Supplementary files to the manuscript

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Supplementary File 1

PRISMA NMA Checklist

Table S1 PRISMA NMA Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	*3*
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	*4*
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	*5-6*
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	*5-6*

METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	*6*
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	*7*
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	*7*
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	*Supplementary File 2*
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	*7*
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	*7*
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	*7*
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	*8-9*
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	*7-8*
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	*8-9*

Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	*8-9*
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	*8-9*
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	*7-8*
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	*8-9*
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	*9* *Figure 1*
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	*Figure 2*
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in	*9*

		the treatment network, and potential biases reflected by the network structure.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	*Supplentary File 3*
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	*Supplementary File 4*
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	*NG*
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	*Figure 3*
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	*13 Supplementary File 8*
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	*Supplementary File 4*
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, *alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	*Supplementary File 6 Supplementary File 14 Supplementary File 15*

DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	*18-19*
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	*20*
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	*20*
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	*3*

PICOS = population, intervention, comparators, outcomes, study design.

***** Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

Supplementary File 2

Search strategy and results

Table S2.1 Search strategy for Ovid-Medline

1	*Glucagon-Like Peptide-1 Receptor/ or glucagon-like peptide-1 agonists.mp. or *Glucagon-Like Peptide 1/
2	glucagon like peptide*.ti,ab.
3	Receptors, Glucagon/ag [Agonists]
4	exenatide.af.
5	liraglutide.af.
6	albiglutide.af.
7	taspoglutide.af.
8	lixisenatide.af.
9	dulaglutide.af.
10	semaglutide.af.
11	Byetta.af.
12	Bydureon.af.
13	Victoza.af.
14	Lyxumia.af.
15	Adlyxin.af.
16	Tanzeum.af.
17	Eperzan.af.
18	Trulicity.af.
19	ZP10A peptide*.af.
20	"AVE 0010".af.
21	GLP 1 Receptor Agonist*.af.
22	GLP 1 RA*.af.
23	GLP 1RA*.af.
24	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25	Dipeptidyl Peptidase 4 inhibitor.mp. or exp *Dipeptidyl-Peptidase IV Inhibitors/
26	dipeptidyl peptidase IV inhibit*.af.
27	Dipeptidyl Peptidase 4 Inhibit*.af.
28	DPP 4 inhibit*.af.
29	DPP4 inhibit*.af.
30	DPP4i.af.
31	DPP IV inhibit*.af.

32	DPPIV inhibit*.af.
33	sitagliptin.af.
34	Januvia.af.
35	Janumet.af.
36	Juvisync.af.
37	vildagliptin.af.
38	Galvus.af.
39	Eucreas.af.
40	Galvus Met.af.
41	saxagliptin.af.
42	Onglyza.af.
43	Kombiglyze XR.af.
44	alogliptin.af.
45	Nesina.af.
46	Oseni.af.
47	Kazano.af.
48	linagliptin.af.
49	Trajenta.af.
50	gemigliptin.af.
51	Gemiglo.af.
52	anagliptin.af.
53	Beskoa.af.
54	teneligliptin.af.
55	Tenelia.af.
56	Trelagliptin.af.
57	PF 734200.af.
58	retagliptin.af.
59	Melogliptin.af.
60	evogliptin.af.
61	Carmegliptin.af.
62	"LC15 0444".af.
63	DA-1229.af.
64	omarigliptin.af.

65	gliptin*.af.
66	dutogliptin.af.
67	or/25-66
68	24 or 67
69	(clinical trial or controlled clinical trial or randomized controlled trial).pt.
70	clinical trials.mp. or exp *Clinical Trial/
71	clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/
72	random*.ti,ab.
73	clinical trial*.ti,ab.
74	controlled trial*.ti,ab.
75	case-control studies/
76	retrospective studies/
77	cohort studies/
78	longitudinal studies/
79	follow-up studies/
80	prospective studies/
81	cohort.ti,ab.
82	longitudinal.ti,ab.
83	follow up.ti,ab.
84	followup.ti,ab.
85	prospective*.ti,ab.
86	retrospective*.ti,ab.
87	nonrandom*.ti,ab.
88	comparison group*.ti,ab.
89	control group*.ti,ab.
90	database*.ti,ab.
91	population*.ti,ab.
92	registries/
93	registries.ti,ab.
94	trial$1 register.ti.
95	trial$1 registers.ti.
96	or/69-95
97	24 and 96

98	67 and 96
99	68 and 96
100	limit 97 to humans
101	limit 97 to animals
102	101 not 100
103	97 not 102
104	limit 98 to humans
105	limit 98 to animals
106	105 not 104
107	98 not 106
108	limit 99 to humans
109	limit 99 to animals
110	109 not 108
111	99 not 110
112	103 or 107
113	meta analysis.pt.
114	Meta-Analysis as Topic/
115	meta analy*.ti.
116	metaanaly*.ti.
117	113 or 114 or 115 or 116
118	24 and 117
119	67 and 117
120	68 and 117
121	limit 118 to humans
122	limit 118 to animals
123	122 not 121
124	118 not 123
125	limit 119 to humans
126	limit 119 to animals
127	126 not 125
128	119 not 127
129	limit 120 to humans
130	limit 120 to animals

131	130 not 129
132	120 not 131
133	103 not 124
134	107 not 128
135	111 not 132
136	133 or 134
137	remove duplicates from 133
138	remove duplicates from 134
139	remove duplicates from 135

Table S2.2 Search strategy for Embase

#1	'glucagon like peptide'/exp
#2	'glucagon like peptide 1'/exp
#3	'glp-1 receptor agonists'
#4	'glucagon like peptide 1 receptor agonists'
#5	'glucagon receptor'/exp
#6	'glucagon-like peptide-1 agonists'
#7	'glp-1 receptor agonist'
#8	'glucagon like peptide 1 receptor agonist'
#9	'glp-1 agonist'
#10	'glp-1 agonists'
#11	'glp-1 ra*'
#12	'exenatide'/exp
#13	'liraglutide'/exp
#14	'albiglutide'/exp
#15	'taspoglutide'/exp
#16	'lixisenatide'/exp
#17	'dulaglutide'/exp
#18	'semaglutide'/exp
#19	'zp10a peptide'
#20	'zp10a peptide 1'
#21	'glp1 ra'
#22	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#23	'dipeptidyl peptidase iv inhibitor'
#24	'dipeptidyl peptidase iv inhibitors'
#25	'dipeptidyl peptidase iv inhibitor'/exp
#26	'dpp 4 inhibitor*'
#27	'dpp iv inhibitor*'
#28	'dpp4i'

#29	'dpp4 i'
#30	'dpp4 inhibitor*'
#31	'dppiv inhibitor*'
#32	'alogliptin'/exp
#33	'sitagliptin'/exp
#34	'gemigliptin'/exp
#35	'linagliptin'/exp
#36	'saxagliptin'/exp
#37	'vildagliptin'/exp
#38	'dutogliptin'/exp
#39	'teneligliptin'/exp
#40	'anagliptin'/exp
#41	'trelagliptin'/exp
#42	'pf-734200'/exp
#43	'melogliptin'/exp
#44	'evogliptin'/exp
#45	'retagliptin'
#46	'carmegliptin'/exp
#47	'lc15 0444'
#48	'tenelia'
#49	'da-1229'
#50	'omarigliptin'/exp
#51	'beskoa'
#52	'gemiglo'
#53	'trajenta'
#54	'kazano'
#55	'oseni'
#56	'nesina'
#57	'kombiglyze xr'
#58	'onglyza'
#59	'eucreas'
#60	'galvus'
#61	'juvisync'
#62	'janumet'
#63	'januvia'
#64	'liptin'
#65	'gliptin'/exp
#66	#23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65
#67	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12

	OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66
#68	'clinical trial'/exp OR 'controlled clinical trial'/exp OR 'randomized controlled trial'/exp
#69	random*
#70	'case-control studies'/exp
#71	'retrospective studies'/exp
#72	'cohort studies'/exp
#73	'longitudinal studies'/exp
#74	'follow up studies'/exp
#75	nonrandom
#76	'prospective studies'/exp
#77	'comparison group'
#78	'control group'/exp
#79	database*
#80	'database'/exp
#81	'registries'/exp
#82	'registration'/exp
#83	#68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82
#84	#22 AND #83
#85	#22 AND #83 AND [humans]/lim
#86	#22 AND #83 AND [animals]/lim
#87	#86 NOT #85
#88	#84 NOT #87
#89	#66 AND #83
#90	#66 AND #83 AND [humans]/lim
#91	#66 AND #83 AND [animals]/lim
#92	#91 NOT #90
#93	#89 NOT #92
#94	#67 AND #83
#95	#67 AND #83 AND [humans]/lim
#96	#67 AND #83 AND [animals]/lim
#97	#96 NOT #95
#98	#94 NOT #97
#99	#88 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim)
#100	#93 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim)

#101	#98 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim)
#102	#99 AND [embase]/lim
#103	#100 AND [embase]/lim
#104	#101 AND [embase]/lim

Table S2.3 Search strategy for Cochrane Library

S45	s42	Limiters - MEDLINE Publication Type: Multicenter Study, Randomized Controlled Trial, Validation Studies, Clinical Conference, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Congresses, Consensus Development Conference, Controlled Clinical Trial, Corrected and Republished Article, Duplicate Publication, Evaluation Studies, Journal Article Search modes - Boolean/Phrase
S44	s17	Limiters - MEDLINE Publication Type: Multicenter Study, Randomized Controlled Trial, Validation Studies, Clinical Conference, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Congresses, Consensus Development Conference, Controlled Clinical Trial, Corrected and Republished Article, Duplicate Publication, Evaluation Studies, Journal Article Search modes - Boolean/Phrase
S43	S41	Limiters - MEDLINE Publication Type: Multicenter Study, Randomized Controlled Trial, Validation Studies, Clinical Conference, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Congresses, Consensus Development Conference, Controlled Clinical Trial, Corrected and Republished Article, Duplicate Publication, Evaluation Studies, Journal Article Search modes - Boolean/Phrase
S42	S17 OR S41	Search modes - Boolean/Phrase
S41	S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40	Search modes - Boolean/Phrase
S40	TX Januvia OR TX Janumet OR TX Juvisync OR TX Galvus OR TX Eucreas OR TX Onglyza OR TX Kombiglyze OR TX Nesina OR TX Oseni OR TX Kazano OR TX Trajenta OR TX	Search modes - Boolean/Phrase

	Gemiglo OR TX Beskoa OR TX Tenelia	
S39	TX Carmegliptin	Search modes - Boolean/Phrase
S38	TX Evogliptin	Search modes - Boolean/Phrase
S37	TX Melogliptin	Search modes - Boolean/Phrase
S36	TX Retagliptin	Search modes - Boolean/Phrase
S35	TX PF-734200	Search modes - Boolean/Phrase
S34	TX Trelagliptin	Search modes - Boolean/Phrase
S33	TX anagliptin	Search modes - Boolean/Phrase
S32	TX gemigliptin	Search modes - Boolean/Phrase
S31	TX LC15 0444	Search modes - Boolean/Phrase
S30	TX teneligliptin	Search modes - Boolean/Phrase
S29	TX dutogliptin	Search modes - Boolean/Phrase
S28	TX linagliptin	Search modes - Boolean/Phrase
S27	TX saxagliptin	Search modes - Boolean/Phrase
S26	TX vildagliptin	Search modes - Boolean/Phrase
S25	TX sitagliptin	Search modes - Boolean/Phrase
S24	TX alogliptin	Search modes - Boolean/Phrase
S23	TX DPP IV inhibit* OR TX DPPIV inhibit*	Search modes - Boolean/Phrase
S22	TX DPP4i	Search modes - Boolean/Phrase
S21	TX DPP 4 inhibit* OR TX DPP4 inhibit*	Search modes - Boolean/Phrase
S20	TX dipeptidyl-peptidase 4 inhibitor OR TX dipeptidyl-peptidase 4 inhibitors	Search modes - Boolean/Phrase
S19	TX dipeptidyl-peptidase iv inhibitors OR TX dipeptidyl-peptidase iv inhibitor	Search modes - Boolean/Phrase
S18	(ZE "dipeptidyl-peptidase iv inhibitors") or (ZE "dipeptidyl-peptidase iv inhibitors administration & dosage") or (ZE "dipeptidyl-peptidase iv inhibitors adverse effects") or (ZE "dipeptidyl-peptidase iv inhibitors pharmacokinetics") or (ZE "dipeptidyl-peptidase iv inhibitors pharmacology") or (ZE "dipeptidyl-peptidase iv inhibitors	Search modes - Boolean/Phrase

	therapeutic use") or (ZE "dipeptidyl-peptidase iv inhibitors toxicity")	
S17	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	Search modes - Boolean/Phrase
S16	TX Byetta OR TX Bydureon OR TX Victoza OR TX Lyxumia OR TX Adlyxin OR TX Tanzeum OR TX Eperzan OR TX Trulicity OR TX AVE 0010	Search modes - Boolean/Phrase
S15	TX GLP 1RA*.	Search modes - Boolean/Phrase
S14	TX GLP 1 RA*.	Search modes - Boolean/Phrase
S13	TX GLP 1 Receptor Agonist*.	Search modes - Boolean/Phrase
S12	TX ZP10A peptide*	Search modes - Boolean/Phrase
S11	TX semaglutide	Search modes - Boolean/Phrase
S10	TX dulaglutide	Search modes - Boolean/Phrase
S9	TX lixisenatide	Search modes - Boolean/Phrase
S8	TX taspoglutide	Search modes - Boolean/Phrase
S7	TX albiglutide	Search modes - Boolean/Phrase
S6	TX liraglutide	Search modes - Boolean/Phrase
S5	TX exenatide	Search modes - Boolean/Phrase
S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase
S3	TX glp-1 OR TX glp1	Search modes - Boolean/Phrase
S2	TX glucagon-like peptide 1 OR TX Glucagon-Like Peptides 1	Search modes - Boolean/Phrase
S1	(ZE "glucagon-like peptide 1") or (ZE "glucagon-like peptide 1 administration & dosage") or (ZE "glucagon-like peptide 1 agonists") or (ZE "glucagon-like peptide 1 analogs & derivatives") or (ZE "glucagon-like peptide 1 drug effects") or (ZE "glucagon-like peptide 1 therapeutic use") or (ZE "glucagon-like peptide-1 receptor agonists")or (ZE "glucagon-like peptide 1 pharmacokinetics") or (ZE	Search modes - Boolean/Phrase

	"glucagon-like peptide 1 pharmacology")	

Search strategy for ClinicalTrials.gov

exenatide OR liraglutide OR albiglutide OR taspoglutide OR lixisenatide OR dulaglutide OR semaglutide OR Byetta OR Bydureon OR Victoza OR Lyxumia OR Adlyxin OR Tanzeum OR Eperzan OR Trulicity OR ‘ZP10A peptide*’ OR ‘AVE 0010’ OR sitagliptin OR Januvia OR Janumet OR Juvisync OR vildagliptin OR Galvus OR Eucreas OR ‘Galvus Met’ OR saxagliptin OR Onglyza OR ‘Kombiglyze XR’ OR alogliptin OR Nesina OR Oseni OR Kazano OR linagliptin OR Trajenta OR gemigliptin OR Gemiglo OR anagliptin OR Beskoa OR teneligliptin OR Tenelia OR Trelagliptin OR ‘PF 734200’ OR retagliptin OR Melogliptin OR evogliptin OR Carmegliptin OR "LC15 0444" OR ‘DA-1229’ OR omarigliptin OR gliptin* OR dutogliptin

Supplementary File 3

References for included trials and boxplots among trials included

Table S3.1 Characteristics of the 292 studies included in the network Meta-analysis.

Study ID	Register number	Treatments	Size	Background medicine	Trial duration (w)	outcome	Age (yrs)	HbA1c (%)	Years of T2DM
3D Trial, Oe H, 2015[1]	NO	DPP4, a-Glu	80	OAD	24	Weight	67.1	7	4
ADDONIS, Gautier JF, 2016[2]	NCT01871558	DPP4, SU	42	Ins	24	Weight	63.7	8.2	12
Ahmann A, 2015[3]	NCT01617434	GLP1RA, placebo	431	NO	26	Weight	58.4	8.3	12.1
Ahren B, 2016[4]	NCT02098395	GLP1RA, placebo	705	Ins	26	Weight	43.2	8.3	21
Apovian CM, 2010[5]	NCT00375492	GLP1RA, placebo	142	Met/SU/SU+Met	24	Weight+WC	54.8	7.6	5.5
Araki E, 2015[6]	NCT01584232	GLP1RA, Insulin	360	OAM	26	Weight	56.8	8	8.8
Arechavaleta R 2009[7]	NCT00701090	DPP4, SU	926	Met	30	Weight	56.3	7.5	6.8
Arjona Ferreira JC 2013-1[8]	NCT00509262	DPP4, SU	291	NO	54	Weight	59.5	7.9	17.5
Arjona Ferreira JC 2013-2[9]	NCT00509236	DPP4, SU	129	NO	54	Weight	59.5	7.9	17.5
Arnolds S, 2010[10]	NCT00971659	DPP4, GLP1RA, placebo	47	Glar+Met	4	Weight	57	8.1	5.7
Aso Y 2015[11]	NO	DPP4, SU	30	NO	12	BMI	64.9	7.9	12.1
AWARD-1, Wysham C, 2014[12]	NCT01064687	GLP1RA, placebo	866	Met+TZD	26	Weight+BMI	55.7	8.1	8.8
AWARD-2, Giorgino F, 2015[13]	NCT01075282	GLP1RA, Insulin	801	Met+SU	78	Weight+BMI	56.7	8.1	9.1
AWARD-3, Umpierrez G, 2014[14]	NCT01126580	GLP1RA, Met	803	Met	52	Weight+BMI	55.6	7.6	2.6
AWARD-4, Blonde L,	NCT01191268	GLP1RA, Insulin	869	Ins	52	Weight+BMI	59.4	8.5	12.7

2015[15]									
AWARD-5, Nauck M, 2014[16]	NCT00734474	DPP4, GLP1RA	916	Diet+exercise /Met	104	Weight+WC	53.9	9.1	7.2
AWARD-7, NCT01621178 , 2017	NCT01621178	GLP1RA, Insulin	466	Ins	26	Weight	64.6	8.6	18.1
AWARD-8, Dungan, 2016[17]	NCT01769378	GLP1RA, placebo	265	NO	24	Weight+BMI	57.8	8.4	7.6
AWARD-9, Pozzilli P, 2017[18]	NCT02152371	GLP1RA, placebo	300	Ins	28	Weight	60.4	NA	13.1
Azar ST, 2016[19]	NCT01917656	GLP1RA, SU	333	Met	33	Weight	54.5	8.3	7.6
Bailey, TS, 2016[20]	NCT01907854	DPP4, GLP1RA	392	Met	26	Weight	56.4	8.3	7.8
Barnett AH, 2007[21]	NCT00099619	GLP1RA, Insulin	228	Met/SU	16	Weight	54.9	9	7.4
Bergenstal R, 2009[22]	NCT00097877	GLP1RA, Insulin	372	Met+SU	24	Weight	52.6	10.2	9
Berndt-Zipfel C, 2013[23]	NO	DPP4, SU	44	Met	24	Weight	58.5	7.4	7.3
Bolli G, 2009[24]	NCT00237237	DPP4, TZD	576	Met	52	Weight	56.6	8.4	6.4
Bosi E, 2007[25]	NCT00099892	DPP4, placebo	544	Met	24	Weight	54.2	8.4	6.3
Bosi E, 2009[26]	NO	DPP4, placebo	879	Met	24	Weight	52.6	8.6	2
Bosi E, 2011[27]	NCT00432276	DPP4, placebo	789	Met+PIG	52	Weight	55.1	NA	7.2
Bouchi R, 2017[28]	NO	GLP1RA, placebo	17	Met	36	Weight	58.6	8	NA
Buse JB, 2004[29]	NCT00039026	GLP1RA, placebo	377	SU	30	Weight	55.3	8.6	6.2
Buse JB, 2011[30]	NCT00765817	GLP1RA, placebo	213	Glar+/-Met/TZD	30	Weight+WC	59	NA	12
CANTATA-D Trial, Lavalle-Gonzalez FJ, 2013[31]	NCT01106677	DPP4, SGLT-2, placebo	1261	Met	26	Weight	55.4	7.9	6.9
Charbonnel B, 2013[32]	NCT01296412	DPP4, GLP1RA	547	SU	26	Weight	57.3	8.2	7.9
Chawla S 2013[33]	NO	DPP4, TZD	50	Met	16	Weight	50.8	8.2	4.3

Chen WJY, 2017[34]	NCT00766857	GLP1RA, Insulin	23	OGLA (Met/Met+SU)	26	BMI+WC	66	7.5	8
Chien MN 2011[35]	NO	DPP4, placebo	97	OAD	24	BMI	73	9.8	13.7
CONFIDENCE, Xu W, 2015[36]	NCT01147627	GLP1RA, Insulin, TZD	169	NO	48	Weight+BMI+WC	50.3	8.1	NA
Cui J 2016[37]	NCT01963845	DPP4, placebo	50	NO	24	Weight+BMI	NA	NA	NA
Davies M, 2013[38]	NCT01003184	GLP1RA, Insulin	194	Met/Met+SU	26	Weight+BMI+WC	58.5	8.4	7.5
Davies MJ, 2009[39]	NCT00360334	GLP1RA, Insulin	204	Met+/- SU/TZD	26	Weight+BMI+WC	56.5	8.6	8.7
Davies MJ, 2016[40]	NCT01620489	GLP1RA, placebo	263	NO	26	BMI	67.2	8	15.1
Davis SN, 2007[41]	NCT00099333	GLP1RA, Insulin	45	SU/Met	16	Weight	53.3	NA	10.9
de Ranitz-Greven, 2014[42]	NO	DPP4, placebo	15	NO	16	Weight	62.4	7.9	5.8
DeFronzo RA, 2005[43]	NCT00039013	DPP4, placebo	314	NO	26	Weight	53.4	NA	NA
DeFronzo RA, 2008[44]	NCT00286455	GLP1RA, placebo	336	Met	30	Weight	53	8.2	5.9
DeFronzo RA, 2010[45]	NCT00135330	GLP1RA, TZD	88	Met	20	Weight+WC	56.5	7.9	4.7
Dei Cas A, 2017[46]	NCT01822548	DPP4, SU	64	NO	48	BMI	62	7.7	6.5
Derosa G, 2010[47]	NO	DPP4, Met	137	TZD	52	Weight+BMI	57.5	8.5	5.5
Derosa G, 2010[48]	NO	DPP4, placebo	167	Met	52	Weight+BMI	53.3	8.2	6.2
Derosa G, 2011[49]	NO	DPP4, placebo	197	OAD	104	Weight+BMI+WC	NA	8.1	NA
Derosa G, 2012[50]	NO	DPP4, SU	153	Met	26	Weight+BMI	58.5	7.9	6.8
Derosa G, 2012[51]	NO	GLP1RA, SU	116	Met	52	Weight+BMI	56.5	8.9	NA
Derosa G, 2013[52]	NO	GLP1RA, SU	101	Met	52	Weight+BMI	55.5	8.8	NA
Derosa G, 2014-1[53]	NO	GLP1RA, placebo	163	Met	52	Weight+BMI+WC	57	8	7.7
Derosa G, 2014-2[53]	NO	DPP4, placebo	169	Met	52	Weight+BMI	53.6	8.1	5.6
Diamant M, 2014[54]	NCT00960661	GLP1RA, Insulin	510	Ins/Met	30	Weight+BMI+WC	59.5	8.2	NA
DUAL-I, Holst JJ, 2016[55]	NCT01336023	GLP1RA, Insulin	827	Met+TZD	26	Weight	55	8.3	7.1

DURATION-2, Bergenstal RM, 2010[56]	NCT00637273	DPP4, GLP1RA, TZD	488	Met	26	Weight	52.5	8.5	5.7
DURATION-3, Diamant M, 2014[57]	NCT00641056	GLP1RA, Insulin	299	Met/Met+SU	156	Weight+WC	58	8.3	7.9
DURATION-4, Russell-Jones D, 2012[58]	NCT00676338	DPP4, GLP1RA, Met, TZD	707	NO	26	Weight	53.7	8.5	2.7
DURATION-8, Frias JP2-1, 2016[59]	NCT02229396	GLP1RA, placebo	458	SGLT-2	28	Weight	54.2	NA	NA
DURATION-8, Frias JP2-2, 2016[59]	NCT02229396	GLP1RA, SGLT-2	457	placebo	28	Weight	54.2	NA	NA
DURATION-NEO-2, Gadde KM, 2017[60]	NCT01652729	DPP4, GLP1RA, placebo	364	Met/antihypertensive and lipid-lowering agents	28	Weight	53.7	NA	8.3
EAGLE D'Alessio D, 2015[61]	NCT01117350	GLP1RA, Insulin	888	Met/SU/Met+SU	24	Weight	57.3	9.1	8.5
EASIE, Aschner P, 2012[62]	NCT00751114	DPP4, Insulin	482	Met	26	Weight	53.6	8.5	4.5
EDIT, Sato S, 2015[63]	NO	DPP4, placebo	49	Ins	24	Weight+WC	66	7.9	19.5
ELEGANT, de Wit HM, 2014[64]	NCT01392898	GLP1RA, Insulin	50	Met/Met+SU/SU	52	Weight+BMI+WC	58	7.3	8
ENDURE, NCT00856284, 2013[65]	NCT00856284	DPP4, SU	2606	Met	104	Weight	55.4	7.6	NA
EUREXA, Gallwitz, B, 2012[66]	NCT00359762	GLP1RA, SU	386	Met	156	Weight	56.4	7.4	5.7
EXAMINE, White WB 2013[67]	NCT00968708	DPP4, placebo	4764	OAD	76	Weight	61	8	7.2
Faber R, 2015[68]	NCT01931982	GLP1RA, placebo	36	NO	22	Weight+WC	57	NA	4

Farngren J, 2016[69]	NCT02020629	GLP1RA, placebo	18	NO	6	Weight	55	7.7	11.7
Farr OM, 2016[70]	NCT01562678	GLP1RA, placebo	56	NO	2.4	Weight+BMI	52.5	NA	NA
Faurschou A, 2015[71]	NCT01460069	GLP1RA, placebo	20	NO	8	Weight	51.3	5.5	NA
Feng W, 2017[71]	NCT03068065	GLP1RA, Met, SU	43	NO	24	Weight+BMI+WC	47.1	9.1	NA
Ferrannini E, 2009[72]	NCT00106340	DPP4, SU	2789	Met	52	Weight	57.5	7.3	5.7
Filozof C, 2010[73]	NCT00396357	DPP4, Met	914	Met	24	Weight	57	7.3	4.7
Filozof C, 2010[74]	NO	DPP4, SU	1007	SU	52	Weight	59.5	8.5	6.6
Fineman MS, 2004[75]	NO	GLP1RA, placebo	123	NO	5	Weight	53.7	NA	NA
Foley JE, 2009[76]	NCT00102388	DPP4, SU	1092	SU	104	Weight	54.8	8.7	2.2
Fonseca V, 2007[77]	NCT00099931	DPP4, placebo	296	Ins	24	Weight	59.2	8.4	14.7
Forst T, 2012[78]	NCT01208012	GLP1RA, placebo	40	Met	6	Weight+BMI+WC	56.4	6.3	4.3
GALIANT, Blonde L, 2009[78]	NCT00396627	DPP4, TZD	2664	Met	12	Weight	55.6	8	5.1
Gallwitz B, 2011[79]	NCT00434954	DPP4, SU	1524	Met	104	Weight	59.8	7.7	NA
Gallwitz B, 2012[80]	NCT00622284	GLP1RA, Insulin	354	Met/SU	26	Weight+BMI	57.1	7.9	5
Gao Y, 2009[81]	NCT00324363	GLP1RA, placebo	401	Met/Met+SU	16	Weight	54.5	8.3	8
Garber AJ, 2008[82]	NCT00099944	DPP4, placebo	408	SU	24	Weight	58.2	8.5	7.2
GetGoal-DUO-1, Riddle MC, 2013[83]	NCT00975286	GLP1RA, placebo	437	Ins	24	Weight	56.2	7.6	9.2
GetGoal-F1, Bolli G, 2013[84]	NCT00763451	GLP1RA, placebo	471	Met	24	Weight	56.1	8	6
GetGoal-L, Riddle MC, 2013[85]	NCT00715624	GLP1RA, placebo	472	Met+/-SU+/-TZD	24	Weight	57.2	8.4	12.5
GetGoal-L-Asia, Seino Y, 2012[86]	NCT00866658	GLP1RA, placebo	307	Ins/SU	24	Weight	58.4	8.5	13.9
GetGoal-M, Ahren B,	NCT00712673	GLP1RA, placebo	665	Met	24	Weight	54.7	8.1	6.1

2013[87]									
GetGoal-M-Asia, Yu Pan C, 2014[88]	NCT01169779	GLP1RA, placebo	379	Met/SU/Met+SU	24	Weight	54.8	7.9	6.6
GetGoal-Mono, Fonseca VA, 2012[89]	NCT00688701	GLP1RA, placebo	348	NO	12	Weight	53.7	8	1.1
GetGoal-O, Meneilly GS, 2017[90]	NCT01798706	GLP1RA, placebo	348	NO	24	Weight	74.2	8.1	14.1
GetGoal-P, Pinget M, 2013[91]	NCT00763815	GLP1RA, placebo	472	TZD+/- Met	24	Weight	55.8	8.1	8.1
GetGoal-S, Rosenstock J, 2014[92]	NCT00713830	GLP1RA, placebo	848	Met+/- SU	24	Weight	57.2	8.3	9.3
Goke B, 2008[93]	NCT00138567	DPP4, Met	462	TZD	104	Weight	54	8.7	2.4
Göke B, 2013[94]	NCT00575588	DPP4, SU	858	Met	104	Weight	57.6	7.7	5.4
Grunberger G, 2012[95]	NO	GLP1RA, placebo	164	NO	12	Weight	56.6	7.3	3.8
GUARD study, Yoon SA, 2016[96]	NCT01968044	DPP4, placebo	130	Ins	12	Weight	66	8.4	16.3
Gudipaty L, 2014[97]	NCT00775684	DPP4, SU	26	NO	26	BMI	55.3	NA	3.9
Gurkan E, 2014[98]	NO	GLP1RA, Insulin	34	Met	26	Weight+BMI+WC	52.7	8	7.2
Harder H, 2004[99]	NO	GLP1RA, placebo	33	SU	8	Weight+WC	60	7.5	4.1
HARMONY-1, Reusch J, 2014[100]	NCT00849056	GLP1RA, placebo	81	Met+TZD/Met	156	Weight	55	8.1	8
HARMONY-2, Nauck, MA, 2016[101]	NCT00849017	GLP1RA, placebo	75	NO	156	Weight	52.9	8.1	4
HARMONY-3, Ahren B, 2014[102]	NCT00838903	DPP4, GLP1RA, placebo, SU	323	Met	156	Weight	54.5	8.1	6
HARMONY-4, Weissman	NCT00838916	GLP1RA, Insulin	211	Met/SU/Met+SU	156	Weight	55.4	8.3	8.7

