

Supplementary Appendix

Comparative effectiveness of GLP-1 receptor agonists on glycemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis

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Appendix 1: Search strategy

Table S1. Search strategy of PubMed

[illegible]

4	(((((IFG[Title/Abstract]) OR (impaired FPG[Title/Abstract])) OR (glucose intolerance[Title/Abstract]))) OR (IGT[Title/Abstract]) OR (impaired glucose[Title/Abstract]))
5	#1 OR #2
6	#3 OR #4
7	#5 AND #6
8	(((((meta analysis[MeSH Terms]) OR (meta analysis as topic[MeSH Terms])) OR (meta analysis[Publication Type])) OR (review[Publication Type])) OR (meta-analysis[Title/Abstract]))
9	#7 NOT #8
10	((((((((((((randomized controlled trial[Publication Type]) OR (controlled clinical trial[Publication Type])) OR (clinical trials as topic[MeSH Terms])) OR (random allocation[MeSH Terms])) OR (randomized controlled trials as topic[MeSH Terms])) OR (clinical trial[Publication Type])) OR (clinical trial[Text Word])) OR (singl*[Text Word])) OR (doubl*[Text Word])) OR (trebl*[Text Word])) OR (tripl*[Text Word])) OR (randomly[Text Word])) OR (trial[Text Word]))
11	#9 AND #10

Table S3. Search strategy of Cochrane Central Register of Controlled Trials
(CENTRAL)

#	Searches
1	(GLP-1 receptor agonist*):ti,ab,kw OR (Glucagon-like peptide-1 agonis*):ti,ab,kw OR (Incretin mimeti*):ti,ab,kw OR (GLP-1 analo*):ti,ab,kw OR ("Glucagon-Like Peptide 1"):ti,ab,kw OR ("glucagon like peptide 1 receptor"):ti,ab,kw OR ("GLP-1"):ti,ab,kw (Word variations have been searched)
2	("liraglutide"):ti,ab,kw OR ("semaglutide"):ti,ab,kw OR ("tirzepatide"):ti,ab,kw OR ("exenatide"):ti,ab,kw OR ("beinaglutide"):ti,ab,kw
3	("dulaglutide"):ti,ab,kw OR ("Albiglutide"):ti,ab,kw OR ("Lixisenatide"):ti,ab,kw OR ("loxenatide"):ti,ab,kw OR ("PEX168"):ti,ab,kw
4	("Mazdutide"):ti,ab,kw OR ("IBI362"):ti,ab,kw OR ("LY3305677"):ti,ab,kw OR ("ITCA 650"):ti,ab,kw OR ("PB-119"):ti,ab,kw
5	("PEGylated exenatide"):ti,ab,kw OR ("Orforglipron"):ti,ab,kw OR ("Retatrutide"):ti,ab,kw OR ("CagriSema"):ti,ab,kw
6	("LY3437943"):ti,ab,kw OR ("LY3502970"):ti,ab,kw OR ("LY-3502970"):ti,ab,kw OR ("OWL 833"):ti,ab,kw OR ("PEG-exenatide"):ti,ab,kw
7	("PB119"):ti,ab,kw OR ("Presendin"):ti,ab,kw OR ("Exendin-4"):ti,ab,kw OR ("EX-4"):ti,ab,kw OR ("AC-2993"):ti,ab,kw
8	("AC-2993-LAR"):ti,ab,kw OR ("LY-2148568"):ti,ab,kw OR ("LY2148568"):ti,ab,kw OR ("Byetta"):ti,ab,kw OR ("Bydureon"):ti,ab,kw
9	("IBI-362"):ti,ab,kw OR ("IBI362"):ti,ab,kw OR ("OXM-3"):ti,ab,kw OR ("OXM3"):ti,ab,kw OR ("LY3305677"):ti,ab,kw
10	("LY-3305677"):ti,ab,kw OR ("Polyethylene Glycol Loxenatide"):ti,ab,kw OR ("PEG loxenatide"):ti,ab,kw OR ("pegloxenatide"):ti,ab,kw OR ("PEX-168"):ti,ab,kw
11	("LAPS-Exendin"):ti,ab,kw OR ("Langlenatide"):ti,ab,kw OR ("LAPS-exendin 4 analogue"):ti,ab,kw OR ("LAPSCA-Exendin4"):ti,ab,kw OR ("LAPS-Exendin4"):ti,ab,kw
12	("LAPS-EXD4"):ti,ab,kw OR ("HM-11260C"):ti,ab,kw OR ("SAR-439977"):ti,ab,kw OR ("ZP-10"):ti,ab,kw OR ("AQVE-10010"):ti,ab,kw
13	("AVE0100"):ti,ab,kw OR ("AVE-0010"):ti,ab,kw OR ("ZP10A PEPTIDE"):ti,ab,kw OR ("Lyxumia"):ti,ab,kw OR ("Adlyxin"):ti,ab,kw
14	("GSK-716155"):ti,ab,kw OR ("PGC-GLP-1"):ti,ab,kw OR ("Tanzeum"):ti,ab,kw OR ("Eperzan"):ti,ab,kw OR ("Syncria"):ti,ab,kw
15	("Albugon"):ti,ab,kw OR ("LY-3298176"):ti,ab,kw OR ("Mounjaro"):ti,ab,kw OR ("NN-9535"):ti,ab,kw OR ("NN-9536"):ti,ab,kw
16	("NN-9931"):ti,ab,kw OR ("NN9924"):ti,ab,kw OR ("Ozempic"):ti,ab,kw OR ("Rybelsus"):ti,ab,kw
17	("Wegovy"):ti,ab,kw OR ("GLP-fc"):ti,ab,kw OR ("LY-2189265"):ti,ab,kw OR ("LY 2189265"):ti,ab,kw
18	("Trulicity"):ti,ab,kw OR ("NN-2211"):ti,ab,kw OR ("NN-9211"):ti,ab,kw OR ("NN-8022"):ti,ab,kw
19	("NNC-901170"):ti,ab,kw OR ("NN 9211"):ti,ab,kw OR ("NN 2211"):ti,ab,kw OR ("LATIN T1D"):ti,ab,kw
20	("Saxenda"):ti,ab,kw OR ("SAXE"):ti,ab,kw OR ("Victoza"):ti,ab,kw
21	#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
22	("type 2 diabetes"):ti,ab,kw OR (diabetes mellitus, type 2):ti,ab,kw OR (diabetes, type 2):ti,ab,kw OR ("type 2 diabetes mellitus"):ti,ab,kw OR (type II):ti,ab,kw
23	(T2D):ti,ab,kw OR ("NIDDM"):ti,ab,kw OR (hyperglyc*):ti,ab,kw OR (prediabet*):ti,ab,kw OR (type 2):ti,ab,kw
24	MeSH descriptor: [Diabetes Mellitus] explode all trees
25	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees
26	MeSH descriptor: [Hyperglycemia] explode all trees
27	MeSH descriptor: [Prediabetic State] explode all trees
28	(IFG):ti,ab,kw OR (impaired FPG):ti,ab,kw OR ("glucose intolerance"):ti,ab,kw OR (IGT):ti,ab,kw OR (impaired glucose):ti,ab,kw

29	#22 or #23 or #24 or #25 or #26 or #27 or #28
30	#21 and #29
31	("meta analysis"):ti,ab,kw OR ("meta analysis"):pt OR (review):pt
32	#30 not #31
33	("randomized clinical trial"):pt OR ("controlled clinical trial"):pt OR ("clinical trial"):ti,ab,kw OR ("random allocation"):ti,ab,kw OR ("clinical trial"):ti,ab,kw
34	("clinical trial") OR (singl*) OR (doubl*) OR (trebl*) OR ("randomly")
35	(trial*):ti,ab,kw OR (group*):ti,ab,kw
36	#33 or #34 or #35
37	#32 and #36

Table S4. Search strategy of Embase

#	Searches
1	'GLP-1 receptor agonis*' OR " Glucagon-like peptide-1 agonis*":ti,ab,kw OR " Incretin mimeti*":ti,ab,kw OR " GLP-1 analo*":ti,ab,kw OR " Glucagon-Like Peptide 1*":ti,ab,kw OR " glucagon like peptide 1 receptor*":ti,ab,kw
2	liraglutide:ti,ab,kw OR semaglutide:ti,ab,kw OR tirzepatide:ti,ab,kw OR exenatide:ti,ab,kw OR polyethylene glycol loxenatide:ti,ab,kw OR dulaglutide:ti,ab,kw OR albiglutide:ti,ab,kw OR lixisenatide:ti,ab,kw OR loxenatide:ti,ab,kw liraglutide:ti,ab,kw OR semaglutide:ti,ab,kw OR tirzepatide:ti,ab,kw OR exenatide:ti,ab,kw OR polyethylene glycol loxenatide:ti,ab,kw OR dulaglutide:ti,ab,kw OR albiglutide:ti,ab,kw OR lixisenatide:ti,ab,kw OR loxenatide:ti,ab,kw OR PEX168:ti,ab,kw OR Mazdutide:ti,ab,kw OR IBI362:ti,ab,kw OR LY3305677:ti,ab,kw OR ITCA 650:ti,ab,kw OR PB-119:ti,ab,kw OR PEGylated exenatide:ti,ab,kw OR Orforglipron:ti,ab,kw OR Retatrutide:ti,ab,kw OR CagriSema:ti,ab,kw OR LY3437943:ti,ab,kw OR LY3502970:ti,ab,kw OR LY-3502970:ti,ab,kw OR OWL 833:ti,ab,kw OR PEG-exenatide:ti,ab,kw OR PB119:ti,ab,kw OR Presendin:ti,ab,kw OR Exendin-4:ti,ab,kw OR EX-4:ti,ab,kw OR AC-2993:ti,ab,kw OR AC-2993-LAR:ti,ab,kw OR LY-2148568:ti,ab,kw OR LY2148568:ti,ab,kw OR Byetta:ti,ab,kw OR Bydureon:ti,ab,kw OR IBI-362:ti,ab,kw OR OXM-3:ti,ab,kw OR OXM3:ti,ab,kw OR LY3305677:ti,ab,kw OR LY-3305677:ti,ab,kw OR Polyethylene Glycol Loxenatide:ti,ab,kw OR PEG loxenatide:ti,ab,kw OR pegloxenatide:ti,ab,kw OR PEX-168:ti,ab,kw OR LAPS-Exendin:ti,ab,kw OR Langlenatide:ti,ab,kw OR LAPS-exendin 4 analogue:ti,ab,kw OR LAPSCA-Exendin4:ti,ab,kw OR LAPS-Exendin4:ti,ab,kw OR LAPS-EXD4:ti,ab,kw OR HM-11260C:ti,ab,kw OR SAR-439977:ti,ab,kw OR ZP-10:ti,ab,kw OR AQVE-10010:ti,ab,kw OR AVE0100:ti,ab,kw OR AVE-0010:ti,ab,kw OR ZP10A PEPTIDE:ti,ab,kw OR Lyxumia:ti,ab,kw OR Adlyxin:ti,ab,kw OR GSK-716155:ti,ab,kw OR PGC-GLP-1:ti,ab,kw OR Tanzeum:ti,ab,kw OR Eperzan:ti,ab,kw OR Syncria:ti,ab,kw OR Albugon:ti,ab,kw OR LY-3298176:ti,ab,kw OR Mounjaro:ti,ab,kw OR NN-9535:ti,ab,kw OR NN-9536:ti,ab,kw OR NN-9931:ti,ab,kw OR NN9924:ti,ab,kw OR NNC-0113-0217:ti,ab,kw OR Ozempic:ti,ab,kw OR Rybelsus:ti,ab,kw OR Wegovy:ti,ab,kw OR GLP-fc:ti,ab,kw OR LY-2189265:ti,ab,kw OR GLP-1-FC:ti,ab,kw OR LY 2189265:ti,ab,kw OR Trulicity:ti,ab,kw OR NN-2211:ti,ab,kw OR NN-9211:ti,ab,kw OR NNC-90-1170:ti,ab,kw OR NN-8022:ti,ab,kw OR NNC-901170:ti,ab,kw OR NNC 90-1170:ti,ab,kw OR NN 9211:ti,ab,kw OR NN 2211:ti,ab,kw OR LATIN T1D:ti,ab,kw OR Saxenda:ti,ab,kw OR SAXE:ti,ab,kw OR Victoza:ti,ab,kw
3	'liraglutide'/exp OR 'semaglutide'/exp OR 'tirzepatide'/exp OR 'exenatide'/exp OR 'beinaglutide'/exp OR 'dulaglutide'/exp OR 'albiglutide'/exp OR 'lixisenatide'/exp OR 'loxenatide'/exp OR 'Efpeglenatide'/exp OR 'polyethylene glycol loxenatide'/exp OR 'PEX168'/exp OR 'Mazdutide'/exp OR 'IBI362'/exp OR 'LY3305677'/exp OR 'ITCA 650'/exp OR 'PB-119'/exp OR 'PEGylated exenatide'/exp OR 'Orforglipron'/exp OR 'Retatrutide'/exp OR 'CagriSema'/exp OR 'LY3437943'/exp OR 'LY3502970'/exp OR 'LY-3502970'/exp OR 'OWL 833'/exp OR 'PEG-exenatide'/exp OR 'PB119'/exp OR 'Presendin'/exp OR 'Exendin-4'/exp OR 'EX-4'/exp OR 'AC-2993'/exp OR 'AC-2993-LAR'/exp OR 'LY-2148568'/exp OR 'LY2148568'/exp OR 'Byetta'/exp OR 'Bydureon'/exp OR 'IBI-362'/exp OR 'OXM-3'/exp OR 'OXM3'/exp OR 'LY3305677'/exp OR 'LY-3305677'/exp OR 'Polyethylene Glycol Loxenatide'/exp OR 'PEG loxenatide'/exp OR 'pegloxenatide'/exp OR 'PEX-168'/exp OR 'LAPS-Exendin'/exp OR 'Langlenatide'/exp OR 'LAPS-exendin 4 analogue'/exp OR 'LAPSCA-Exendin4'/exp OR 'LAPS-Exendin4'/exp OR 'LAPS-EXD4'/exp OR 'HM-11260C'/exp OR 'SAR-439977'/exp OR 'ZP-10'/exp OR 'AQVE-10010'/exp OR 'AVE0100'/exp OR 'AVE-0010'/exp OR 'ZP10A PEPTIDE'/exp OR 'Lyxumia'/exp OR 'Adlyxin'/exp OR 'GSK-716155'/exp OR 'PGC-GLP-1'/exp OR 'Tanzeum'/exp OR 'Eperzan'/exp OR 'Syncria'/exp OR 'Albugon'/exp OR 'LY-3298176'/exp OR 'Mounjaro'/exp OR 'NN-9535'/exp OR 'NN-9536'/exp OR 'NN-9931'/exp OR 'NN9924'/exp OR 'NNC-0113-0217'/exp OR 'Ozempic'/exp OR 'Rybelsus'/exp OR 'Wegovy'/exp OR 'GLP-fc'/exp OR 'LY-2189265'/exp OR 'GLP-1-FC'/exp OR 'LY

