.
		High	GLP-1 receptor agonist: 73 per 1000	SGLT-2 inhibitor: 67 per 1000	6 fewer per 1000 (from 21 fewer to 13 more)	Moderate due to serious imprecision	There is probably no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on kidney failure in people with diabetes and chronic kidney disease.
		Very high	GLP-1 receptor agonist: 119 per 1000	SGLT-2 inhibitor: 109 per 1000	10 fewer per 1000 (from 34 fewer to 20 more)	Moderate due to serious imprecision	There is probably no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on kidney failure in people with diabetes and established cardiovascular disease and chronic kidney disease.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 5 Hospitalisation for heart failure

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 0.70 (0.63 to 0.77)	Very low	Placebo: 5 per 1000	SGLT-2 inhibitor: 3 per 1000	2 fewer per 1000 (from 1 fewer to 2 fewer)	Moderate due to indirectness	SGLT-2 inhibitor therapy probably reduces hospitalisation for heart failure in people with diabetes and few or no risk factors for cardiovascular disease.
		Low	Placebo: 30 per 1000	SGLT-2 inhibitor: 21 per 1000	9 fewer per 1000 (from 7 fewer to 11 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 80 per 1000	SGLT-2 inhibitor: 57 per 1000	23 fewer per 1000 (from 17 fewer to 28 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure in people with diabetes and established cardiovascular disease.
		High	Placebo: 105 per 1000	SGLT-2 inhibitor: 76 per 1000	29 fewer (from 22 fewer to 36 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure in people with diabetes and chronic kidney disease.
		Very high	Placebo: 235 per 1000	SGLT-2 inhibitor: 177 per 1000	58 fewer (from 44 fewer to 73 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 5 Hospitalisation for heart failure

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
GLP-1 receptor agonist versus placebo	OR 0.94 (0.85 to 1.03)	Very low	Placebo: 5 per 1000	GLP-1 receptor agonist: 5 per 1000	0 fewer per 1000 (from 0 fewer to 1 fewer)	Moderate due to indirectness	GLP-1 receptor agonist therapy probably has little or no effect on hospitalisation for heart failure in people with diabetes and few or no risk factors for cardiovascular disease.
		Low	Placebo: 30 per 1000	GLP-1 receptor agonist: 28 per 1000	2 fewer per 1000 (from 4 fewer to 1 more)	High	GLP-1 receptor agonist therapy has little or no effect on hospitalisation for heart failure in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 80 per 1000	GLP-1 receptor agonist: 76 per 1000	4 fewer per 1000 (from 11 fewer to 2 more)	High	GLP-1 receptor agonist therapy has little or no effect on hospitalisation for heart failure in people with diabetes and established cardiovascular disease.
		High	Placebo: 105 per 1000	GLP-1 receptor agonist: 99 per 1000	6 fewer per 1000 (from 14 fewer to 3 more)	High	GLP-1 receptor agonist therapy has little or no effect on hospitalisation for heart failure in people with diabetes and chronic kidney disease.
		Very high	Placebo: 235 per 1000	GLP-1 receptor agonist: 224 per 1000	11 fewer per 1000 (from 28 fewer to 5 more)	High	GLP-1 receptor agonist therapy probably has little or no effect on hospitalisation for heart failure in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 5 Hospitalisation for heart failure

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 0.74 (0.65 to 0.85)	Very low	GLP-1 receptor agonist: 5 per 1000	SGLT-2 inhibitor: 4 per 1000	1 fewer per 1000 (from 1 fewer to 2 fewer)	Moderate due to indirectness	SGLT-2 inhibitor therapy probably reduces hospitalisation for heart failure compared with GLP-1 receptor agonist therapy in people with diabetes and few or no risk factors for cardiovascular disease.
		Low	GLP-1 receptor agonist: 28 per 1000	SGLT-2 inhibitor: 21 per 1000	7 fewer per 1000 (from 4 fewer to 10 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure compared with GLP-1 receptor agonist therapy in people with diabetes and cardiovascular risk factors.
		Moderate	GLP-1 receptor agonist: 75 per 1000	SGLT-2 inhibitor: 57 per 1000	18 fewer per 1000 (from 11 fewer to 25 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure compared with GLP-1 receptor agonist therapy in people with diabetes and established cardiovascular disease.
		High	GLP-1 receptor agonist: 98 per 1000	SGLT-2 inhibitor: 74 per 1000	24 fewer per 1000 (from 13 fewer to 32 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure compared with GLP-1 receptor agonist therapy in people with diabetes and chronic kidney disease.
		Very high	GLP-1 receptor agonist: 222 per 1000	SGLT-2 inhibitor: 174 per 1000	48 fewer (from 27 fewer to 66 fewer)	High	SGLT-2 inhibitor therapy reduces hospitalisation for heart failure compared with GLP-1 receptor agonist therapy in people with diabetes and established cardiovascular disease and chronic kidney disease.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 6 Severe hypoglycaemia