PN, 2014[103]									
HARMONY-5, Home PD, 2015[104]	NCT00839527	GLP1RA, placebo	170	Met+SU	156	Weight	55.2	8.2	8.9
HARMONY-6, Rosenstock J, 2014[92]	NCT00976391	GLP1RA, Insulin	263	Ins	60	Weight	55.6	8.5	11
Harrtori A, 2017[105]	UMIN000004674	DPP4, a-Glu	74	NO	24	Weight+BMI	64.4	7.2	NA
Hartley P, 2015[106]	NCT01189890	DPP4, SU	444	NO	30	Weight	70.7	7.8	8.7
Hegazy SK, 2015[107]	NO	DPP4, Met	40	NO	12	BMI	NA	8.1	NA
Heine RJ, 2005[108]	NCT00082381	GLP1RA, Insulin	475	Met+SU	26	Weight	58.9	8.3	9.6
Hissa MRN, 2015[109]	NO	DPP4, SU	36	Met	16	Weight	57.4	8.9	4.3
Hong ES, 2012[110]	NCT01100125	DPP4, Insulin	124	OAD	24	Weight+WC	59.2	9.2	NA
Iacobellis G, 2017[111]	NCT02014740	GLP1RA, placebo	85	Met	26	BMI	50.9	6.5	NA
Idorn T, 2016-1[112]	NCT01394341	GLP1RA, placebo	20	NO	12	Weight	61.9	7.9	12.9
Idorn T, 2016-2[112]	NCT01394341	GLP1RA, placebo	20	NO	12	Weight	67.1	6.7	14.1
Inagaki N, 2012[113]	NCT00935532	GLP1RA, Insulin	426	Met/Met+TZD	26	Weight	57.1	8.5	8.9
INDORSE study, Lovshin JA, 2017[114]	NCT02406443	DPP4, placebo	36	NO	4	BMI	59.9	7.2	7.4
INICOM, Lim S, 2017[115]	NCT01787396	DPP4, Met	433	Met	24	Weight	53.9	8.7	3.9
Inoue Y, 2015[116]	UMIN 000007009	GLP1RA, Insulin	82	NO	24	Weight	60.4	6.5	9
Ito M, 2011[117]	NO	DPP4, placebo	51	OAD	24	Weight+BMI	67.5	6.7	NA
Iwamoto K, 2009[118]	NCT00612794	GLP1RA, placebo	19	SU/Met/Met+SU/TZD	10	Weight	59.6	7.4	6.1
Iwamoto Y, 2010[119]	NCT00127192	DPP4, a-Glu	380	NO	12	Weight	59.2	7.6	5.4
Iwamoto Y, 2010[119]	NO	DPP4, placebo	363	NO	12	Weight	59.8	7.6	5.4
Jeon HJ, 2011[120]	NO	DPP4, SU	106	Met	32	Weight	54.5	8.1	5.9
Kadowaki T, 2009[121]	NCT00382239	DPP4, placebo	194	SU	12	Weight	59.4	8.4	8.8

Kadowaki T, 2011[122]	NCT00577824	GLP1RA, placebo	114	SU/Met/Met+SU/TZD	12	Weight	59.7	8	10.9
Kadowaki T, 2013[123]	NCT01026194	GLP1RA, placebo	178	SU+/Biguanide+/TZD	24	Weight+WC	58.4	8.6	11.9
Kadowaki T, 2014[124]	NCT00974090	DPP4, placebo	204	TZD	12	Weight	60.4	8	7.4
Kaku K, 2010[125]	NCT00395746	GLP1RA, placebo	262	SU	52	Weight	59.7	8.4	10.3
Kato H, 2015[126]	NO	DPP4, SU	20	NO	24	BMI	58.5	7.3	NA
Kawamori R, 2012[127]	NCT00654381	DPP4, placebo	396	NO	12	Weight+BMI+WC	60.6	8	NA
Ke W, 2016[128]	NCT01471808	GLP1RA, placebo	31	Ins	12	Weight	42.2	10.1	NA
Kendall DM, 2005[129]	NCT00035984	GLP1RA, placebo	733	Met/Met+SU	30	Weight	55.3	8.5	8.9
Kikuchi M, 2009[130]	NO	DPP4, placebo	148	NO	12	BMI	59.6	7.4	5.9
Kikuchi M, 2010[131]	NCT00325117	DPP4, placebo	197	SU	12	Weight	59.8	7.9	8.7
Kim D, 2007[132]	NCT00103935	GLP1RA, placebo	43	Met	15	Weight	55	8.5	4.4
Koren S, 2012[133]	NO	DPP4, SU	80	Met	12	Weight+BMI+WC	59	8.3	7.8
Kumarathurai P, 2017[134]	NCT01595789	GLP1RA, placebo	48	liraglutide Met	12	Weight+WC	62.5	6.5	NA
Kutoh E, 2012[135]	UMIN 000006860	DPP4, placebo	51	NO	12	BMI	49.2	10.3	NA
LEAD-1, Marre M, 2009[136]	NCT00318422	GLP1RA, TZD, placebo	1041	SU	26	Weight+BMI	56.1	8.5	NA
LEAD-2, Nauck M, 2009[137]	NCT00318461	GLP1RA, SU, placebo	1077	Met	104	Weight	56.7	8.4	7.4
LEAD-3, Garber A, 2011[138]	NCT00294723	GLP1RA, SU	733	Met/SU/Biguanide/Met+TZD	156	Weight	53	8.3	5.4
LEAD-4, Zinman B, 2009[139]	NCT00333151	GLP1RA, placebo	533	Met+TZD	26	Weight	55	8.5	9
LEAD-5, Russell-Jones D, 2009[139]	NCT00331851	GLP1RA, Insulin, placebo	347	Met+SU	26	Weight	57.5	8.3	9.4
Leiter LA, 2014[140]	NCT01098539	DPP4, GLP1RA	276	OAD	52	Weight	63.3	8.2	11.2

Lewin AJ, 2012[141]	NCT00819091	DPP4, placebo	245	SU	18	Weight	54.9	8.6	NA
Li CJ, 2012[142]	NO	GLP1RA, Insulin	84	Ins	12	Weight+BMI+WC	52	8.7	9
Li CJ, 2014[143]	NO	DPP4, GLP1RA	178	Ins	24	Weight+BMI	47.1	8.6	5.5
Li F, 2017[144]	NO	DPP4, Met	27	NO	12	Weight+BMI+WC	54.1	8.5	NA
Li FF, 2017[145]	NO	GLP1RA, placebo	36	Ins	5	Weight	48.7	9.3	NA
LIBRA, Retnakaran R, 2014[146]	NCT01270789	GLP1RA, placebo	51	Met/SU/Met+SU	48	BMI+WC	58.2	6.3	2.3
Lind M, 2015[147]	EudraCT 2012-001941-42	GLP1RA, placebo	122	NO	24	Weight	63.6	9	17.1
Liutkus J, 2010[148]	NCT00603239	GLP1RA, placebo	165	TZD/TZD+Met	26	Weight+WC	54.7	8.2	6.3
LixiLan-O, Davies, MJ, 2017[149]	NCT02058147	GLP1RA, Insulin	698	Met	30	Weight	58.4	8.1	9.8
L-STEP study Fujitani Y, 2016[150]	UMIN000008591	DPP4, a-Glu	359	NO	12	Weight+BMI	61	7	NA
Luo N, 2015[151]	NO	DPP4, placebo	30	Ins	12	BMI	37	10.1	20
Macauley M, 2015[152]	NCT01356381	DPP4, placebo	44	NO	24	Weight	61.4	6.4	NA
Masanori A, 2016[153]	UMIN000018445	DPP4, Insulin	82	Ins	24	Weight+BMI	66.6	6.5	NA
MASTER Mikada A, 2014[154]	NO	DPP4, a-Glu	28	NO	24	Weight+BMI	59	7.2	NA
Mastushima Y, 2016[155]	UMIN000003503	DPP4, a-Glu	238	a-Glu	12	Weight+BMI	63.2	7.9	NA
Mathieu C, 2014[156]	NCT01388361	GLP1RA, Insulin	176	Met+Ins	26	Weight	61	7.7	12.4
Matikainen N, 2006[157]	NO	DPP4, placebo	31	NO	4	Weight	55.2	6.9	5.1
Matthews DR, 2010[158]	NO	DPP4, SU	3118	Met	104	Weight	57.5	7.3	5.7
Mensberg P, 2017[159]	NCT01455441	GLP1RA, placebo	33	NO	16	Weight+BMI	56.1	8.1	4.9
Mita T, 2016-1[160]	NO	DPP4, placebo	297	NO	104	BMI	64.6	7.3	8.6
Mita T, 2016-2[160]	NO	DPP4, placebo	236	NO	104	BMI	63.7	8.1	17.3

Miya A, 2017[161]	NR	GLP1RA, placebo	26	Met	12	Weight+BMI	62.3	7.2	20.2
Mohan V, 2009[162]	NCT00289848	DPP4, placebo	503	NO	18	Weight	50.9	8.7	2
Moretto TJ, 2008[163]	NCT00381342	GLP1RA, placebo	232	NO	24	Weight	54	7.8	1.7
Moses RG, 2016[164]	NCT01076075	DPP4, placebo	339	NO	54	Weight	54.9	8.4	7.8
Nauck M, 2007[165]	NCT00094770	DPP4, SU	514	Met	104	Weight	56.7	7.7	6.3
Nauck MA, 2007[166]	NCT00082407	DPP4, SU	756	Met	52	WC	56.7	7.7	6.4
Nauck MA, 2007[165]	NCT00094770	DPP4, placebo	507	Met	26	Weight	54.8	7.9	6
Nauck MA, 2009[167]	NCT00286442	GLP1RA, Insulin	428	Met/SU	52	Weight	58.7	8.6	9.9
NCT00620282, 2011	NCT00620282	GLP1RA, SU, placebo	47	Met	12	Weight	58.5	NA	6.8
NCT00701935, 2013	NCT00701935	GLP1RA, placebo	75	NO	26	Weight	58.1	NA	NA
NCT00993187, 2014	NCT00993187	DPP4, SU	290	Met	30	Weight	53.9	8	4.2
NCT01149421, 2015	NCT01149421	GLP1RA, placebo	755	NO	26	Weight	56.5	7.9	8.3
NCT01195090, 2011	NCT01195090	DPP4, TZD	119	Met+SU	24	Weight	59.1	8.4	NA
NCT01289119, 2013	NCT01289119	DPP4, placebo	175	NO	16	Weight	52.3	NA	2
NCT01289119, 2013-1	NCT01289119	DPP4, placebo	190	Met	16	Weight	53.1	NA	5.4
NCT01289119, 2013-2	NCT01289119	DPP4, placebo	122	TZD	16	Weight	52.2	NA	5.3
NCT01438814, 2014	NCT01438814	DPP4, placebo	611	Met	14	Weight	53	8	NA
NCT01644500, 2012	NCT01644500	GLP1RA, SU	695	NO	26	Weight+BMI	52.8	NA	NA
NCT01648582, 2012	NCT01648582	GLP1RA, Insulin	768	Met/SU	52	Weight+BMI	55	NA	NA
NCT01733758, 2013	NCT01733758	GLP1RA, placebo	489	NO	24	Weight	58.4	118	NA
Nogueira KC, 2014[168]	NO	DPP4, SU	35	Met+SU	24	Weight+BMI	57	8	10.9
Nomoto H, 2016[169]	UMIN000004955	DPP4, SU	90	SU	26	BMI	61	7.4	NA
Nonaka K, 2008[170]	NCT00371007	DPP4, placebo	151	NO	12	Weight	55.3	7.6	4.1
Ohira M, 2014[171]	NO	DPP4, Met	70	NO	24	Weight+BMI	60.4	NA	NA
Oyama J, 2016[172]	UMIN000004490	DPP4, placebo	442	Ins	96	BMI	69.4	7	NA

Oz Gul O, 2011[173]	NO	DPP4, placebo	44	NO	12	Weight+BMI	56.5	6.8	NA
Pan C, 2008[174]	NCT00110240	DPP4, a-Glu	661	NO	24	Weight	51.8	8.6	1.2
Park KS, 2017[175]	NCT01812122	DPP4, SU	32	NO	24	Weight+WC	60	8.4	7.4
Pi-Sunyer FX, 2007[176]	NCT00120536	DPP4, placebo	350	NO	24	Weight	51.2	8.4	2.2
Pratley R, 2011[177]	NCT00700817	DPP4, GLP1RA	644	Met	78	Weight+WC	55.3	8.4	6.2
Pratley RE, 2009-1[178]	NCT00286468	DPP4, SU	488	SU	24	Weight	56.5	NA	7.7
Pratley RE, 2009-2[178]	NCT00286494	DPP4, placebo	488	NO	26	Weight	55.4	8	7.6
Probstfield JL, 2016[179]	NCT01524705	GLP1RA, Insulin	89	Met/Ins	26	Weight	62	7.9	NA
Ratner R, 2010[180]	NCT00460941	GLP1RA, placebo	129	Met	8	Weight	56.5	7.9	6.5
Ratner RE, 2010[181]	NO	GLP1RA, placebo	529	Met	13	Weight	56.2	7.6	6.6
RELEASE de Boer SA, 2017[182]	NCT02015299	DPP4, placebo	40	NO	26	Weight	63	6.3	NA
Ristic S, 2005[183]	NO	DPP4, placebo	273	NO	12	Weight	55.9	7.7	2.7
Roden M, 2013[184]	NCT01177813	DPP4, SGLT-2, placebo	899	NO	24	Weight+WC	55	NA	NA
Roden M, 2015[185]	NCT01289990	DPP4, placebo	451	NO	76	Weight	55	7.9	NA
Rosenstock J, 2007-1[186]	NCT00101803	DPP4, TZD	228	NO	24	Weight	51.9	8.7	2
Rosenstock J, 2007-2[186]	NCT00101803	DPP4, placebo	363	TZD	24	Weight	51.3	8.8	2
Rosenstock J, 2008-1[187]	NO	DPP4, placebo	270	Met	12	Weight	54	7.9	1.2
Rosenstock J, 2008-2[187]	NO	DPP4, placebo	73	Met	6	Weight	52.1	7.7	0.4
Rosenstock J, 2009[188]	NCT00286429	DPP4, placebo	372	Ins	26	Weight	55.4	9.6	12.6
Rosenstock J, 2009[189]	NCT00518115	DPP4, TZD	391	TZD	26	Weight	52.8	8.8	3.2
Rosenstock J, 2010[190]	NCT00395512	DPP4, SU	419	NO	52	Weight	69.9	7.5	6.1
Rosenstock J, 2010[191]	NCT00395512	DPP4, SGLT-2	261	Met	24	Weight	54.5	9	7.8
Rosenstock J, 2013[192]	NCT00707993	GLP1RA, placebo	113	Met	16	Weight+WC	53.5	8	4.9
Rosenstock J, 2015[193]	NCT01606007	DPP4, TZD	240	NO	26	Weight	52.2	8.8	3.2

Rosenstock J, 2016[194]	NCT01768559	GLP1RA, Insulin	885	NO	26	Weight	59.8	7.8	NA
SAIS2, Nomoto H, 2015[195]	UMIN000005331	GLP1RA, Insulin	31	NO	14	BMI	60.3	8.7	NA
Saito D, 2017[196]	UMIN000010849	DPP4, Insulin	24	Ins	24	BMI	60.9	7.9	12.4
Samocha-Bonet D, 2014[197]	NCT00673894	DPP4, placebo	26	Met	4	Weight	65	7.1	3.3
Satoh-Asahara N, 2013[198]	NO	DPP4, placebo	48	NO	12	BMI	60	8.3	NA
Savvidou S, 2016[199]	NR	GLP1RA, placebo	103	Ins	26	Weight+BMI+WC	62.9	NA	12
SCALE, Davies MJ, 2015-1[200]	NCT01272232	GLP1RA, placebo	826	NO	68	BMI	54.9	7.9	7.3
SCALE, Davies MJ, 2015-2[200]	NCT01272232	GLP1RA, placebo	827	NO	68	Weight+WC	54.9	7.9	7.3
Scalzo RL, 2017[201]	NCT01364584	GLP1RA, placebo	23	NO	13	Weight+BMI	64	7.3	6.5
Scherbaum WA, 2008-1[202]	NCT00300287	DPP4, placebo	131	NO	108	Weight	63.1	6.6	2.3
Scherbaum Wa, 2008-2[203]	NCT00101712	DPP4, placebo	306	NO	52	Weight	63	6.8	2.6
Schweizer A, 2009[204]	NO	DPP4, Met	335	NO	24	Weight	70.9	7.8	3
Seino Y, 2008[205]	NCT00154414	DPP4, placebo	230	a-Glu	12	Weight	62.1	8	7.8
Seino Y, 2010[206]	NCT00393718	DPP4, placebo	288	Met	12	Weight	52.6	8	6.3
Seino Y, 2011[207]	NCT01263483	GLP1RA, placebo	135	OAD	14	Weight	57.7	NA	8
Seino Y, 2012[208]	NCT01318109	GLP1RA, SU	395	Diet+exercise	52	Weight	58.3	8.3	8.3
Seino Y, 2014[209]	NCT01098461	GLP1RA, placebo	211	Diet+exercise	16	Weight	57.8	8.6	7.3
Seino Y, 2016[210]	NCT01572740	GLP1RA, placebo	256	Ins	36	Weight	60.5	8.8	14.5
Shi L, 2017[211]	NO	GLP1RA, a-Glu	31	Met	13	BMI+WC	41.5	9.6	2.3

Shi Xiulin, 2017[212]	NCT01776788	GLP1RA, placebo	129	Ins	104	BMI+WC	45	10.1	NA
Shimoda S, 2014[213]	UMIN000009544	DPP4, SU	50	NO	12	BMI	63.1	7.4	NA
Silva GM, 2016	NCT02607410	DPP4, Insulin	35	SU/Met	52	Weight+BMI	56.7	8.1	10.9
SMART study NCT02243176[214]	NCT02243176	DPP4, a-Glu	481	NO	24	Weight	55.6	8.2	5.2
Smits, M M-1, 2016[215]	NCT01744236	DPP4, GLP1RA, placebo	51	NO	12	Weight+BMI	62.7	7.3	8.2
Srivastava S, 2012[216]	NO	DPP4, SU	50	Met	18	BMI	NA	8.3	NA
START Terauchi Y, 2017[217]	NCT01183104	DPP4, SU	261	NO	52	Weight	70.5	7.5	NA
START-J Hibuse T, 2014[218]	NO	DPP4, placebo	26	SU/Met/Met+SU	12	BMI+WC	60.3	7.6	4.4
STEADFAST Hassanein M, 2014[219]	NCT01758380	DPP4, SU	557	Met	16	Weight	54.5	7	4.8
Strozik A, 2015[220]	NO	DPP4, placebo	61	Met	12	Weight+BMI	51	7.9	NA
Su Y, 2014 -1[221]	NO	DPP4, placebo	600	NO	24	Weight	48.1	8.6	NA
Su Y, 2014-2[222]	NO	DPP4, placebo	508	AGI	12	Weight	49.2	8.8	NA
Sun X, 2017[223]	NO	DPP4, placebo	206	NO	16	Weight+BMI	28.9	NA	NA
SUSTAIN-1, Sorli, C, 2017[224]	NCT02054897	GLP1RA, placebo	387	NO	30	Weight+BMI+WC	53.7	8.1	4.2
SUSTAIN-2, Ahren, 2016[225]	NCT01930188	DPP4, GLP1RA	1163	NO	56	Weight+BMI+WC	55.1	8.1	6.6
SUSTAIN-4, Aroda VR, 2017[226]	NCT02128932	GLP1RA, Insulin	1082	NO	30	Weight+BMI+WC	56.5	8.2	8.6
Suzuki K, 2014[227]	NO	DPP4, GLP1RA	40	NO	24	Weight	57.6	9.5	2.2
Tai H, 2016[228]	NCT02798172	DPP4, placebo	81	Met	26	BMI+WC	53.6	8.2	6.6

Takeshita Y, 2015[229]	no. 000004953	DPP4, a-Glu	60	NO	16	Weight+BMI+WC	63.5	6.8	9.7
Takeshita Y, 2015[230]	UMIN 000007051	DPP4, GLP1RA	112	NO	12	Weight+BMI+WC	64.7	8.1	NA
Takihata M, 2013[231]	NO	DPP4, TZD	115	Met/SU/Met+SU	24	Weight+BMI	60.5	7.4	NA
Tanaka K, 2015[232]	UMIN000004243	GLP1RA, Met	46	NO	24	Weight+WC	52.9	7.9	5.1
Tanaka T, 2014[233]	NO	DPP4, SU	80	Met/TZD	12	Weight	64	7.4	9.4
Tang A, 2015[234]	NCT01399645	GLP1RA, Insulin	35	Met	12	Weight+BMI+WC	60.5	7.8	NA
T-emerge-1, Raz I, 2012[235]	NCT00744926	GLP1RA, placebo	354	NO	24	WC	54.8	7.6	2.4
T-emerge-3, Henry RR, 2012[236]	NCT00744367	GLP1RA, placebo	313	Met+TZD	24	Weight+WC	54.1	8.1	7.7
T-emerge-4, Bergenstal RM, 2012[237]	NCT00754988	DPP4, GLP1RA	546	Met	156	Weight	55.9	8	5.9
T-emerge-5, Nauk M, 2013[238]	NCT00755287	GLP1RA, Insulin	1028	Met/SU	24	Weight	57.7	8.3	9.3
T-emerge-6, Pratley RE, 2013[239]	NCT00909597	GLP1RA, TZD	740	Met/SU/Met+SU	24	Weight+WC	56.4	8.3	8.8
T-emerge-7, Hollander P, 2013[240]	NCT00823992	GLP1RA, placebo	292	Met	24	Weight+WC	53.5	7.6	5.1
Ten Kulve JS, 2016[241]	NCT01363609	GLP1RA, Insulin	40	NO	24	Weight+BMI+WC	NA	7.1	NA
Terauchi Y, 2014[242]	NCT01001104	GLP1RA, placebo	145	Met	12	Weight	52.2	8	4.6
Tian M, 2016[243]	NO	DPP4, placebo	135	NO	12	Weight+BMI	NA	8.1	NA
Tonneijck L, 2017[244]	NCT02276196	GLP1RA, Insulin	35	NO	8	Weight+WC	61.5	8.1	12.5
Treat 4 Ramadan Trial, Brady EM, 2014[245]	NO	GLP1RA, SU	100	Met	12	Weight	51.9	7.7	NA
TROICA study, Ahn CH,	NCT01990469	DPP4, placebo	219	Met+SU	24	Weight+WC	60.9	8.2	12.9

2016[246]									
Umpierrez GE, 2011[247]	NCT00630825	GLP1RA, placebo	256	OAD	16	Weight+WC	56.7	8.2	7.8
Van Gaal L, 2014[248]	NCT00976937	DPP4, GLP1RA	312	Met	24	Weight	43.1	8.1	4.4
van Raalte, DH, 2016[249]	NCT00097500	GLP1RA, Insulin	69	NO	64	Weight	58.4	7.5	4.9
Vanderheiden, A, 2016[250]	NCT01505673	GLP1RA, placebo	66	Ins	26	Weight+BMI	54.2	NA	NA
Vilsboll T, 2010[251]	NCT00395343	DPP4, placebo	641	Ins	24	Weight	57.8	8.7	12.5
Violante R, 2012[252]	NCT00870194	DPP4, placebo	208	Exetide,Met	20	Weight+WC	56	7.9	8
VISUAL, Hong AR, 2015[253]	NCT01099137	DPP4, SU	309	Met	24	Weight	59.3	8.6	13.1
von Scholten, B J, 2017[254]	NCT02545738	GLP1RA, placebo	54	standard therapy	28	Weight	66	NA	16
Wang MM, 2015[255]	NO	DPP4, a-Glu	81	Met	52	Weight	64.7	8.3	13.2
Wu WJ, 2015[256]	NO	DPP4, placebo	57	NO	24	Weight	52	8	NA
Wu, Jin-dan, 2011[257]	NO	GLP1RA, placebo	23	NO	16	Weight+BMI	55.6	NA	6.2
Yang HK, 2015[258]	NO	DPP4, placebo	106	NO	24	Weight+BMI	56.2	7.1	3.6
Yang W, 2011[259]	NCT00614120	GLP1RA, SU	907	Met	16	Weight	53.3	8.6	7.5
Yokoh H, 2015[260]	NO	DPP4, a-Glu	116	NO	24	Weight	58.5	7.6	6.8
Yokoyama H, 2014[261]	NO	DPP4, GLP1RA	74	SU	24	Weight+BMI	61.3	7.8	11.3
Yoon KH, 2011[262]	NCT00397631	DPP4, placebo	520	TZD	24	Weight	50.9	9.5	2.1
Yuan GH, 2012[263]	NO	GLP1RA, Met	59	NO	26	Weight+BMI+WC	57.7	8.2	NA
Zinman B, 2007[264]	NCT00099320	GLP1RA, placebo	233	TZD+- Met	16	Weight	56.1	7.9	7.7

Note: DPP4: dipeptidyl-peptidase IV inhibitors, GLP1RA: glucagon-like peptide-1 receptor agonists, Ins: insulin, SU: sulfonylureas, Met: metformin, SGLT-2: Sodium-Glucose co-Transporter 2, TZD: thiazolidinediones, a-Glu: alpha-glucosidase; OAM: oral antihyperglycemic medication, included sulfonylureas (SU; glibenclamide, gliclazide, or glimepiride) and/or biguanides, OAD: oral antidiabetic drug, OGLA: oral glucose-lowering agent, Glar: glargine;PIG:piolitazone.

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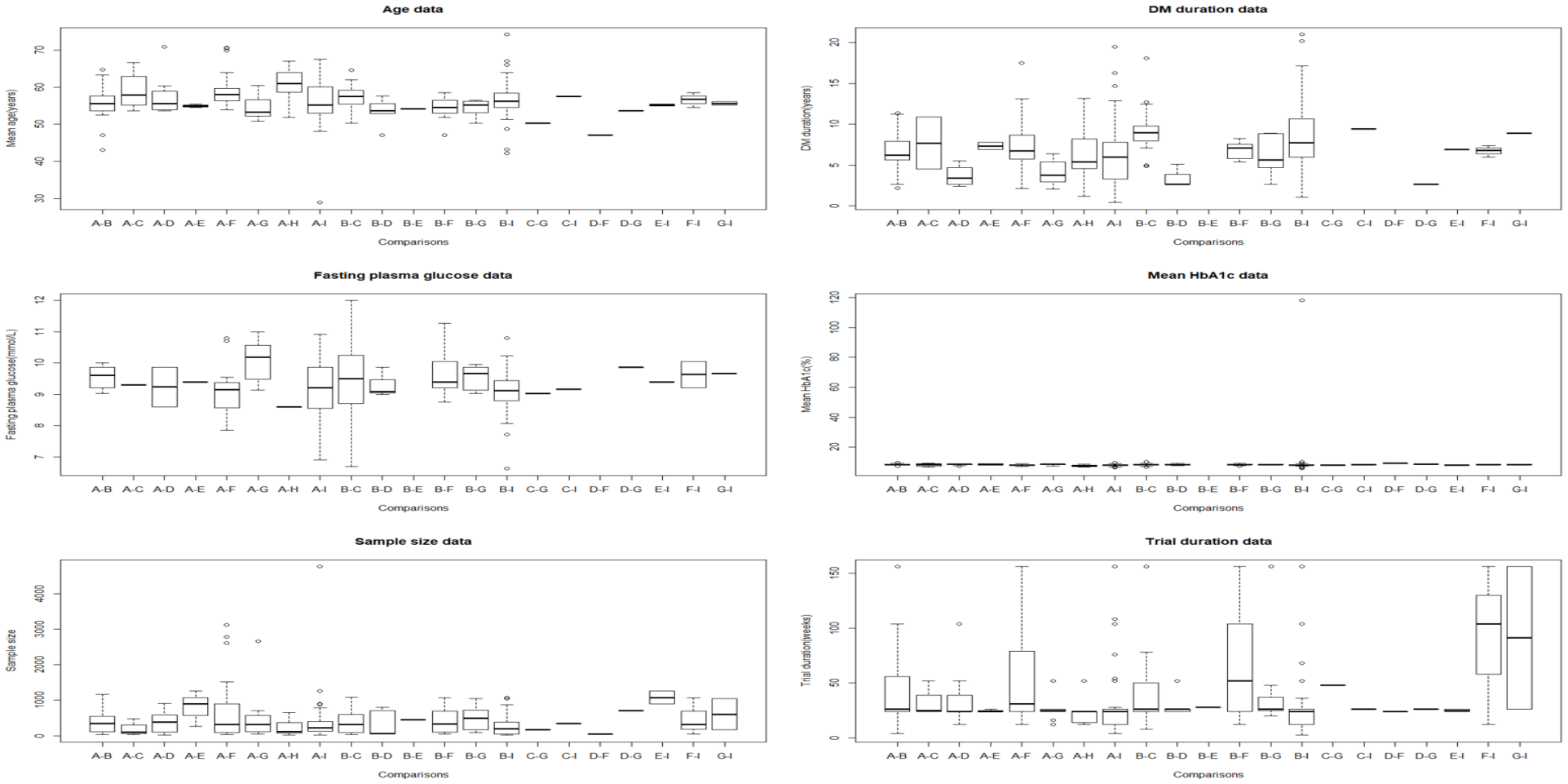

Figure S1.1 Boxplots among trials included: weight.