	2189265'/exp OR 'Trulicity'/exp OR 'NN-2211'/exp OR 'NN-9211'/exp OR 'NNC-90-1170'/exp OR 'NN-8022'/exp OR 'NNC-901170'/exp OR 'NNC 90-1170'/exp OR 'NN 9211'/exp OR 'NN 2211'/exp OR 'LATIN T1D'/exp OR 'Saxenda'/exp OR 'SAXE'/exp OR Victoza
4	'type 2 diabetes':ti,ab,kw OR 'diabetes mellitus, type 2':ti,ab,kw OR 'diabetes, type 2':ti,ab,kw OR 'type 2 diabetes mellitus':ti,ab,kw OR 't2d':ti,ab,kw OR 'niddm':ti,ab,kw OR 'hyperglycemia':ti,ab,kw OR 'prediabetes':ti,ab,kw
5	ifg:ti,ab,kw OR 'impaired glucose':ti,ab,kw OR 'impaired fpg':ti,ab,kw OR 'glucose intolerance':ti,ab,kw OR igt:ti,ab,kw
6	#1 OR #2 OR #3
7	#4 OR #5
8	#6 AND #7
9	review:it OR 'meta analysis':ti,ab,kw
10	#8 NOT #9
11	'controlled clinical trial'/exp OR 'randomized controlled trial':ti,ab,kw OR 'clinical study'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'placebo'/exp OR singl* OR doubl* OR trebl* OR tripl* OR randomly
12	#10 AND #11

Appendix 2: Characteristics of included studies

Table S2.1: Baseline of characteristics of included studies

Study	Trial registration	Country and region	Design	Follow-up duration	Number of participants	Randomised treatments	Dose and frequency	Diabetes duration (mean $\pm$ SD), years	Age (mean $\pm$ SD), years	Male %	BMI (mean $\pm$ SD), kg/m ²	HbA1c (mean $\pm$ SD), %	Background hypoglycemic intervention
Ahmadi 2019¹	NCT02113332	Sweden	RCT	24 weeks	122	Placebo:59 liraglutide:63	1.8 mg QD sc	17.0 $\pm$ 8.2 17.3 $\pm$ 7.7	63.6 $\pm$ 7.7 63.8 $\pm$ 8.2	66.1% 63.5%	33.5 $\pm$ 4.0 33.7 $\pm$ 4.3	8.96 $\pm$ 1.10 8.98 $\pm$ 0.99	insulin with/or metformin
Ahmann 2015²	NN2211-3917	Argentina, Canada, Finland, Germany, India, Mexico, the Netherlands, Serbia, USA	RCT	26 weeks	450	Placebo:225 Liraglutide:225	1.8 mg QD sc	12.1 $\pm$ 6.8 12.1 $\pm$ 7.1	57.5 $\pm$ 11.1 59.3 $\pm$ 9.2	60.4% 53.3%	32.2 $\pm$ 5.7 32.3 $\pm$ 5.6	8.30 $\pm$ 0.90 8.20 $\pm$ 0.80	metformin with/or insulin glargine or insulin detemir
Ahren 2014³	NCT00838903	Sweden	RCT	104 weeks	1049	Placebo:104 Sitagliptin:313 Glimepiride:317 Albiglutide:315	100 mg QD po 2 mg QD po 30 mg QW sc	6.7 $\pm$ 6.6 5.8 $\pm$ 4.8 6.0 $\pm$ 4.8 6.0 $\pm$ 4.3	56.1 $\pm$ 10.0 54.3 $\pm$ 9.8 54.4 $\pm$ 10.0 54.3 $\pm$ 10.1	49.5% 46.0% 51.5% 44.7%	32.8 $\pm$ 5.4 32.5 $\pm$ 5.4 32.5 $\pm$ 5.5 32.7 $\pm$ 5.6	8.10 $\pm$ 0.50 8.10 $\pm$ 0.86 8.10 $\pm$ 0.87 8.10 $\pm$ 0.86	metformin
Aroda 2019⁴	NCT02906930	Algeria, Bulgaria, Czech Republic, Japan, Mexico, Russia, Serbia, Turkey, USA	RCT	26 weeks	703	Placebo:178 Semaglutide:175 Semaglutide:175 Semaglutide:175	3 mg QD po 7 mg QD po 14 mg QD po	3.4 $\pm$ 4.6 3.8 $\pm$ 5.3 3.6 $\pm$ 5.1 3.4 $\pm$ 4.4	54 $\pm$ 11 55 $\pm$ 11 56 $\pm$ 11 54 $\pm$ 11	50.0% 50.9% 53.1% 49.1%	32.2 $\pm$ 6.9 31.8 $\pm$ 6.3 31.6 $\pm$ 6.4 31.7 $\pm$ 6.6	7.90 $\pm$ 0.70 7.90 $\pm$ 0.70 8.00 $\pm$ 0.60 8.00 $\pm$ 0.70	none
Blevins 2011⁵	Not provided	USA	RCT	24 weeks	252	Exenatide:129 Exenatide:123	2 mg QW sc 5 μ g BID sc		56 $\pm$ 11 55 $\pm$ 10	60.0% 55.0%	33.6 $\pm$ 5.5 33.0 $\pm$ 5.3		none
Blonde 2020⁶	NCT02964247	India	RCT	26 weeks	302	Placebo:100 Liraglutide:202	1.8 mg QD sc	9.6 $\pm$ 6.7 10.1 $\pm$ 7.2	56.0 $\pm$ 9.9 54.7 $\pm$ 10.1	58.0% 62.0%	32.6 $\pm$ 6.5 32.0 $\pm$ 6.0	8.00 $\pm$ 0.60 8.00 $\pm$ 0.70	SGLT2i and metformin
Buse 2013⁷	NCT01029886	Argentina, Australia, Austria, Belgium, Canada, Czech Republic, France, Germany, Hungary, Israel, Italy, Mexico, Poland, Romania, Slovakia, South Africa, South Korea, Spain, China	RCT	26 weeks	911	Exenatide:461 Liraglutide:450	2 mg QW sc 1.8 mg QD sc	8 $\pm$ 6 9 $\pm$ 6	57 $\pm$ 9.4 57 $\pm$ 9.6	54.0% 55.0%	32.3 $\pm$ 5.6 32.3 $\pm$ 5.4	8.50 $\pm$ 1.00 8.40 $\pm$ 1.00	metformin, pioglitazone, sulfonylurea
Buse 2009⁸	NCT00518882	USA	RCT	26 weeks	464	Exenatide:231 Liraglutide:233	10 μ g BID sc 1.8 mg QD sc	8.5 $\pm$ 6.2 7.9 $\pm$ 5.9	56.3 $\pm$ 9.8 57.1 $\pm$ 10.8	49.0% 55.0%	32.9 $\pm$ 5.5 32.9 $\pm$ 5.7	8.20 $\pm$ 1.00 8.10 $\pm$ 1.00	metformin, sulphonylurea

Capehorn 2020⁹	NN9535-4339	Bulgaria, Czech Republic, Finland, France, Hungary, Italy, Poland, Slovenia, Spain, Sweden, UK	RCT	30 weeks	577	Semaglutide:290 Liraglutide:287	1.0 mg QW sc 1.2 mg QD sc	9.6 ± 6.1 8.9 ± 5.7	60.1 ± 10.5 58.9 ± 10.0	55.2% 58.2%	33.7 ± 6.6 33.7 ± 7.0	8.20 ± 0.90 8.30 ± 1.00	sulfonylurea, metformin and SGLT2i
Davies 2015¹⁰	NCT01272232	France, Germany, Israel, South Africa, Spain, Sweden, Turkey, United Kingdom, England, Scotlandonly, USA	RCT	56 weeks	846	Placebo:212 Liraglutide:423 Liraglutide:211	3.0 mg QD sc 1.8 mg QD sc	6.7 ± 5.07 7.5 ± 5.65 7.4 ± 5.16	54.7 ± 9.8 55.0 ± 10.8 54.9 ± 10.7	45.8% 52.0% 51.2%	37.4 ± 7.1 37.1 ± 6.5 37.0 ± 6.9		metformin, sulfonylurea, glitazone or diet and exercise only
Drucker 2008¹¹	NCT00308139.	Not provided	RCT	30 weeks	295	Exenatide:148 Exenatide:147	2 mg QW sc 10 µg BID sc	7 ± 6 6 ± 5	55 ± 10 55 ± 10	55.0% 51.0%	35 ± 5 35 ± 5	8.30 ± 1.00 8.30 ± 1.00	diet modification and exercise, or pharmacological treatment with metformin, a sulphonylurea, a thiazolidinedione,
Frias 2018¹²	NCT03131687	Poland, Puerto Rico, Slovakia, USA	RCT	26 weeks	316	placebo: 51 LY3298176: 52 LY3298176: 55 LY3298176: 51 LY3298176: 53 Dulaglutide: 54	1mg QW sc 5mg QW sc 10mg QW sc 15mg QW sc 1.5mg QW sc	8.6 ± 7.0 7.8 ± 5.4 8.9 ± 5.7 7.9 ± 5.8 8.5 ± 6.1 9.3 ± 7.1	56.6 ± 8.9 57.4 ± 8.9 57.9 ± 8.2 56.5 ± 9.9 56.0 ± 7.6 58.7 ± 7.8	57.0% 56.0% 62.0% 59.0% 42.0% 44.0%	32.4 ± 6.0 32.9 ± 6.1 32.9 ± 5.7 32.6 ± 5.8 32.2 ± 6.2 32.4 ± 5.4	8.00 ± 0.90 8.20 ± 0.90 8.20 ± 1.00 8.20 ± 1.10 8.10 ± 1.10 8.10 ± 1.00	metformin or other drugs
Frias 2019¹³	NCT31050143	Caucasia, Asia, Africa, USA	RCT	18 weeks	318	Placebo: 82 Dulaglutide: 81 Dulaglutide: 79 Dulaglutide: 76	1.5 mg QW sc 3.0 mg QW sc 4.5 mg QW sc	7.8 ± 7.4 7.9 ± 5.6 7.5 ± 6.0 9.0 ± 5.8	56.5 ± 8.9 57.7 ± 9.8 55.9 ± 10.7 57.1 ± 9.6	59.3% 49.1% 44.3% 47.4%	33.2 ± 6.0 32.2 ± 4.8 34.4 ± 6.0 32.2 ± 5.4	8.10 ± 0.80 8.00 ± 0.80 8.20 ± 0.90 8.10 ± 0.80	metformin
Grunberger 2012¹⁴	Not provided	Multinational	RCT	12 weeks	164	Placebo: 32 Dulaglutide: 35 Dulaglutide: 34 Dulaglutide: 34 Dulaglutide: 29	0.1 mg QW sc 0.5 mg QW sc 1.0 mg QW sc 1.5 mg QW sc	3.9 ± 4.7 3.9 ± 3.2 3.7 ± 3.8 3.3 ± 2.5 4.6 ± 4.1	55.0 ± 9.3 56.3 ± 9.2 56.9 ± 9.1 57.2 ± 8.8 57.5 ± 7.9	56.3% 31.4% 47.1% 47.1% 44.8%	32.1 ± 5.2 32.9 ± 4.8 32.3 ± 5.4 32.2 ± 4.5 31.0 ± 4.3	7.40 ± 0.60 7.10 ± 0.60 7.20 ± 0.60 7.30 ± 0.70 7.30 ± 0.40	metformin
Iwamoto 2009¹⁵	NCT00612794	Japan	RCT	10 weeks	29	Placebo: 10 Exenatide: 10 Exenatide: 9	0.8 mg QW sc 2.0 mg QW sc	7 ± 5 6 ± 6 5 ± 4	61 ± 8 56 ± 11 58 ± 9	40.0% 50.0% 88.9%	26.4 ± 3.3 26.5 ± 2.8 26.1 ± 2.9	7.50 ± 0.90 7.40 ± 0.70 7.30 ± 0.80	none
Ji 2021¹⁶	NCT03520972	China	RCT	12 weeks	250	Placebo: 62 PB-119: 62 PB-119: 63 PB-119: 63	75 µg QW sc 150 µg QW sc 200 µg QW sc	2.66 ± 3.92 3.20 ± 4.31 3.28 ± 3.94 3.48 ± 4.44	50.7 ± 10.81 50.8 ± 8.93 51.4 ± 9.77 50.5 ± 10.24	59.7% 77.4% 65.1% 49.2%		8.74 ± 0.71 8.57 ± 0.84 8.77 ± 0.95 8.65 ± 0.79	none