		Anticipated absolute effects over 5 years				
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 0.90 (0.70,1.16)	Placebo: 25 per 1000	SGLT-2 inhibitor: 23 per 1000	2 fewer per 1000 (from 8 fewer to 4 more)	High	SGLT-2 inhibitor therapy does not incur severe hypoglycaemia
GLP-1 receptor agonist versus placebo	OR 0.92 (0.79,1.08)	Placebo: 25 per 1000	GLP-1 receptor agonist: 24 per 1000	2 fewer per 1000 (from 5 fewer to 2 more)	High	GLP-1 receptor agonist therapy does not incur severe hypoglycaemia
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 0.98 (0.73,1.31)	GLP-1 receptor agonist: 23 per 1000	SGLT-2 inhibitor: 23 per 1000	0 fewer per 1000 (from 6 fewer to 7 more)	Moderate due to serious imprecision	There probably is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on serious hypoglycaemia

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 7 Blindness

		Anticipated absolute effects over 5 years				
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 0.17 (0.01,4.07)	Placebo: 1 per 1000	SGLT-2 inhibitor: 0 per 1000	1 fewer per 1000 (from 1 fewer to 4 more)	Low due to very serious imprecision	SGLT-2 inhibitor therapy may have no effect on blindness.
GLP-1 receptor agonist versus placebo	OR 1.00 (0.23, 4.41)	Placebo: 1 per 1000	GLP-1 receptor agonist: 1 per 1000	0 fewer per 1000 (from 1 fewer to 4 more)	Low due to very serious imprecision	GLP-1 receptor agonist therapy may have no effect on blindness.
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 0.99 (0.57,1.73)	GLP-1 receptor agonist: 1 per 1000	SGLT-2 inhibitor: 1 per 1000	0 fewer per 1000 (from 0 fewer to 1 more)	Low due to very serious imprecision	There may be no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on blindness.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 8 Health-related quality of life

Comparison	Standardised mean difference (95% CI)	Certainty in treatment effects	Plain text summary
SGLT-2 inhibitor versus placebo	0.14 (-0.08 to 0.36)	Low due to very serious imprecision	SGLT-2 inhibitors may have no effect on health-related quality of life.
GLP-1 receptor agonist versus placebo	0.13 (0.03 to 0.23)	Low due to very serious imprecision	GLP-1 receptors may increase health-related quality of life.
SGLT-2 inhibitor versus GLP-1 receptor agonist	0.01 (-0.19 to 0.20)	Low due to very serious imprecision	There may be no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on health-related quality of life.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 9 Body weight

Comparison	Mean difference (95% CI)	Certainty in treatment effects	Plain text summary
SGLT-2 inhibitor versus placebo	-1.92 kg (-2.23 to -1.62)	Low due to very serious inconsistency	SGLT-2 inhibitors may lower body weight.
GLP-1 receptor agonist versus placebo	-1.45 kg (-1.72 to -1.18)	Low due to very serious inconsistency	GLP-1 receptor agonists may lower body weight.
SGLT-2 inhibitor versus GLP-1 receptor agonist	-0.47 kg (-0.85 to -0.09)	Moderate due to serious inconsistency	SGLT-2 inhibitors probably reduce body weight more than GLP-1 receptor agonists.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 10 Amputation

Comparison	Relative effect	Anticipated absolute effects over 5 years: Baseline risk	Risk with control	Risk with intervention	Anticipated absolute effects (95% CI) over 5 years	Certainty in treatment effects (GRADE)	Plain text summary
SGLT-2 inhibitor versus placebo	OR 1.14 (0.96, 1.35)	Very low	Placebo: 10 per 1000	SGLT-2 inhibitor: 11 per 1000	1 more per 1000 (from 1 fewer to 4 more)	Low due to serious imprecision and indirectness	SGLT-2 inhibitor therapy may have no effect on amputation in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 12 per 1000	SGLT-2 inhibitor: 13 per 1000	2 more per 1000 (from 1 fewer to 4 more)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has no effect on amputation in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 45 per 1000	SGLT-2 inhibitor: 50 per 1000	6 more per 1000 (from 2 fewer to 16 more)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has no effect on amputation in people with diabetes and established cardiovascular disease.
		High	Placebo: 55 per 1000	SGLT-2 inhibitor: 61 per 1000	8 more per 1000 (from 2 fewer to 19 more)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has no effect on amputation in people with diabetes and chronic kidney disease
		Very high	Placebo: 94 per 1000	Placebo: 104 per 1000	13 more per 1000 (from 4 fewer to 23 more)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has no effect on amputation in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 10 Amputation

		Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Baseline risk**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
GLP-1 receptor agonist versus placebo	OR 0.33 (0.01, 8.18)	Very low	Placebo: 10 per 1000	GLP-1 receptor agonist: 3 per 1000	7 fewer per 1000 (from 10 fewer to 72 more)	Very low due to very serious imprecision and indirectness	The effect of GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and few or no cardiovascular risk factors.
		Low	Placebo: 12 per 1000	GLP-1 receptor agonist: 4 per 1000	8 fewer per 1000 (from 12 fewer to 86 more)	Low due to very serious imprecision	The effect of GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and cardiovascular risk factors.
		Moderate	Placebo: 45 per 1000	GLP-1 receptor agonist: 15 per 1000	30 fewer per 1000 (from 45 fewer to 324 more)	Low due to very serious imprecision	The effect of GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and established cardiovascular disease.
		High	Placebo: 55 per 1000	GLP-1 receptor agonist: 18 per 1000	37 fewer per 1000 (from 54 fewer to 395 more)	Low due to very serious imprecision	The effect of GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and chronic kidney disease.
		Very high	Placebo: 94 per 1000	GLP-1 receptor agonist: 31 per 1000	63 fewer (from 93 fewer to 676 more)	Low due to very serious imprecision	The effect of GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and established cardiovascular disease and chronic kidney disease.

Table 10 Amputation

Comparison	Relative effect	Anticipated absolute effects over 5 years: Baseline risk	Risk with control	Risk with intervention	Anticipated absolute effects (95% CI) over 5 years	Certainty in treatment effects (GRADE)	Plain text summary
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 3.43 (0.14, 84.5)	Very low	GLP-1 receptor agonist: 3 per 1000	SGLT-2 inhibitor: 10 per 1000	7 more per 1000 (from 3 fewer to 250 more)	Very low due to very serious imprecision and indirectness	Whether there is an important difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and few or no cardiovascular risk factors.
		Low	GLP-1 receptor agonist: 4 per 1000	SGLT-2 inhibitor: 13 per 1000	10 more per 1000 (from 3 fewer to 334 more)	Low due to very serious imprecision	Whether there is an important difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and cardiovascular risk factors.
		Moderate	GLP-1 receptor agonist: 15 per 1000	SGLT-2 inhibitor: 50 per 1000	36 more per 1000 (from 13 fewer to 1000 more)	Low due to very serious imprecision	Whether there is an important difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and established cardiovascular disease.
		High	GLP-1 receptor agonist: 18 per 1000	SGLT-2 inhibitor: 60 per 1000	42 more per 1000 (from 15 fewer to 1000 more)	Low due to very serious imprecision	Whether there is an important difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and chronic kidney disease.
		Very high	GLP-1 receptor agonist: 31 per 1000	SGLT-2 inhibitor: 103 per 1000	72 more per 1000 (from 27 fewer to 1000 more)	Low due to very serious imprecision	Whether there is an important difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on amputation is uncertain in people with diabetes and established cardiovascular disease and chronic kidney disease.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 11 Neuropathic pain

		Anticipated absolute effects over 5 years				
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	NA	Placebo: 2 per 1000	SGLT-2 inhibitor: NA	NA	NA	Whether SGLT-2 inhibitor therapy has an effect on neuropathic pain is uncertain.
GLP-1 receptor agonist versus placebo	OR 0.33 (0.01,8.19)	Placebo: 2 per 1000	GLP-1 receptor agonist: 1 per 1000	1 fewer per 1000 (from 2 fewer to 14 more)	Very low due to very serious imprecision and inconsistency between studies	Whether GLP-1 receptor agonist therapy has an effect on neuropathic pain is uncertain.
SGLT-2 inhibitor versus GLP-1 receptor agonist	NA	GLP-1 receptor agonist: 1 per 1000	SGLT-2 inhibitor: NA	NA	NA	Whether there is any difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on neuropathic pain or not is uncertain.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 12 Diabetic ketoacidosis

	Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 1.04 (0.61, 1.78)	Placebo: 2 per 1000	SGLT-2 inhibitor: 2 per 1000	0 more per 1000 (from 1 fewer to 2 more)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has no effect on diabetic ketoacidosis.
GLP-1 receptor agonist versus placebo	OR 0.61 (0.33, 1.11)	Placebo: 2 per 1000	GLP-1 receptor agonist: 1 per 1000	1 fewer per 1000 (from 1 fewer to 0)	Moderate due to serious imprecision	GLP-1 receptor agonist therapy probably has no effect on diabetic ketoacidosis.
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 1.71 (0.79, 3.69)	GLP-1 receptor agonist: 1 per 1000	SGLT-2 inhibitor: 2 per 1000	1 more per 1000 (from 0 to 3 more)	Moderate due to serious imprecision	There probably is no difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 13 Serious hyperglycaemia

		Anticipated absolute effects over 5 years				
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 0.59 (0.35, 1.01)	Placebo: 25 per 1000	SGLT-2 inhibitor: 15 per 1000	10 fewer per 1000 (from 0 to 16 fewer)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably decreases serious hyperglycaemia.
GLP-1 receptor agonist versus placebo	OR 0.40 (0.25, 0.64)	Placebo: 25 per 1000	GLP-1 receptor agonist: 10 per 1000	15 fewer per 1000 (from 9 to 19 fewer)	High	GLP-1 receptor agonist therapy decreases serious hyperglycaemia.
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 1.48 (0.75, 2.93)	GLP-1 receptor agonist: 10 per 1000	SGLT-2 inhibitor: 15 per 1000	5 more per 1000 (from 2 fewer to 19 more)	Moderate due to serious imprecision	There probably is no difference in serious hyperglycaemia between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 14 Genital infection

	Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 3.50 (3.01, 4.07)	Placebo: 73 per 1000	SGLT-2 inhibitor: 216 per 1000	143 more per 1000 (from 119 more to 170 more)	High	SGLT-2 inhibitor therapy increases genital infection.
GLP-1 receptor agonist versus placebo	OR 0.70 (0.34, 1.44)	Placebo: 73 per 1000	GLP-1 receptor agonist: 52 per 1000	21 fewer per 1000 (from 47 fewer to 29 more)	Moderate due to serious imprecision	GLP-1 receptor agonist therapy probably does not increase genital infection.
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 5.00 (2.45, 10.2)	GLP-1 receptor agonist: 50 per 1000	SGLT-2 inhibitor: 208 per 1000	158 more per 1000 (from 64 to 299 more)	High	SGLT-2 inhibitors increase genital infection compared with GLP-1 receptor agonists.

CI= confidence interval. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 15 Fournier gangrene

	Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitors versus placebo	OR 0.56 (0.16, 19.2)	Placebo: 1 per 1000	SGLT-2 inhibitor: 1 per 1000	0 fewer per 1000 (1 fewer to 18 more)	Low due to very serious imprecision	Whether or not SGLT-2 inhibitor therapy has an effect on Fournier gangrene is uncertain.
GLP-1 receptor agonist versus placebo	NA	Placebo: 1 per 1000	GLP-1 receptor agonist: NA	NA	NA	Whether or not GLP-1 receptor agonist therapy has an effect on Fournier gangrene is uncertain.
SGLT-2 inhibitor versus GLP-1 receptor agonist	NA	GLP-1 receptor agonist: NA	SGLT-2 inhibitor: NA	NA	NA	Whether SGLT-2 inhibitor or GLP-1 receptor agonist therapy have different effects on Fournier gangrene is uncertain.

CI= confidence interval. NA = not available. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 16 Severe gastrointestinal events

	Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	NA	Placebo: 44 per 1000	SGLT-2 inhibitor: NA	NA	NA	Whether or not SGLT-2 inhibitor therapy has an effect on severe gastrointestinal events is uncertain.
GLP-1 receptor agonist versus placebo	OR 2.46(1.22, 4.97)	Placebo: 44	GLP-1 receptor agonist: 102 per 1000	58 more per 1000 (from 9 to 142 more)	Low due to serious imprecision and inconsistency between studies	GLP-1 receptor agonists may increase severe gastrointestinal events.
SGLT-2 inhibitor versus GLP-1 receptor agonist	NA	GLP-1 receptor agonist: NA	SGLT-2 inhibitor: NA	NA	NA	Whether there is a difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on serious gastrointestinal events is uncertain.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 17 Pancreatic cancer