Note: A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT2: sodium-dependent glucose transporters 2, SU: sulphanylureas; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

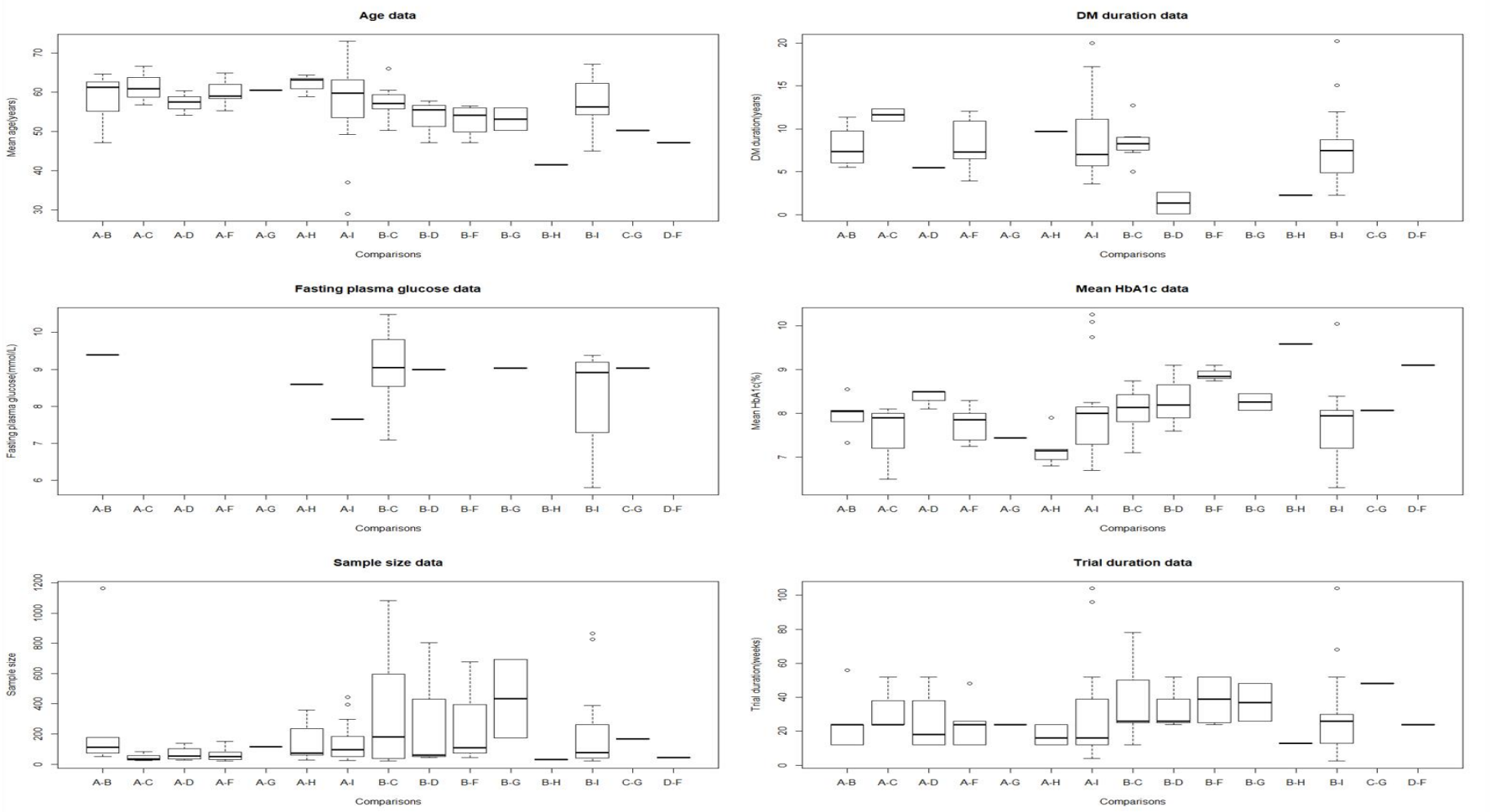

Figure S1.2 Boxplots among trials included: body mass index.

Note: A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT2: sodium-dependent glucose transporters 2, SU: sulphanylureas; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

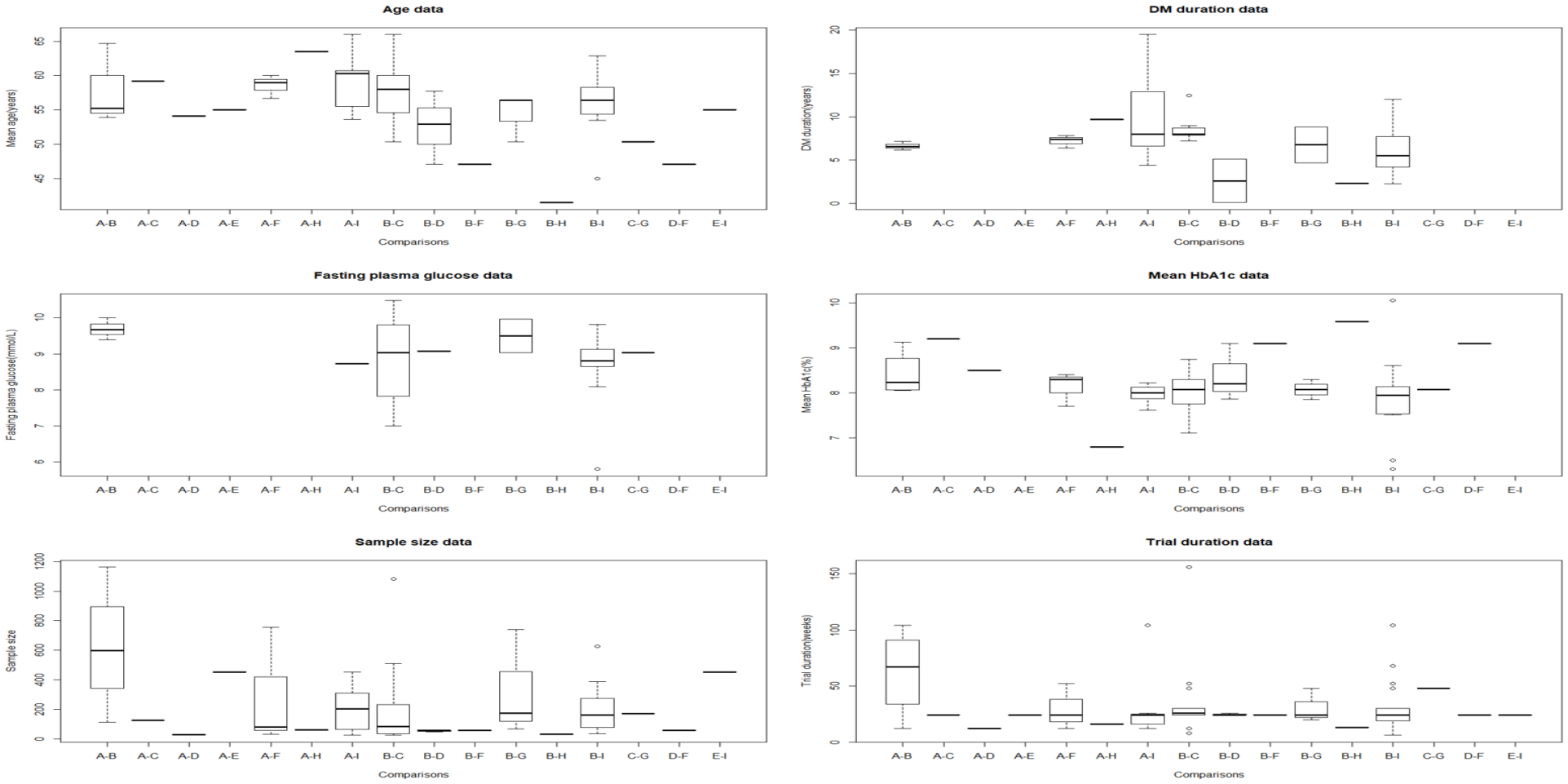

Figure S1.3 Boxplots among trials included: waist circumference.

Note: A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT2: sodium-dependent glucose transporters 2, SU: sulphanylureas; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

Supplementary File 4

Risk of bias assessment

Risk of bias summary: it is a summary table of review authors' judgments for each risk of bias entry for each study

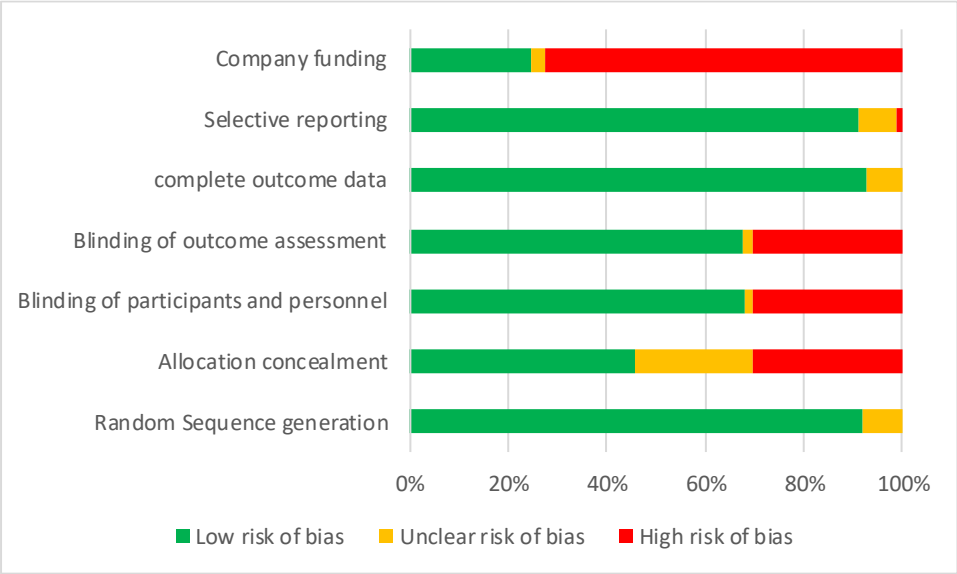

Figure S2.1 Summary of risk of bias: weight

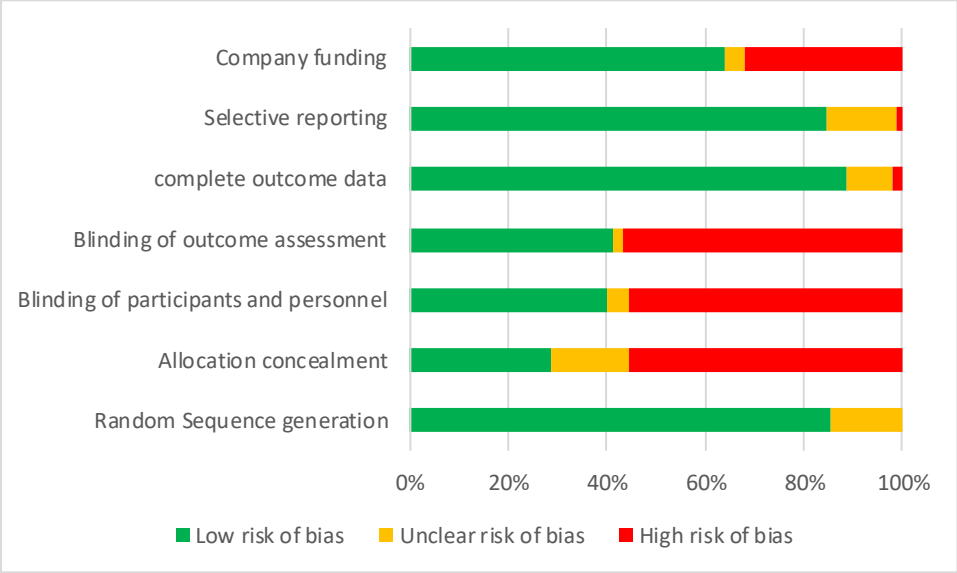

Figure S2.2 Summary of risk of bias: body mass index

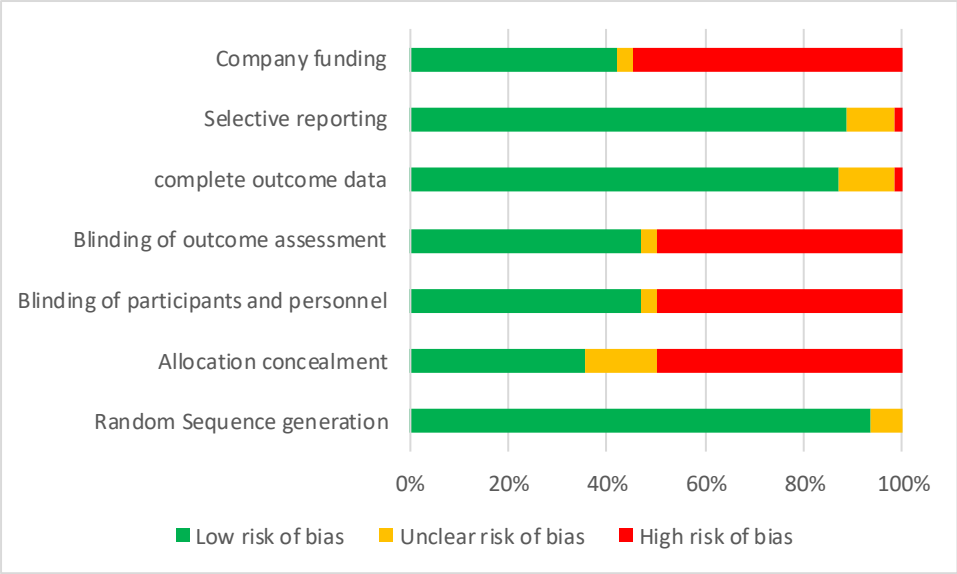

Figure S2.3 Summary of risk of bias: waist circumference

Table S4.1 Summary table of review authors' judgments for each risk of bias entry for each study

Study ID	Register number	Outcome	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	complete outcome data	Selective reporting	Company funding
3D Trial, Oe H, 2015	NO	Weight	Low	High	High	High	Low	Low	Low
ADDONIS, Gautier JF, 2016	NCT01871558	Weight	Low	High	High	High	Low	Low	High
Ahmann A, 2015	NCT01617434	Weight	Low	Unclear	Low	Low	Low	High	High
Ahren B, 2016	NCT02098395	Weight	Low	Low	Low	Low	Low	Low	High
Apovian CM, 2010	NCT00375492	Weight+WC	Low	Unclear	Low	Low	Low	Low	High
Araki E, 2015	NCT01584232	Weight	Low	High	High	High	Low	Low	High
Arechavaleta R 2009	NCT00701090	Weight	Low	Low	Low	Low	Low	Low	High
Arjona Ferreira JC 2013-1	NCT00509262	Weight	Low	Low	Low	Low	Low	Low	High
Arjona Ferreira JC 2013-2	NCT00509236	Weight	Low	Low	Low	Low	Low	Low	High
Arnolds S, 2010	NCT00971659	Weight	Low	High	High	High	Low	Low	Low
Aso Y 2015	NO	BMI	Unclear	High	High	High	Low	Unclear	Low
AWARD-1, Wysham C, 2014	NCT01064687	Weight+BMI	Low	Low	Low	Low	Low	Low	High
AWARD-2, Giorgino F, 2015	NCT01075282	Weight+BMI	Low	High	High	High	Low	Low	High
AWARD-3, Umpierrez G, 2014	NCT01126580	Weight+BMI	Low	Low	Low	Low	Low	Low	High
AWARD-4, Blonde L, 2015	NCT01191268	Weight+BMI	Low	High	High	High	Low	Low	High
AWARD-5, Nauck M, 2014	NCT00734474	Weight+WC	Low	Low	Low	Low	Low	Low	High
AWARD-7, NCT01621178 , 2017	NCT01621178	Weight	Low	High	High	High	Low	Low	High
AWARD-8, Dungan, 2016	NCT01769378	Weight+BMI	Low	Low	Low	Low	Low	Low	High
AWARD-9, Pozzilli P, 2017	NCT02152371	Weight	Low	Low	Low	Low	Low	Low	High
Azar ST, 2016	NCT01917656	Weight	Low	High	High	High	Low	Low	High
Bailey, TS, 2016	NCT01907854	Weight	Low	Low	Low	Low	Low	Low	High
Barnett AH, 2007	NCT00099619	Weight	Low	High	High	High	Low	Low	High
Bergenstal R, 2009	NCT00097877	Weight	Low	High	High	High	Low	Low	High
Berndt-Zipfel C, 2013	NO	Weight	Low	High	High	High	Low	Low	High

Bolli G, 2009	NCT00237237	Weight	Low	Low	Low	Low	Low	Low	High
Bosi E, 2007	NCT00099892	Weight	Low	Unclear	Low	Low	Low	Low	High
Bosi E, 2009	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Low	High
Bosi E, 2011	NCT00432276	Weight	Low	Low	Low	Low	Low	Low	High
Bouchi R, 2017	NO	Weight	Unclear	High	High	High	Low	Low	Low
Buse JB, 2004	NCT00039026	Weight	Low	Unclear	Low	Low	Low	Unclear	High
Buse JB, 2011	NCT00765817	Weight+WC	Low	Unclear	Low	Low	Low	Low	High
CANTATA-D Trial, Lavalle-Gonzalez FJ, 2013	NCT01106677	Weight	Low	Low	Low	Low	Low	Low	Low
Charbonnel B, 2013	NCT01296412	Weight	Low	High	High	High	Low	Low	High
Chawla S 2013	NO	Weight	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Chen WJY, 2017	NCT00766857	BMI+WC	Low	High	High	High	High	Low	Low
Chien MN 2011	NO	BMI	Low	High	High	High	Low	Low	Unclear
CONFIDENCE, Xu W, 2015	NCT01147627	Weight+BMI+WC	Low	High	High	High	Unclear	Low	Low
Cui J 2016	NCT01963845	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Davies M, 2013	NCT01003184	Weight+BMI+WC	Low	High	High	High	Low	Low	High
Davies MJ, 2009	NCT00360334	Weight+BMI+WC	Low	High	High	High	Low	Low	High
Davies MJ, 2016	NCT01620489	BMI	Low	Low	Low	Low	High	Low	High
Davis SN, 2007	NCT00099333	Weight	Low	High	High	High	Unclear	Unclear	Unclear
de Ranitz-Greven, 2014	NO	Weight	Low	Low	Low	Unclear	Low	Unclear	Low
DeFronzo RA, 2005	NCT00039013	Weight	Low	Low	Low	Low	Low	Low	High
DeFronzo RA, 2008	NCT00286455	Weight	Low	Unclear	Low	Low	Low	Low	High
DeFronzo RA, 2010	NCT00135330	Weight+WC	Low	High	High	High	Low	Low	High
Dei Cas A, 2017	NCT01822548	BMI	Low	High	High	High	Low	Low	Low
Derosa G, 2010	NO	Weight+BMI	Low	Low	Low	Low	Unclear	Unclear	High
Derosa G, 2010	NO	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Derosa G, 2011	NO	Weight+BMI	Low	Low	Low	Low	Low	Unclear	High
Derosa G, 2012	NO	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Derosa G, 2012	NO	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Derosa G, 2013	NO	Weight+BMI+WC	Low	Low	Low	Low	Low	Low	Low
Derosa G, 2014-1	NO	Weight+BMI+WC	Low	Low	Low	Low	Low	Low	Low

Derosa G, 2014-2	NO	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Diamant M, 2014	NCT00960661	Weight+BMI+WC	Low	High	High	High	Low	Low	High
DUAL-I, Holst JJ, 2016	NCT01336023	Weight	Low	High	High	High	Low	Low	High
DURATION-2, Bergenstal RM, 2010	NCT00637273	Weight	Low	Low	Low	Low	Low	Low	High
DURATION-3, Diamant M, 2014	NCT00641056	Weight+WC	Low	High	High	High	Low	Low	High
DURATION-4, Russell-Jones D, 2012	NCT00676338	Weight	Low	Low	Low	Low	Low	Low	High
DURATION-8, Frias JP2-1, 2016	NCT02229396	Weight	Low	Unclear	Low	Low	Low	Low	High
DURATION-8, Frias JP2-2, 2016	NCT02229396	Weight	Low	Unclear	Low	Low	Low	Low	High
DURATION-NEO-2, Gadde KM, 2017	NCT01652729	Weight	Low	High	High	High	Low	Low	High
EAGLE D'Alessio D, 2015	NCT01117350	Weight	Low	High	High	High	Low	Low	High
EASIE, Aschner P, 2012	NCT00751114	Weight	Low	High	High	High	Low	Low	High
EDIT, Sato S, 2015	NO	Weight+WC	Low	Low	Low	Low	Low	Low	Low
ELEGANT, de Wit HM, 2014	NCT01392898	Weight+BMI+WC	Low	High	High	High	Low	Low	High
ENDURE, NCT00856284, 2013	NCT00856284	Weight	Low	Unclear	Low	Low	Low	Low	High
EUREXA, Gallwitz, B, 2012	NCT00359762	Weight	Low	High	High	High	Low	Low	High
EXAMINE, White WB 2013	NCT00968708	Weight	Low	Unclear	Low	Low	Low	Low	High
Faber R, 2015	NCT01931982	Weight+WC	Low	Low	Low	Low	Low	Low	Low
Farngren J, 2016	NCT02020629	Weight	Low	High	High	High	Low	Low	Low
Farr OM, 2016	NCT01562678	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Faurschou A, 2015	NCT01460069	Weight	Low	Low	Low	Low	Low	Low	Low
Feng W, 2017	NCT03068065	Weight+BMI+WC	Low	High	High	High	Low	Low	Low
Ferrannini E, 2009	NCT00106340	Weight	Low	Unclear	Low	Low	Low	Low	High
Filozof C, 2010	NCT00396357	Weight	Low	Unclear	Low	Low	Low	Low	High
Filozof C, 2010	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Unclear	High
Fineman MS, 2004	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Unclear	High
Foley JE, 2009	NCT00102388	Weight	Low	Unclear	Low	Low	Low	Low	High
Fonseca V, 2007	NCT00099931	Weight	Low	Unclear	Low	Low	Low	Low	High
Forst T, 2012	NCT01208012	Weight+BMI+WC	Low	High	High	High	Low	Low	Low

GALIANT, Blonde L, 2009	NCT00396627	Weight	Low	High	High	High	Low	Low	High
Gallwitz B, 2011	NCT00434954	Weight+BMI	Low	High	High	High	Low	Low	High
Gallwitz B, 2012	NCT00622284	Weight	Low	Low	Low	Low	Low	Low	High
Gao Y, 2009	NCT00324363	Weight	Low	Low	Low	Low	Low	Low	High
Garber AJ, 2008	NCT00099944	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-DUO-1, Riddle MC, 2013	NCT00975286	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-F1, Bolli G, 2013	NCT00763451	Weight	Low	Unclear	Low	Low	Low	Low	High
GetGoal-L, Riddle MC, 2013	NCT00715624	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-L-Asia, Seino Y, 2012	NCT00866658	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-M, Ahren B, 2013	NCT00712673	Weight	Low	Unclear	Low	Low	Low	Low	High
GetGoal-M-Asia, Yu Pan C, 2014	NCT01169779	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-Mono, Fonseca VA, 2012	NCT00688701	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-O, Meneilly GS, 2017	NCT01798706	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-P, Pinget M, 2013	NCT00763815	Weight	Low	Low	Low	Low	Low	Low	High
GetGoal-S, Rosenstock J, 2014	NCT00713830	Weight	Low	Unclear	Low	Low	Low	Low	High
Goke B, 2008	NCT00138567	Weight	Low	Low	Low	Low	Low	Low	High
Göke B, 2013	NCT00575588	Weight	Low	Low	Low	Low	Low	Low	High
Grunberger G, 2012	NO	Weight	Low	Low	Low	Low	Low	Unclear	High
GUARD study, Yoon SA, 2016	NCT01968044	Weight	Low	Low	Low	Low	Low	Low	High
Gudipaty L, 2014	NCT00775684	BMI	Low	High	High	High	Low	Low	Low
Gurkan E, 2014	NO	Weight+BMI+WC	Low	High	High	High	Low	Low	Low
Harder H, 2004	NO	Weight+WC	Unclear	Unclear	Low	Low	Low	Unclear	Unclear
HARMONY-1, Reusch J, 2014	NCT00849056	Weight	Low	Unclear	Low	Low	Low	Low	High
HARMONY-2, Nauck, MA, 2016	NCT00849017	Weight	Low	Low	Low	Low	Low	Low	High
HARMONY-3, Ahren B, 2014	NCT00838903	Weight	Low	Unclear	Low	Low	Low	Low	High
HARMONY-4, Weissman PN, 2014	NCT00838916	Weight	Low	High	High	High	Low	Low	High
HARMONY-5, Home PD, 2015	NCT00839527	Weight	Low	Low	Low	Low	Low	Low	High

HARMONY-6, Rosenstock J, 2014	NCT00976391	Weight	Low	High	High	High	Low	Low	High
Harrtori A, 2017	UMIN000004674	Weight+BMI	Low	High	High	High	Low	Low	Low
Hartley P, 2015	NCT01189890	Weight	Low	Low	Low	Low	Low	Low	High
Hegazy SK, 2014	NO	BMI	Unclear	Unclear	Low	Low	Low	Low	Low
Heine RJ, 2005	NCT00082381	Weight	Low	High	High	High	Low	Low	High
Hissa MRN, 2015	NO	Weight	Unclear	High	High	High	Low	Low	High
Hong ES, 2012	NCT01100125	Weight+WC	Low	High	High	High	Unclear	Unclear	Low
Iacobellis G, 2017	NCT02014740	BMI	Low	High	High	High	Low	Low	Low
Idorn T, 2016-1	NCT01394341	Weight	Low	Low	Low	Low	Unclear	Low	High
Idorn T, 2016-2	NCT01394341	Weight	Low	Low	Low	Low	Unclear	Low	High
Inagaki N, 2012	NCT00935532	Weight	Low	High	High	High	Low	Low	High
INDORSE study, Lovshin JA, 2017	NCT02406443	BMI	Low	Low	Low	Low	Low	Low	High
INICOM, Lim S, 2017	NCT01787396	Weight	Low	Low	Low	Low	Low	Low	High
Inoue Y, 2015	UMIN 000007009	Weight	Low	High	High	High	Low	Low	Low
Ito M, 2011	NO	Weight+BMI	Unclear	High	High	High	Low	Unclear	Low
Iwamoto K, 2009	NCT00612794	Weight	Low	Low	Low	Low	Low	Low	High
Iwamoto Y, 2010	NCT00127192	Weight	Low	Low	Low	Low	Low	Low	High
Iwamoto Y, 2010	NO	Weight	Unclear	Unclear	Low	Low	Low	Low	High
Jeon HJ, 2011	NO	Weight	Unclear	High	High	High	Low	Low	Low
Kadowaki T, 2009	NCT00382239	Weight	Low	Low	Low	Low	Low	Low	High
Kadowaki T, 2011	NCT00577824	Weight+WC	Low	Low	Low	Low	Low	Low	High
Kadowaki T, 2013	NCT01026194	Weight	Low	Unclear	Low	Low	Low	Low	High
Kadowaki T, 2014	NCT00974090	Weight	Low	Low	Low	Low	Low	Low	High
Kaku K, 2010	NCT00395746	Weight	Low	Unclear	Low	Low	Low	Low	High
Kato H, 2015	NO	BMI	Low	High	High	High	Low	Low	Unclear
Kawamori R, 2012	NCT00654381	Weight+BMI+WC	Low	Low	Low	Low	Low	Low	High
Ke W, 2016	NCT01471808	Weight	Low	High	High	High	Low	Low	Low
Kendall DM, 2005	NCT00035984	Weight	Low	Unclear	Low	Low	Low	Low	High
Kikuchi M, 2009	NO	BMI	Unclear	Unclear	Low	Low	Low	Low	High