Jiang 2022 ¹⁷	NCT04466904	China	RCT	12 weeks	42	Placebo: 12		3.46 ± 1.01	50.2 ± 8.5	50.0%	26.5 ± 2.7	8.30 ± 0.70	metformin
						Dulaglutide: 6	1.5 mg QW sc	2.89 ± 0.70	50.7 ± 4.8	100%	26.6 ± 3.0	8.30 ± 1.40	
						Mazutide: 8	3.0 mg QW sc	1.98 ± 0.45	58.6 ± 5.3	75.0%	24.1 ± 1.4	8.90 ± 0.70	
						Mazutide: 8	4.5 mg QW sc	4.31 ± 1.15	47.9 ± 8.9	37.5%	25.7 ± 3.4	8.80 ± 1.00	
						Mazutide: 8	6.0 mg QW sc	6.05 ± 2.37	54.6 ± 10.6	62.5%	26.0 ± 2.2	8.50 ± 1.10	
Koska 2021 ¹⁸	NCT02162550	USA	RCT	18 months	163/122	Placebo: 54		6 ± 4	64 ± 7	98.0%	33 ± 6	8.10 ± 1.30	Multiple oral antidiabetic drugs
						Exenatide: 109	2 mg QW sc	6 ± 4	63 ± 8	95.0%	33 ± 6	7.80 ± 1.20	
Ludvik 2018 ¹⁹	NCT02597049	Austria, Czech Republic, Germany, Hungary, Israel, Mexico, Spain, USA	RCT	24 weeks	423	Placebo: 140		8.87 ± 6.13	57.1 ± 9.6	47.0%	32.39 ± 4.98	8.05 ± 0.66	SGLT2i, metformin
						Dulaglutide: 142	1.5 mg QW sc	9.21 ± 5.74	56.2 ± 9.3	54.0%	32.87 ± 5.56	8.04 ± 0.65	
						Dulaglutide: 141	0.75mg QW sc	10.05 ± 6.56	58.6 ± 9.1	49.0%	32.77 ± 6.27	8.04 ± 0.61	
Moretto 2008 ²⁰	NCT00381342	United States, Puerto Rico, Romania, Russia, India	RCT	24 weeks	233	Placebo: 78		1 ± 2	53 ± 9	55%	32 ± 5	7.80 ± 0.90	none
						Exenatide: 77	5 µg BID sc	2 ± 3	54 ± 10	62%	32 ± 5	7.90 ± 1.00	
						Exenatide: 78	10 µg BID sc	2 ± 3	55 ± 10	52%	31 ± 5	7.80 ± 1.00	
Nauck 2014 ²¹	NCT00734474	Multinational	RCT	52 weeks	1098	Placebo: 177		7 ± 5	55 ± 9	51.0%	31 ± 4	8.10 ± 1.10	metformin or other drugs
						Dulaglutide: 304	1.5 mg QW sc		54 ± 10	48.0%	31 ± 5	8.10 ± 1.10	
						Dulaglutide: 302	0.75 mg QWsc		54 ± 10	44.0%	31 ± 4	8.10 ± 1.10	
						Sitagliptin: 315	100 mg QD po		54 ± 10	48.0%	31 ± 4	8.10 ± 1.10	
Odawara 2016 ²²	NCT01558271	Japan	RCT	26 weeks	422	Dulaglutide: 281	0.75 mg QWsc	5.8 ± 5.6	57.9 ± 9.4	81.0%	25.6 ± 3.6	8.15 ± 0.77	none
						Liraglutide: 141	0.9 mg QD sc	6.3 ± 6.0	57.9 ± 10.4	83.0%	25.5 ± 3.5	8.08 ± 0.89	
Pinget 2013 ²³	NCT00763815	Austria, Canada, France, Germany, Greece, India, Guatemala, Mexico, Peru, Puerto Rico, Romania, Turkey, America	RCT	24 weeks	484	Placebo: 161		8.1 ± 5.6	55.3 ± 9.5	51.0%	34.4 ± 7.0	8.10 ± 0.80	pioglitazone with or without metformin
						Lixisenatide: 323	20 µg QD sc	8.1 ± 5.4	56.0 ± 9.5	53.0%	33.7 ± 6.7	8.10 ± 0.90	
Pratley 2019 ²⁴	NCT02863419	Croatia, Czech Republic, Germany, Hungary, Japan, Latvia, Poland, Slovakia, South Africa, Ukraine, United Arab Emirates, USA	RCT	52 weeks	711	Placebo: 142		7.8 ± 5.5	57 ± 10	52.0%	32.9 ± 6.1	7.90 ± 0.70	metformin, SGLT2i, or short-term insulin
						Semaglutide: 285	14 mg QD po	7.8 ± 5.7	56 ± 10	52.0%	32.5 ± 5.9	8.00 ± 0.70	
						Liraglutide: 284	1.8 mg QD sc	7.3 ± 5.3	56 ± 10	52.0%	33.4 ± 6.7	8.00 ± 0.70	
Pratley 2010 ²⁵	NCT00700817	Europe, USA, Canada	RCT	26 weeks	665	Liraglutide: 225	1.2 mg QD sc	6.0 ± 4.5	55.9 ± 9.6	52.0%	32.6 ± 5.2	8.40 ± 0.80	metformin
						Liraglutide: 221	1.8 mg QD sc	6.4 ± 5.4	55.0 ± 9.1	52.0%	33.1 ± 5.1	8.40 ± 0.70	
						Sitagliptin: 219	100 mg QD po	6.3 ± 5.4	55.0 ± 9.0	55.0%	32.6 ± 5.4	8.50 ± 0.70	
Rosenstock 2018 ²⁶	NCT01455857	USA	RCT	39 weeks	460	Placebo: 154		8.6 ± 6.0	54.7 ± 9.1	40.3%	33.7 ± 5.5	8.50 ± 0.80	metformin, sulfonylureas, or pioglitazone monotherapy or in any combination
						ITCA 650: 153	40 µg QD sc	9.1 ± 6.2	55.5 ± 10.3	41.8%	33.1 ± 5.1	8.50 ± 0.80	
						ITCA 650: 153	60 µg QD sc	8.9 ± 6.9	54.7 ± 9.6	40.5%	33.8 ± 5.2	8.50 ± 0.80	

Rosenstock 2019²⁷	NCT02057172	Czech Republic, Germany, Hungary, the Netherlands, Spain, Sweden, USA	RCT	13 weeks	252	Placebo: 37		6.3 ± 5.1	55 ± 9	43.0%	31 ± 5	metformin with/without sulfonylurea
						Efpeglenatide: 37	0.3 mg QW sc	7.1 ± 6.2	56 ± 11	65.0%	32 ± 5	
						Efpeglenatide: 37	1 mg QW sc	5.1 ± 3.3	55 ± 9	51.0%	32 ± 5	
						Efpeglenatide: 33	2 mg QW sc	5.8 ± 5.2	56 ± 10	55.0%	32 ± 4	
						Efpeglenatide: 36	3 mg QW sc	5.9 ± 4.8	54 ± 10	64.0%	32 ± 5	
						Efpeglenatide: 36	4 mg QW sc	6.1 ± 6.4	56 ± 10	50.0%	31 ± 6	
						Liraglutide: 36	1.8 mg QD sc	6.4 ± 4.8	54 ± 11	44.0%	32 ± 4	
Rosenstock 2021²⁸	NCT03954834	India, Japan, Mexico, USA	RCT	40 weeks	478	Placebo: 115		4.5 ± 5.9	53.6 ± 12.8	49.0%	31.7 ± 6.1	none
						Tirzepatide: 121	5mg QW sc	4.6 ± 5.1	54.1 ± 11.9	46.0%	32.2 ± 7.0	
						Tirzepatide: 121	10mg QW sc	4.9 ± 5.6	55.8 ± 10.4	60.0%	32.2 ± 7.6	
						Tirzepatide: 121	15 mg QW sc	4.8 ± 5.0	52.9 ± 12.3	52.0%	31.5 ± 5.5	
Seino 2008²⁹	NCT00154414 CTI-050131	Japan	RCT	14 weeks	225	Placebo: 46		7.48 ± 5.65	57.5 ± 8.7	63.0%	23.77 ± 2.63	none or oral antidiabetic drug
						Liraglutide: 45	0.1 mg QD sc	7.15 ± 5.14	56.5 ± 8.4	68.9%	24.26 ± 2.77	
						Liraglutide: 46	0.3 mg QD sc	6.78 ± 4.69	56.8 ± 8.8	69.6%	23.93 ± 3.09	
						Liraglutide: 45	0.6 mg QD sc	8.87 ± 6.77	60.0 ± 7.0	62.2%	23.74 ± 2.78	
						Liraglutide: 44	0.9 mg QD sc	7.62 ± 4.92	55.5 ± 7.6	40.5%	23.59 ± 3.04	
Shuai 2021³⁰	NCT02477865	China	RCT	24 weeks	361	Placebo: 121		1.83 ± 1.01	51.5 ± 10.9	72.7%	26.3 ± 3.4	with or without oral antidiabetic drug
						PEX168: 124	100 µg QW sc	1.12 ± 0.73	50.5 ± 10.4	66.9%	27.0 ± 3.7	
						PEX168: 116	200 µg QW sc	1.62 ± 0.88	52.4 ± 11.5	55.2%	26.4 ± 3.3	
Sorli 2017³¹	NCT02054897	Canada, Italy, Japan, Mexico, Russia, South Africa, UK, USA	RCT	30 weeks	387	Placebo: 129		4.06 ± 5.48	53.9 ± 11.0	54.0%	32.40 ± 6.86	none
						Semaglutide: 128	0.5 mg QD sc	4.81 ± 6.10	54.6 ± 11.1	47.0%	32.46 ± 7.62	
						Semaglutide: 130	1.0 mg QD sc	3.62 ± 4.88	52.7 ± 11.9	62.0%	33.92 ± 8.43	
Terauchi 2014³²	NCT01001104	Japan	RCT	12 weeks	145	Placebo: 37		4.7 ± 4.5	51.7 ± 9.7	78.4%	27.4 ± 4.5	none
						Dulaglutide: 36	0.25mg QW sc	4.3 ± 3.5	52.3 ± 8.8	75.0%	26.8 ± 4.5	
						Dulaglutide: 37	0.5mg QW sc	4.9 ± 4.0	52.5 ± 9.2	62.2%	26.7 ± 3.8	
						Dulaglutide: 35	0.75 mg QW sc	4.6 ± 4.5	52.2 ± 7.8	80.0%	27.1 ± 3.7	
Umpierrez 2014³³	NCT01126580	Multinational	RCT	52 weeks	807	Dulaglutid: 269	1.5 mg QW sc	3 ± 2	56 ± 10	42.0%	34 ± 6.0	none
						Dulaglutide: 270	0.75 mg QW sc	3 ± 2	56 ± 11	44.0%	33 ± 6.0	
						Metformin: 268	2000mg QD po	3 ± 2	55 ± 10	45.0%	33 ± 5.0	
Vanderheid en 2016³⁴	NCT01505673	Multinational	RCT	6 months	71	Placebo: 36		18.4 ± 3.3	55.5 ± 6.6	39.0%	41.6 ± 10.4	Insulin
						Liraglutide: 35	1.8 mg QD sc	16.3 ± 2.6	52.8 ± 8.1	34.0%	40.7 ± 6.7	
Wysham 2016³⁵	NCT01104701	Multinational	RCT	20 weeks	110	Exenatide 2 mg: 29	2 mg QW sc	6.0 ± 5.5	49.0 ± 9.8	65.5%	33.8 ± 5.4	metformin, pioglitazone
						Exenatide: 26	5 mg QMS sc	5.0 ± 3.6	50.0 ± 10.1	57.7%	33.4 ± 6.0	
						Exenatide: 28	8 mg QMS sc	6.4 ± 5.9	52.3 ± 10.7	82.1%	34.0 ± 6.0	
						Exenatide: 27	11 mg QMS sc	6.7 ± 5.8	49.9 ± 10.6	55.6%	33.8 ± 5.7	
Yabe 2020³⁶	NCT03015220	Japan	RCT	52 weeks	458	Semaglutide: 131	3 mg QD po	9.4 ± 6.3	59 ± 10	76.0%	25.8 ± 4.5	sulfonylurea, glinide, thiazolidinedione, alpha-glucosidase inhibitor, or SGLT2i
						Semaglutide: 132	7 mg QD po	9.3 ± 6.3	58 ± 11	68.0%	26.8 ± 5.0	
						Semaglutide: 130	14 mg QD po	9.1 ± 6.4	57 ± 10	77.0%	26.3 ± 5.2	
						Dulaglutide: 65	0.75 mg QW sc	9.9 ± 6.3	61 ± 9	78.0%	26.0 ± 4.0	