	Anticipated absolute effects over 5 years					
Comparison	**Relative effect**	**Risk with control**	**Risk with intervention**	**Anticipated absolute effects (95% CI) over 5 years**	**Certainty in treatment effects (GRADE)**	**Plain text summary**
SGLT-2 inhibitor versus placebo	OR 1.77 (0.55, 5.75)	Placebo: 4 per 1000	SGLT-2 inhibitor: 7 per 1000	3 more per 1000 (2 fewer to 19 more	Low due to very serious imprecision	Whether or not SGLT-2 inhibitor therapy has an effect on pancreatic cancer is uncertain.
GLP-1 receptor agonist versus placebo	OR 1.19 (0.78, 1.81)	Placebo: 4 per 1000	GLP-1 receptor agonist: 5 per 1000	1 more per 1000 (1 fewer to 3 more)	Moderate due to serious imprecision	GLP-1 receptor therapy probably has little or no effect on pancreatic cancer
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 1.49 (0.43, 5.19)	GLP-1 receptor agonist: 5 per 1000	SGLT-2 inhibitor: 7 per 1000	2 more per 1000 (3 fewer to 21 more)	Low due to very serious imprecision	Whether there is a difference between SGLT-2 inhibitor therapy and GLP-1 receptor agonist therapy on pancreatic cancer is uncertain.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 18 Pancreatitis

Comparison	Anticipated absolute effects over 5 years			Anticipated absolute effects (95% CI) over 5 years	Certainty in treatment effects (GRADE)	Plain text summary
	Relative effect	Risk with control	Risk with intervention			
SGLT-2 inhibitor versus placebo	OR 0.64 (0.39, 1.05)	Placebo: 5 per 1000	SGLT-2 inhibitor: 3 per 1000	2 fewer per 1000 (3 fewer to 0)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has no effect on pancreatitis.
GLP-1 receptor agonist versus placebo	OR 1.18 (0.90, 1.56)	Placebo: 5 per 1000	GLP-1 receptor agonist: 6 per 1000	1 more per 1000 (1 fewer to 3 more)	Moderate due to serious imprecision	GLP-1 receptor agonist therapy probably has no effect on pancreatitis.
SGLT-2 inhibitor versus GLP-1 receptor agonist	OR 0.54 (0.31, 0.94)	GLP-1 receptor agonist: 6 per 1000	SGLT-2 inhibitor: 3 per 1000	3 fewer per 1000 (4 fewer to 0)	Moderate due to serious imprecision	SGLT-2 inhibitor therapy probably has lower odds of pancreatitis than GLP-1 receptor agonist therapy.

CI= confidence interval. OR = odds ratio. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Table 19 Glycated haemoglobin A1C

Comparison	Mean difference (95% CI)	Certainty in treatment effects	Plain text summary
SGLT-2 inhibitor versus placebo	-0.60% (-0.67 to -0.54)	Low due to serious imprecision and inconsistency	SGLT-2 inhibitor therapy may lower glycated haemoglobin A1C.
GLP-1 receptor agonist versus placebo	-0.89% (-0.95 to -0.82)	Low due to serious imprecision and inconsistency	GLP-1 receptor therapy may lower glycated haemoglobin A1C.
SGLT-2 inhibitor versus GLP-1 receptor agonist	0.28% (0.19 to 0.37)	High	GLP-1 receptor agonist therapy lowers glycated haemoglobin A1C more than SLGT-2 inhibitor therapy.

CI= confidence interval. We used the point estimate of absolute effect for GLP-1 receptor agonists, obtained from GLP-1 receptor agonists versus placebo, to calculate absolute effect for SGLT-2 inhibitors *v* GLP-1 receptor agonists.

Appendix 9 Subgroup and meta-regression analysis for SGLT-2 inhibitors and GLP-1 receptor agonists compared to placebo for the outcome of all-cause mortality

SGLT-2 inhibitor versus placebo		
Subgroup	**Odds ratio (95% confidence interval)**	**P value for subgroup heterogeneity**
High cardiovascular risk	0.85 (0.78-0.92)	0.99
Low cardiovascular risk	0.85 (0.70-1.03)	
Body mass index 30 kg/m^2 or higher	0.86 (0.79-0.93)	0.66
Body mass index lower than 30 kg/m^2	0.81 (0.65-1.02)	
Trial duration 12 months or longer	0.85 (0.79-0.91)	0.58
Trial duration <12 months	1.03 (0.52-2.05)	
Chronic kidney disease	0.85 (0.79-0.92)	0.80
No chronic kidney disease	0.83 (0.68-1.02)	
GLP-1 receptor agonists versus placebo		
High cardiovascular risk	0.90 (0.82-1.00)	0.55
Low cardiovascular risk	0.87 (0.80-0.94)	
Body mass index 30 kg/m^2 or higher	0.88 (0.82-0.94)	0.38
Body mass index lower than 30 kg/m^2	0.33 (0.03-3.21)	
Trial duration 12 months or longer	0.88 (0.83-0.94)	0.97
Trial duration <12 months	0.89 (0.52-1.54)	
Chronic kidney disease	Not estimable	
No chronic kidney disease		