Kikuchi M, 2010	NCT00325117	Weight	Low	Low	Low	Low	Low	Low	High
Kim D, 2007	NCT00103935	Weight	Low	Low	Low	Low	Low	Low	High
Koren S, 2012	NO	Weight+BMI+WC	Low	High	High	High	Unclear	Unclear	Low
Kumarathurai P, 2017	NCT01595789	Weight+WC	Low	Low	Low	Unclear	Low	Low	High
Kutoh E, 2012	UMIN 000006860	BMI	Low	High	High	High	Low	Low	Low
LEAD-1, Marre M, 2009	NCT00318422	Weight+BMI	Low	Unclear	Low	Low	Low	Low	High
LEAD-2, Nauck M, 2009	NCT00318461	Weight	Low	Low	Low	Low	Low	Low	High
LEAD-3, Garber A, 2011	NCT00294723	Weight	Low	Unclear	Low	Low	Low	Low	High
LEAD-4, Zinman B, 2009	NCT00333151	Weight	Low	Low	Low	Low	Low	Low	High
LEAD-5, Russell-Jones D, 2009	NCT00331851	Weight	Low	Low	Low	Low	Low	Low	High
Leiter LA, 2014	NCT01098539	Weight	Low	Low	Low	Low	Low	Low	High
Lewin AJ, 2012	NCT00819091	Weight	Low	Low	Low	Low	Low	Low	High
Li CJ, 2012	NO	Weight+BMI+WC	Low	High	High	High	Low	Low	Low
Li CJ, 2014	NO	Weight+BMI	Low	Low	Low	Low	Low	Unclear	Low
Li F, 2017	NO	Weight+BMI+WC	Low	High	High	High	Low	Low	Unclear
Li FF, 2017	NO	Weight	Unclear	High	High	High	Low	Low	Low
LIBRA, Retnakaran R, 2014	NCT01270789 EudraCT	BMI+WC	Low	Unclear	Low	Low	Unclear	Unclear	High
Lind M, 2015	2012-001941-42	Weight	Low	Low	Low	Low	Low	Low	High
Liutkus J, 2010	NCT00603239	Weight+WC	Low	Low	Low	Low	Low	Low	High
LixiLan-O, Davies, MJ, 2017	NCT02058147	Weight	Low	High	High	High	Low	Low	High
L-STEP study Fujitani Y, 2016	UMIN000008591	Weight+BMI	Low	Unclear	Unclear	Unclear	Unclear	Unclear	High
Luo N, 2015	NO	BMI	Unclear	Unclear	Low	Low	Low	Low	Low
Macauley M, 2015	NCT01356381	Weight	Low	Low	Low	Low	Low	Low	High
Masanori A, 2016	UMIN000018445	Weight+BMI	Low	High	High	High	Low	Low	Low
MASTER Mikada A, 2014	NO	Weight+BMI	Low	High	High	High	Low	Low	Low
Mastushima Y, 2016	UMIN000003503	Weight+BMI	Low	High	High	High	Low	Low	Low
Mathieu C, 2014	NCT01388361	Weight	Low	High	High	High	Low	Low	High
Matikainen N, 2006	NO	Weight	Low	Low	Low	Low	Low	Low	High
Matthews DR, 2010	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Unclear	High
Mensberg P, 2017	NCT01455441	Weight+BMI	Low	Low	Low	Low	Low	Low	Low

Mita T, 2016-1	NO	BMI	Low	High	High	High	Low	Low	Low
Mita T, 2016-2	NO	BMI	Low	High	High	High	Low	Low	High
Miya A, 2017	NR	Weight+BMI	Low	High	High	High	Low	Unclear	Low
Mohan V, 2009	NCT00289848	Weight	Low	Low	Low	Low	Low	Low	High
Moretto TJ, 2008	NCT00381342	Weight	Low	Low	Low	Low	Low	Low	High
Moses RG, 2016	NCT01076075	Weight	Low	Low	Low	Low	Low	Low	High
Nauck M, 2007	NCT00094770	Weight	Low	Unclear	Low	Low	Low	Low	High
Nauck MA, 2007	NCT00082407	Weight	Low	High	High	High	Low	Low	High
Nauck MA, 2007	NCT00094770	WC	Low	Low	Low	Low	Low	Low	High
Nauck MA, 2009	NCT00286442	Weight	Low	Low	Low	Low	Low	Low	High
NCT00620282, 2011	NCT00620282	Weight	Low	Low	Low	Low	Low	Low	High
NCT00701935, 2013	NCT00701935	Weight	Low	Unclear	Low	Low	Low	Low	High
NCT00993187, 2014	NCT00993187	Weight	Low	Low	Low	Low	Low	Low	High
NCT01149421, 2015	NCT01149421	Weight	Low	Unclear	Low	Low	Low	Low	High
NCT01195090, 2011	NCT01195090	Weight	Low	High	High	High	Low	Low	Low
NCT01289119, 2013	NCT01289119	Weight	Low	Low	Low	Low	Low	Low	High
NCT01289119, 2013-1	NCT01289119	Weight	Low	Low	Low	Low	Low	Low	High
NCT01289119, 2013-2	NCT01289119	Weight	Low	Low	Low	Low	Low	Low	High
NCT01438814, 2014	NCT01438814	Weight	Low	Low	Low	Low	Low	Low	High
NCT01644500, 2012	NCT01644500	Weight+BMI	Low	Unclear	Low	Low	Low	Low	High
NCT01648582, 2012	NCT01648582	Weight+BMI	Low	High	High	High	Low	Low	High
NCT01733758, 2013	NCT01733758	Weight	Low	Unclear	Low	Low	Low	Low	High
Nogueira KC, 2014	NO	Weight+BMI	Low	High	High	High	Low	Low	Low
Nomoto H, 2016	UMIN000004955	BMI	Low	High	High	High	Low	Low	Low
Nonaka K, 2008	NCT00371007	Weight	Low	Low	Low	Low	Low	Low	High
Ohira M, 2014	NO	Weight+BMI	Low	High	High	High	Low	Low	Unclear
Oyama J, 2016	UMIN000004490	BMI	Low	High	High	High	Low	Low	Low
Oz Gul O, 2011	NO	Weight+BMI	Unclear	Unclear	Unclear	Low	Low	Low	Low
Pan C, 2008	NCT00110240	Weight	Low	Low	Low	Low	Low	Low	High
Park KS, 2017	NCT01812122	Weight+WC	Low	High	High	High	Low	Low	Low
Pi-Sunyer FX, 2007	NCT00120536	Weight	Low	Unclear	Low	Low	Low	Low	High

Pratley R, 2011	NCT00700817	Weight+WC	Low	High	High	High	Low	Low	High
Pratley RE, 2009-1	NCT00286468	Weight	Low	Unclear	Low	Low	Low	Low	High
Pratley RE, 2009-2	NCT00286494	Weight	Low	Low	Low	Low	Low	Low	High
Probstfield JL, 2016	NCT01524705	Weight	Low	High	High	High	Low	Low	Low
Ratner R, 2010	NCT00460941	Weight	Low	Low	Low	Low	Low	Low	High
Ratner RE, 2010	NO	Weight	Low	Low	Low	Low	Unclear	Unclear	Low
RELEASE de Boer SA, 2017	NCT02015299	Weight	Low	Low	Low	Low	Low	Low	Low
Ristic S, 2005	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear
Roden M, 2013	NCT01177813	Weight+WC	Low	Low	Low	Low	Low	Low	High
Roden M, 2015	NCT01289990	Weight	Low	Low	Low	Low	Low	Low	High
Rosenstock J, 2007-1	NCT00101803	Weight	Low	Unclear	Low	Low	Low	Low	High
Rosenstock J, 2007-2	NCT00101803	Weight	Low	Unclear	Low	Low	Low	Low	High
Rosenstock J, 2008-1	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Unclear	High
Rosenstock J, 2008-2	NO	Weight	Unclear	Unclear	Low	Low	Unclear	Unclear	High
Rosenstock J, 2009	NCT00286429	Weight	Low	Low	Low	Low	Low	Low	High
Rosenstock J, 2009	NCT00518115	Weight+WC	Low	Unclear	Low	Low	Low	Low	High
Rosenstock J, 2010	NCT00395512	Weight	Low	Unclear	Low	Low	Low	Low	High
Rosenstock J, 2010	NCT00395512	Weight	Low	Unclear	Low	Low	Low	Low	High
Rosenstock J, 2013	NCT00707993	Weight	Low	Unclear	Low	Low	Low	Low	High
Rosenstock J, 2015	NCT01606007	Weight	Low	Low	Low	Low	Low	Low	High
Rosenstock J, 2016,	NCT01768559	Weight	Low	High	High	High	Low	Low	High
SAIS2, Nomoto H, 2015	UMIN000005331	BMI	Low	High	High	High	Low	Unclear	Low
Saito D, 2017	UMIN000010849	BMI	Low	High	High	High	Low	Low	Low
Samocha-Bonet D, 2014	NCT00673894	Weight	Low	High	High	High	Low	Low	Low
Satoh-Asahara N, 2013	NO	BMI	Unclear	High	High	High	Low	Low	Low
Savvidou S, 2016	NR	Weight+BMI+WC	Low	High	High	High	Low	Low	Low
SCALE, Davies MJ, 2015-1	NCT01272232	BMI	Low	Low	Low	Low	Low	Low	High
SCALE, Davies MJ, 2015-2	NCT01272232	Weight+WC	Low	Low	Low	Low	Low	Low	High
Scalzo RL, 2017	NCT01364584	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Scherbaum WA, 2008-1	NCT00300287	Weight	Low	Unclear	Low	Low	Low	Low	High
Scherbaum Wa, 2008-2	NCT00101712	Weight	Low	Unclear	Low	Low	Low	Low	High

Schweizer A, 2009	NO	Weight	Low	Low	Low	Low	Low	Low	High
Seino Y, 2008	NCT00154414	Weight	Low	Low	Low	Low	Low	Low	High
Seino Y, 2010	NCT00393718	Weight	Low	Unclear	Low	Low	Low	Low	High
Seino Y, 2011	NCT01263483	Weight	Low	Low	Low	Low	Low	Low	High
Seino Y, 2012	NCT01318109	Weight	Low	Low	Low	Low	Low	Low	High
Seino Y, 2014	NCT01098461	Weight	Low	Unclear	Low	Low	Low	Low	High
Seino Y, 2016	NCT01572740	Weight	Low	Low	Low	Low	Low	Low	High
Shi L, 2017	NO	BMI+WC	Unclear	High	High	High	Low	Unclear	Low
Shi Xiulin, 2017	NCT01776788	BMI+WC	Low	High	High	High	Low	Low	Low
Shimoda S, 2014	UMIN000009544	BMI	Low	High	High	High	Low	Low	Low
Silva GM, 2016	NCT02607410	Weight+BMI	Low	High	High	High		Low	Low
SMART study NCT02243176	NCT02243176	Weight	Low	High	High	High	Low	Low	High
Smits, M M-1, 2016	NCT01744236	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Srivastava S, 2012	NO	BMI	Low	High	High	High	Low	Low	High
START Terauchi Y, 2017	NCT01183104	Weight	Low	High	High	High	Low	Low	High
START-J Hibuse T, 2014	NO	BMI+WC	Unclear	Unclear	Unclear	Low	Low	Low	High
STEADFAST Hassanein M, 2014	NCT01758380	Weight	Low	Low	Low	Low	Low	Low	High
Strozik A, 2015	NO	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Su Y, 2014 -1	NO	Weight	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Su Y, 2014-2	NO	Weight	Unclear	Unclear	Low	Low	Low	Low	Unclear
Sun X, 2017	NO	Weight+BMI	Unclear	Unclear	Low	Low	Low	Low	Low
SUSTAIN-1, Sorli, C, 2017	NCT02054897	Weight+BMI+WC	Low	Low	Low	Low	Low	Low	High
SUSTAIN-2, Ahren, 2016	NCT01930188	Weight+BMI+WC	Low	Low	Low	Low	Low	Low	High
SUSTAIN-4, Aroda VR, 2017	NCT02128932	Weight+BMI+WC	Low	High	High	High	Low	Low	High
Suzuki K, 2014	NO	Weight	Unclear	High	High	High	Low	Low	Low
Tai H, 2016	NCT02798172	BMI+WC	Low	High	High	High	Low	Low	Low
Takeshita Y, 2015	no. 000004953	Weight+BMI+WC	Low	High	High	High	Low	High	High
Takeshita Y, 2015	UMIN 000007051	Weight+BMI+WC	Low	High	High	High	Low	Low	Low
Takihata M, 2013	NO	Weight+BMI	Low	High	High	High	Low	Low	Low
Tanaka K, 2015	UMIN000004243	Weight+WC	Low	High	High	High	Low	Low	High

Tanaka T, 2014	NO	Weight	Low	High	High	High	Low	Low	Unclear
Tang A, 2015	NCT01399645	Weight+BMI+WC	Low	Low	Low	Unclear	Unclear	Unclear	Low
T-emerge-1, Raz I, 2012	NCT00744926	WC	Low	Unclear	Low	Low	Low	Low	High
T-emerge-3, Henry RR, 2012	NCT00744367	Weight+WC	Low	Low	Low	Low	Low	Low	High
T-emerge-4, Bergenstal RM, 2012	NCT00754988	Weight	Low	Low	Low	Low	Low	Low	High
T-emerge-5, Nauk M, 2013	NCT00755287	Weight	Low	High	High	High	Low	Low	High
T-emerge-6, Pratley RE, 2013	NCT00909597	Weight+WC	Low	Low	Low	Low	Low	Low	High
T-emerge-7, Hollander P, 2013	NCT00823992	Weight+WC	Low	Low	Low	Low	Low	Low	High
Ten Kulve JS, 2016	NCT01363609	Weight+BMI+WC	Low	High	High	High	Low	Low	Low
Terauchi Y, 2014	NCT01001104	Weight	Low	Unclear	Low	Low	Low	Low	High
Tian M, 2016	NO	Weight+BMI	Unclear	Unclear	Low	Low	Low	Low	Low
Tonneijck L, 2017	NCT02276196	Weight+WC	Low	High	High	High	Low	Low	Low
Treat 4 Ramadan Trial, Brady EM, 2014	NO	Weight	Low	High	High	High	Low	Low	High
TROICA study, Ahn CH, 2016	NCT01990469	Weight+WC	Low	Low	Low	Low	Low	Low	High
Umpierrez GE, 2011	NCT00630825	Weight+WC	Low	Low	Low	Low	Low	Low	High
Van Gaal L, 2014	NCT00976937	Weight	Low	Unclear	Low	Low	Low	Low	High
van Raalte, DH, 2016	NCT00097500	Weight	Low	High	High	High	Low	Low	High
Vanderheiden, A, 2016	NCT01505673	Weight+BMI	Low	Low	Low	Low	Low	Low	Low
Vilsboll T, 2010	NCT00395343	Weight	Low	Low	Low	Low	Low	Low	High
Violante R, 2012	NCT00870194	Weight+WC	Low	Unclear	Low	Low	Low	Low	High
VISUAL, Hong AR, 2015	NCT01099137	Weight	Low	Low	Low	Low	Low	Low	Low
von Scholten, B J, 2017	NCT02545738	Weight	Low	Low	Low	Low	Low	High	High
Wang MM, 2015	NO	Weight	Unclear	High	High	High	Low	Low	High
Wu WJ, 2015	NO	Weight	Low	Low	Low	Low	Low	Low	Low
Wu, Jin-dan, 2011	NO	Weight+BMI	Unclear	Unclear	Low	Low	Low	Unclear	High
Yang HK, 2015	NO	Weight+BMI	Unclear	Unclear	Low	Low	Unclear	Unclear	High
Yang W, 2011	NCT00614120	Weight	Low	Unclear	Low	Low	Low	Low	High
Yokoh H, 2015	NO	Weight	Low	High	High	High	Low	Low	Low
Yokoyama H, 2014	NO	Weight+BMI	Low	High	High	High	Low	Low	Low

Yoon KH, 2011	NCT00397631	Weight	Low	Unclear	Low	Low	Low	Low	High
Yuan GH, 2012	NO	Weight+BMI+WC	Unclear	Unclear	Unclear	Low	Low	Low	Low
Zinman B, 2007	NCT00099320	Weight	Low	Low	Low	Low	Low	Low	High

Supplementary File 5

Effects of incretin-based regimens on weight, body mass index and waist circumference by standard pairwise meta-analysis

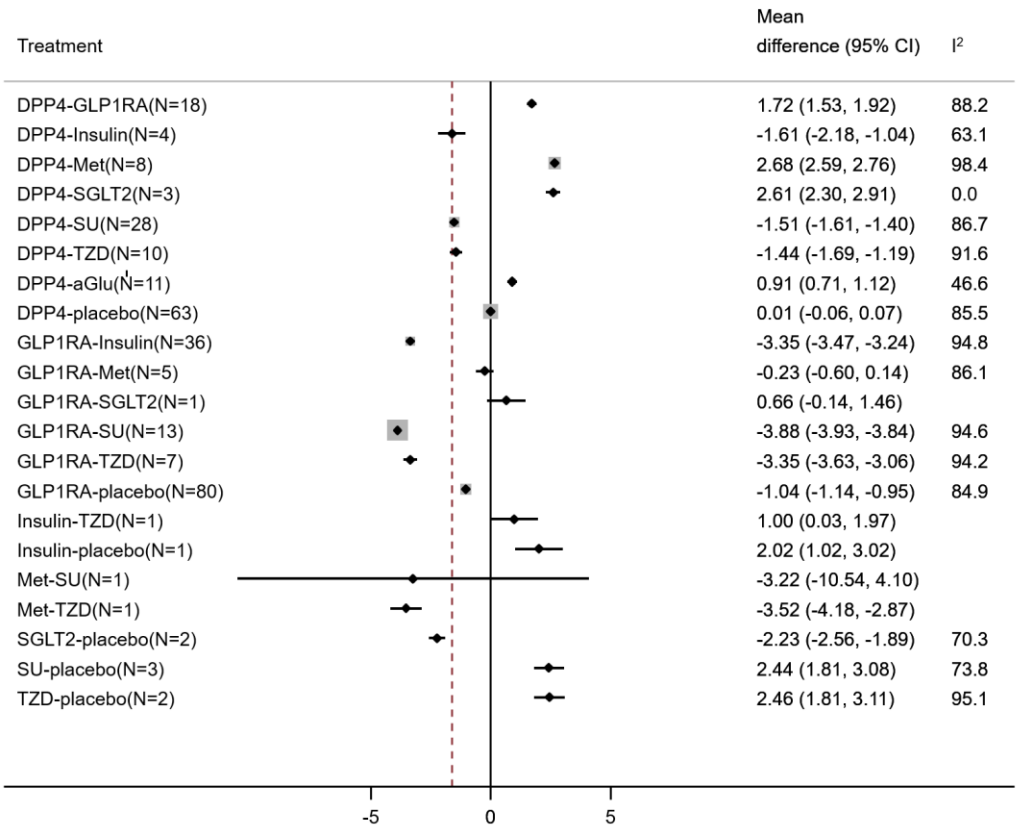

Figure S3.1 Results of standard pairwise comparisons: weight.

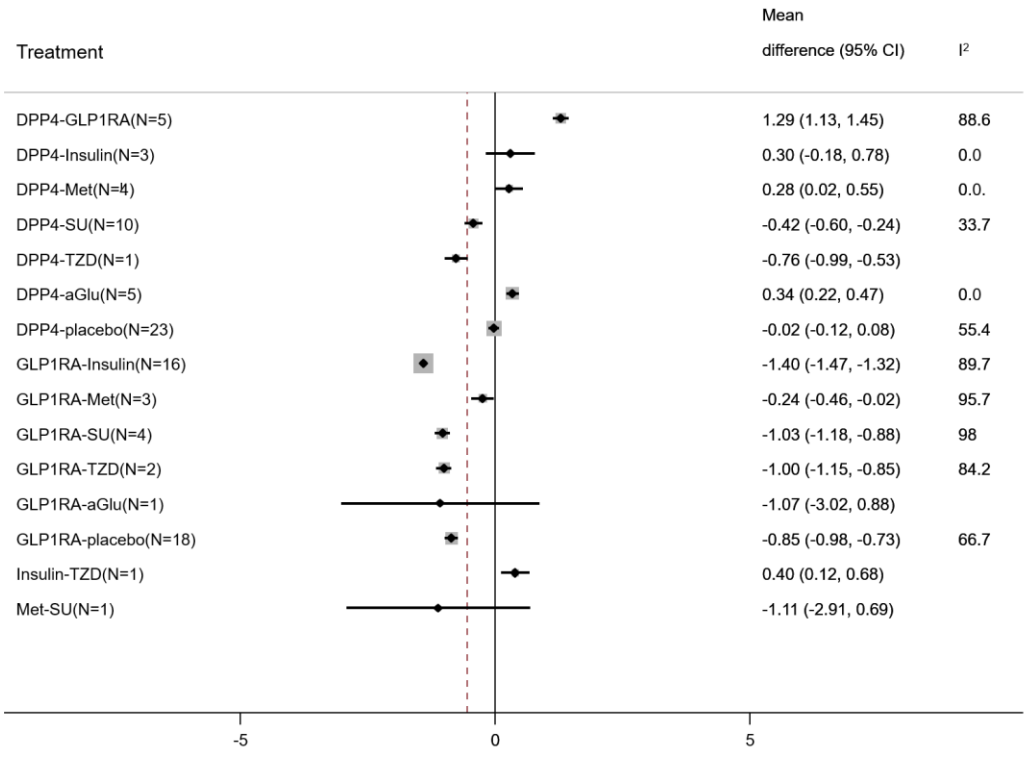

Figure S3.2 Results of standard pairwise comparisons: body mass index.

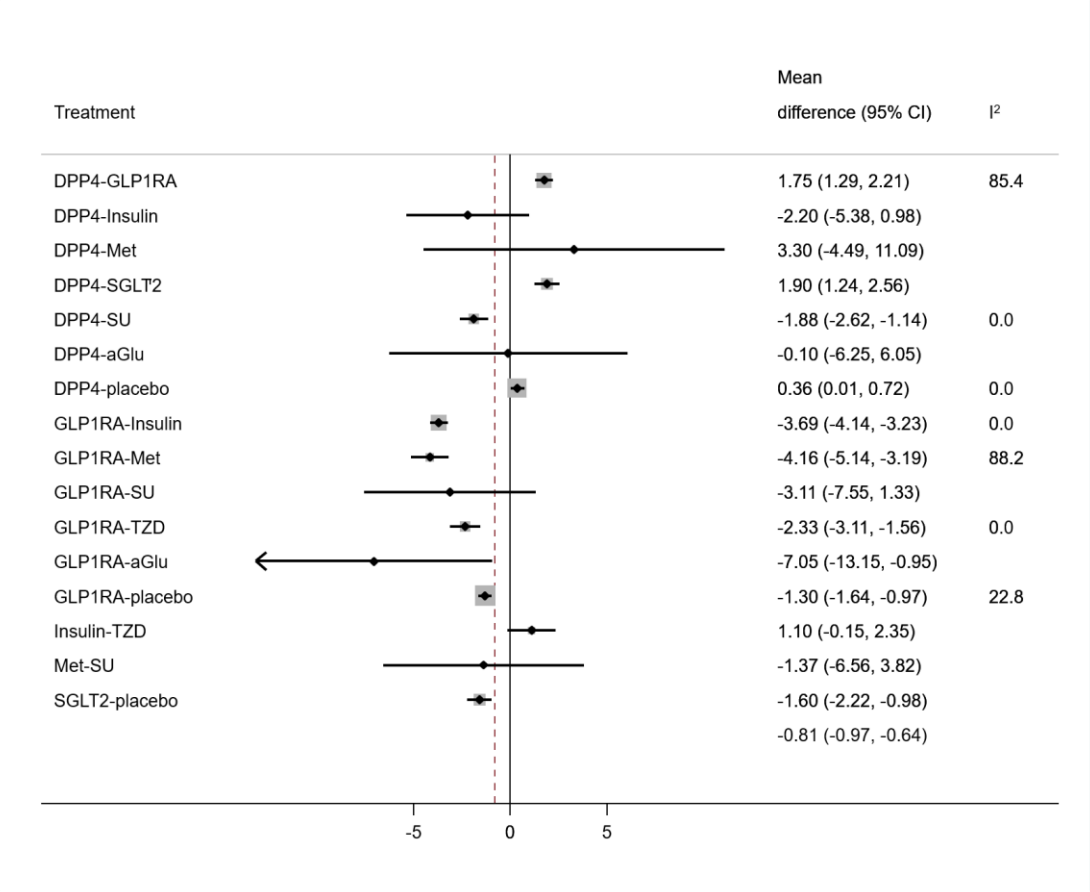

Figure S3.3 Results of standard pairwise comparisons: waist circumference.

Note: DPP4: dipeptidyl-peptidase IV inhibitors; GLP1RA: Glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT2: Sodium-Glucose co-Transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; aGlu: alpha-glucosidase.

Supplementary File 6

Sensitivity network meta-analyses

DPP4	1.72 (1.53,1.92)	-1.61 (-2.18,-1.04)	2.68 (2.59,2.76)	2.61 (2.30,2.91)	-1.51 (-1.61,-1.40)	-1.44 (-1.69,-1.19)	0.91 (0.71,1.12)	0.01 (-0.06,0.07)
1.63 (1.30,1.97)	GLP1RA	-3.35 (-3.47,-3.24)	-0.23 (-0.60,0.14)	0.66 (-0.14,1.46)	-3.88 (-3.93,-3.84)	-3.35 (-3.63,-3.06)	NA	-1.04 (-1.14,-0.95)
-1.70 (-3.67,0.27)	-3.34 (-5.29,-1.38)	Insulin	NA	NA	NA	1.00 (0.03,1.97)	NA	2.02 (1.02,3.02)
1.07 (0.29,1.84)	-0.57 (-1.37,0.23)	2.77 (0.67,4.87)	Met	NA	-3.22 (-10.54,4.10)	-3.52 (-4.18,-2.87)	NA	NA
2.55 (1.52,3.57)	0.91 (-0.13,1.95)	4.25 (2.04,6.45)	1.48 (0.21,2.75)	SGLT2	NA	NA	NA	-2.23 (-2.56,1.89)
-1.46 (-1.91,-1.01)	-3.09 (-3.60,-2.59)	0.24 (-1.77,2.25)	-2.52 (-3.41,-1.64)	-4.00 (-5.11,-2.90)	SU	NA	NA	2.44 (1.81,3.08)
-1.93 (-2.65,-1.20)	-3.56 (-4.30,-2.83)	-0.23 (-2.31,1.85)	-3.00 (-4.01,-1.98)	-4.47 (-5.72,-3.23)	-0.47 (-1.31,0.37)	TZD	NA	2.46 (1.81,3.11)
1.07 (-0.18,2.31)	-0.57 (-1.86,0.72)	2.77 (0.44,5.10)	0.00 (-1.46,1.47)	-1.48 (-3.09,0.13)	2.53 (1.20,3.85)	3.00 (1.56,4.44)	aGlu	NA
0.33 (0.06,0.61)	-1.30 (-1.57,-1.03)	2.04 (0.08,3.99)	-0.73 (-1.53,0.06)	-2.21 (-3.24,-1.18)	1.79 (1.30,2.28)	2.26 (1.52,3.00)	-0.73 (-2.01,0.54)	placebo

Figure S4.1a Results of sensitivity analysis (by excluding studies with no allocation concealment) for weight

DPP4	1.74 (1.54,1.94)	-1.61 (-2.18,-1.04)	2.68 (2.59,2.76)	2.61 (2.30,2.91)	-1.51 (-1.61,-1.40)	-1.44 (-1.69,-1.19)	0.97 (0.76,1.18)	0.08 (0.01,0.15)
1.68 (1.36,2.00)	GLP1RA	-3.35 (-3.46,-3.23)	-0.31 (-0.69,0.08)	0.66 (-0.14,1.46)	-3.88 (-3.93,-3.84)	-3.35 (-3.63,-3.06)	NA	-1.01 (-1.11,-0.91)
-2.07 (-2.58,-1.57)	-3.75 (-4.16,-3.34)	Insulin	NA	NA	NA	1.00 (0.03,1.97)	NA	2.02 (1.02,3.02)
1.02 (0.28,1.76)	-0.65 (-1.42,0.11)	3.10 (2.23,3.96)	Met	NA	-3.22 (-10.54,4.10)	-3.52 (-4.18,-2.87)	NA	NA
2.57 (1.52,3.61)	0.89 (-0.17,1.95)	4.64 (3.51,5.77)	1.55 (0.27,2.82)	SGLT2	NA	NA	NA	-2.23 (-2.56,-1.89)
-1.53 (-1.94,-1.12)	-3.21 (-3.67,-2.74)	0.54 (-0.06,1.15)	-2.55 (-3.39,-1.72)	-4.10 (-5.21,-2.98)	SU	NA	NA	2.80 (2.07,3.53)
-1.83 (-2.43,-1.22)	-3.50 (-4.12,-2.88)	0.25 (-0.48,0.97)	-2.85 (-3.77,-1.93)	-4.40 (-5.59,-3.20)	-0.30 (-1.01,0.42)	TZD	NA	2.46 (1.81,3.11)
0.80 (-0.05,1.65)	-0.88 (-1.79,0.03)	2.87 (1.89,3.86)	-0.22 (-1.35,0.90)	-1.77 (-3.12,-0.42)	2.33 (1.38,3.27)	2.63 (1.58,3.67)	aGlu	NA
0.38 (0.10,0.66)	-1.30 (-1.57,-1.02)	2.46 (1.97,2.94)	-0.64 (-1.41,0.13)	-2.19 (-3.24,-1.14)	1.91 (1.45,2.38)	2.21 (1.58,2.84)	-0.42 (-1.31,0.48)	placebo

Figure S4.1b Results of sensitivity analysis (by excluding studies with sample size less than 50) for weight

DPP4	**1.29 (1.12,1.45)**	0.03 (-0.18,0.78)	**0.28 (0.02,0.55)**	**-0.42 (-0.60,-0.24)**	**-0.76 (-0.99,-0.53)**	**0.34 (0.22,0.47)**	-0.02 (-0.12,0.08)
0.86 (0.30,1.43)	**GLP1RA**	**-1.40 (-1.47,-1.32)**	**-0.24 (-0.46,-0.02)**	**-1.03 (-1.18,-0.88)**	**-0.10 (-1.15,-0.85)**	-1.07 (-3.02,0.88)	**-0.85 (-0.98,-0.73)**
-0.07 (-1.58,1.44)	-0.93 (-2.34,0.47)	**Insulin**	NA	NA	**0.40 (0.12,0.68)**	NA	NA
0.33 (-0.64,1.30)	-0.53 (-1.45,0.38)	0.40 (-1.28,2.08)	**Met**	-1.11 (-2.91,0.69)	NA	NA	NA
-0.99 (-1.89,-0.09)	**-1.86 (-2.66,-1.05)**	-0.92 (-2.54,0.70)	**-1.32 (-2.52,-0.12)**	**SU**	NA	NA	NA
-0.01 (-1.65,1.62)	-0.88 (-2.42,0.66)	0.06 (-2.02,2.14)	-0.34 (-2.13,1.45)	0.98 (-0.76,2.71)	**TZD**	NA	NA
0.30 (-1.24,1.84)	-0.56 (-2.20,1.07)	0.37 (-1.78,2.52)	-0.03 (-1.85,1.79)	1.29 (-0.49,3.07)	0.31 (-1.93,2.56)	**aGlu**	NA
-0.12 (-0.59,0.34)	**-0.99 (-1.47,-0.51)**	-0.05 (-1.54,1.43)	-0.45 (-1.44,0.53)	0.87 (-0.03,1.76)	-0.11 (-1.72,1.50)	-0.42 (-2.03,1.18)	**placebo**