Yamada 2020 ³⁷	NCT03018028	Japan	RCT	52 weeks	243	Placebo: 49		8.4 ± 6.0	59 ± 9	18.0%	25.1 ± 3.9	8.30 ± 1.10	metformin, sulphonylurea, glinide, α -glucosidase inhibitor, DPP-4i, SGLT2i
						Liraglutide: 48	0.9 mg QD sc	6.7 ± 5.2	59 ± 10	19.0%	26.9 ± 4.8	8.30 ± 0.80	
						Semaglutide: 49	3 mg QD po	7.4 ± 5.5	58 ± 9	27.0%	26.5 ± 4.6	8.10 ± 0.80	
						Semaglutide: 49	7 mg QD po	7.4 ± 5.6	60 ± 10	27.0%	26.3 ± 3.5	8.30 ± 1.00	
						Semaglutide: 48	14 mg QD po	7.9 ± 5.9	61 ± 9	17.0%	24.7 ± 4.1	8.00 ± 0.90	
Zinman 2019 ³⁸	NCT03086330	Austria, Canada, Japan, Norway, Russia, USA	RCT	30 weeks	302	Placebo: 151		9.6 ± 5.9	56.6 ± 10.1	57.6%	32.7 ± 6.9	8.10 ± 0.80	SGLT-2i, sulphonylurea or metformin
						Semaglutide: 151	1.0 mg QW sc	9.8 ± 6.3	57.5 ± 8.9	68.9%	31.1 ± 6.2	8.00 ± 0.80	
Frias 2021 ³⁹	NCT03987919	USA, Argentina, Australia, Brazil, Canada, Israel, Mexico, UK	RCT	40 weeks	1878	Tirzepatide: 470	5 mg QW sc	9.1 ± 7.2	56.3 ± 10.0	56.4%	33.8 ± 6.9		metformin
						Tirzepatide: 469	10 mg QW sc	8.4 ± 5.9	57.2 ± 10.5	49.3%	34.3 ± 6.6		
						Tirzepatide: 470	15 mg QW sc	8.7 ± 6.9	55.9 ± 10.4	54.5%	34.5 ± 7.1		
						Semaglutide: 469	1 mg QW sc	8.3 ± 5.8	56.9 ± 10.8	52.0%	34.2 ± 7.2		
Ahmann 2018 ⁴⁰	NCT01885208	Europe, South America, USA	RCT	56 weeks	809	Semaglutide: 404	1.0 mg QW sc	9.0	56.4	54.2%	34.0	8.40	metformin, thiazolidinedione s, sulphonylureas
						Exenatide: 405	2.0 mg ER QW sc	9.4	56.7	56.3%	33.6	8.30	
Ahren 2017 ⁴¹	NCT01930188	Europe (Bulgaria, Czech Republic, Hungary, Norway, Portugal, Romania, Spain, Sweden, Turkey, and Ukraine), Argentina, Hong Kong China, India, Japan, Mexico, Russia, South Africa, Thailand	RCT	56 weeks	1231	Semaglutide: 410	0.5mg QW sc	6.4 ± 4.7	54.8 ± 10.2	51.0%	32.4 ± 6.2	8.00 ± 0.90	metformin, pioglitazone, rosiglitazone
						Semaglutide: 410	1mg QW sc	6.7 ± 5.6	56.0 ± 9.4	50.0%	32.5 ± 6.5	8.00 ± 0.90	
						Sitagliptin: 411	100mg QD po	6.6 ± 5.1	54.6 ± 10.4	51.0%	32.5 ± 5.8	8.20 ± 0.90	
Blonde 2015 ⁴²	NCT01191268	Argentina, Australia, Belgium, Brazil, Canada, Denmark, Greece, Hungary, Mexico, Poland, Russia, Spain, Sweden, Taiwan, USA	RCT	52 weeks	884	Dulaglutide: 293	0.75mg QW sc	12.4 ± 6.9	59.3 ± 9.0	50.0%	33.1 ± 5.2	8.40 ± 1.03	any combination of basal, basal with prandial, or premixed insulin, with or without oral hypoglycaemic drugs
						Dulaglutide: 295	1.5mg QW sc	12.8 ± 7.2	58.9 ± 9.6	54.0%	32.0 ± 5.1	8.46 ± 1.08	
Chen 2016 ⁴³	NCT01965509	China	RCT	12 weeks	120	Placebo: 38		6.46 ± 7.92	53.5 ± 10.2	68.4%	27.2 ± 4.5	8.28 ± 1.05	metformin
						PEX168: 42	100 µg QW sc	4.42 ± 6.42	52.6 ± 8.4	53.7%	27.2 ± 3.6	8.23 ± 0.88	
						PEX168: 40	200 µg QW sc	4.00 ± 5.67	49.8 ± 10.9	56.4%	26.3 ± 3.3	8.34 ± 1.15	
Dahl 2022 ⁴⁴	NCT04039503	USA, Japan, Czech Republic, Germany, Poland, Puerto Rico, Slovakia, and Spain	RCT	40 weeks	475	Placebo: 120		12.9 ± 7.4	60 ± 10	55.0%	33.2 ± 6.3	8.37 ± 0.84	insulin glargine with/without metformin
						Tirzepatide :116	5mg QW sc	14.1 ± 8.1	61 ± 10	53.0%	33.6 ± 5.9	8.30 ± 0.88	
						Tirzepatide: 119	10mg QW sc	12.6 ± 6.2	60 ± 10	61.0%	33.4 ± 6.2	8.36 ± 0.83	
						Tirzepatide: 120	15mg QW sc	13.7 ± 7.5	62 ± 10	54.0%	33.4 ± 5.9	8.23 ± 0.86	
De Fronzo 2005 ⁴⁵	NA	USA	RCT	30 weeks	336	Placebo:113		6.6 ± 6.1	54 ± 9	67.0%	34 ± 6	8.20 ± 1.00	metformin
						Exenatide 5 µg: 110	5 µg BID sc	6.2 ± 5.9	53 ± 11	57.0%	34 ± 6	8.30 ± 1.10	
						Exenatide 10 µg: 113	10 µg BID sc	4.9 ± 4.7	52 ± 11	68.0%	34 ± 6	8.20 ± 1.00	

Del Prato 2020⁴⁶	NCT02081118	USA	RCT	17 weeks	207	Placebo: 50		7.2 ± 5.3	54.7 ± 9.9	46.0%	32.4 ± 4.2	7.90 ± 0.70	metformin
						Efpeglenatide: 52	8 mg QW sc	7.1 ± 7.4	56.7 ± 8.1	36.5%	32.1 ± 4.7	7.90 ± 0.80	
						Efpeglenatide: 52	12mg QW sc	7.4 ± 6.2	56.0 ± 9.5	53.8%	33.0 ± 4.6	7.60 ± 0.70	
						Efpeglenatide: 53	16mg QW sc	7.2 ± 4.6	56.4 ± 9.5	47.2%	30.7 ± 4.0	7.90 ± 0.70	
Dungan 2014⁴⁷	NCT01624259	Czech Republic, Germany, Hungary, Mexico, Poland, Romania, Spain, Slovakia, USA	RCT	26 weeks	599	Dulaglutide: 299	1.5mg QW sc	7.1 ± 5.4	56.5 ± 9.3	46.0%	33.5 ± 5.1	8.10 ± 0.80	metformin
						Liraglutide: 300	1.8mg QW sc	7.3 ± 5.4	56.8 ± 9.9	50.0%	33.6 ± 5.2	8.10 ± 0.80	
Frias 2021⁴⁸	NCT03495102	USA, Austria, Canada, Greece, Hungary, Israel, Italy, Mexico, Poland, Puerto Rico, Romania, Russian, Slovakia, Spain, China Taiwan	RCT	52 weeks	1842	Dulaglutide: 612	1.5 mg QW sc	7.6 ± 5.8	57.8 ± 9.7	48.7%	34.4 ± 6.4	8.60 ± 0.90	metformin
						Dulaglutide: 616	3.0 mg QW sc	7.6 ± 5.5	56.9 ± 10.2	53.2%	34.3 ± 6.2	8.60 ± 1.00	
						Dulaglutide: 614	4.5 mg QW sc	7.7 ± 5.8	56.6 ± 10.2	51.8%	34.0 ± 6.2	8.60 ± 0.90	
Giorgino 2015⁴⁹	NCT01075282	Argentina, Australia, Italy, Belgium, Canada, Croatia, Czech Republic, France, Greece, Hungary, India, Korea, Mexico, Poland, Romania, Slovakia, Spain, Sweden, China Taiwan	RCT	52 weeks	810	Dulaglutide: 272	0.75mg QW sc	9.0 ± 6.0	57.0 ± 9.0	50.0%	32.0 ± 5.0	8.10 ± 1.00	metformin, glimepiride
						Dulaglutide: 273	1.5mg QW sc	9.0 ± 6.0	56.0 ± 10.0	43.0%	31.0 ± 5.0	8.20 ± 1.00	
Heise 2022⁵⁰	NCT03951753	Germany	RCT	28 weeks	127	Placebo:28		10.95 ± 6.78	60.4 ± 7.6	75.0%	32.24 ± 3.96	7.90 ± 0.51	metformin
						Tirzepatide: 45	15 mg QW sc	10.24 ± 5.80	61.1 ± 7.1	69.0%	31.28 ± 5.01	7.83 ± 0.72	
						Semaglutide: 44	1 mg QW sc	12.73 ± 6.10	63.7 ± 5.9	77.0%	30.82 ± 3.84	7.70 ± 0.60	
Inagaki 2022⁵¹	NCT03861052	Japan	RCT	52 weeks	636	Tirzepatide: 159	5mg QW sc	4.52 ± 1.02	56.8 ± 10.1	71.0%	28.6 ± 5.4	8.20 ± 0.90	none
						Tirzepatide: 158	10mg QW sc	5.12 ± 1.17	56.2 ± 10.3	75.0%	28.0 ± 4.1	8.20 ± 0.90	
						Tirzepatide: 160	15mg QW sc	5.12 ± 1.17	56.0 ± 10.7	83.0%	28.1 ± 4.4	8.20 ± 0.90	
						Dulaglutide: 159	0.75mg QW sc	5.01 ± 1.22	57.5 ± 10.2	74.0%	27.8 ± 3.7	8.20 ± 0.90	
Kadowaki 2022⁵²	NCT03861039	Japan	RCT	52 weeks	443	Tirzepatide: 148	5mg QW sc	8.51 ± 1.44	57.7 ± 11.0	80.0%	27.7 ± 4.3	8.50 ± 1.10	sulfonylureas, biguanides, α-glucosidase inhibitors, thiazolidinedione, glinides, or SGLT2i
						Tirzepatide: 147	10mg QW sc	9.13 ± 1.35	56.9 ± 11.2	77.0%	27.6 ± 4.0	8.60 ± 1.00	
						Tirzepatide: 148	15mg QW sc	8.59 ± 1.50	56.5 ± 10.4	70.0%	28.4 ± 5.9	8.60 ± 1.10	
Kadowaki 2011⁵³	NCT00577824	Japan	RCT	24 weeks	179	Placebo:35		12.4 ± 6.5	56.3 ± 11.4	68.6%	25.8 ± 4.2	8.10 ± 0.90	sulfonylurea, biguanide, thiazolidine derivative
						Exenatide: 72	5 µg BID sc	12.2 ± 6.3	58.5 ± 9.3	68.1%	25.0 ± 4.1	8.30 ± 0.80	
						Exenatide: 72	10 µg BID sc	11.6 ± 7.0	59.4 ± 9.8	68.1%	25.8 ± 3.9	8.20 ± 1.00	