Figure S4.2a Results of sensitivity analysis (by excluding studies with no allocation concealment) for body mass index

DPP4	**1.29 (1.13,1.45)**	0.00 (-1.60,1.60)	**0.29 (0.02,0.55)**	**-0.43 (-0.61,-0.25)**	**-0.76 (-0.98,-0.53)**	**0.33 (0.20,0.46)**	-0.01 (-0.10,0.10)
0.89 (0.54,1.24)	**GLP1RA**	**-1.44 (-1.52,-1.36)**	**-0.24 (-0.46,-0.02)**	**-1.03 (-1.18,-0.88)**	**-1.00 (-1.15,-0.85)**	NA	**-0.85 (-0.97,-0.72)**
-0.63 (-1.13,-0.13)	**-1.51 (-1.89,-1.14)**	**Insulin**	NA	NA	**0.40 (0.12,0.68)**	NA	NA
0.32 (-0.29,0.92)	-0.57 (-1.17,0.03)	**0.94 (0.24,1.65)**	**Met**	-1.11 (-2.91,0.69)	NA	NA	NA
-0.80 (-1.29,-0.32)	**-1.69 (-2.19,-1.20)**	-0.18 (-0.79,0.44)	**-1.12 (-1.85,-0.40)**	**SU**	NA	NA	NA
-0.35 (-1.05,0.34)	**-1.24 (-1.90,-0.58)**	0.28 (-0.44,0.99)	-0.67 (-1.54,0.20)	0.45 (-0.35,1.25)	**TZD**	NA	NA
0.29 (-0.42,1.00)	-0.60 (-1.39,0.19)	**0.92 (0.05,1.78)**	-0.03 (-0.96,0.90)	**1.10 (0.24,1.95)**	0.64 (-0.35,1.63)	**aGlu**	NA
-0.14 (-0.44,0.16)	**-1.03 (-1.38,-0.69)**	0.48 (-0.02,0.99)	-0.46 (-1.10,0.18)	**0.66 (0.13,1.19)**	0.21 (-0.51,0.92)	-0.43 (-1.20,0.33)	**placebo**

Figure S4.2b Results of sensitivity analysis (by excluding studies with sample size less than 50) for body mass index

DPP4	**1.75 (1.29,2.21)**	-2.20 (-5.38,0.98)	3.30 (-4.49,11.09)	**1.90 (1.24,2.56)**	**-1.88 (-2.62,-1.14)**	NA	**0.36 (0.01,0.72)**
1.61 (0.95,2.26)	**GLP1RA**	**-3.69 (-4.14,-3.23)**	**-4.16 (-5.14,-3.19)**	NA	-3.11 (-7.55,1.33)	**-2.33 (-3.11,-1.56)**	**-1.30 (-1.64,-0.97)**
0.61 (-7.13,8.35)	-1.00 (-8.72,6.72)	**Insulin**	NA	NA	NA	1.10 (-0.15,2.35)	NA
-3.49 (-5.22,-1.76)	**-5.10 (-6.71,-3.49)**	-4.10 (-11.98,3.78)	**Met**	NA	-1.37 (-6.56,3.82)	NA	NA
1.94 (0.75,3.14)	0.34 (-0.91,1.58)	1.34 (-6.48,9.15)	**5.44 (3.40,7.47)**	**SGLT2**	NA	NA	**-1.60 (-2.22,-0.98)**
-2.10 (-3.56,-0.64)	**-3.71 (-5.31,-2.11)**	-2.71 (-10.59,5.17)	1.39 (-0.87,3.66)	**-4.04 (-5.93,-2.16)**	**SU**	NA	NA
-0.49 (-2.16,1.17)	**-2.10 (-3.63,-0.57)**	-1.10 (-8.97,6.77)	**3.00 (0.78,5.22)**	**-2.44 (-4.41,-0.46)**	1.61 (-0.60,3.82)	**TZD**	NA
0.39 (-0.21,0.98)	**-1.22 (-1.67,-0.78)**	-0.22 (-7.95,7.51)	**3.88 (2.21,5.54)**	**-1.56 (-2.75,-0.36)**	**2.49 (0.91,4.06)**	0.88 (-0.71,2.47)	**placebo**

Figure S4.3a Results of sensitivity analysis (by excluding studies with no allocation concealment) for waist circumference

DPP4	**1.75 (1.29,2.21)**	-2.20 (-5.38,0.98)	NA	**1.90 (1.24,2.56)**	**-1.90 (-2.64,-1.15)**	NA	**0.37 (0.01,0.73)**	NA
1.67 (1.19,2.15)	**GLP1RA**	**-3.72 (-4.18,-3.27)**	**-4.93 (-5.98,-3.88)**	NA	-3.11 (-7.55,1.33)	**-2.33 (-3.11,-1.56)**	NA	**-1.37 (-1.72,-1.02)**
-2.02 (-2.77,-1.26)	**-3.69 (-4.28,-3.10)**	**Insulin**	NA	NA	NA	1.10 (-0.15,2.35)	NA	NA
-3.14 (-4.56,-1.73)	**-4.82 (-6.15,-3.48)**	-1.13 (-2.59,0.33)	**Met**	NA	-1.37 (-6.56,3.82)	NA	NA	NA
1.92 (0.96,2.88)	0.25 (-0.75,1.25)	**3.94 (2.78,5.10)**	**5.06 (3.40,6.73)**	**SGLT2**	NA	NA	NA	**-1.60 (-2.22,-0.98)**
-1.85 (-2.84,-0.86)	**-3.52 (-4.61,-2.43)**	0.17 (-1.07,1.40)	1.29 (-0.40,2.99)	**-3.77 (-5.14,-2.40)**	**SU**	NA	NA	NA
-0.73 (-1.77,0.31)	**-2.40 (-3.32,-1.48)**	**1.29 (0.28,2.29)**	**2.42 (0.79,4.04)**	**-2.65 (-4.01,-1.29)**	1.12 (-0.31,2.55)	**TZD**	NA	NA
-0.10 (-6.31,6.11)	-1.77 (-8.00,4.46)	1.92 (-4.34,8.18)	3.04 (-3.33,9.42)	-2.02 (-8.31,4.27)	1.75 (-4.54,8.04)	0.63 (-5.67,6.93)	**aGlu**	NA
0.34 (-0.11,0.79)	**-1.33 (-1.73,-0.94)**	**2.35 (1.65,3.06)**	**3.48 (2.09,4.87)**	**-1.58 (-2.53,-0.63)**	**2.19 (1.11,3.27)**	**1.07 (0.06,2.07)**	0.44 (-5.79,6.67)	**placebo**

Figure S4.3b Results of sensitivity analysis (by excluding studies with sample size less than 50) for waist circumference

Note: Treatments were reported in alphabetical order. Results of direct comparisons were listed in the upper triangle, and the estimation was calculated as the row-defining treatment compared with the column-defining treatment. Results of network meta-analysis were listed in the lower triangle, and the estimation was calculated as the column-defining treatment compared with the row-defining treatment. NA: not available. DPP4: dipeptidyl-peptidase IV inhibitors; GLP1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinedione; aGlu: alpha-glucosidase.

Supplementary File 7

Contribution plots for the incretin-based regimens network on weight, body mass index and waist circumference.

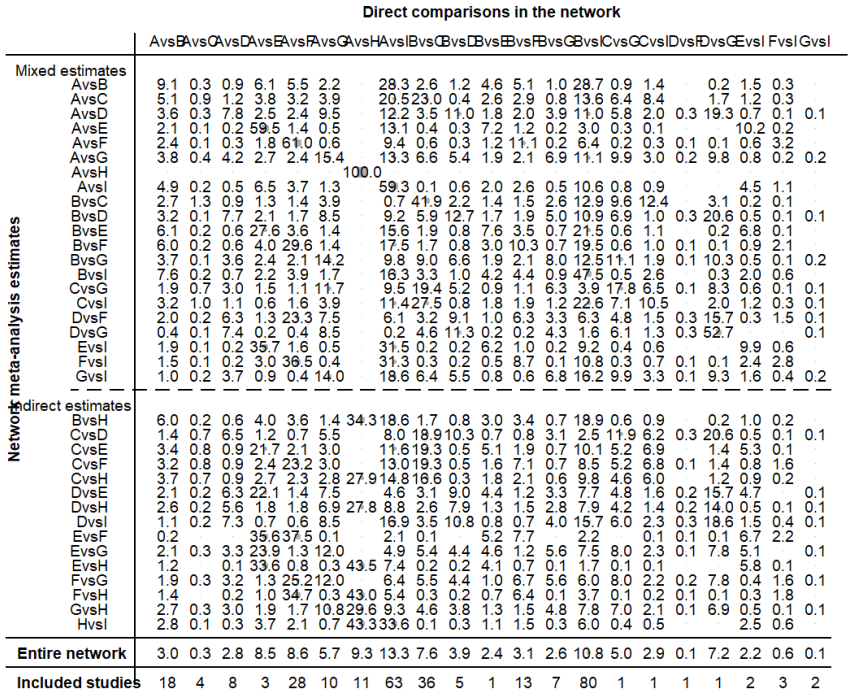

Figure S5.1 Contribution plot for the incretin-based regimens network: weight

Note: The size of the squares is proportional to the percentage contribution of the column-defining direct comparison to the row-defining network estimate. A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT-2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; a-Glu: alpha-glucosidase inhibitor; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

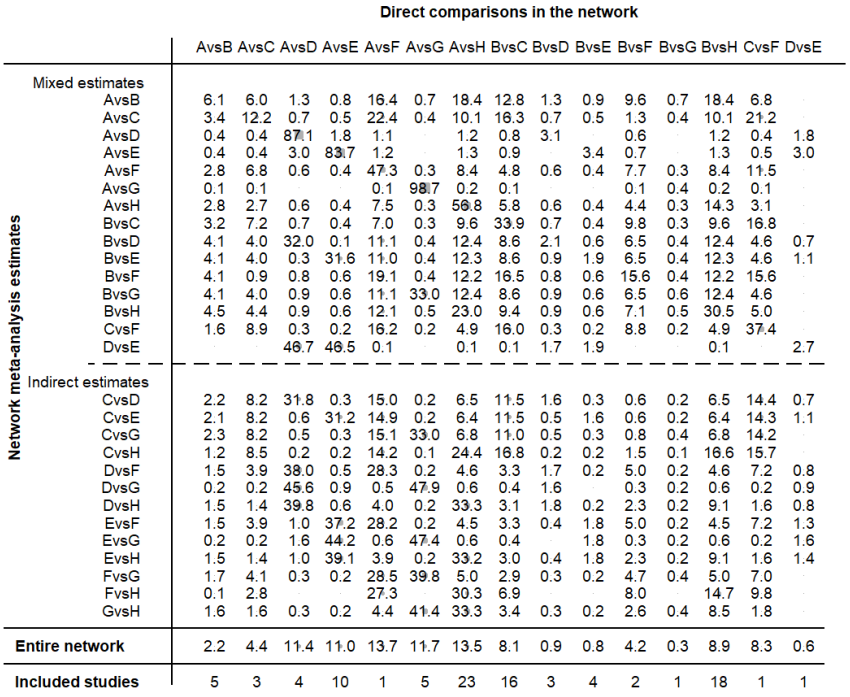

Figure S5.2 Contribution plot for the incretin-based regimens network: body mass index

Note: The size of the squares is proportional to the percentage contribution of the column-defining direct comparison to the row-defining network estimate. A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SU, F=TZD, G=a-Glu, H=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SU: sulphanylureas; a-Glu: alpha-glucosidase inhibitor; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

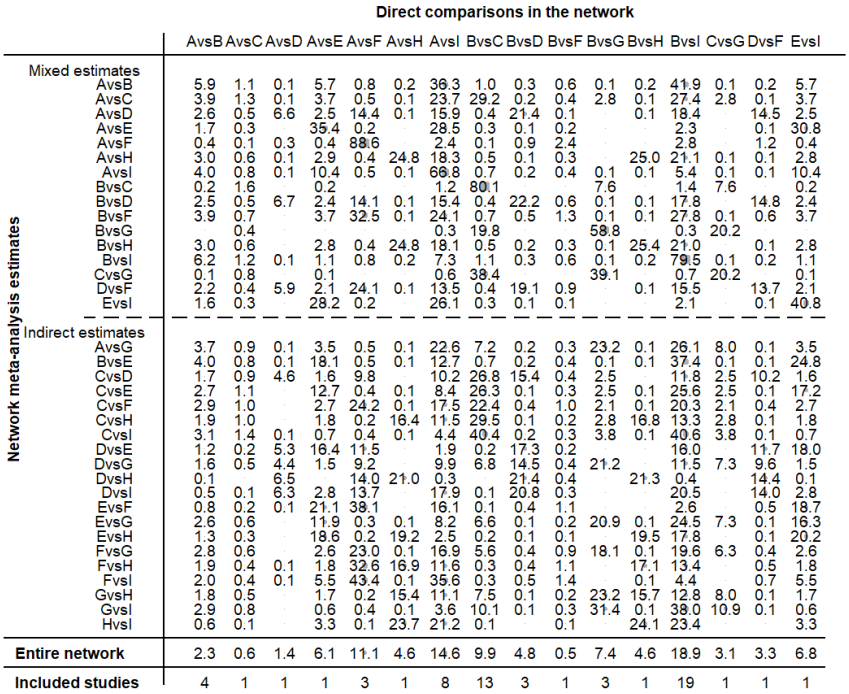

Figure S5.3 Contribution plot for the incretin-based regimens network: waist circumference

Note: The size of the squares is proportional to the percentage contribution of the column-defining direct comparison to the row-defining network estimate. A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT-2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; a-Glu: alpha-glucosidase inhibitor; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

Supplementary File 8

Assessment of inconsistency: results of the loop-specific approach and the node-splitting model

a. Evaluation of the local inconsistency: forest plots of inconsistence check for all closed loops in network

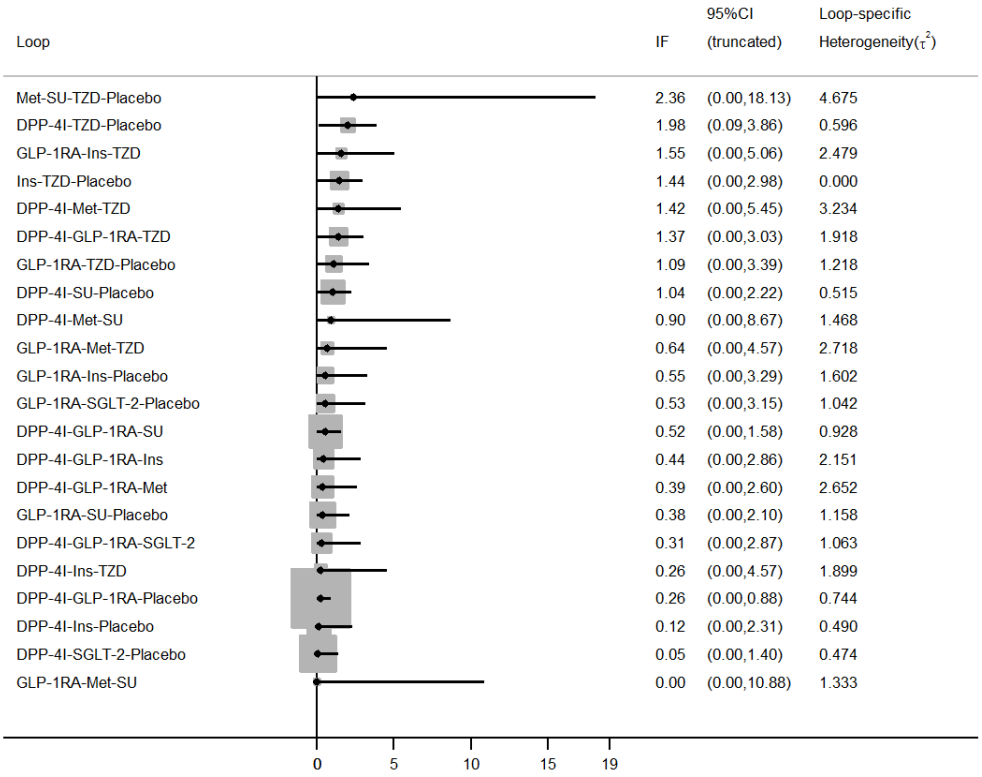

Figure S6.1 Forest plots of inconsistency: weight

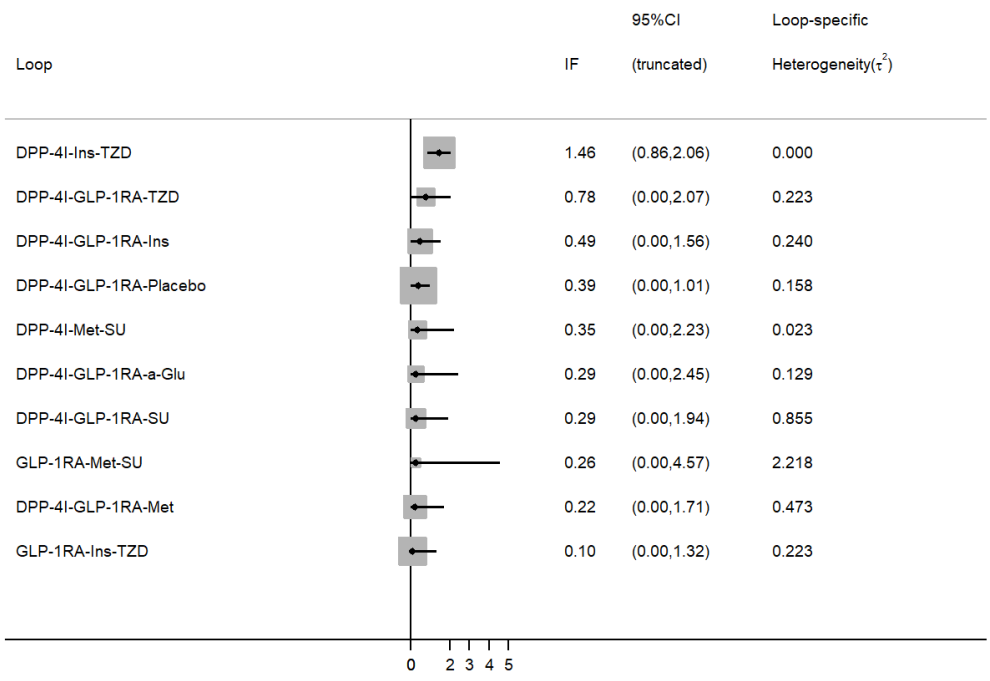

Figure S6.2 Forest plots of inconsistency: body mass index

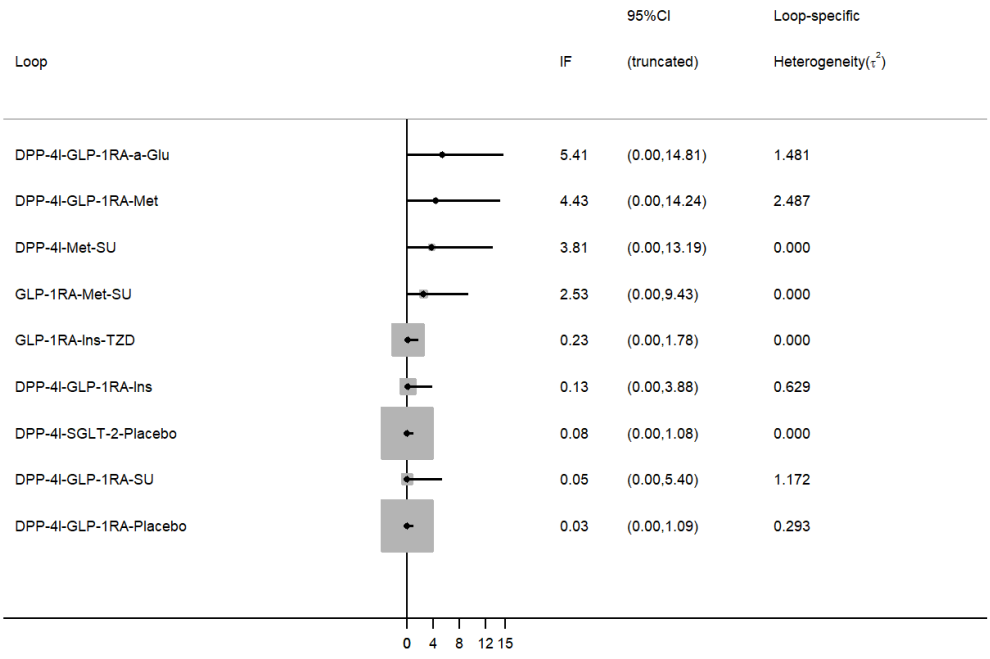

Figure S6.3 Forest plots of inconsistency: waist circumference

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Ins: insulin; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulfonylurea TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

b. Evaluation of the inconsistency by node-splitting model

Table S5.1 Summary of node splitting model results: weight

Comparisons	Direct		Indirect		Difference		
	Coef.	SE	Coef.	SE	Coef.	SE	P-value
DPP4-placebo	-0.12	0.20	-0.68	0.30	0.56	0.36	0.119
DPP4-GLP1RA	-1.59	0.34	-1.72	0.22	0.13	0.41	0.752
DPP4-Insulin	3.80	0.71	1.96	0.30	1.84	0.77	0.016
DPP4-Met	-0.84	0.50	-1.30	0.67	0.46	0.84	0.583
DPP4-SGLT2	-2.56	0.84	-2.47	1.16	-0.09	1.43	0.951
DPP4-SU	1.41	0.27	2.47	0.43	-1.06	0.51	0.038
DPP4-TZD	1.30	0.45	3.03	0.59	-1.73	0.74	0.019
DPP4-aGlu	-0.20	0.43	-0.32	5.82	0.12	5.83	0.984
GLP1RA-placebo	1.24	0.19	1.80	0.32	-0.56	0.37	0.127
GLP1RA-Insulin	3.75	0.24	5.36	0.68	-1.61	0.72	0.025
GLP1RA-Met	0.55	0.64	0.77	0.55	-0.22	0.84	0.796
GLP1RA-SGLT2	-0.66	1.43	-0.91	0.78	0.25	1.62	0.880
GLP1RA-SU	4.06	0.40	2.92	0.33	1.15	0.52	0.026
GLP1RA-TZD	4.38	0.54	2.97	0.50	1.41	0.73	0.055
Insulin-placebo	-1.99	1.60	-2.55	0.27	0.56	1.63	0.731
Insulin-TZD	-1.00	1.43	-0.24	0.44	-0.76	1.49	0.610
Met-SU	3.22	1.43	2.66	0.47	0.56	1.51	0.709
Met-TZD	3.52	1.43	2.85	0.56	0.67	1.53	0.663
SGLT2-placebo	2.39	1.07	2.12	0.90	0.27	1.41	0.850
SU-placebo	-2.62	0.95	-1.95	0.27	-0.66	1.00	0.504
TZD-placebo	-5.67	1.19	-1.82	0.40	-3.85	1.26	0.002

Table S5.2 Summary of node splitting model results: body mass index

Comparisons	Direct		Indirect		Difference		
	Coef.	SE	Coef.	SE	Coef.	SE	P-value
DPP4-placebo	0.16	0.23	-0.14	0.35	0.30	0.41	0.468
DPP4-GLP1RA	-0.97	0.39	-1.02	0.22	0.05	0.45	0.910
DPP4-Insulin	-0.03	0.48	0.45	0.29	-0.48	0.56	0.388
DPP4-Met	-0.18	0.41	-0.43	0.48	0.25	0.64	0.695
DPP4-SU	0.68	0.26	0.95	0.44	-0.28	0.51	0.590
DPP4-TZD	0.76	0.82	-0.01	0.57	0.77	1.00	0.441
DPP4-aGlu	-0.28	0.37	0.10	0.84	-0.38	0.92	0.681
GLP1RA-placebo	0.98	0.27	1.21	0.32	-0.24	0.42	0.571
GLP1RA-Insulin	1.39	0.21	1.01	0.50	0.38	0.54	0.483
GLP1RA-Met	0.60	0.48	0.84	0.45	-0.25	0.66	0.709
GLP1RA-SU	1.92	0.41	1.65	0.33	0.27	0.53	0.615
GLP1RA-TZD	1.09	0.58	1.50	0.74	-0.41	0.94	0.660
GLP1RA-aGlu	1.07	0.83	0.72	0.42	0.35	0.93	0.705
Insulin-TZD	-0.40	0.82	0.07	0.58	-0.47	1.01	0.639
Met-SU	1.11	0.83	1.01	0.41	0.10	0.92	0.915

Table S5.3 Summary of node splitting model results: waist circumference

Comparisons	Direct		Indirect		Difference		
	Coef.	SE	Coef.	SE	Coef.	SE	P-value
DPP4-placebo	-0.30	0.70	-0.88	0.79	0.58	1.06	0.584
DPP4-GLP1RA	-1.39	0.86	-2.27	0.64	0.88	1.07	0.414
DPP4-Insulin	2.20	1.73	1.02	0.72	1.18	1.87	0.528
DPP4-Met	-3.30	1.68	0.23	1.03	-3.53	1.97	0.073
DPP4-SGLT2	-1.90	1.78	-2.46	3.38	0.56	3.83	0.884
DPP4-SU	1.16	1.00	0.88	1.62	0.28	1.91	0.883
DPP4-aGlu	0.10	1.65	5.30	1.72	-5.20	2.39	0.029
GLP1RA-placebo	1.29	0.46	1.84	0.92	-0.55	1.03	0.590
GLP1RA-Insulin	3.07	0.48	4.06	1.61	-0.99	1.68	0.557
GLP1RA-Met	2.05	0.97	-1.12	1.64	3.17	1.90	0.096
GLP1RA-SU	3.11	1.73	3.01	1.09	0.10	2.05	0.959
GLP1RA-TZD	2.54	1.00	1.28	3.09	1.26	3.25	0.697
GLP1RA-aGlu	7.05	1.65	1.81	1.72	5.24	2.39	0.028
Insulin-TZD	-1.10	1.73	-0.53	1.26	-0.57	2.14	0.789
Met-SU	1.37	1.73	2.13	1.45	-0.76	2.26	0.738
SGLT2-placebo	1.60	1.82	1.04	3.31	0.56	3.83	0.884

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP1RA: glucagon-like peptide-1 receptor agonists; Ins: insulin; Met: metformin; SGLT2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; aGlu: alpha-glucosidase.

Supplementary File 9

Predictive intervals plots for the incretin-based regimens network on weight, body mass index and waist circumference.

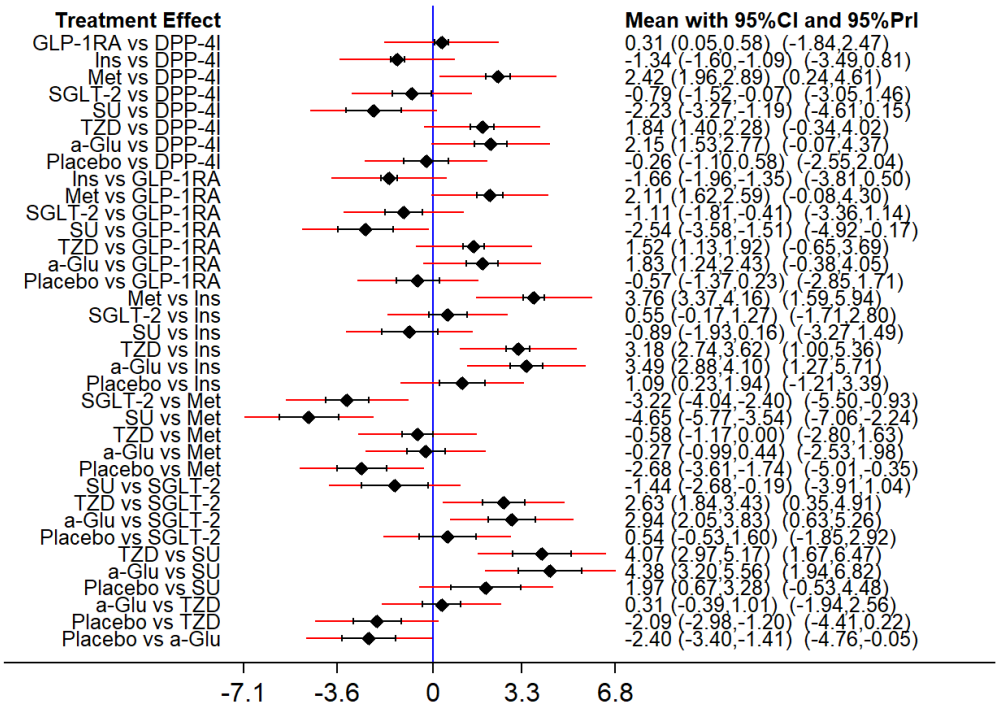

Figure S7.1 Predictive intervals plot: weight

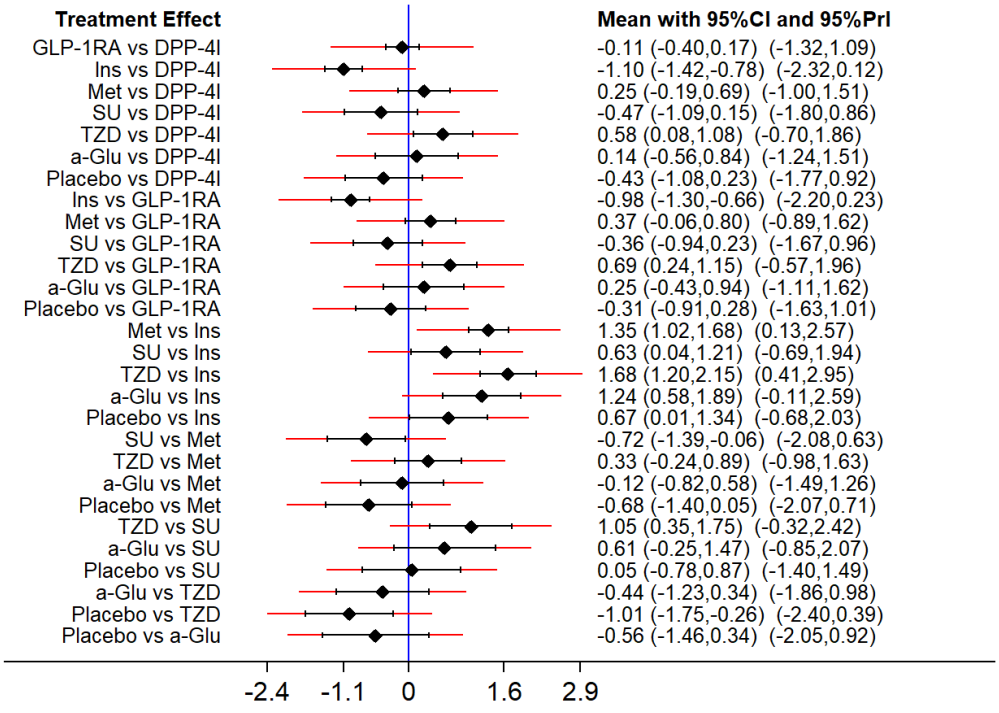

Figure S7.2 Predictive intervals plot: body mass index

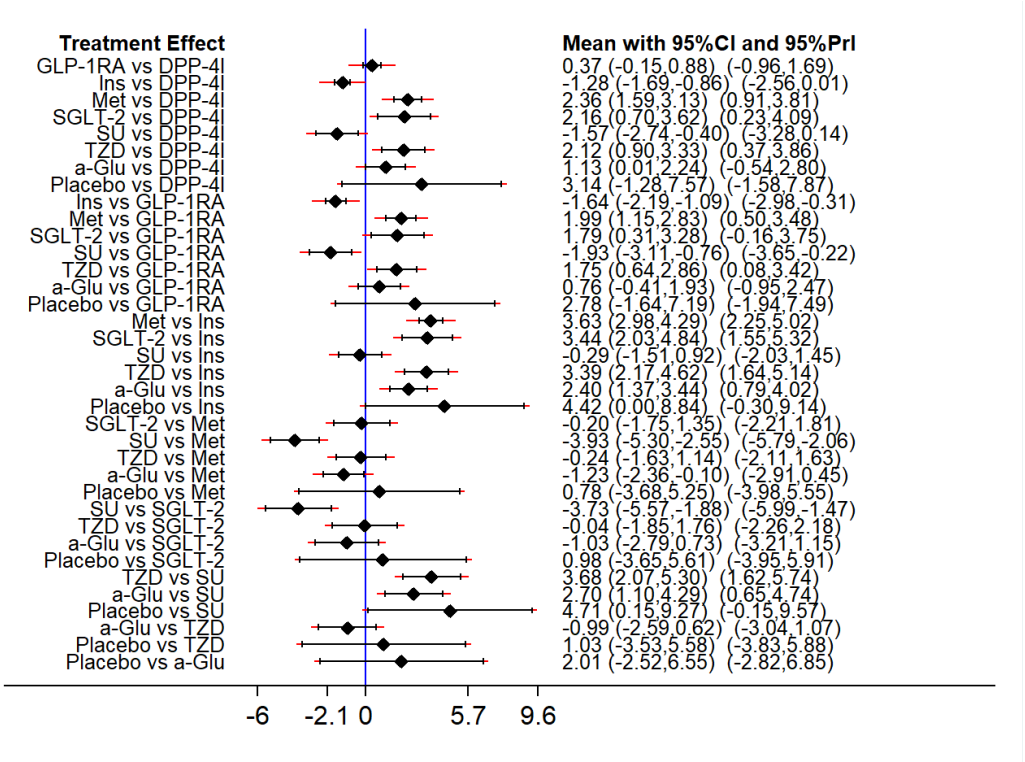

Figure S7.3 Predictive intervals plot: waist circumference

Note: The graph presents the network estimates for all pairwise comparisons. Black horizontal lines represent the confidence intervals, and red horizontal lines represent the predictive intervals. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Ins: insulin; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

Supplementary File 10

Comparison-adjusted funnel plots for weight, body mass index and waist circumference

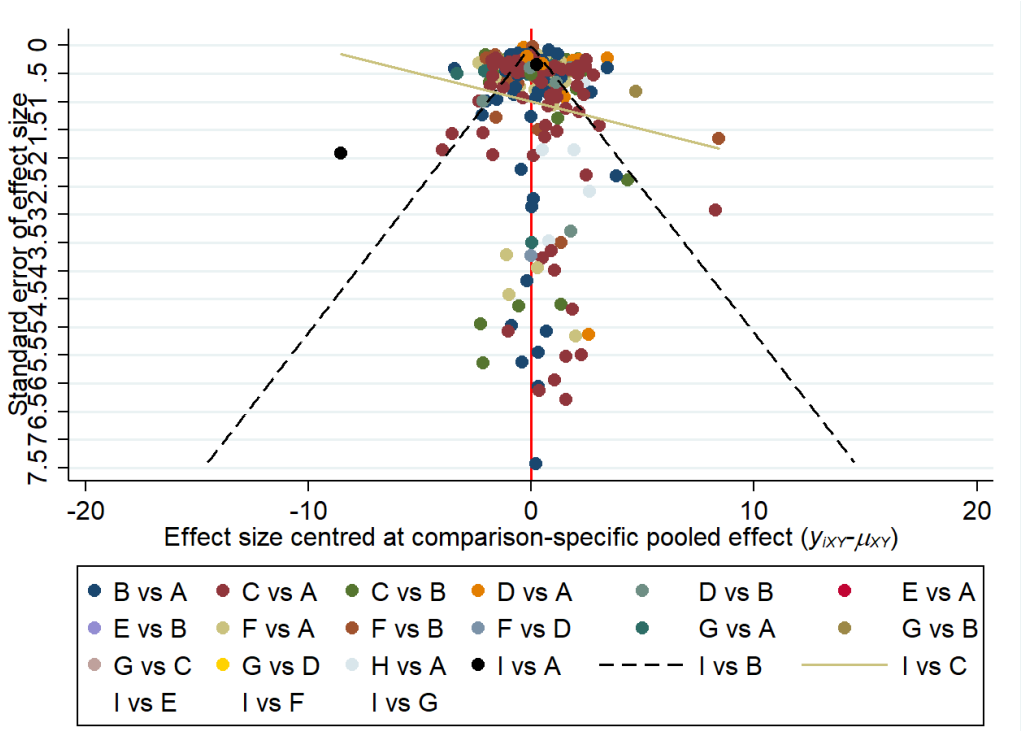

Figure S8.1 Comparison-adjusted funnel plot: weight

A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT-2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; a-Glu: alpha-glucosidase inhibitor; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

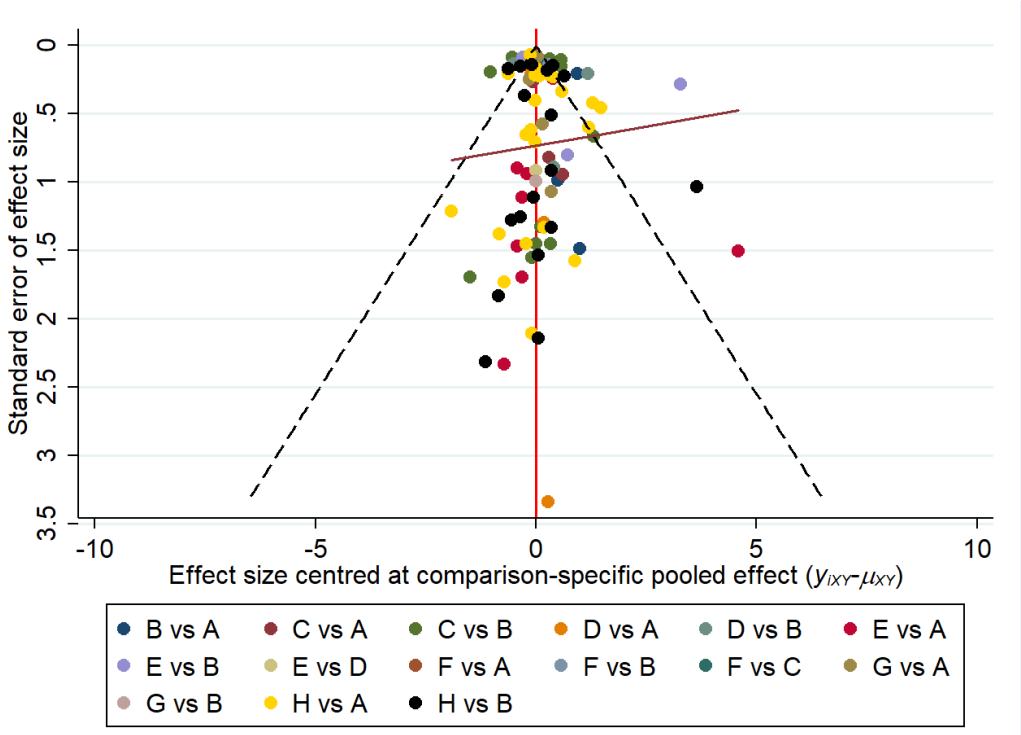

Figure S8.2 Comparison-adjusted funnel plot: body mass index

A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SU, F=TZD, G=a-Glu, H=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SU: sulphanylureas; a-Glu: alpha-glucosidase inhibitor; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

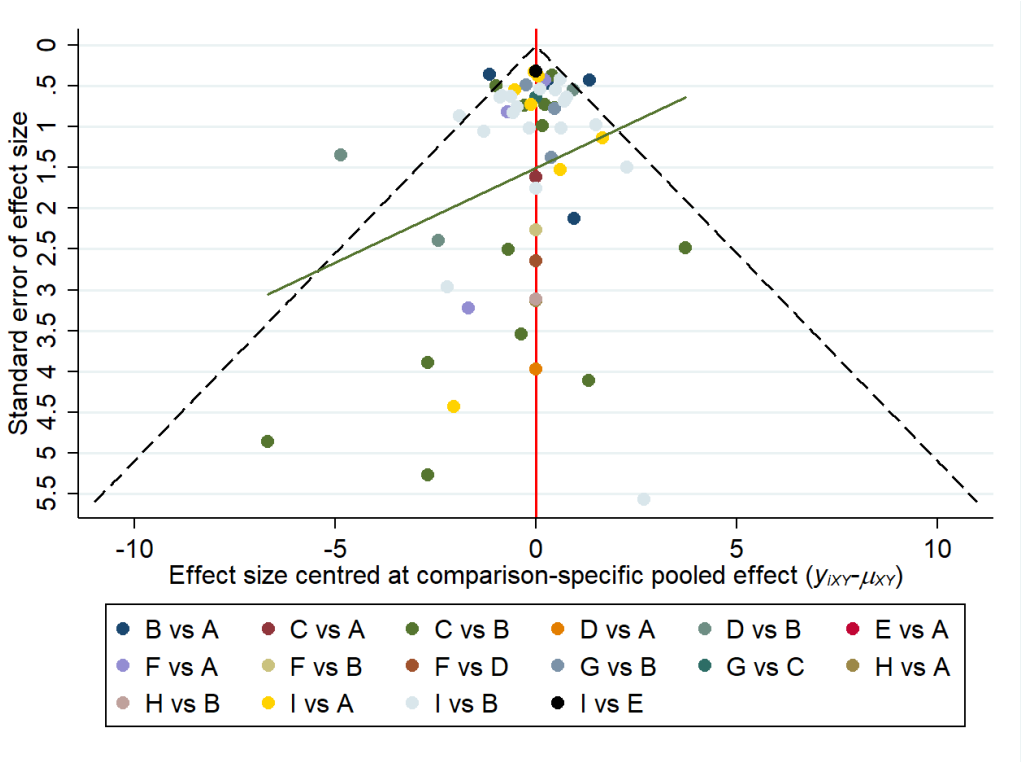

Figure S8.3 Comparison-adjusted funnel plot: waist circumference

A=DPP-4I, B=GLP-1RA, C=Insulin, D=Met, E=SGLT-2, F=SU, G=TZD, H=a-Glu, I=Placebo. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; a-Glu: alpha-glucosidase inhibitor; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

Supplementary File 11

Plots of cumulative ranking probability (SUCRA)

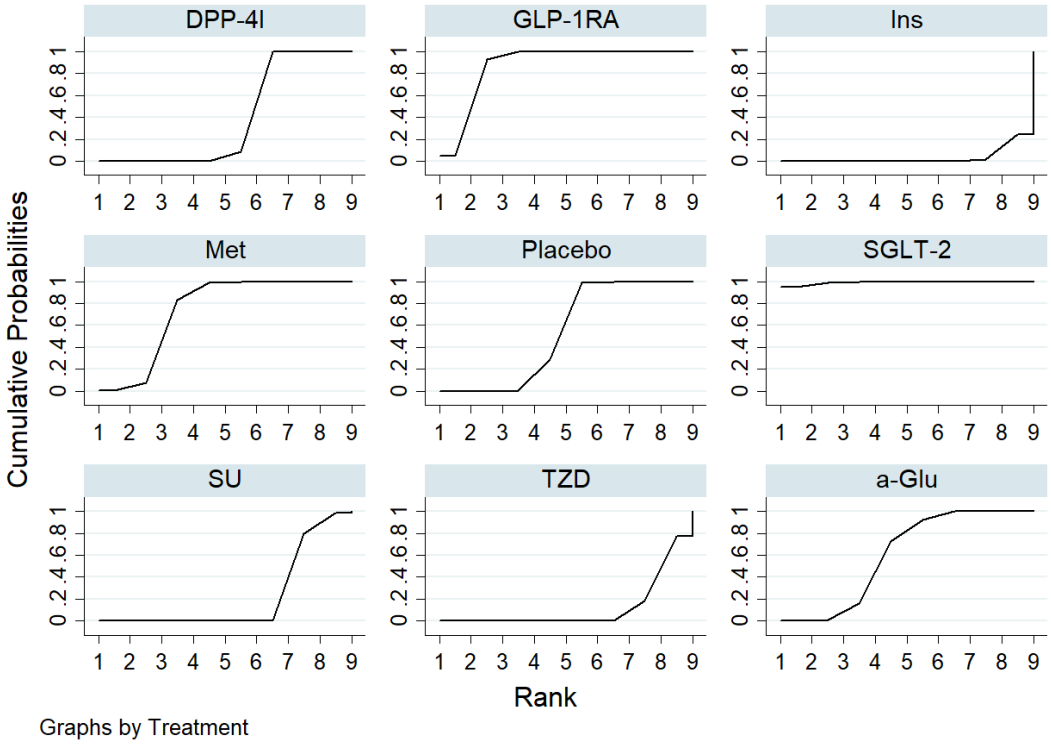

Figure S9.1 Plots of cumulative ranking probability: weight

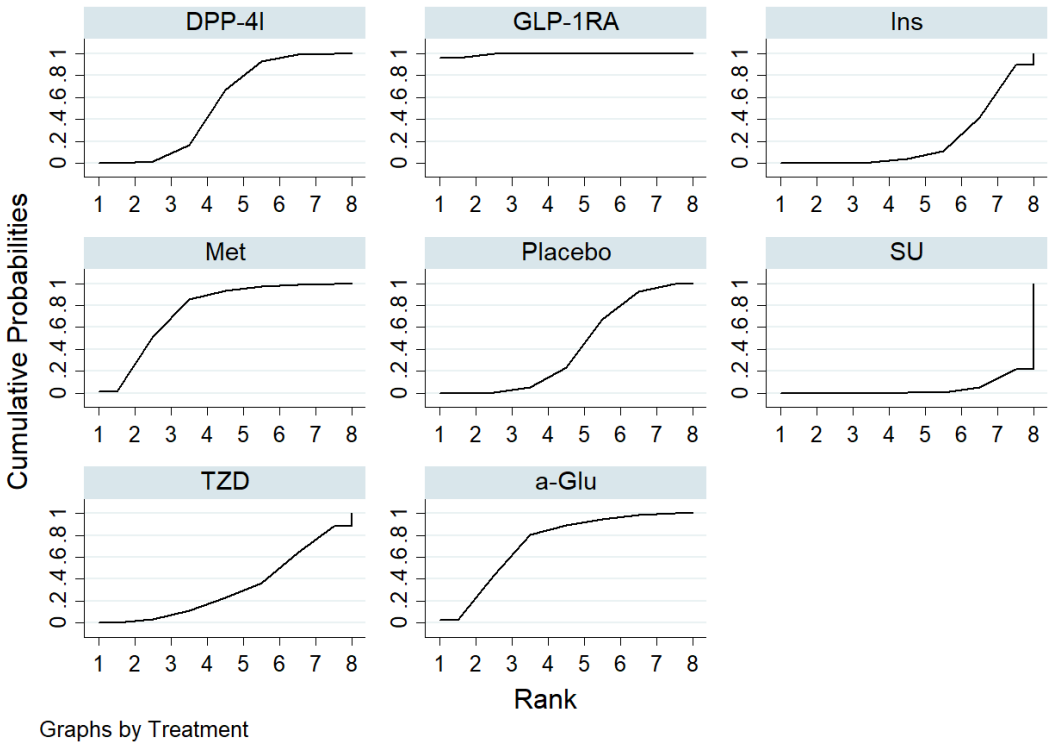

Figure S9.2 Plots of cumulative ranking probability: body mass index

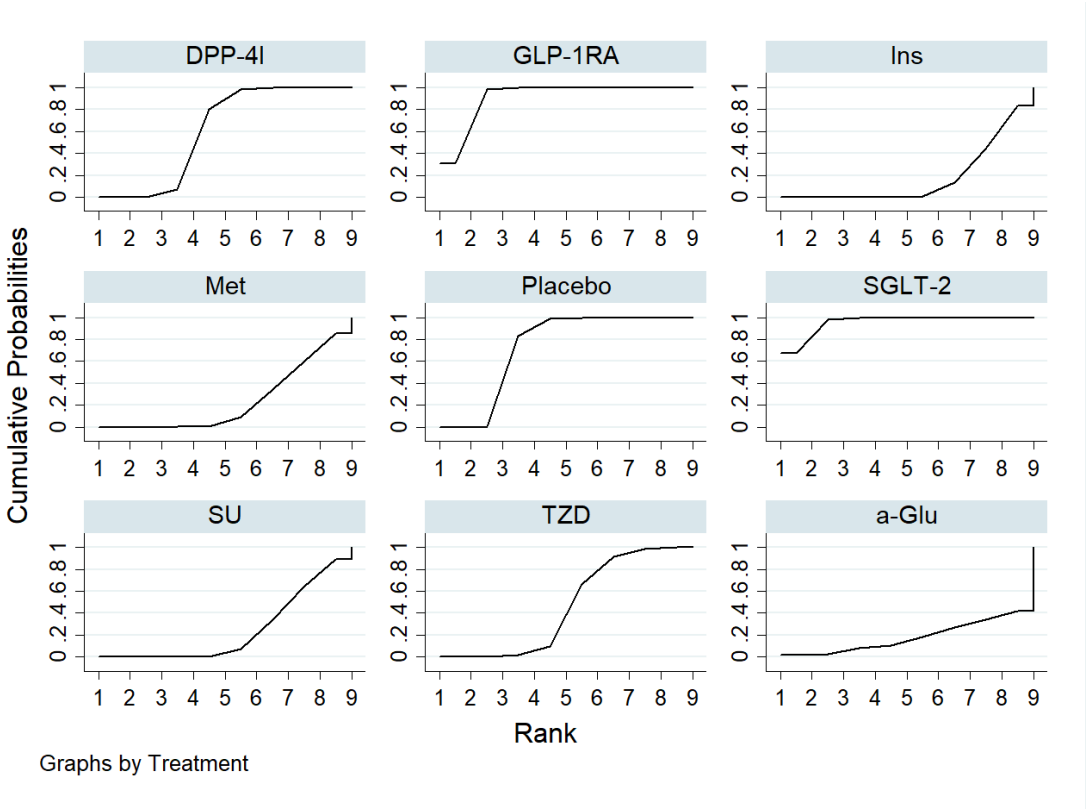

Figure S9.3 Plots of cumulative ranking probability: waist circumference

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Ins: insulin; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; a-Glu: alpha-glucosidase. Ranking: probability of being the best safety, of being the second safety, the third safety and so on, among the 8 (body mass index) or 9 treatments (weight and waist circumference).

Supplementary File 12

Contribution summary of risk of bias assessments

a. Contribution summary of risk of bias assessments for any direct comparisons included in the network meta-analysis

Table S6.1 Contribution summary of risk of bias assessments

Direct comparison	Risk of bias assessment		
	Weight	**Body mass index**	**Waist circumference**
DPP4-GLP1RA	Low	High	High
DPP4-Insulin	High	High	High
DPP4-Met	Low	High	High
DPP4-SGLT2	Low	NA	Low
DPP4-SU	Low	High	High
DPP4-TZD	Unclear	High	NA
DPP4-aGlu	High	High	High
DPP4-placebo	Low	High	Low
GLP1RA-Insulin	High	High	High
GLP1RA-Met	High	High	High
GLP1RA-SGLT2	Unclear	NA	NA
GLP1RA-SU	Unclear	Unclear	High
GLP1RA-TZD	Low	High	High
GLP1RA-aGlu	NA	High	High
GLP1RA-placebo	Low	Low	Low
Insulin-TZD	High	High	High
Insulin-placebo	Low	NA	NA
Met-SU	High	High	High
Met-TZD	Low	NA	NA
SGLT2-placebo	Low	NA	Low
SU-placebo	Low	NA	NA
TZD-placebo	Unclear	NA	NA

Note: DPP4: dipeptidyl-peptidase IV inhibitors; GLP1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; aGlu: alpha-glucosidase. NA: No direct comparison.

b. The contribution of direct comparisons to mixed or indirect comparisons by risk of bias classification

Table S6.2 Summary of the contribution of direct comparisons: weight

Comparisons	Risk of bias assessment		
	Low (%)	Unclear (%)	High (%)
DPP4-GLP1RA	83.0	11.9	5.1
DPP4-Insulin	59.8	9.4	30.8
DPP4-Met	65.5	13.4	21.1
DPP4-SGLT2	90.0	8.9	1.1
DPP4-SU	85.7	12.9	1.4
DPP4-TZD	58.2	19.6	22.2
DPP4-aGlu	0.0	0.0	100.0
DPP4-placebo	92.5	5.9	1.6
GLP1RA-Insulin	38.3	6.8	54.9
GLP1RA-Met	62.0	12.2	25.8
GLP1RA-SGLT2	83.9	12.5	3.6
GLP1RA-SU	82.0	14.7	3.3
GLP1RA-TZD	54.9	18.4	26.7
GLP1RA-aGlu	54.7	7.8	37.5
GLP1RA-placebo	84.6	10.3	5.1
Insulin-Met	50.8	7.1	42.1
Insulin-SGLT2	64.2	10.0	25.8
Insulin-SU	62.5	11.7	25.8
Insulin-TZD	42.7	13.8	43.5
Insulin-aGlu	43.1	6.7	50.2
Insulin-placebo	55.7	7.7	36.6
Met-SGLT2	69.5	13.2	17.3
Met-SU	67.6	14.9	17.5
Met-TZD	68.5	9.0	22.5
Met-aGlu	47.3	9.8	42.9
Met-placebo	69.1	10.1	20.8
SGLT2-SU	86.7	13.0	0.3
SGLT2-TZD	63.8	17.9	18.3
SGLT2-aGlu	50.9	5.1	44.0
SGLT2-placebo	91.4	7.7	0.9
SU-TZD	61.6	19.8	18.6
SU-aGlu	48.9	7.4	43.7
SU-placebo	89.4	9.6	1.0
TZD-aGlu	40.8	13.7	45.5
TZD-placebo	62.2	15.6	22.2
aGlu-placebo	52.4	3.4	44.2
entire	62.5	11.3	26.2

Table S6.3 Summary of the contribution of direct comparisons: body mass index

Comparisons	Risk of bias assessment		
	Low (%)	Unclear (%)	High (%)
DPP4-GLP1RA	18.4	0.9	80.7
DPP4-Insulin	10.1	0.5	89.4
DPP4-Met	1.2	0.0	98.8
DPP4-SU	1.3	3.4	95.3
DPP4-TZD	8.4	0.4	91.2
DPP4-aGlu	0.2	0.0	99.8
DPP4-placebo	14.3	0.4	85.3
GLP1RA-Insulin	9.6	0.4	90.0
GLP1RA-Met	12.4	0.6	87.0
GLP1RA-SU	12.3	1.9	85.8
GLP1RA-TZD	12.2	0.6	87.2
GLP1RA-aGlu	12.4	0.6	87.0
GLP1RA-placebo	30.5	0.6	68.9
Insulin-Met	6.5	0.3	93.2
Insulin-SU	6.4	1.6	92.0
Insulin-TZD	4.9	0.2	94.9
Insulin-aGlu	6.8	0.3	92.9
Insulin-placebo	16.6	0.2	83.2
Met-SU	0.1	1.9	98.0
Met-TZD	4.6	0.2	95.2
Met-aGlu	0.6	0.0	99.4
Met-placebo	9.1	0.2	90.7
SU-TZD	4.5	1.8	93.7
SU-aGlu	0.6	1.8	97.6
SU-placebo	9.1	1.8	89.1
TZD-aGlu	5.0	0.2	94.8
TZD-placebo	14.7	0.0	85.3
aGlu-placebo	8.5	0.2	91.3
enrite	8.9	0.8	90.3

Table S6.4 Summary of the contribution of direct comparisons: waist circumference

Comparisons	Risk of bias assessment		
	Low (%)	Unclear (%)	High (%)
DPP4-GLP1RA	89.6	0.0	10.4
DPP4-Insulin	58.5	0.0	41.5
DPP4-Met	39.3	0.0	60.7
DPP4-SGLT2	97.0	0.0	3.0
DPP4-SU	6.0	0.0	94.0
DPP4-TZD	55.7	0.0	44.3
DPP4-aGlu	45.1	0.0	54.9
DPP4-placebo	93.0	0.0	7.0

GLP1RA-Insulin	3.0	0.0	97.0
GLP1RA-Met	38.0	0.0	62.0
GLP1RA-SGLT2	93.0	0.0	7.0
GLP1RA-SU	59.3	0.0	40.7
GLP1RA-TZD	0.6	0.0	99.4
GLP1RA-aGlu	44.7	0.0	55.3
GLP1RA-placebo	89.0	0.0	11.0
Insulin-Met	25.2	0.0	74.8
Insulin-SGLT2	63.9	0.0	36.1
Insulin-SU	43.2	0.0	56.8
Insulin-TZD	1.5	0.0	98.5
Insulin-aGlu	28.4	0.0	71.6
Insulin-placebo	46.4	0.0	53.6
Met-SGLT2	52.3	0.0	47.7
Met-SU	32.8	0.0	67.2
Met-TZD	24.4	0.0	75.6
Met-aGlu	0.8	0.0	99.2
Met-placebo	44.0	0.0	56.0
SGLT2-SU	58.5	0.0	41.5
SGLT2-TZD	60.9	0.0	39.1
SGLT2-aGlu	59.1	0.0	40.9
SGLT2-placebo	97.2	0.0	2.8
SU-TZD	41.7	0.0	58.3
SU-aGlu	28.6	0.0	71.4
SU-placebo	51.0	0.0	49.0
TZD-aGlu	27.3	0.0	72.7
TZD-placebo	42.8	0.0	57.2
aGlu-placebo	51.2	0.0	48.8
entire	46.4	0.0	53.6

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Ins: insulin; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; a-Glu: alpha-glucosidase.

c. The contribution summary of direct comparisons to mixed or indirect comparisons by risk of bias classification