Ludvik 2021⁵⁴	NCT03882970	Argentina, Austria, Italy, Greece, Hungary, Poland, Puerto Rico, Romania, South Korea, Spain, China Taiwan, Ukraine, USA	RCT	52 weeks	1437	Tirzepatide:358 Tirzepatide:360 Tirzepatide:359	5 mg QW sc 10 mg QW sc 15 mg QW sc	8.5 ± 5.8 8.4 ± 6.6 8.5 ± 6.5	57.2 ± 10.1 57.4 ± 9.7 57.5 ± 10.2	56.0% 54.0% 54.0%	33.6 ± 5.9 33.4 ± 6.2 33.7 ± 6.1	8.17 ± 0.89 8.18 ± 0.89 8.21 ± 0.94	sulfonylureas, biguanides, α-glucosidase inhibitors, thiazolidinedione, glinides, or SGLT2i
Miyagawa 2015⁵⁵	NCT01558271	Japan	RCT	52 weeks	492	Placebo: 70 Liraglutide: 141 Dulaglutide: 281	0.9 mg QD sc 0.75 mg QW sc	6.3 ± 5.1 6.3 ± 6.0 6.8 ± 5.6	57.7 ± 8.3 57.9 ± 10.4 57.2 ± 9.6	79.0% 83.0% 81.0%	25.2 ± 3.2 25.5 ± 3.5 25.6 ± 3.6	8.20 ± 0.83 8.08 ± 0.89 8.15 ± 0.77	none or sulphonylurea
Nauck 2016⁵⁶	NCT00849017	USA, Mexico	RCT	52 weeks	301	Placebo:101 Albiglutide: 101 Albiglutide: 99	30mg QW sc 50mg QW sc	4.3 ± 4.0 3.4 ± 3.7 4.2 ± 4.6	53.1 ± 11.7 53.6 ± 10.9 52.0 ± 11.8	57.4% 57.4% 50.5%	33.0 ± 5.4 33.7 ± 5.1 33.9 ± 5.5	8.00 ± 0.90 8.00 ± 0.80 8.20 ± 0.90	none
Pan 2014⁵⁷	NCT01169779	China, Malaysia, Thailand	RCT	24 weeks		placebo: 194 Lixisenatide:196	20µg QD sc	6.8 ± 4.8 6.5 ± 4.6	55.1 ± 10.5 54.5 ± 10.3	46.9% 51.5%	27.1 ± 3.8 26.8 ± 3.9	7.85 ± 0.71 7.95 ± 0.81	
Pratley 2018⁵⁸	NCT02648204	Bulgaria, Croatia, Finland, Germany, Greece, China Hong Kong, India, Spain, Ireland, Latvia, Lithuania, Portugal, Romania, Slovakia, UK, USA	RCT	40 weeks	1201	Semaglutide: 301 Semaglutide: 300 Dulaglutide: 300 Dulaglutide: 300	0.5 mg QW sc 1.0 mg QW sc 0.75 mg QW sc 1.5 mg QW sc	7.7 ± 5.9 7.3 ± 5.7 7.0 ± 5.5 7.6 ± 5.6	56 ± 10.9 55 ± 10.6 55 ± 10.4 56 ± 10.6	56.0% 54.0% 54.0% 57.0%	33.7 ± 7.1 33.6 ± 6.5 33.6 ± 6.9 33.1 ± 6.6	8.30 ± 0.90 8.20 ± 0.90 8.20 ± 0.90 8.20 ± 0.90	metformin
Ratner 2010⁵⁹		USA	RCT	13 weeks	542	Placebo:109 Lixisenatide:55 Lixisenatide:52 Lixisenatide:55 Lixisenatide:54 Lixisenatide:53 Lixisenatide:56 Lixisenatide:54 Lixisenatide:54	5 µg QD sc 10 µg QD sc 20 µg QD sc 30 µg QD sc 5 µg BID sc 5 µg BID sc 5 µg BID sc 5 µg BID sc	7.1 ± 5.4 7.2 ± 4.9 6.2 ± 4.1 6.4 ± 6.8 6.0 ± 4.8 6.2 ± 6.0 6.4 ± 5.0 6.6 ± 5.1 7.0 ± 5.4	56.3 ± 9.2 56.8 ± 7.8 55.4 ± 9.2 55.4 ± 9.9 56.5 ± 8.7 57.1 ± 8.2 56.0 ± 7.9 56.7 ± 8.3 55.3 ± 9.1	56.0% 47.3% 59.6% 50.9% 50.0% 47.2% 51.8% 37.0% 42.6%	31.7 ± 4.2 30.7 ± 4.6 31.9 ± 4.0 32.0 ± 4.3 31.6 ± 3.6 31.6 ± 4.2 32.8 ± 4.4 32.7 ± 4.4 32.3 ± 4.5	7.53 ± 0.60 7.58 ± 0.70 7.52 ± 0.60 7.58 ± 0.70 7.52 ± 0.70 7.60 ± 0.60 7.54 ± 0.60 7.61 ± 0.70 7.46 ± 0.50	metformin
Riddle 2013^{60 61}	NCT007715624	Brazil, Canada, Chile, UK, Egypt, France, USA Germany, India, Italy, Korea, Mexico, Puerto Rico, Russia, Turkey	RCT	24 weeks	495	Placebo: 167 Lixisenatide: 238	20 mg QD sc	12.4 ± 6.3 12.5 ± 7.0	57 ± 10 57 ± 10	49.0% 45.0%	32.6 ± 6.3 31.9 ± 6.2		metformin, basal insulin
Rodbard 2018⁶¹	NCT02305381	Germany, Japan, Serbia, Slovakia, USA	RCT	30 weeks	396	Placebo: 133 Semaglutide: 131 Semaglutide: 132	0.5mg QW sc 1mg QW sc	13.3 12.9 13.7	58.8 58.5	59.1 53.4% 56.1% 58.8%	53.4% 31.8 32.8 32.0	8.40 8.40 8.30	basal insulin therapy alone /combination with metformin
Rosenstock 2019⁶²	NCT02607865	USA, Argentina, Mexico, France, Germany, India, Israel, Brazil, Japan, UK, Romania, Russia, South Africa, Turkey, Ukraine	RCT	78 weeks	1864	Semaglutide: 466 Semaglutide: 465 Semaglutide: 465 Sitagliptin: 467	3 mg QD sc 7 mg QD sc 14 mg QD sc 100 mg QD sc	8.4 ± 6.1 8.3 ± 5.8 8.7 ± 6.1 8.8 ± 6.0	58 ± 10.0 58 ± 10.0 57 ± 10.0 58 ± 10.0	54.5% 52.7% 53.1% 51.0%	32.6 ± 6.7 32.6 ± 6.4 32.3 ± 6.3 32.5 ± 6.2	8.30 ± 1.00 8.40 ± 1.00 8.30 ± 0.90 8.30 ± 0.90	metformin

Rosenstock 2014⁶³	NCT00713830	Bulgaria, Czech Republic, Egypt, Germany, India, Israel, Japan, Korea, The Netherlands, Romania, Russia, Taiwan, Thailand, Tunisia, Turkey, USA	RCT	24 weeks	859	Placebo: 285 Lixisenatide: 574	20µg QD sc	9.8 ± 6.2 9.1 ± 6.0	57.8 ± 10.1 57.0 ± 9.8	52.6% 49.5%	30.4 ± 6.6 30.1 ± 6.6	8.20 ± 0.80 8.30 ± 0.90	metformin, sulphonylurea
Seino 2014⁶⁴	NCT01098461	Japan	RCT	16 weeks	212	placebo: 53 Albiglutide: 52 Albiglutide: 54 Albiglutide: 53	15 mg QW sc 30 mg QW sc 30 mg BIWsc	6.7 ± 7.8 6.3 ± 4.6 7.8 ± 5.4 7.2 ± 5.6	57.5 ± 11.1 53.3 ± 10.3 58.0 ± 9.3 59.1 ± 8.5	69.8% 61.5% 70.4% 77.4%	25.0 ± 3.0 25.3 ± 3.5 25.0 ± 3.8 25.3 ± 3.8	8.57 ± 0.79 8.54 ± 0.82 8.54 ± 0.86 8.54 ± 0.81	none
Seino 2012⁶⁵		Japan, Korea, China Taiwan, Philippines	RCT	24 weeks	311	Placebo: 157 Lixisenatide: 154	20 µg QD sc	14.1 ± 7.7 13.7 ± 7.7	58.0 ± 10.1 58.7 ± 10.2	51.0% 44.85	25.2 ± 3.9 25.4 ± 3.7	8.52 ± 0.78 8.54 ± 0.73	basal insulin with/without sulphonylurea
Wang 2018⁶⁶	NCT01648582	China, Russia, Mexico and South Korea	RCT	52 weeks	774	Dulaglutide: 257 Dulaglutide: 258	0.75 mg QW sc 1.5 mg QW sc	8.1 ± 5.3 7.9 ± 4.8	54.5 ± 10.0 55.0 ± 9.6	56.7% 53.4%	27.0 ± 3.8 26.6 ± 3.7	8.30 ± 1.10 8.50 ± 1.20	insulin glargine
Frias2021⁶⁷	NCT03989232	USA, Bulgaria, Canada, Czechia, Greece, Hungary, Japan, Poland, Puerto Rico, Slovakia, Ukraine	RCT	40 weeks	961	Semaglutide: 481 Semaglutide: 480	1mg QW sc 2mg QW sc	9.8 ± 6.2 9.2 ± 6.2	58.2 ± 9.9 57.9 ± 10.0	59% 58%	34.4 ± 7.2 34.8 ± 6.8	8.8 ± 0.6 8.9 ± 0.6	Metformin alone/with sulfonylurea
Gao 2020⁶⁸	NCT02477969	China	RCT	24 weeks	587	Placebo: 179 PEX168: 179 PEX168: 175	100 µg QW sc 200 µg QW sc	4.7 ± 3.4 4.3 ± 3.5 4.8 ± 3.2	52.3 ± 10.7 53.6 ± 10.5 52.8 ± 10.6	54.7% 60.6% 57.0%	26.9 ± 3.9 26.0 ± 3.5 26.6 ± 3.8	8.6 ± 0.9 8.5 ± 0.9 8.5 ± 0.9	metformin
Aroda2023⁶⁹	NCT04707469	Australia, Bulgaria, Canada, Croatia, Czechia, Estonia, Germany, Hungary, India, Poland, Slovakia, Slovenia, Taiwan China, USA	RCT	52 weeks	1606	Semaglutide: 536 Semaglutide: 535 Semaglutide: 535	14 mg QD po 25 mg QD po 50 mg QD po	9.4 ± 5.9 9.7 ± 6.7 8.9 ± 5.9	58.4 ± 10.4 58.8 ± 10.7 57.6 ± 11.2	61.0% 57.0% 57.0%	33.7 ± 6.1 34.1 ± 6.5 33.7 ± 6.2	8.9 ± 0.8 9.0 ± 0.8 8.9 ± 0.7	metformin, sulfonylurea, SGLT2i, or DPP-4i
Frias2022⁷⁰	NCT03353350	Germany, Poland, Ukraine, UK, USA	RCT	56 weeks	406	Placebo: 102 Efpeglenatide: 100 Efpeglenatide: 101 Efpeglenatide: 103	2 mg QW sc 4mg QW sc 6mg QW sc	5.0 ± 4.9 5.3 ± 5.3 4.9 ± 5.0 5.2 ± 5.2	59.5 ± 11.7 58.6 ± 10.5 56.3 ± 11.5 59.6 ± 10.7	50.0% 55.0% 51.5% 59.2%	34.8 ± 7.1 34.4 ± 6.4 33.8 ± 6.6 33.8 ± 6.9	8.0 ± 0.9 8.1 ± 0.9 8.1 ± 0.9 8.1 ± 1.0	multiple hypoglycemic treatments
Frias2023⁷¹	NCT04982575	USA	RCT	32 weeks	92	CagriSema: 31 Semaglutide: 31 Cagrilintide: 30	2.4mg QW sc 2.4mg QW sc 2.4mg QW sc	6.4 ± 3.8 9.2 ± 8.3 10.7 ± 9.1	56 ± 10 57 ± 10 62 ± 7	58% 58% 77%	35.9 ± 5.7 36.2 ± 7.2 34.4 ± 6.1	8.5 ± 0.8 8.6 ± 0.7 8.1 ± 0.8	metformin
Frias 2023⁷²	NCT05048719	USA, Hungary, Poland, and Slovakia	RCT	26 weeks	383	Placebo: 55 Orforglipron: 51 Orforglipron: 56 Orforglipron: 47 Orforglipron: 61 Orforglipron: 63 Dulaglutide: 50	3mg QD po 12mg QD po 24mg QD po 36mg QD po 45mg QD po 1.5mg QW sc	7.8 ± 2.12 5.0 ± 2.25 7.1 ± 2.22 5.9 ± 1.65 5.9 ± 1.55 6.8 ± 2.60 7.9 ± 2.10	58.3 ± 9.5 59.0 ± 9.4 57.4 ± 9.2 60.5 ± 9.1 59.7 ± 9.2 58.5 ± 9.4 58.8 ± 10.2	51% 51% 64% 64% 59% 63% 60%	35.8 ± 6.2 35.3 ± 8.2 34.8 ± 6.3 34.1 ± 7.7 34.4 ± 5.4 36.4 ± 6.9 35.4 ± 8.0	8.1 ± 0.9 8.0 ± 0.8 8.2 ± 0.9 8.2 ± 0.9 8.0 ± 0.7 8.1 ± 0.9 8.0 ± 0.7	metformin