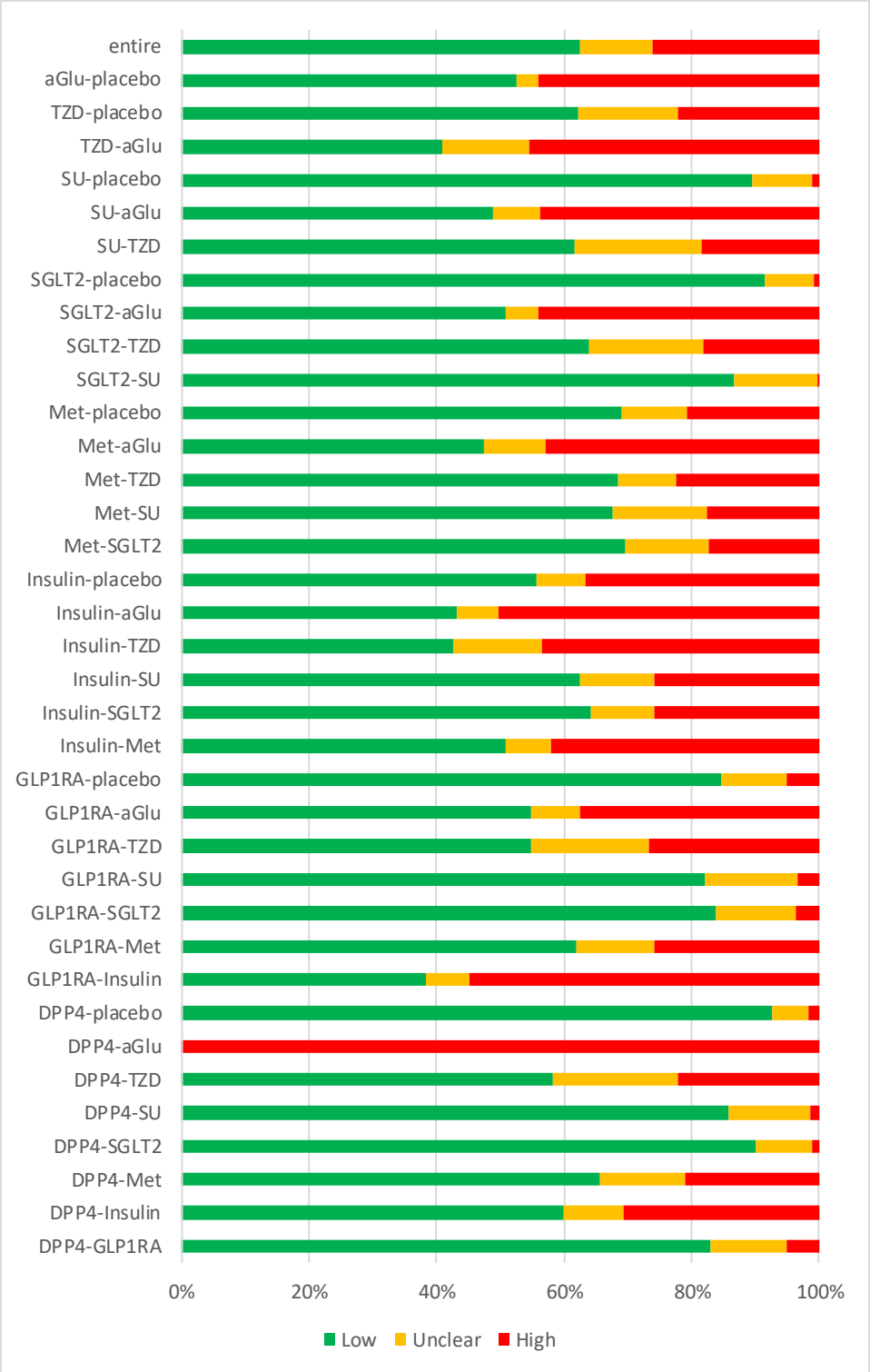

Figure S10.1 The contribution summary of direct comparisons: weight

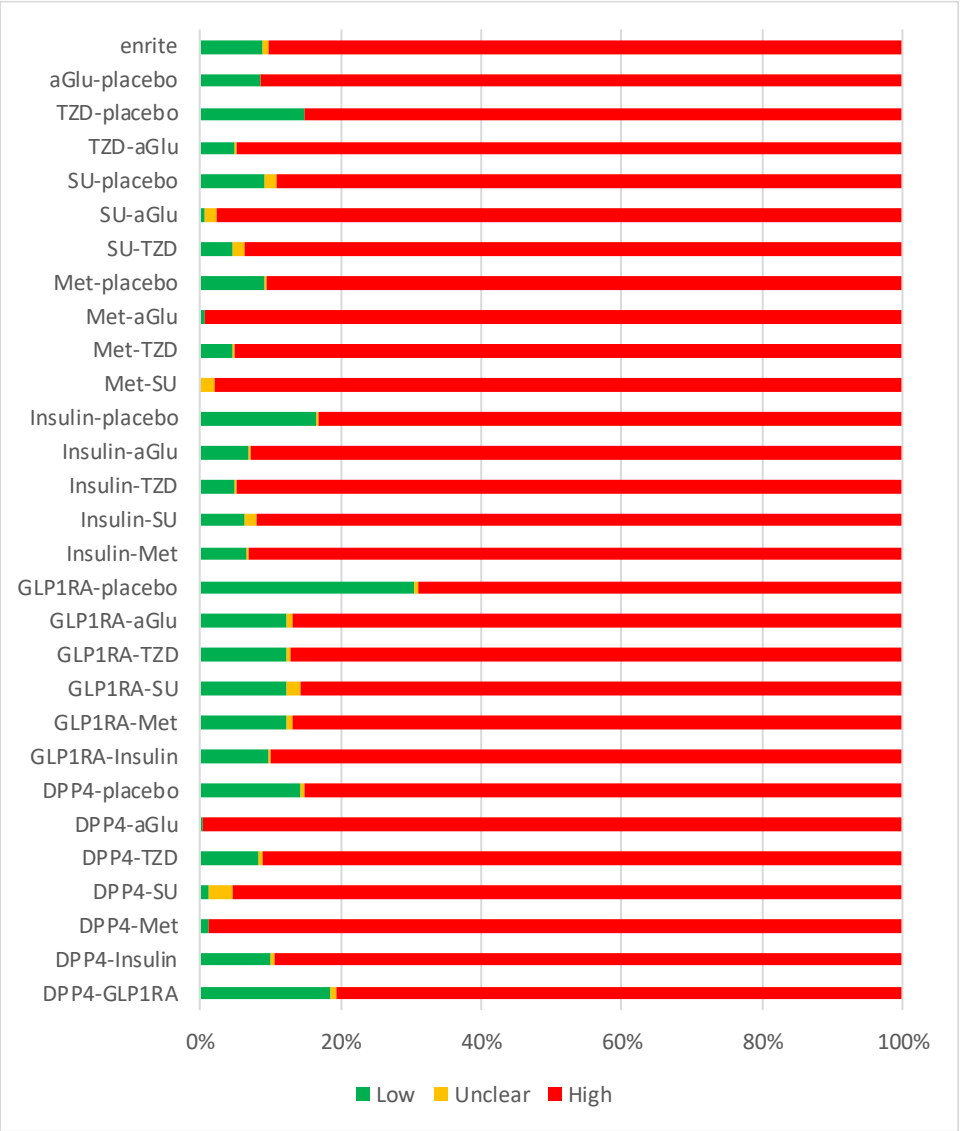

Figure S10.2 The contribution summary of direct comparisons: body mass index

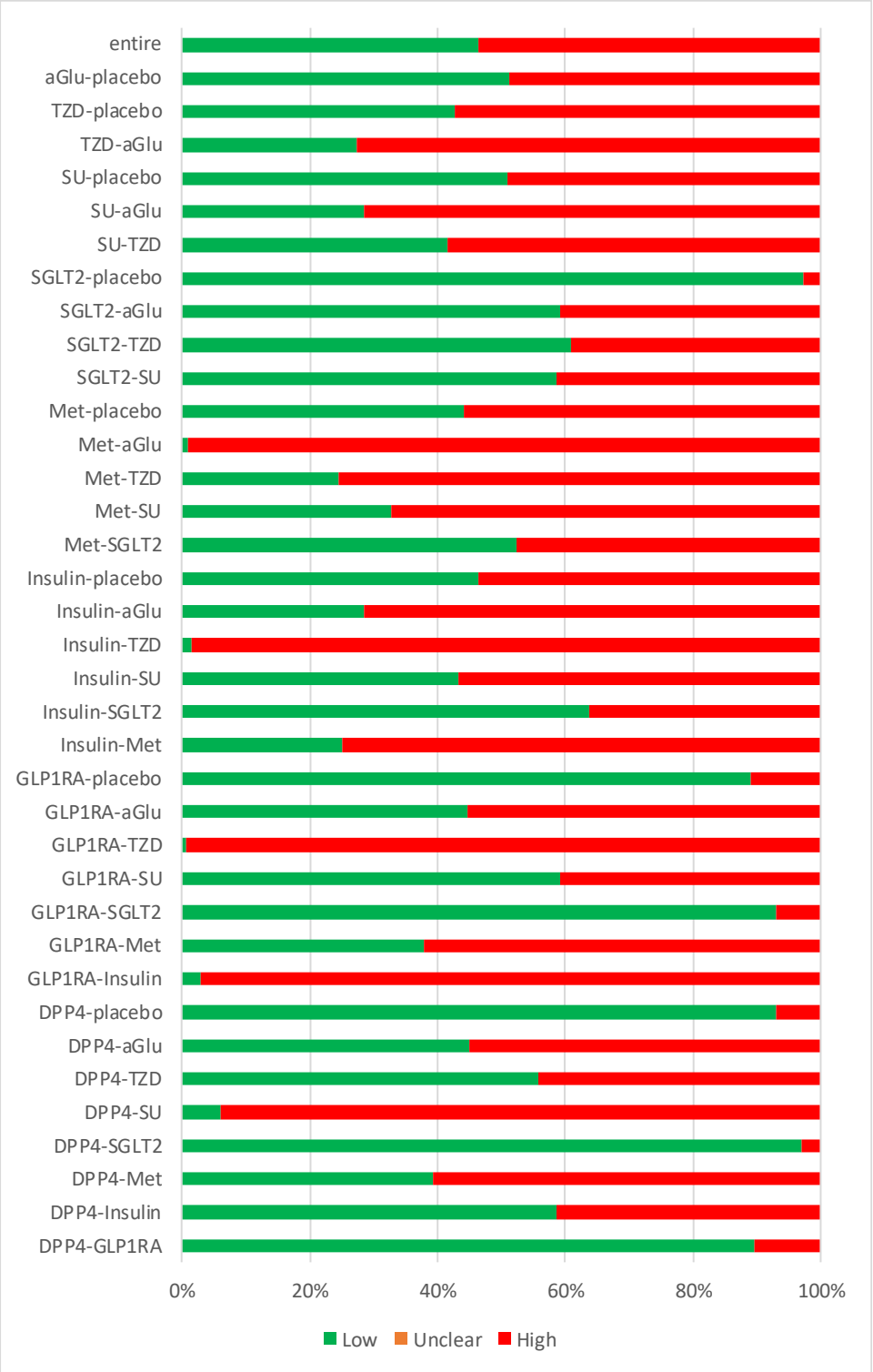

Figure S10.3 The contribution summary of direct comparisons: waist circumference

Note: DPP4: dipeptidyl-peptidase IV inhibitors; GLP1RA: glucagon-like peptide-1 receptor agonists; Ins: insulin; Met: metformin; SGLT2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; aGlu: alpha-glucosidase.

Supplementary File 13

Evaluation of the quality of evidence using GRADE framework

Table S7.1 Evaluation of the quality of evidence using GRADE framework: weight

Comparison	**Study limitation**	**Imprecision** WMD (95% CI)	**Heterogeneity and inconsistency**	**Indirectness**	**Publication bias**	**Confidence in OR for risk of dizziness**
DPP4-GLP1RA	5.1% of the estimate from studies at high risk, 11.9% at moderate risk, and 83.0% at low risk.	1.66 (1.35,1.96) No concerns	Severe heterogeneity according to I^2 (88.2%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.752).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)
DPP4-Insulin	30.8% of the estimate from studies at high risk, 9.4% at moderate risk, and 59.8% at low risk.	-2.11 (-2.59,-1.62) No concerns	Moderate heterogeneity according to I^2 (63.1%) and P-value (0.043) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.016).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation and heterogeneity and inconsistency)
DPP4-Met	21.1% of the estimate from studies at high risk, 13.4% at moderate risk, and 65.5% at	1.11 (0.41,1.81) Some concerns	Severe heterogeneity according to I2 (98.4%) and P-value (0.000) in direct comparisons. No inconsistency between	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation , heterogeneity and

	low risk.		direct and indirect estimate (Node-split p=0.583).			inconsistency, publication bias)
DPP4-SGLT2	1.1% of the estimate from studies at high risk, 8.9% at moderate risk, and 90.0% at low risk.	2.54 (1.51,3.58) No concerns	Mild heterogeneity according to I2 (0.0%) and P-value (0.722) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.951).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	High
DPP4-SU	1.4% of the estimate from studies at high risk, 12.9% at moderate risk, and 85.7% at low risk.	-1.52 (-1.92,-1.13) No concerns	Severe heterogeneity according to I^2 (0.000%) and P-value (0.440) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.038).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)
DPP4-TZD	22.2% of the estimate from studies at high risk, 19.6% at moderate risk, and 58.2% at low risk.	-1.83 (-2.43,-1.24) No concerns	Severe heterogeneity according to I^2 (91.6%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.019).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation and heterogeneity and inconsistency)

DPP4-aGlu	100.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 0.0% at low risk.	0.57 (-0.23,1.37) Some concerns	Mild heterogeneity according to I^2 (46.6%) and P-value (0.044) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.984).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to heterogeneity and inconsistency and study limitation (for two levels))
DPP4-placebo	1.6% of the estimate from studies at high risk, 5.9% at moderate risk, and 92.5% at low risk.	0.31 (0.05,0.58) No concerns	Severe heterogeneity according to I^2 (85.5%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.119).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)
GLP1RA-Insulin	54.9% of the estimate from studies at high risk, 6.8% at moderate risk, and 38.3% at low risk.	-3.76 (-4.16,-3.37) No concerns	Severe heterogeneity according to I^2(94.8%) and P-value(0.859) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.025).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation, heterogeneity and inconsistency)
GLP1RA-Met	25.8% of the estimate from	-0.55 (-1.27,0.17) Some concerns	Severe heterogeneity according to I^2(86.1%) and	The treatment effects were not significantly	The funnel plot for the direct comparison is not	Low (Downgrade by

	studies at high risk, 12.2% at moderate risk, and 62% at low risk.		P-value(0.000) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.796).	influenced by clinical modifiers in the subgroup analyses.	suggestive of any dominant publication bias.	two levels due to study limitation and heterogeneity and inconsistency)
GLP1RA-SGLT2	3.6% of the estimate from studies at high risk, 12.5% at moderate risk, and 83.9% at low risk.	0.89 (-0.16,1.93) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.880).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	High
GLP1RA-SU	3.3% of the estimate from studies at high risk, 14.7% at moderate risk, and 82% at low risk.	-3.18 (-3.62,-2.74) No concerns	Severe heterogeneity according to I^2 (94.6%) and P-value (0.000) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.026).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)
GLP1RA-TZD	26.7% of the estimate from studies at high risk, 18.4% at moderate risk, and 54.9% at	-3.49 (-4.10,-2.88) No concerns	Severe heterogeneity according to I^2 (94.2%) and P-value (0.000) in direct comparisons. No inconsistency between	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation and

	low risk.		direct and indirect estimate (Node-split p=0.055).			heterogeneity and inconsistency)
GLP1RA-aGlu	37.5% of the estimate from studies at high risk, 7.8% at moderate risk, and 54.7% at low risk.	-1.09 (-1.94,-0.23) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
GLP1RA-placebo	5.1% of the estimate from studies at high risk, 10.3% at moderate risk, and 84.6% at low risk.	-1.34 (-1.60,-1.09) No concerns	Severe heterogeneity according to I^2 (84.9%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.127).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)
Insulin-Met	42.1% of the estimate from studies at high risk, 7.1% at moderate risk, and 50.8% at low risk.	3.22 (2.40,4.04) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Insulin-SGLT2	25.8% of the estimate from studies at high risk,	4.65 (3.54,5.77) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison,	The treatment effects were not significantly influenced by clinical	No head-to-head study.	Moderate (Downgrade by one level due to

	10.0% at moderate risk, and 64.2% at low risk.		and no node-splitting inconsistency.	modifiers in the subgroup analyses.		study limitation)
Insulin-SU	25.8% of the estimate from studies at high risk, 11.7% at moderate risk, and 62.5% at low risk.	0.58 (-0.00,1.17) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Insulin-TZD	43.5% of the estimate from studies at high risk, 13.8% at moderate risk, and 42.7% at low risk.	0.27 (-0.44,0.99) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.610).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Insulin-aGlu	50.2% of the estimate from studies at high risk, 6.7% at moderate risk, and 43.1% at low risk.	2.68 (1.74,3.61) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Insulin-placebo	36.6% of the estimate from studies at high risk,	2.42 (1.96,2.89) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between	The treatment effects were not significantly influenced by clinical	Only one head-to-head study.	Moderate (Downgrade by one level due to

	7.7% at moderate risk, and 55.7% at low risk.		direct and indirect estimate (Node-split p=0.731).	modifiers in the subgroup analyses.		study limitation)
Met-SGLT2	17.3% of the estimate from studies at high risk, 13.2% at moderate risk, and 69.5% at low risk.	1.44 (0.19,2.68) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	High
Met-SU	17.5% of the estimate from studies at high risk, 14.9% at moderate risk, and 67.6% at low risk.	-2.63 (-3.43,-1.84) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.709).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	High
Met-TZD	22.5% of the estimate from studies at high risk, 9.0% at moderate risk, and 68.5% at low risk.	-2.94 (-3.83,-2.05) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.663).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Met-aGlu	42.9% of the estimate from studies at high risk,	-0.54 (-1.60,0.53) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison,	The treatment effects were not significantly influenced by clinical	No head-to-head study.	Moderate (Downgrade by one level due to

	9.8% at moderate risk, and 47.3% at low risk.		and no node-splitting inconsistency.	modifiers in the subgroup analyses.		study limitation)
Met-placebo	20.8% of the estimate from studies at high risk, 10.1% at moderate risk, and 69.1% at low risk.	-0.79 (-1.52,-0.07) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
SGLT2-SU	0.3% of the estimate from studies at high risk, 13.0% at moderate risk, and 86.7% at low risk.	-4.07 (-5.17,-2.97) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	High
SGLT2-TZD	18.3% of the estimate from studies at high risk, 17.9% at moderate risk, and 63.8% at low risk.	-4.38 (-5.56,-3.20) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
SGLT2-aGlu	44% of the estimate from studies at high risk, 5.1% at moderate risk, and	-1.97 (-3.28,-0.67) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting	The treatment effects were not significantly influenced by clinical modifiers in the	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)

	50.9% at low risk.		inconsistency.	subgroup analyses.		
SGLT2-placebo	0.9% of the estimate from studies at high risk, 7.7% at moderate risk, and 91.4% at low risk.	-2.23 (-3.27,-1.19) Some concerns	Moderate heterogeneity according to I^2 (70.3%) and P-value (0.067) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.850).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)
SU-TZD	18.6% of the estimate from studies at high risk, 19.8% at moderate risk, and 61.6% at low risk.	-0.31 (-1.01,0.39) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
SU-aGlu	43.7% of the estimate from studies at high risk, 7.4% at moderate risk, and 48.9% at low risk.	2.09 (1.20,2.98) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
SU-placebo	1.0% of the estimate from studies at high risk, 9.6% at moderate risk, and	1.84 (1.40,2.28) Some concerns	Moderate heterogeneity according to I^2 (73.8%) and P-value (0.022) in direct comparisons.	The treatment effects were not significantly influenced by clinical modifiers in the	The funnel plot for the direct comparison is not suggestive of any dominant publication	Moderate (Downgrade by one level due to heterogeneity and

	89.4% at low risk.		No inconsistency between direct and indirect estimate (Node-split p=0.504).	subgroup analyses.	bias.	inconsistency)
TZD-aGlu	45.5% of the estimate from studies at high risk, 13.7% at moderate risk, and 40.8% at low risk.	2.40 (1.41,3.40) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
TZD-placebo	22.2% of the estimate from studies at high risk, 15.6% at moderate risk, and 62.2% at low risk.	2.15 (1.53,2.77) No concerns	Severe heterogeneity according to I^2 (95.1%) and P-value (0.000) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.002).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation, heterogeneity and inconsistency)
aGlu-placebo	44.2% of the estimate from studies at high risk, 3.4% at moderate risk, and 52.4% at low risk.	-0.26 (-1.10,0.58) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Ranking of	26.2% of the	SUCRA plots	High heterogeneity in	The treatment effects	The	Low

treatment	estimate from studies at high risk, 11.3% at moderate risk, and 62.5% at low risk.	suggested no imprecision in a ranking of treatments.	network meta-analyses according to global I^2 (91.4%). No inconsistency in test of global inconsistency according to Q statistic (Q=27.75, P=0.479), and few inconsistency in local inconsistency.	were not significantly influenced by clinical modifiers in the subgroup analyses.	comparison-adjusted funnel plot for the network is not suggestive of any dominant publication bias.	(Downgrade by two level due to study limitation, heterogeneity and inconsistency)

Table S7.2 Evaluation of the quality of evidence using GRADE framework: body mass index

Comparison	**Study limitation**	**Imprecision** WMD (95% CI)	**Heterogeneity and inconsistency**	**Indirectness**	**Publication bias**	**Confidence in OR for risk of headache**
DPP4-GLP1RA	80.7% of the estimate from studies at high risk, 0.9% at moderate risk, and 18.4% at low risk.	0.98 (0.66,1.30) Some concerns	Severe heterogeneity according to I^2 (88.6%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.910).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation (for two levels), heterogeneity and inconsistency)
DPP4-Insulin	89.4% of the estimate from studies at high risk,	-0.37 (-0.80,0.06) No concerns	Mild heterogeneity according to I^2 (0.0%) and P-value (0.730) in direct	The treatment effects were not significantly influenced by clinical	The funnel plot for the direct comparison is not suggestive of any	Low (Downgrade by two levels due to

	0.5% at moderate risk, and 10.1% at low risk.		comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.388).	modifiers in the subgroup analyses.	dominant publication bias.	study limitation (for two levels))
DPP4-Met	98.8% of the estimate from studies at high risk, 0.0% at moderate risk, and 1.2% at low risk.	0.36 (-0.23,0.94) Some concerns	Mild heterogeneity according to I^2 (0.0%) and P-value (0.913) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.695).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation (for two levels))
DPP4-SU	95.3% of the estimate from studies at high risk, 3.4% at moderate risk, and 1.3% at low risk.	-0.69 (-1.15,-0.24) Some concerns	Mild heterogeneity according to I^2 (33.7%) and P-value (0.138) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.590).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation (for two levels))
DPP4-TZD	91.2% of the estimate from studies at high risk, 0.4% at moderate risk, and 8.4% at low risk.	-0.25 (-0.94,0.43) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.441).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))

DPP4-aGlu	99.8% of the estimate from studies at high risk, 0.0% at moderate risk, and 0.2% at low risk.	0.31 (-0.28,0.91) Some concerns	Mild heterogeneity according to I^2 (0.0%) and P-value (0.899) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.681).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation (for two levels))
DPP4-placebo	85.3% of the estimate from studies at high risk, 0.4% at moderate risk, and 14.3% at low risk.	-0.11 (-0.40,0.17) No concerns	Moderate heterogeneity according to I^2 (55.4%) and P-value (0.001) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.468).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation (for two levels) and heterogeneity and inconsistency)
GLP1RA-Insulin	90% of the estimate from studies at high risk, 0.4% at moderate risk, and 9.6% at low risk.	-1.35 (-1.68,-1.02) No concerns	Severe heterogeneity according to I^2 (89.7%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.483).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation (for two levels), heterogeneity and inconsistency)
GLP1RA-Met	87.0% of the estimate from	-0.63 (-1.21,-0.04) Some concerns	Severe heterogeneity according to I^2 (95.7%) and	The treatment effects were not significantly	The funnel plot for the direct comparison is not	Very low (Downgrade by

	studies at high risk, 0.6% at moderate risk, and 12.4% at low risk.		P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.709).	influenced by clinical modifiers in the subgroup analyses.	suggestive of any dominant publication bias.	three levels due to study limitation (for two levels), heterogeneity and inconsistency)
GLP1RA-SU	85.8% of the estimate from studies at high risk, 1.9% at moderate risk, and 12.3% at low risk.	-1.68 (-2.15,-1.20) No concerns	Severe heterogeneity according to I^2 (98.0%) and P-value (0.000) in direct comparisons. There is inconsistency between direct and indirect estimate (Node-split p=0.615).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation (for two levels), heterogeneity and inconsistency)
GLP1RA-TZD	87.2% of the estimate from studies at high risk, 0.6% at moderate risk, and 12.2% at low risk.	-1.24 (-1.89,-0.58) Some concerns	Severe heterogeneity according to I^2 (84.2%) and P-value (0.012) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.660).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation (for two levels), heterogeneity and inconsistency)
GLP1RA-aGlu	87.0% of the estimate from studies at high risk, 0.6% at moderate	-0.67 (-1.34,-0.01) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate	The treatment effects were not significantly influenced by clinical modifiers in the	Only one head-to-head study.	Low (Downgrade by two levels due to study limitation

	risk, and 12.4% at low risk.		(Node-split p=0.705).	subgroup analyses.		(for two levels))
GLP1RA-placebo	68.9% of the estimate from studies at high risk, 0.6% at moderate risk, and 30.5% at low risk.	-1.10 (-1.42,-0.78) No concerns	Moderate heterogeneity according to I^2 (66.7%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.571).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation, heterogeneity and inconsistency)
Insulin-Met	93.2% of the estimate from studies at high risk, 0.3% at moderate risk, and 6.5% at low risk.	0.72 (0.06,1.39) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Insulin-SU	92.0% of the estimate from studies at high risk, 1.6% at moderate risk, and 6.4% at low risk.	-0.33 (-0.89,0.24) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Insulin-TZD	94.9% of the estimate from studies at high risk,	0.12 (-0.58,0.82) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between	The treatment effects were not significantly influenced by clinical	Only one head-to-head study.	Low (Downgrade by two levels due to

	0.2% at moderate risk, and 4.9% at low risk.		direct and indirect estimate (Node-split p=0.639).	modifiers in the subgroup analyses.		study limitation (for two levels))
Insulin-aGlu	92.9% of the estimate from studies at high risk, 0.3% at moderate risk, and 6.8% at low risk.	0.68 (-0.05,1.40) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Insulin-placebo	83.2% of the estimate from studies at high risk, 0.2% at moderate risk, and 16.6% at low risk.	0.25 (-0.19,0.69) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Met-SU	98.0% of the estimate from studies at high risk, 1.9% at moderate risk, and 0.1% at low risk.	-1.05 (-1.75,-0.35) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.915).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Met-TZD	95.2% of the estimate from studies at high risk,	-0.61 (-1.47,0.25) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison,	The treatment effects were not significantly influenced by clinical	No head-to-head study.	Low (Downgrade by two levels due to

	0.2% at moderate risk, and 4.6% at low risk.		and no node-splitting inconsistency.	modifiers in the subgroup analyses.		study limitation (for two levels))
Met-aGlu	99.4% of the estimate from studies at high risk, 0.0% at moderate risk, and 0.6% at low risk.	-0.05 (-0.87,0.78) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Met-placebo	90.7% of the estimate from studies at high risk, 0.2% at moderate risk, and 9.1% at low risk.	-0.47 (-1.09,0.15) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
SU-TZD	93.7% of the estimate from studies at high risk, 1.8% at moderate risk, and 4.5% at low risk.	0.44 (-0.34,1.23) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
SU-aGlu	97.6% of the estimate from studies at high risk,	1.01 (0.26,1.75) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison,	The treatment effects were not significantly influenced by clinical	No head-to-head study.	Low (Downgrade by two levels due to

	1.8% at moderate risk, and 0.6% at low risk.		and no node-splitting inconsistency.	modifiers in the subgroup analyses.		study limitation (for two levels))
SU-placebo	89.1% of the estimate from studies at high risk, 1.8% at moderate risk, and 9.1% at low risk.	0.58 (0.08,1.08) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
TZD-aGlu	94.8% of the estimate from studies at high risk, 0.2% at moderate risk, and 5% at low risk.	0.56 (-0.34,1.46) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
TZD-placebo	85.3% of the estimate from studies at high risk, 0.0% at moderate risk, and 14.7% at low risk.	0.14 (-0.56,0.84) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
aGlu-placebo	91.3% of the estimate from studies at high risk,	-0.43 (-1.08,0.23) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison,	The treatment effects were not significantly influenced by clinical	No head-to-head study.	Low (Downgrade by two levels due to

	0.2% at moderate risk, and 8.5% at low risk.		and no node-splitting inconsistency.	modifiers in the subgroup analyses.		study limitation (for two levels))
Ranking of treatment	90.3% of the estimate from studies at high risk, 0.8% at moderate risk, and 8.9% at low risk.	SUCRA plots suggested no imprecision in a ranking of treatments.	High heterogeneity in network meta-analyses according to global I^2 (84.5%). No inconsistency in test of global inconsistency according to Q statistic (Q=5.26, P=0.949), and few inconsistency in local inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The comparison-adjusted funnel plot for the network is not suggestive of any dominant publication bias.	Very low (Downgrade by three levels due to study limitation(for two levels), heterogeneity and inconsistency)

Table S7.3 Evaluation of the quality of evidence using GRADE framework: waist circumference

Comparison	**Study limitation**	**Imprecision** WMD (95% CI)	**Heterogeneity and inconsistency**	**Indirectness**	**Publication bias**	**Confidence in OR for risk of dizziness**
DPP4-GLP1RA	10.4% of the estimate from studies at high risk, 0.0% at moderate risk, and 89.6% at low risk.	1.64 (1.09,2.19) No concerns	Severe heterogeneity according to I^2 (85.4%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to heterogeneity and inconsistency)

			(Node-split p=0.414).			
DPP4-Insulin	41.5% of the estimate from studies at high risk, 0.0% at moderate risk, and 58.5% at low risk.	-1.99 (-2.83,-1.15) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.528).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Moderate (Downgrade by one level due to study limitation)
DPP4-Met	60.7% of the estimate from studies at high risk, 0.0% at moderate risk, and 39.3% at low risk.	-1.79 (-3.28,-0.31) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.073).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Moderate (Downgrade by one level due to study limitation)
DPP4-SGLT2	3.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 97.0% at low risk.	1.93 (0.76,3.11) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.884).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	High
DPP4-SU	94.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 6.0% at low risk.	-1.75 (-2.86,-0.64) Some concerns	Mild heterogeneity according to I2 (0.0%) and P-value (0.525) in direct comparisons. No inconsistency between direct and indirect estimate	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitations (for two levels))

			(Node-split p=0.883).			
DPP4-TZD	44.3% of the estimate from studies at high risk, 0.0% at moderate risk, and 55.7% at low risk.	-0.76 (-1.93,0.41) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
DPP4-aGlu	54.9% of the estimate from studies at high risk, 0.0% at moderate risk, and 45.1% at low risk.	-2.78 (-7.19,1.64) Major concerns	Only one head-to-head study and no heterogeneity. There is inconsistency between direct and indirect estimate (Node-split p=0.029).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Very low (Downgrade by three levels due to study limitation, imprecision and heterogeneity and inconsistency)
DPP4-placebo	7.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 93.0% at low risk.	0.37 (-0.15,0.88) Some concerns	Mild heterogeneity according to I^2 (0.0%) and P-value (0.830) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.584).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	High
GLP1RA-Insulin	97.0% of the estimate from studies at high risk,	-3.63 (-4.29,-2.98) No concerns	Mild heterogeneity according to I^2 (0.0%) and P-value (0.544) in direct	The treatment effects were not significantly influenced by clinical	The funnel plot for the direct comparison is not suggestive of any	Low (Downgrade by two levels due to