Garvey2023 ⁷³	NCT04657003	Argentina, Brazil, India, Japan, Russia, Taiwan China, USA	RCT	72 weeks	938	Placebo: 315	10mg QW sc	18.1 ± 11.7	54.7 ± 10.5	50%	36.6 ± 7.3	7.89 ± 0.84	any oral glycemic-lowering agent
						Tirzepatide: 312	15 mg QW sc	17.6 ± 12.0	54.3 ± 10.7	49%	36.0 ± 6.4	8.00 ± 0.84	
						Tirzepatide: 311		17.5 ± 11.0	53.6 ± 10.6	49%	35.7 ± 6.1	8.07 ± 0.99	
Pratt2023 ⁷⁴	NCT04426474	Germany, USA	RCT	12 weeks	68	Placebo:17	9mg QD po	8.63 ± 4.89	56.0 ± 6.0	58.8%	31.31 ± 4.86	8.09 ± 0.75	metformin
						Orforglipron:9	15mg QD po	13.48 ± 8.29	57.7 ± 6.4	44.4%	30.14 ± 4.60	8.02 ± 0.62	
						Orforglipron:10	21mg QD po	15.02 ± 11.97	59.6 ± 4.6	70.0%	30.39 ± 3.61	7.84 ± 0.74	
						Orforglipron:14	27mg QD po	9.48 ± 5.48	55.3 ± 8.0	71.4%	32.60 ± 5.48	8.36 ± 1.31	
						Orforglipron:9	45mg QD po	7.60 ± 4.39	58.8 ± 4.6	77.8%	30.62 ± 3.55	7.82 ± 0.69	
						Orforglipron:9		10.38 ± 4.78	62.8 ± 4.4	44.4%	29.82 ± 2.64	7.93 ± 0.79	
Rosenstock 2023 ⁷⁵	NCT04867785	USA	RCT	24 weeks	281	Placebo:45	0.5 mg QW sc	8.7 ± 8.3	57.6 ± 10.8	49%	33.8 ± 4.9	8.4 ± 1.1	metformin
						Retatrutide:47	4 mg QW sc	8.8 ± 6.7	57.2 ± 9.7	51%	34.7 ± 5.6	8.3 ± 1.2	
						Retatrutide:23	escalation	8.1 ± 6.6	57.7 ± 8.1	65%	36.3 ± 7.4	8.1 ± 0.9	
						Retatrutide:24	4 mg QW sc	10.5 ± 7.6	57.6 ± 10.0	50%	34.0 ± 6.5	8.2 ± 1.2	
						Retatrutide:26	8 mg QW sc slow	7.2 ± 6.4	57.0 ± 7.4	38%	35.0 ± 6.4	8.3 ± 1.1	
						Retatrutide:24	escalation	6.0 ± 5.8	53.8 ± 9.0	38%	34.1 ± 5.9	8.2 ± 1.3	
						Retatrutide:46	8 mg QW sc fast	7.9 ± 6.9	54.4 ± 9.7	43%	35.5 ± 6.9	8.3 ± 1.1	
						dulaglutide:46	escalation	7.2 ± 6.5	54.9 ± 10.4	28%	36.3 ± 6.8	8.2 ± 0.9	
							12 mg QW sc						
							escalation						
Urva2022 ⁷⁶	NCT04143802	USA	RCT	12 weeks		Placebo:15	1.5 mg QW sc	9.2 ± 6.0	58.8 ± 6.4	20%	32.3 ± 6.2	8.83 ± 1.06	metformin
						dulaglutide:5	0.5 mg QW sc	14.2 ± 4.5	59.8 ± 7.5	80%	30.1 ± 2.0	8.50 ± 0.86	
						Retatrutide:9	1.5 mg QW sc	10.7 ± 5.2	59.2 ± 6.6	44%	33.3 ± 6.3	8.07 ± 0.74	
						Retatrutide:9	3 mg QW sc	9.0 ± 5.8	56.8 ± 5.7	33%	32.4 ± 6.1	8.87 ± 0.79	
						Retatrutide:11	6 mg QW sc slow	10.2 ± 4.6	56.8 ± 8.0	55%	31.7 ± 5.1	8.65 ± 0.98	
						Retatrutide:11	escalation	12.9 ± 7.7	55.8 ± 10.7	64%	33.7 ± 3.9	9.05 ± 0.81	
						Retatrutide:12	12 mg QW sc	10.0 ± 5.4	61.5 ± 6.3	67%	30.5 ± 3.6	8.45 ± 0.92	
							slow escalation						

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride. SC, subcutaneous injections; PO, oral intake; QD, once daily; QW, once weekly; BID, twice daily; BIW: twice weekly; QMS, once monthly suspension.

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Table S2.2: GLP-1RA list

GLP-1RA Drug	Synonyms	Drug type	Company	Highest phase	Drug approved country/region	ATC	Note
Albiglutide	GSK-716155, PGC-GLP-1, Tanzeum, Eperzan, Syncria, Albugon	Fusion protein	GSK Plc	Approved	United States, European Union, Canada	A10BJ04	
CagriSema	Cagrilintide/Semaglutide	Recombinant polypeptide	Novo Nordisk	Phase 3	-	-	GLP-1/Amylin receptor dual agonist
Dulaglutide	GLP-fc, LY-2189265, GLP-1-FC, LY 2189265, Trulicity	Fusion protein	Eli Lilly & Co.	Approved	United States, China, European Union, Japan, Canada, India, Iceland, Liechtenstein, Norway	A10BJ05	
Efpeglenatide	LAPS-Exendin, Langlenatide, LAPS-exendin 4 analogue, LAPSCA-Exendin4, LAPS-Exendin4, LAPS-EXD4, HM-11260C, SAR-439977	Fusion protein	Hanmi Pharmaceutical Co., Ltd.	Phase 3	-	-	
Exenatide	Presendin, Exendin-4, EX-4, AC-2993, AC-2993-LAR, LY-2148568, LY2148568, Byetta, Bydureon	Synthetic peptide	Eli Lilly & Co.; Amylin Pharmaceuticals, Inc.	Approved	United States, China, European Union, Japan	A10BJ01	
ITCA 650	-	Small molecule drug	Intarcia Therapeutics, Inc.	Phase 3	-	-	Subdermal osmotic exenatide mini-pump
Liraglutide	NN-2211, NN-9211, NNC-90-1170, NN-8022, NNC-901170, NNC 90-1170, NN 9211, NN 2211, LATIN T1D, Saxenda, SAXE, Victoza	Recombinant polypeptide	Novo Nordisk	Approved	United States, China, European Union, Japan, Canada	A10BJ02	
Lixisenatide	des-38-proline-exendin-4 (Heloderma suspectum)-(1-39)-peptidylpenta-L-lysyl-L-lysineamide, DesPro38Exendin-4(1-39)-Lys6-NH2, ZP-10, AQVE-10010, AVE0100, AVE-	Synthetic peptide	Zealand Pharma	Approved	United States, China, European Union, Japan, Canada, Australia, India, Argentina, Brazil, Switzerland, Chile, Colombia, Ecuador, Hong Kong, Israel, Iceland, South Korea,	A10BJ03	

	0010, ZP10A PEPTIDE, Lyxumia, Adlyxin				Kuwait, Liechtenstein, Mexico, Norway, Russia, Singapore, Turkey, Taiwan Province, Ukraine		
Mazdutide	IBI-362, IBI362, OXM-3, OXM3, LY3305677, LY-3305677	Synthetic peptide	Eli Lilly & Co.	Phase 3	-	-	GLP-1/GCG receptor dual agonist
Orforglipron	LY3502970, LY-3502970, OWL 833	Small molecule drug	Eli Lilly & Co.	Phase 3	-	-	
PEGylated exenatide	PEG-exenatide, PB-119, PB119	Synthetic peptide	PegBio Co., Ltd	Phase 3	-	-	
polyethylene glycol loxenatide	Polyethylene Glycol Loxenatide, PEG loxenatide, pegloxenatide, PEX-168, PEX168	Synthetic peptide	Jiangsu Hansoh Pharmaceutical Co. Ltd.	Approved	China	A10B	
Retatrutide	LY3437943	Synthetic peptide	Eli Lilly & Co.	Phase 3	-	-	GLP-1/GIP/GCG receptor triple agonist
Semaglutide	NN-9535, NN-9536, NN-9931, NN9924, NNC-0113-0217, Ozempic, Rybelsus, Wegovy	Synthetic peptide	Novo Nordisk	Approved	United States, China, European Union, Japan	A10BJ06	
Tirzepatide	LY3298176, LY-3298176, GIP/GLP-1 RA, Mounjaro	Synthetic peptide	Eli Lilly & Co.	Approved	United States, Japan	-	GLP-1/GIP receptor dual agonist

Abbreviations: ATC: anatomical therapeutic chemical; GIP, gastric inhibitory polypeptide; GCG, glucagon.

Appendix 3: List of data extracted from the included randomized clinical trials

Data category	List of variables
Study	Primary author, year of publication, duration of study, total number of patients in each group
Patients	Sex, age, nationality, diabetes duration, HbA1c and BMI at baseline
Interventions	Drug class, dose and duration of the primary intervention and strategies used for implementing them
Efficacy outcome	Mean of change in HbA1c (%), FPG (mmol/L), weight (kg), BMI, waist circumference (cm), HDL (mmol/L), LDL (mmol/L), TC (mmol/L), TG (mmol/L), with respective standard deviation from baseline
Adverse events	Various adverse events reported in included trials

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Appendix 4: Risk of bias of randomized clinical trials

Figure S4: Overall risk of bias presented as percentage of each risk of bias item across all included studies. Green = Low risk, Red = High risk, Yellow = Some concerns.

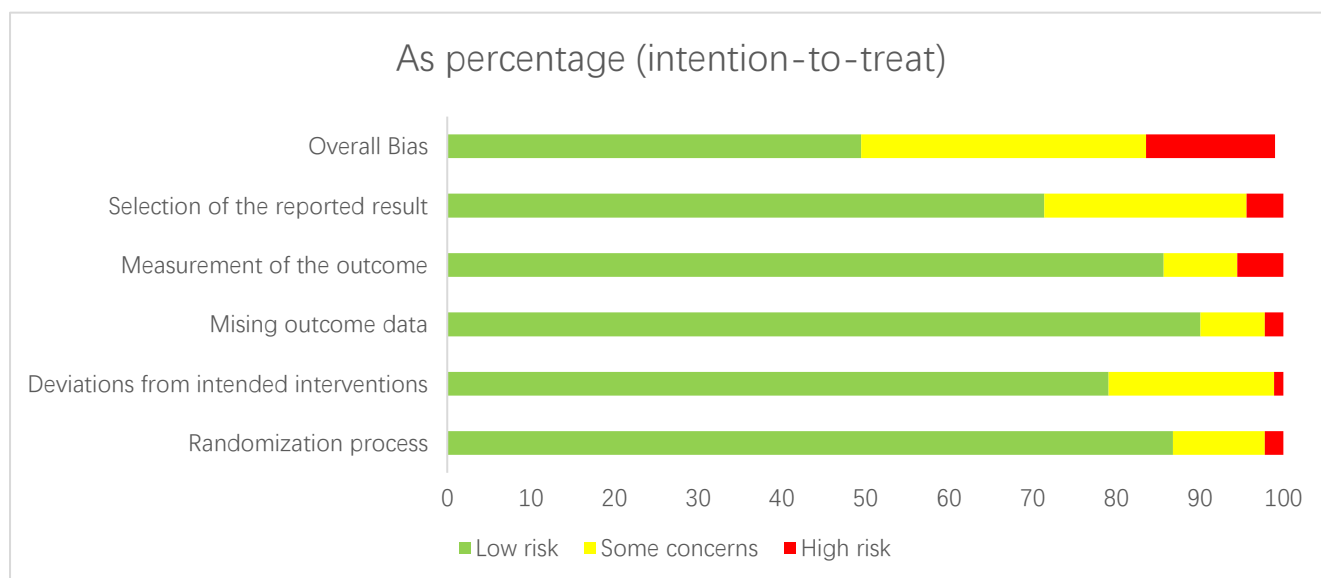


Table S4: Study level risk of bias assessment using Cochrane risk of bias tool 2.0 for assessing risk of bias of randomized clinical trials.

Unique ID	Study ID	Randomization process	Deviations from intended interventions	Mising outcome data	Measurement of the outcome	Selection of the reported result	Over all
Ahmadi2019	NCT02113332	Low	Low	Low	Low	Low	Low
Ahmann2015	NN2211-3917	Low	Low	Low	Low	Low	Low
Ahren2014	NCT00838903	Low	Low	High	High	Some concerns	High
Aroda2019	NCT02906930	Low	Low	Low	Low	Low	Low
Blevins2011	NA	Low	Some concerns	Low	Low	Low	Some concerns
Blonde2020	NCT02964247	Low	Low	Low	Low	Low	Low
Buse2013	NCT01029886	Low	Some concerns	Low	Low	Low	Some concerns
Buse2009	NCT00518882	Low	Some concerns	Low	Low	Low	Some concerns
Capehorn2020	NN9535-4339	Low	Some concerns	Low	Low	Low	Some concerns
Davies2015	NCT01272232	Low	Low	Some concerns	Low	Low	Some concerns
Drucker2008	NCT00308139	Low	Low	Low	Low	Low	Low
Frias2018	NCT03131687	Low	Low	Low	Low	Low	Low
Frias2019	NCT31050143	High	Low	Low	Low	Low	High
Grunberger2012	NA	Low	Low	Low	Low	Low	Low
Iwamoto2009	NCT00612794	Low	Some concerns	Low	Low	Low	Some concerns
Ji2021	NCT03520972	Low	Low	Low	Low	Low	Low
Jiang2022	NCT04466904	Low	Low	Low	Low	Low	Low
Koska2021	NCT02162550	Low	Low	Low	Low	Low	Low
Ludvik2018	NCT02597049	Low	Low	Low	Low	Low	Low
Moretto2008	NCT00381342	Low	Low	Low	Low	Low	Low
Nauck2014	NCT00734474	Low	Low	Low	Low	Low	Low
Odawara2016	NCT01558271	Low	Low	Low	Low	Some concerns	Some concerns
Pinger2013	NCT00763815	Low	Some concerns	Low	Low	Low	Some concerns
Pratley2019	NCT02863419	Low	Low	Low	Low	Low	Low
Pratley2010	NCT00700817	Low	Low	Some concerns	Low	Low	Some concerns
Rosenstock2018	NCT01455857	Low	Low	Low	Low	Low	Low
Rosenstock 2019	NCT02057172	Some concerns	Low	Low	Low	Some concerns	High
Rosenstock2021	NCT03954834	Low	Low	Low	Low	Low	Low
Seino2008	NCT00154414	Low	Low	Low	Low	Low	Low
Shuai2021	NCT02477865	High	Low	Low	Low	Some concerns	High
Sorli2017	NCT02054897	Low	Low	Low	Low	Low	Low
Terauchi2014	NCT01001104	Low	Low	Low	Low	Low	Low
Umpierrez2014	NCT01126580	Low	Low	Low	Low	Low	Low
Vanderheiden2016	NCT01505673	Low	Low	Low	Low	Low	Low
Wysham2016	NCT01104701	Low	Low	Low	High	Some concerns	High
Yabe2020	NCT03015220	Low	Low	Low	Low	Low	Low
Yamada2020	NCT03018028	Low	Low	Low	Low	Low	Low
Zinman2019	NCT03086330	Low	Low	Low	Low	Low	Low
Frías2021	NCT03987919	Low	Low	Low	Low	Low	Low
DeFronzo2005	NA	Low	Low	Low	Low	High	High
Del Prato2020	NCT02081118	Low	Low	Some concerns	Low	Some concerns	Some concerns
Frias2021	NCT03495102	Low	Low	Some concerns	Low	High	High
Kadowaki2011	NCT00577824	Low	Low	Some concerns	Low	Some concerns	Some concerns
Ludvik2021	NCT03882970	Low	Low	Low	Low	Low	Low
Nauck2016	NCT00849017	Low	Low	Low	Low	Low	Low

Pratley2018	NCT02648204	Low	Low	Low	Low	Low	Low
Ratner2010	NA	Low	Low	Low	Low	Low	Low
Riddle2013	NCT007715624	Low	Low	Low	Low	Low	Low
Seino2014	NCT01098461	Some concerns	Low	Low	Low	Some concerns	Some concerns
Seino2012	NA	Some concerns	Low	Low	Low	Some concerns	Some concerns
Heise2022	NCT03951753	Low	Low	Low	Low	Low	Low
Ahmann2018	NCT01885208	Low	Some concerns	Low	Low	Low	Some concerns
Ahren2017	NCT01930188	Low	Low	Low	Low	Low	Low
Blonde 2015	NCT01191268	Low	Some concerns	Some concerns	Low	Low	Some concerns
Chen 2016	NCT01965509	Some concerns	Low	Low	Some concerns	Some concerns	Some concerns
Dahl 2022	NCT04039503	Low	Low	Low	Low	Low	Low
Dungan 2014	NCT01624259	Low	Low	Low	Low	Low	Low
Giorgino2015	NCT01075282	Some concerns	Low	Low	Low	Some concerns	Some concerns
Inagaki 2022	NCT03861052	Low	Low	Low	Low	Low	Low
Kadowaki 2022	NCT03861039	Low	Low	Low	Low	Low	Low
Miyagawa 2015	NCT01558271	Low	Low	Low	Some concerns	Some concerns	Some concerns
Pan 2014	NCT01169779	Low	Low	Low	Some concerns	Some concerns	Some concerns
Rodbard 2018	NCT02305381	Low	Low	Low	Some concerns	High	High
Rosenstock2019	NCT02607865	Low	Low	Low	Low	Low	Low
Rosenstock 2014	NCT00713830	Some concerns	Low	Low	High	High	High
Wang 2018	NCT01648582	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
Frias,2021	NCT03989232	Low	Low	Low	Low	Low	Low
Aroda 2023	NCT04707469	Low	Low	Low	Low	Low	Low
Frias,2022	NCT03353350	Low	Some concerns	Low	Low	Low	Some concerns
Frias,2023	NCT04982575	Low	Low	Low	Low	Low	Low
Frias 2023	NCT05048719	Low	Low	Low	Low	Low	Low
Gao 2020	NCT02477969	Low	Low	Some concerns	Low	Some concerns	Some concerns
Garvey 2023	NCT04657003	Low	Low	Low	Low	Low	Low
Pratt 2023	NCT04426474	Low	Low	Low	Low	Some concerns	Some concerns
Rosenstock 2023	NCT04867785	Low	Low	Low	Low	Low	Low
Urva 2022	NCT04143802	Low	Low	High	Low	Low	High

Appendix 5: Evaluation of inconsistency and heterogeneity

Table S5.1: Global consistency

Clinical outcome	Chi square	P value
HbA1c	18.94	0.5258
PFG	22.30	0.3246
Body weight	6.08	0.9119
BMI	2.99	0.8105
Waist circumference	7.05	0.0702
HDL	0.70	0.8740
LDL	6.21	0.1020
TG	1.88	0.3899
TC	3.88	0.2750

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Table S5.2: Side-splitting of HbA1c. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison	Direct		Indirect		Difference		
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Albiglutide v.s. Placebo	1.010196	.1858212	.8287283	36.10177	.181468	36.10225	0.996
CagriSema v.s. Semaglutide	.4000001	.39438	-.4875302	703.3394	.8875303	703.3395	0.999
Liraglutide v.s. Dulaglutide	.1405345	.169211	-.0625698	.1325139	.2031044	.2149187	0.345
Dulaglutide v.s. Mazdutide	-.5899999	.543167	-2.1715	.879162	1.5815	1.127501	0.161
Dulaglutide v.s. Orforglipron	-.7175051	.2958948	-.1418027	.3548137	-.5757024	.467939	0.219
Dulaglutide v.s. Placebo	1.0417	.1069788	.9456347	.1465279	.0960649	.1814791	0.597
Dulaglutide v.s. Retatrutide	-.136956	.2774511	-.5913831	.5530991	.4544271	.6463778	0.482
Dulaglutide v.s. Semaglutide	-.2003691	.2127641	-.2554687	.1294505	.0550996	.2489085	0.825
Dulaglutide v.s. Tirzepatide	-.9675652	.2230793	-.6562665	.1638432	-.3112987	.2776399	0.262
Efpeglenatide v.s. Liraglutide	-.2397865	.3089369	-.2776906	.218802	.0379041	.3814788	0.921
Efpeglenatide v.s. Placebo	.7245514	.1720204	.7729484	.5816305	-.048397	.6110658	0.937
Exenatide v.s. Liraglutide	-.2934627	.2151302	-.1791232	.1564295	-.1143395	.2659747	0.667
Exenatide v.s. Placebo	.8397442	.1441074	.6649272	.1876451	.174817	.2365944	0.460
Exenatide v.s. Semaglutide	-.6	.2914599	-.4403104	.1509303	-.1596896	.3282207	0.627
ITCA 650 v.s. Placebo	.9099998	.2960574	1.721679	604.7255	-.8116789	604.7256	0.999
Liraglutide v.s. Placebo	1.099688	.1033708	.7969379	.1397316	.3027503	.1738853	0.082
Liraglutide v.s. Semaglutide	-.3776726	.1688977	-.1739266	.138379	-.2037459	.218344	0.351
Lixisenatide v.s. Placebo	.5991026	.1324913	1.849504	267.291	-1.250401	267.291	0.996
Mazdutide v.s. Placebo	2.37	.4568535	.7884996	1.01581	1.5815	1.1275	0.161
Orforglipron v.s. Placebo	1.361676	.2441679	2.102848	.5574309	-.7411715	.6169521	0.230
PEG-Loxenatide v.s. Placebo	1.019917	.1832241	1.673032	417.3849	-.6531156	417.385	0.999
PEGylated exenatide v.s. Placebo	.97	.2988408	1.531057	547.5853	-.5610572	547.5854	0.999
Placebo v.s. Retatrutide	-1.354805	.2811711	-.9003783	.5476577	-.4544269	.6463779	0.482
Placebo v.s. Semaglutide	-1.157042	.1104185	-1.420999	.1507675	.2639563	.1871976	0.159
Placebo v.s. Tirzepatide	-1.699831	.1325818	-2.044991	.2564945	.34516	.2900046	0.234
Semaglutide v.s. Tirzepatide	-.2499322	.2841028	-.6106111	.1593395	.3606789	.3257385	0.268

Table S5.3: Side-splitting of FPG. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison		Direct		Indirect		Difference		
		Coef.	Std.Err.	Coef.	Std.Err.	Coef.	Std.Err.	P> z
Placebo	v.s.	-.8675887	.1184598	-.565361	.1707751	-.3022277	.208392	0.147
Dulaglutide								
Placebo	v.s.	-.2920277	.1946545	-1.464318	.6728239	1.17229	.7100549	0.099
Efpeglenatide								
Placebo	v.s.	-.6636427	.2967267	-.5991547	.2453683	-.064488	.3850017	0.867
Exenatide								
Placebo	v.s.	-.7694818	.1326122	-.7882901	.1799365	.0188083	.2238542	0.933
Liraglutide								
Placebo	v.s.	-.878	.4774491	-.525148	1.060385	-.352852	1.208058	0.770
Mazdutide								
Placebo	v.s.	-1.68122	.2716064	-1.289606	.6526367	-.3916141	.7199863	0.586
Orforglipron								
Placebo	v.s.	-.4544676	.3393247	-1.720447	.6463936	1.26598	.7528192	0.093
Retatrutide								
Placebo	v.s.	-1.051346	.1562587	-1.052108	.1993066	.0007624	.2563193	0.998
Semaglutide								
Placebo	v.s.	-1.643477	.1570611	-1.751809	.293449	.1083321	.3386902	0.749
Tirzepatide								
Cagrisema	v.s.	.4008349	.3968502	-2.099082	.633.0851	2.499917	.633.0852	0.997
Semaglutide								
Dulaglutide	v.s.	-.1053652	.1857264	.073342	.1648169	-.1787071	.2482851	0.472
Liraglutide								
Dulaglutide	v.s.	.0637257	.548634	-.2891262	.9514679	.3528519	1.208058	0.770
Mazdutide								
Dulaglutide	v.s.	-.7350531	.3427681	-.9895634	.3853908	.2545103	.5240047	0.627
Orforglipron								
Dulaglutide	v.s.	-.2720405	.3382577	.9939393	.648069	-1.26598	.752819	0.093
Retatrutide								
Dulaglutide	v.s.	-.2305168	.3155471	-.293749	.1592971	.0632322	.3534764	0.858
Semaglutide								
Dulaglutide	v.s.	-.9273527	.2383804	-.8778575	.1971344	-.0494952	.310477	0.873
Tirzepatide								
Efpeglenatide	v.s.	-.0055962	.3512486	-.5783333	.2545441	.5727371	.4386792	0.192
Liraglutide								
Exenatide	v.s.	-.2955678	.3233209	-.0690098	.242823	-.226558	.4043506	0.575
Liraglutide								
Exenatide	v.s.	-.3307052	.3182352	-.4856754	.251561	.1549702	.4056558	0.702
Semaglutide								
Liraglutide	v.s.	-.380303	.2249216	-.2128306	.1734483	-.1674724	.2840356	0.555
Semaglutide								
Semaglutide	v.s.	-.5260827	.3785672	-.6401659	.1903018	.1140832	.4234557	0.788
Tirzepatide								

Abbreviations: FPG, fasting plasma glucose.