	0.0% at moderate risk, and 3.0% at low risk.		comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.557).	modifiers in the subgroup analyses.	dominant publication bias.	study limitation (for two levels))
GLP1RA-Met	62.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 38.0% at low risk.	-3.44 (-4.84,-2.03) No concerns	Severe heterogeneity according to I^2 (88.2%) and P-value (0.000) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.096).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	Low (Downgrade by two levels due to study limitation, heterogeneity and inconsistency)
GLP1RA-SGLT2	7.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 93.0% at low risk.	0.29 (-0.92,1.51) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to imprecision)
GLP1RA-SU	40.7% of the estimate from studies at high risk, 0.0% at moderate risk, and 59.3% at low risk.	-3.39 (-4.62,-2.17) No concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.959).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Moderate (Downgrade by one level due to study limitation)
GLP1RA-TZD	99.4% of the estimate from	-2.40 (-3.44,-1.37) No concerns	Mild heterogeneity according to I^2 (0.0%) and	The treatment effects were not significantly	The funnel plot for the direct comparison is not	Low (Downgrade by

	studies at high risk, 0.0% at moderate risk, and 0.6% at low risk.		P-value (0.717) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.697).	influenced by clinical modifiers in the subgroup analyses.	suggestive of any dominant publication bias.	two levels due to study limitation (for two levels))
GLP1RA-aGlu	55.3% of the estimate from studies at high risk, 0.0% at moderate risk, and 44.7% at low risk.	-4.42 (-8.84,0.00) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.028).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Low (Downgrade by two levels due to study limitation and heterogeneity and inconsistency)
GLP1RA-placebo	11.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 89.0% at low risk.	-1.28 (-1.69,-0.86) No concerns	Mild heterogeneity according to I^2 (22.8%) and P-value (0.179) in direct comparisons. No inconsistency between direct and indirect estimate (Node-split p=0.590).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The funnel plot for the direct comparison is not suggestive of any dominant publication bias.	High
Insulin-Met	74.8% of the estimate from studies at high risk, 0.0% at moderate risk, and 25.2% at	0.20 (-1.35,1.75) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)

	low risk.					
Insulin-SGLT2	36.1% of the estimate from studies at high risk, 0.0% at moderate risk, and 63.9% at low risk.	3.93 (2.55,5.30) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
Insulin-SU	56.8% of the estimate from studies at high risk, 0.0% at moderate risk, and 43.2% at low risk.	0.24 (-1.14,1.63) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)
Insulin-TZD	98.5% of the estimate from studies at high risk, 0.0% at moderate risk, and 1.5% at low risk.	1.23 (0.10,2.36) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0789).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Low (Downgrade by two levels due to study limitation (for two levels))
Insulin-aGlu	71.6% of the estimate from studies at high risk, 0.0% at moderate risk, and 28.4% at	-0.78 (-5.25,3.68) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)

	low risk.					
Insulin-placebo	53.6% of the estimate from studies at high risk, 0.0% at moderate risk, and 46.4% at low risk.	2.36 (1.59,3.13) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Moderate (Downgrade by one level due to study limitation)
Met-SGLT2	47.7% of the estimate from studies at high risk, 0.0% at moderate risk, and 52.3% at low risk.	3.73 (1.88,5.57) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Moderate (Downgrade by one level due to study limitation)
Met-SU	67.2% of the estimate from studies at high risk, 0.0% at moderate risk, and 32.8% at low risk.	0.04 (-1.76,1.85) Major concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.738).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)
Met-TZD	75.6% of the estimate from studies at high risk, 0.0% at moderate risk, and 24.4% at	1.03 (-0.73,2.79) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Low (Downgrade by two levels due to study limitation and imprecision)

	low risk.					
Met-aGlu	99.2% of the estimate from studies at high risk, 0.0% at moderate risk, and 0.8% at low risk.	-0.98 (-5.61,3.65) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Very low (Downgrade by three levels due to study limitation (for two levels) and imprecision)
Met-placebo	56.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 44.0% at low risk.	2.16 (0.70,3.62) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Moderate (Downgrade by one level due to study limitation)
SGLT2-SU	41.5% of the estimate from studies at high risk, 0.0% at moderate risk, and 58.5% at low risk.	-3.68 (-5.30,-2.07) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Moderate (Downgrade by one level due to study limitation)
SGLT2-TZD	39.1% of the estimate from studies at high risk, 0.0% at moderate risk, and 60.9% at	-2.70 (-4.29,-1.10) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study..	Moderate (Downgrade by one level due to study limitation)

	low risk.					
SGLT2-aGlu	40.9% of the estimate from studies at high risk, 0.0% at moderate risk, and 59.1% at low risk.	-4.71 (-9.27,-0.15) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
SGLT2-placebo	2.8% of the estimate from studies at high risk, 97.2% at moderate risk, and 100.0% at low risk.	-1.57 (-2.74,-0.40) Some concerns	Only one head-to-head study and no heterogeneity. No inconsistency between direct and indirect estimate (Node-split p=0.884).	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	Only one head-to-head study.	High
SU-TZD	58.3% of the estimate from studies at high risk, 0.0% at moderate risk, and 41.7% at low risk.	0.99 (-0.62,2.59) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
SU-aGlu	71.4% of the estimate from studies at high risk, 0.0% at moderate risk, and 28.6% at low risk.	-1.03 (-5.58,3.53) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)

SU-placebo	49.0% of the estimate from studies at high risk, 0.0% at moderate risk, and 51.0% at low risk.	2.12 (0.90,3.33) No concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
TZD-aGlu	72.7% of the estimate from studies at high risk, 0.0% at moderate risk, and 27.3% at low risk.	-2.01 (-6.55,2.52) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)
TZD-placebo	57.2% of the estimate from studies at high risk, 0.0% at moderate risk, and 42.8% at low risk.	1.13 (0.01,2.24) Some concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Moderate (Downgrade by one level due to study limitation)
aGlu-placebo	48.8% of the estimate from studies at high risk, 0.0% at moderate risk, and 51.2% at low risk.	3.14 (-1.28,7.57) Major concerns	No head-to-head study and no heterogeneity. Only indirect comparison, and no node-splitting inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	No head-to-head study.	Low (Downgrade by two levels due to study limitation and imprecision)

Ranking of treatment	53.6% of the estimate from studies at high risk, 0.0% at moderate risk, and 46.4% at low risk.	SUCRA plots suggested no imprecision in a ranking of treatments.	Mild heterogeneity in network meta-analyses according to global I^2 (36.7%). No significant inconsistency in test of global inconsistency according to Q statistic (Q=3.79, P = 0.925), and few inconsistency in local inconsistency.	The treatment effects were not significantly influenced by clinical modifiers in the subgroup analyses.	The comparison-adjusted funnel plot for the network is not suggestive of any dominant publication bias.	Moderate (Downgrade by one level due to study limitation)

Note: WMD: weighted mean difference; DPP4: dipeptidyl-peptidase IV inhibitors; GLP1RA: glucagon-like peptide-1 receptor agonists; INS: insulin; Met: metformin; SGLT2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinediones; aGlu: alpha-glucosidase. The item impression was judged by CINeMA: Confidence in Network Meta-Analysis [Software]. Institute of Social and Preventive Medicine, University of Bern, 2017. Available from cinema.ispm.ch

Supplementary File 14

Subgroup network meta-analyses for weight, body mass index and waist circumference compared with placebo

Table S8.1 Subgroup network meta-analyses compared with placebo: weight

Characteristics (No. of studies)	DPP-4I	GLP-1RA	Insulin	Metformin	SGLT-2	SU	TZD	a-Glu
All trials (262)	0.31 (0.05,0.58)	-1.34 (-1.60,-1.00)	2.42 (1.96,2.89)	-0.79 (-1.52,-0.07)	-2.23 (-3.27,-1.19)	1.84 (1.40,2.28)	2.15 (1.53,2.77)	-0.26 (-1.10,0.58)
Mean age								
≤60 years(208)	0.49 (0.19,0.79)	-1.23 (-1.51,-0.90)	2.63 (2.13,3.12)	-0.75 (-1.56,0.06)	-2.12 (-3.16,-1.07)	2.12 (1.64,2.60)	2.28 (1.63,2.92)	-0.12 (-1.17,0.93)
>60 years (50)	-0.33 (-0.84,0.19)	-1.88 (-2.54,-1.2)	1.11 (-0.05,2.27)	-1.01 (-2.41,0.39)	NA	0.36 (-0.64,1.35)	1.66 (-0.21,3.53)	-0.91 (-2.14,0.32)
DM duration								
≤5 years (48)	0.51 (-0.04,1.07)	-1.03 (-1.67,-0.39)	3.14 (1.68,4.60)	-0.80 (-1.77,0.16)	NA	1.45 (0.11,2.79)	1.35 (0.26,2.43)	-0.40 (-2.45,1.66)
5-10 years (117)	0.43 (0.05,0.82)	-1.26 (-1.61,-0.90)	2.69 (2.07,3.30)	-1.37 (-3.23,0.48)	-2.30 (-3.76,-0.84)	1.98 (1.41,2.54)	3.58 (2.55,4.60)	-0.46 (-1.75,0.83)
>10 years (24)	-0.16 (-0.96,0.63)	-1.63 (-2.18,-1.08)	1.12 (-0.02,2.25)	NA	NA	0.93 (-0.49,2.36)	NA	0.84 (-3.42,5.09)
Mean HbA1c								
≤7.5% (39)	-0.28 (-1.33,0.77)	-1.82 (-2.96,-0.68)	2.34 (0.31,4.36)	0.45 (-2.35,3.25)	NA	1.06 (-0.27,2.40)	1.71 (-1.12,4.54)	-0.36 (-2.17,1.45)
7.5%-8.0% (63)	0.34 (-0.03,0.72)	-1.07 (-1.49,-0.64)	1.75 (0.85,2.64)	-1.23 (-2.34,-0.13)	-2.57 (-4.05,-1.09)	2.22 (1.54,2.90)	1.99 (0.60,3.37)	-0.64 (-1.86,0.59)
8.0%-8.5% (89)	0.22 (-0.23,0.68)	-1.32 (-1.70,-0.95)	2.33 (1.70,2.96)	-0.47 (-1.71,0.77)	NA	2.08 (1.30,2.87)	2.83 (2.05,3.60)	-0.13 (-2.03,1.77)
>8.5% (43)	0.87 (-0.02,1.75)	-1.32 (-2.25,-0.39)	3.55 (2.10,4.99)	-0.83 (-2.95,1.29)	-1.53 (-4.64,1.57)	2.55 (0.93,4.18)	0.45 (-1.51,2.40)	-0.43 (-3.45,2.58)

Trial duration								
≤24 weeks (148)	0.48 (0.23,0.74)	-1.05 (-1.31,-0.79)	3.05 (2.32,3.78)	-0.05 (-0.82,0.72)	-2.00 (-3.07,-0.92)	1.13 (0.53,1.73)	2.35 (1.62,3.08)	-0.22 (-0.87,0.44)
24-48 weeks (60)	0.04 (-0.68,0.77)	-1.77 (-2.30,-1.24)	1.89 (1.12,2.66)	-0.98 (-2.62,0.65)	-2.60 (-4.24,-0.96)	1.61 (0.50,2.71)	1.18 (0.14,2.21)	NA
>48 weeks (54)	-0.07 (-0.87,0.73)	-1.79 (-2.73,-0.85)	1.97 (0.61,3.33)	-2.38 (-4.24,-0.52)	NA	1.91 (0.92,2.91)	4.67 (2.46,6.88)	0.93 (-3.70,5.56)
Sample size								
≤500 (202)	0.37 (0.03,0.70)	-1.35 (-1.67,-1.03)	2.54 (1.93,3.16)	-0.77 (-1.74,0.21)	-2.02 (-3.80,-0.25)	1.91 (1.29,2.53)	2.22 (1.36,3.08)	-0.07 (-1.05,0.92)
>500 (60)	0.20 (-0.24,0.64)	-1.34 (-1.80,-0.89)	2.24 (1.54,2.95)	-0.82 (-1.90,0.26)	-2.41 (-3.57,-1.26)	1.74 (1.11,2.36)	2.09 (1.22,2.95)	-1.10 (-2.99,0.79)
Sponsors								
With industry (190)	0.36 (0.07,0.65)	-1.25 (-1.53,-0.98)	2.41 (1.91,2.92)	-1.00 (-1.85,-0.14)	-2.03 (-3.28,-0.79)	1.94 (1.46,2.42)	2.25 (1.54,2.95)	-0.49 (-1.59,0.62)
Unclear & without industry (72)	0.06 (-0.59,0.71)	-1.91 (-2.61,-1.21)	2.49 (1.25,3.72)	-0.44 (-1.90,1.01)	-2.72 (-4.64,-0.80)	1.34 (0.13,2.55)	1.73 (0.36,3.10)	-0.15 (-1.52,1.23)

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinedione; a-Glu: alpha-glucosidase; NA: not available.

Table S8.2 Subgroup network meta-analyses compared with placebo: body mass index

Characteristics (No. of studies)	**DPP-4I**	**GLP-1RA**	**Insulin**	**Metformin**	**SU**	**TZD**	**a-Glu**
All trials (91)	-0.11 (-0.40,0.17)	-1.10 (-1.42,-0.78)	0.25 (-0.19,0.69)	-0.47 (-1.09,0.15)	0.58 (0.08,1.08)	0.14 (-0.56,0.84)	-0.43 (-1.08,0.23)

Mean age							
≤60 years(56)	-0.09 (-0.49,0.32)	-1.11 (-1.51,-0.71)	0.39 (-0.16,0.95)	-0.51 (-1.27,0.25)	0.60 (-0.02,1.23)	-0.05 (-0.98,0.87)	-0.45 (-1.66,0.75)
>60 years (29)	0.06 (-0.19,0.32)	-0.56 (-1.00,-0.13)	-0.19 (-0.66,0.28)	-0.14 (-0.68,0.40)	0.43 (-0.01,0.87)	0.82 (0.35,1.30)	-0.27 (-0.63,0.09)
DM duration							
≤5 years (11)	0.08 (-1.30,1.47)	-0.75 (-1.75,0.25)	0.96 (-0.81,2.74)	-0.19 (-1.65,1.27)	0.08 (-3.43,3.59)	NA	0.32 (-2.30,2.95)
5-10 years (28)	-0.03 (-0.47,0.40)	-1.10 (-1.54,-0.66)	0.54 (-0.11,1.20)	-0.43 (-1.61,0.75)	0.88 (-0.01,1.76)	NA	-0.03 (-2.40,2.34)
>10 years (12)	-0.05 (-0.88,0.79)	-1.08 (-2.13,-0.03)	-0.16 (-1.36,1.03)	NA	-0.02 (-2.09,2.05)	NA	NA
Mean HbA1c							
≤7.5% (25)	-0.25 (-0.77,0.26)	-1.53 (-2.56,-0.51)	-0.37 (-1.79,1.04)	NA	-0.00 (-1.04,1.03)	0.51 (-0.60,1.61)	-0.62 (-1.38,0.13)
7.5%-8.0% (15)	-0.32 (-1.11,0.47)	-1.31 (-2.07,-0.55)	-0.11 (-1.20,0.99)	-1.57 (-3.03,-0.11)	0.66 (-0.62,1.95)	NA	-0.52 (-2.36,1.32)
8.0%-8.5% (29)	-0.10 (-0.41,0.21)	-0.87 (-1.19,-0.55)	0.57 (0.13,1.01)	0.01 (-0.61,0.63)	0.36 (-0.46,1.19)	0.17 (-0.43,0.77)	NA
>8.5% (12)	0.69 (-0.91,2.30)	-1.15 (-3.14,0.84)	0.45 (-2.03,2.94)	-0.21 (-3.61,3.18)	1.21 (-1.29,3.71)	NA	-0.08 (-3.78,3.63)
Trial duration							
≤24 weeks (49)	-0.08 (-0.44,0.28)	-1.03 (-1.51,-0.56)	-0.12 (-0.84,0.60)	-0.34 (-1.25,0.57)	0.32 (-0.46,1.10)	0.68 (-0.37,1.73)	-0.40 (-1.02,0.22)
24-48 weeks (23)	-0.42 (-0.86,0.01)	-0.75 (-1.03,-0.48)	0.96 (0.62,1.30)	0.66 (0.02,1.30)	0.06 (-0.36,0.49)	0.35 (-0.07,0.77)	NA

>48 weeks (19)	-0.29 (-0.87,0.30)	-1.24 (-1.99,-0.49)	-0.27 (-1.32,0.78)	-1.10 (-2.31,0.10)	1.33 (-0.01,2.67)	NA	NA
Sample size						NA	NA
≤500 (80)	-0.08 (-0.38,0.21)	-1.19 (-1.55,-0.83)	0.22 (-0.31,0.75)	-0.22 (-0.92,0.48)	0.73 (0.18,1.28)	0.27 (-0.57,1.12)	-0.40 (-1.07,0.26)
>500 (11)	0.26 (-0.84,1.35)	-0.99 (-1.64,-0.35)	0.33 (-0.43,1.08)	-1.25 (-2.36,-0.15)	-0.25 (-1.34,0.83)	-0.12 (-1.21,0.97)	NA
Sponsors							NA
With industry (31)	-0.05 (-0.69,0.60)	-0.87 (-1.45,-0.30)	0.54 (-0.23,1.31)	-1.13 (-2.72,0.45)	0.93 (-0.04,1.91)	0.00 (-1.57,1.58)	-0.35 (-1.95,1.25)
Unclear & without industry (60)	-0.18 (-0.48,0.11)	-1.33 (-1.72,-0.95)	-0.06 (-0.61,0.49)	-0.34 (-0.93,0.26)	0.39 (-0.17,0.94)	0.11 (-0.57,0.79)	-0.54 (-1.18,0.10)

Table S8.3 Subgroup network meta-analyses compared with placebo: waist circumference

Characteristics (No. of studies)	**DPP-4I**	**GLP-1RA**	**Insulin**	**Metformin**	**SGLT-2**	**SU**	**TZD**	**a-Glu**
All trials (56)	0.37 (-0.15,0.88)	-1.28 (-1.69,-0.86)	2.36 (1.59,3.13)	2.16 (0.70,3.62)	-1.57 (-2.74,-0.40)	2.12 (0.90,3.33)	1.13 (0.01,2.24)	3.14 (-1.28,7.57)
Mean age								
≤60 years(43)	0.49 (-0.17,1.14)	-1.19 (-1.65,-0.73)	2.51 (1.68,3.34)	2.16 (0.64,3.68)	-1.51 (-2.78,-0.24)	2.22 (0.90,3.54)	1.24 (0.06,2.42)	5.86 (-0.39,12.11)
>60 years (11)	0.37 (-0.20,0.94)	-2.16 (-3.72,-0.61)	-0.76 (-5.80,4.28)	NA	NA	NA	NA	0.47 (-5.71,6.64)
DM duration								
≤5 years (11)	2.40	-0.84	NA	4.26	NA	NA	1.88	6.21

	(-6.42,11.22)	(-1.86,0.17)		(2.14,6.38)			(-1.37,5.14)	(-0.16,12.57)
5-10 years (26)	0.47 (-0.26,1.20)	-1.22 (-1.79,-0.65)	2.78 (1.75,3.80)	-1.92 (-4.86,1.02)	NA	2.20 (0.84,3.56)	0.88 (-0.73,2.49)	0.57 (-5.73,6.87)
>10 years (6)	0.35 (-0.94,1.64)	-1.22 (-2.05,-0.38)	-4.22 (-13.79,5.36)	NA	NA	NA	NA	NA
Mean HbA1c								
≤8.0% (21)	0.55 (-0.31,1.41)	-1.30 (-1.96,-0.65)	1.43 (-2.14,4.99)	-2.00 (-4.88,0.88)	NA	2.65 (1.11,4.18)	1.42 (-1.51,4.36)	0.65 (-5.64,6.93)
>8.0% (31)	0.20 (-0.53,0.93)	-1.44 (-2.05,-0.83)	2.22 (1.33,3.12)	3.06 (1.43,4.69)	NA	1.51 (-0.35,3.36)	0.93 (-0.33,2.19)	5.61 (-0.63,11.85)
Trial duration								
≤24 weeks (32)	0.45 (0.04,0.86)	-1.08 (-1.52,-0.63)	2.67 (0.47,4.87)	-1.31 (-3.52,0.90)	-1.53 (-2.09,-0.98)	1.54 (0.04,3.04)	1.09 (0.09,2.10)	3.29 (-1.06,7.63)
24-48 weeks (14)	0.30 (-0.81,1.41)	-1.04 (-1.91,-0.16)	2.61 (1.53,3.68)	4.06 (2.45,5.68)	NA	NA	1.60 (-0.08,3.28)	NA
>48 weeks (10)	-0.78 (-2.27,0.70)	-2.32 (-3.54,-1.10)	1.36 (-1.44,4.17)	NA	NA	1.32 (-1.11,3.75)	NA	NA
Sample size								
≤500 (47)	0.41 (-0.18,1.00)	-1.23 (-1.66,-0.80)	2.57 (1.67,3.48)	2.39 (0.89,3.90)	NA	1.66 (-0.05,3.37)	1.51 (0.11,2.91)	3.19 (-1.21,7.58)
>500 (9)	0.01 (-1.59,1.61)	-1.70 (-3.34,-0.06)	1.73 (-0.48,3.94)	NA	-1.74 (-3.65,0.16)	2.11 (-0.52,4.74)	0.40 (-2.29,3.09)	NA
Sponsors								
With industry (32)	0.44 (-0.10,0.99)	-1.25 (-1.69,-0.81)	2.35 (1.52,3.19)	-1.95 (-4.80,0.91)	-1.53 (-2.58,-0.48)	2.54 (1.13,3.96)	0.97 (-0.36,2.30)	NA
Unclear & without	0.22	-1.41	2.44	2.88	NA	1.54	1.36	3.00

industry (24)	(-1.02,1.47)	(-2.47,-0.35)	(0.65,4.23)	(0.58,5.17)	(-0.66,3.75)	(-0.90,3.63)	(-1.56,7.57)

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinedione; a-Glu: alpha-glucosidase; NA: not available.

Supplementary File 15

Meta-regression for network meta-analyses compared with placebo

Table S9.1 Results of univariate meta-regression: weight

Variables (No. of studies) Scale	Comparison	Regression coefficient (95% CI)	Standard error	P value
Age	DPP-4I VS Placebo	-0.49 (-1.06,0.08)	0.29	0.09
(260)	GLP-1RA VS Placebo	0.18 (-0.43,0.79)	0.31	0.57
Per 10 years	Insulin VS Placebo	-0.59 (-2.12,0.94)	0.78	0.94
	Met VS Placebo	0.24 (-1.22,1.69)	0.74	0.75
	SGLT-2 VS Placebo	-6.41 (-39.26,26.45)	16.76	0.70
	SU VS Placebo	**-1.00 (-1.98,-0.02)**	0.50	0.05
	TZD VS Placebo	0.89 (-1.34,3.12)	1.14	0.43
	a-Glu VS Placebo	0.26 (-1.79,2.30)	1.04	0.81
HbA1c	DPP-4I VS Placebo	**0.52 (0.05,0.99)**	0.24	0.03
(237)	GLP-1RA VS Placebo	0.02 (-0.00,0.04)	0.01	0.10
Per 1%	Insulin VS Placebo	0.65 (-0.04,1.35)	0.36	0.07
	Met VS Placebo	-0.36 (-1.90,1.19)	0.79	0.65
	SGLT-2 VS Placebo	0.97 (-1.90,3.84)	1.46	0.51
	SU VS Placebo	0.76 (-0.19,1.70)	0.48	0.12
	TZD VS Placebo	-1.22 (-2.95,0.52)	0.88	0.17
	a-Glu VS Placebo	0.08 (-1.14,1.57)	0.76	0.92
DM duration	DPP-4I VS Placebo	-0.06 (-0.14,0.02)	0.04	0.12
(205)	GLP-1RA VS Placebo	**-0.08 (-0.15,-0.01)**	0.03	0.02
Per 1 years	Insulin VS Placebo	**-0.22 (-0.40,-0.05)**	0.09	0.01
	Met VS Placebo	0.49 (-0.20,1.17)	0.35	0.16
	SGLT-2 VS Placebo	0.52 (-2.63,3.68)	1.61	0.75
	SU VS Placebo	-0.11 (-0.25,0.04)	0.07	0.14
	TZD VS Placebo	**0.59 (0.28,0.89)**	0.16	0.00
	a-Glu VS Placebo	0.08 (-0.28,0.43)	0.18	0.67

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinedione; a-Glu: alpha-glucosidase.

Table S9.2 Results of multivariate meta-regression in 190 studies: weight

Comparison	Variables	Scale	Regression coefficient (95% CI)	Standard error	P value
DPP-4I VS Placebo	Age	Per 10 years	-0.19 (-1.22,0.85)	0.53	0.72
	HbA1c	Per 1%	0.25 (-0.41,0.90)	0.33	0.46
	DM duration	Per 1 years	-0.04 (-0.15,0.06)	0.06	0.42
GLP-1RA VS Placebo	Age	Per 10 years	**0.70 (0.00,1.40)**	0.36	0.05
	HbA1c	Per 1%	0.20 (-0.49,0.89)	0.35	0.58
	DM duration	Per 1 years	**-0.11 (-0.19,-0.04)**	0.04	0.00
Insulin VS Placebo	Age	Per 10 years	2.57 (-0.77,5.90)	1.70	0.13
	HbA1c	Per 1%	**1.46 (0.29,2.62)**	0.60	0.01
	DM duration	Per 1 years	**-0.41 (-0.69,-0.13)**	0.14	0.01
Met VS Placebo	Age	Per 10 years	0.37 (-1.42,2.16)	0.91	0.69
	HbA1c	Per 1%	-0.37 (-2.11,1.37)	0.89	0.67
	DM duration	Per 1 years	0.43 (-0.28,1.14)	0.36	0.23
SGLT-2 VS Placebo	Age	Per 10 years	NA	NA	NA
	HbA1c	Per 1%	0.73 (-1.93,3.39)	1.36	0.59
	DM duration	Per 1 years	NA	NA	NA
SU VS Placebo	Age	Per 10 years	-1.05 (-2.47,0.37)	0.72	0.15
	HbA1c	Per 1%	-0.18 (-1.28,0.93)	0.56	0.76
	DM duration	Per 1 years	-0.05 (-0.22,0.12)	0.09	0.58
TZD VS Placebo	Age	Per 10 years	-4.89 (-11.41,1.63)	3.32	0.14
	HbA1c	Per 1%	-3.01 (-6.57,0.55)	1.82	0.10
	DM duration	Per 1 years	**0.65 (0.25,1.05)**	0.20	0.00
a-Glu VS Placebo	Age	Per 10 years	2.97 (-3.18,9.12)	3.14	0.34

	HbA1c	Per 1%	1.59 (-1.93,5.11)	1.80	0.38
	DM duration	Per 1 years	-0.15 (-0.76,0.46)	0.31	0.64

Note: DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinedione; a-Glu: alpha-glucosidase; NA: not available.

Table S9.3 Results of network meta analysis before and after regression: weight

Comparison	Before adjustment	Age	HbA1c	DM duration	Age/HbA1c/DM duration
DPP-4I	**0.31**	**0.28**	**0.56**	**0.33**	**0.47**
VS Placebo	**(0.05,0.58)**	**(0.01,0.56)**	**(0.22,0.91)**	**(0.03,0.62)**	**(0.08,0.86)**
GLP-1RA	**-1.34**	**-1.30**	**-1.29**	**-1.25**	**-1.03**
VS Placebo	**(-1.60,-1.09)**	**(-1.56,-1.04)**	**(-1.57,-1.02)**	**(-1.51,-0.98)**	**(-1.43,-0.63)**
Insulin	**2.42**	**2.50**	**2.65**	**2.73**	**3.28**
VS Placebo	**(1.96,2.89)**	**(2.02,2.98)**	**(2.13,3.17)**	**(2.18,3.29)**	**(2.59,3.97)**
Met	**-0.79**	**-0.87**	-0.92	1.13	0.76
VS Placebo	**(-1.52,-0.07)**	**(-1.60,-0.14)**	(-1.88,0.05)	(-1.72,3.98)	(-2.46,3.97)
SGLT-2	**-2.23**	-3.43	**-2.03**	**-2.21**	**-2.11**
VS Placebo	**(-3.27,-1.19)**	(-9.56,2.71)	**(-3.62,-0.45)**	**(-3.91,-0.51)**	**(-3.58,-0.64)**
SU	**1.84**	**1.84**	**2.35**	**1.77**	**1.86**
VS Placebo	**(1.40,2.28)**	**(1.39,2.30)**	**(1.65,3.06)**	**(1.30,2.25)**	**(1.13,2.59)**
TZD	**2.15**	**2.37**	**2.06**	**4.01**	**2.69**
VS Placebo	**(1.53,2.77)**	**(1.62,3.12)**	**(1.34,2.79)**	**(2.95,5.07)**	**(0.82,4.56)**
a-Glu	-0.26	-0.45	-0.39	-0.14	0.05
VS Placebo	(-1.10,0.58)	(-1.40,0.49)	(-1.90,1.12)	(-1.46,1.18)	(-2.10,2.20)

Table S9.4 Ranking probability after meta-regression

Treatment	Weight	
	SUCRA	Rank
Placebo	57.4	3
DPP-4I	56.6	4
GLP-1RA	64.1	2
Insulin	3.0	9
Met	52.6	6
SGLT-2	93.2	1
SU	27.5	8
TZD	55.8	5
a-Glu	39.8	7

Note: Results were reported after the meta-regression of age, HbA1c and DM duration. DPP-4I: dipeptidyl-peptidase IV inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; Met: metformin; SGLT-2: sodium-glucose co-transporter 2; SU: sulphanylureas; TZD: thiazolidinedione; a-Glu: alpha-glucosidase.