Table S5.4: Side-splitting of weight. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison		Direct		Indirect		Difference		
		Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Placebo	v.s.	-.9882329	1.121488	.2910047	1.674687	-1.279238	2.017323	0.526
Dulaglutide								
Placebo	v.s.	-2.651436	.8334561	-.6773573	1.788804	-1.974079	1.973419	0.317
Liraglutide								
Placebo	v.s.	-1.29	1.974305	-3.152089	4.041494	1.862089	4.598857	0.686
Mazdutide								
Placebo	v.s.	-3.45	1.832668	-1.377472	3.951384	-2.072528	4.497462	0.645
Orforglipron								
Placebo	v.s.	-4.63	2.726679	-.3578394	7.198327	-4.272161	7.962825	0.592
Retatrutide								
Placebo	v.s.	-2.544041	.7234505	-5.990598	.9676204	3.446557	1.20794	0.004
Semaglutide								
Placebo	v.s.	-7.424487	1.077885	-1.170287	3.735965	-6.2542	3.998961	0.118
Tirzepatide								
Dulaglutide	v.s.	-1.43	1.924057	.4320889	4.113555	-1.862089	4.598858	0.686
Mazdutide								
Dulaglutide	v.s.	-2.05	1.820275	-4.122529	3.968528	2.072529	4.497458	0.645
Orforglipron								
Dulaglutide	v.s.	-2.03	3.589158	-6.30216	5.956013	4.27216	7.962826	0.592
Retatrutide								
Dulaglutide	v.s.	-5.11	1.331039	-1.620256	1.232543	-3.489744	1.814063	0.054
Semaglutide								
Dulaglutide	v.s.	-3.300656	1.427016	-9.352569	1.278464	6.051913	1.931855	0.002
Tirzepatide								
Exenatide	v.s.	-2.8	1.567292	-7.490981	3518.286	4.690981	3518.286	0.999
Semaglutide								
Liraglutide	v.s.	-2.7	1.574146	-.7259222	1.190147	-1.974078	1.97342	0.317
Semaglutide								

Table S5.5: Side-splitting of BMI. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison	Direct		Indirect		Difference		P> z
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	
Placebo v.s. Dulaglutide	-.7584166	.5169923	-.7153564	.607924	-.0430602	.798943	0.957
Placebo v.s. Liraglutide	-.9615052	.2285539	.1083288	.5550158	-1.069834	.601838	0.075
Placebo v.s. Orforglipron	-1.99	.6901276	-2.381143	1.527281	.3911433	1.734907	0.822
Placebo v.s. Semaglutide	-1.000565	.2132208	-2.151344	.3838959	1.150779	.4408413	0.009
Placebo v.s. Tirzepatide	-3.053274	.436799	-.8886008	1.465515	-2.164673	1.547763	0.162
Dulaglutide v.s. Orforglipron	-1.39	.6613493	-.9988566	1.565015	-.3911434	1.734908	0.822
Dulaglutide v.s. Semaglutide	-1	.5637179	-.1320704	.5325146	-.8679296	.7754673	0.263
Dulaglutide v.s. Tirzepatide	-1.153352	.5780195	-3.410155	.6525466	2.256804	.8759732	0.010
Exenatide v.s. Semaglutide	-1.4	.5823807	-2.56109	1136.39	1.16109	1136.39	0.999
Liraglutide v.s. Semaglutide	-.8996062	.3925248	-.0986321	.3666822	-.8009741	.537149	0.136

Abbreviations: BMI, body mass index.

Table S5.6: Side-splitting of waist circumference. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison	Direct		Indirect		Difference		
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Placebo v.s. Dulaglutide	-.9882329	1.121488	.2910047	1.674687	-1.279238	2.017323	0.526
Placebo v.s. Liraglutide	-2.651436	.8334561	-.6773573	1.788804	-1.974079	1.973419	0.317
Placebo v.s. Mazdutide	-1.29	1.974305	-3.152089	4.041494	1.862089	4.598857	0.686
Placebo v.s. Orforglipron	-3.45	1.832668	-1.377472	3.951384	-2.072528	4.497462	0.645
Placebo v.s. Retatrutide	-4.63	2.726679	-.3578394	7.198327	-4.272161	7.962825	0.592
Placebo v.s. Semaglutide	-2.544041	.7234505	-5.990598	.9676204	3.446557	1.20794	0.004
Placebo v.s. Tirzepatide	-7.424487	1.077885	-1.170287	3.735965	-6.2542	3.998961	0.118
Dulaglutide v.s. Mazdutide	-1.43	1.924057	.4320889	4.113555	-1.862089	4.598858	0.686
Dulaglutide v.s. Orforglipron	-2.05	1.820275	-4.122529	3.968528	2.072529	4.497458	0.645
Dulaglutide v.s. Retatrutide	-2.03	3.589158	-6.30216	5.956013	4.27216	7.962826	0.592
Dulaglutide v.s. Semaglutide	-5.11	1.331039	-1.620256	1.232543	-3.489744	1.814063	0.054
Dulaglutide v.s. Tirzepatide	-3.300656	1.427016	-9.352569	1.278464	6.051913	1.931855	0.002
Exenatide v.s. Semaglutide	-2.8	1.567292	-7.490981	3518.286	4.690981	3518.286	0.999
Liraglutide v.s. Semaglutide	-2.7	1.574146	-.7259222	1.190147	-1.974078	1.97342	0.317

Table S5.7: Side-splitting of HDL. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison		Direct		Indirect		Difference		
		Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Placebo	v.s.	.0596108	.0317801	-.0067061	.0240592	.0663169	.0441089	0.133
Exenatide								
Placebo	v.s.	.0614143	.0416246	.0006071	.0319953	.0608072	.0529931	0.251
Liraglutide								
Placebo	v.s.	-.0088532	.0074118	.0971736	.0118235	-.1060268	.0139546	0.000
Semaglutide								
Exenatide	v.s.	.0040793	.0310812	.0081196	.0423539	-.0040404	.0524029	0.939
Liraglutide								
Exenatide	v.s.	.02	.0350405	-.0284609	.0295173	.0484609	.045816	0.290
Semaglutide								
Liraglutide	v.s.	.02	.0362719	-.0358981	.030676	.0558981	.0475044	0.239
Semaglutide								
Semaglutide	v.s.	.1629982	.0775481	3.393126	552.3029	-3.230128	552.3029	0.995
Tirzepatide								
Placebo	v.s.	.0596108	.0317801	-.0067061	.0240592	.0663169	.0441089	0.133
Exenatide								
Placebo	v.s.	.0614143	.0416246	.0006071	.0319953	.0608072	.0529931	0.251
Liraglutide								
Placebo	v.s.	-.0088532	.0074118	.0971736	.0118235	-.1060268	.0139546	0.000
Semaglutide								
Exenatide	v.s.	.0040793	.0310812	.0081196	.0423539	-.0040404	.0524029	0.939
Liraglutide								
Exenatide	v.s.	.02	.0350405	-.0284609	.0295173	.0484609	.045816	0.290
Semaglutide								
Liraglutide	v.s.	.02	.0362719	-.0358981	.030676	.0558981	.0475044	0.239
Semaglutide								
Semaglutide	v.s.	.1629982	.0775481	3.393126	552.3029	-3.230128	552.3029	0.995
Tirzepatide								

Abbreviations: HDL, high-density lipoprotein.

Table S5.8: Side-splitting of LDL. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison		Direct		Indirect		Difference		
		Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Placebo	v.s.	.23	.1197301	-.1586715	.0899699	.3886715	.1497661	0.009
Exenatide								
Placebo	v.s.	-.2176084	.1008083	-.007262	.11705	-.2103464	.1544084	0.173
Liraglutide								
Placebo	v.s.	-.1813839	.0891143	-.1103092	.1422923	-.0710747	.1678841	0.672
Semaglutide								
Exenatide	v.s.	-.04	.1137061	-.2128479	.1366556	.1728479	.1777747	0.331
Liraglutide								
Exenatide	v.s.	-.03	.1460589	-.2230016	.1203406	.1930016	.1892487	0.308
Semaglutide								
Liraglutide	v.s.	-.09	.1532214	-.0045569	.1129104	-.0854431	.1903301	0.653
Semaglutide								
Semaglutide	v.s.	.02	.1887358	4.293933	949.0817	-4.273933	949.0817	0.996
Tirzepatide								

Abbreviations: LDL, low-density lipoprotein.

Table S5.9: Side-splitting of TC. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison		Direct		Indirect		Difference		
		Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Placebo	v.s.	.53	.2193591	-.3673317	.1863805	.8973317	.2878474	0.002
Exenatide								
Placebo	v.s.	-.17	.3367563	-.1650294	.2883822	-.0049706	.4433611	0.991
Liraglutide								
Placebo	v.s.	-.7379036	.1792963	.0358	.2435973	-.7737035	.302543	0.011
Semaglutide								
Exenatide	v.s.	-.0996573	.2412449	-.3049767	.3314079	.2053194	.4099139	0.616
Liraglutide								
Exenatide	v.s.	-.1	.2786983	-.7595583	.2410086	.6595583	.3684534	0.073
Semaglutide								
Liraglutide	v.s.	-.18	.3305755	-.406116	.2835447	.226116	.4355201	0.604
Semaglutide								
Semaglutide	v.s.	-.06333	.319004	.9722882	.820.4632	-1.035618	.820.4632	0.999
Tirzepatide								

Abbreviations: TC, total cholesterol; Abbreviation.

Table S5.10: Side-splitting of TG. Inconsistency test between direct and indirect treatment comparisons in mixed treatment comparison.

Comparison	Direct		Indirect		Difference		
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z
Placebo v.s. Liraglutide	-.4891101	.2180239	.0394901	.3113614	-.5286002	.3801128	0.164
Placebo v.s. Semaglutide	-.159647	.1784684	-.6882379	.3356325	.5285909	.3801119	0.164
Exenatide v.s. Liraglutide	-.18	.3746939	-.2753768	.413293	.0953768	.557859	0.864
Exenatide v.s. Semaglutide	-.22	.3423803	-.1246256	.4404322	-.0953744	.5578573	0.864
Liraglutide v.s. Semaglutide	-.27	.3125594	.2282687	.2446321	-.4982687	.3969109	0.209
Semaglutide v.s. Tirzepatide	-.61	.347609	.860223	1310.52	-1.470223	1310.52	0.999

Abbreviations: TG, triglyceride.

Table S5.11: Heterogeneity score by each comparison for main model of HbA1c

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Liraglutide	Placebo	0.01	0.07
Dulaglutide	Placebo	0.07	0.08
Tirzepatide	Placebo	0.04	0.08
Semaglutide	Placebo	0.03	0.07
Exenatide	Placebo	0.05	0.08
Albiglutide	Placebo	0.00	0.08
Lixisenatide	Placebo	0.00	0.08
Mazdutide	Placebo	0.00	0.08
Liraglutide	Exenatide	0.00	0.08
Liraglutide	Dulaglutide	0.00	0.08
Liraglutide	Semaglutide	0.03	0.08
Liraglutide	Lixisenatide	NA	0.08
Dulaglutide	Semaglutide	0.10	0.08
Dulaglutide	Tirzepatide	0.20	0.08
Semaglutide	Tirzepatide	0.00	0.08
Dulaglutide	Mazdutide	0.00	0.08
Semaglutide	Exenatide	0.00	0.08

Table S5.12: Heterogeneity score by each comparison for main model of FPG

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Liraglutide	Placebo	0.04	0.10
Dulaglutide	Placebo	0.08	0.07
Tirzepatide	Placebo	0.04	0.08
Semaglutide	Placebo	0.05	0.10
Exenatide	Placebo	0.00	0.09
Albiglutide	Placebo	0.00	0.04
Lixisenatide	Placebo	0.01	0.09
Efpeglenatide	Placebo	0.00	0.09
Loxenatide	Placebo	0.00	0.09
Mazdutide	Placebo	0.00	0.00
ITCA 650	Placebo	NA	0.09
PEGylated exenatide	Placebo	0.00	0.09
Loxenatide	Placebo	0.00	0.08
Orforglipron	Placebo	0.00	0.09
Retatrutide	Placebo	0.00	0.09
Liraglutide	Semaglutide	0.04	0.09
Liraglutide	Efpeglenatide	NA	0.09
Liraglutide	Exenatide	NA	0.08
Liraglutide	Dulaglutide	0.03	0.09
Liraglutide	Semaglutide	NA	0.09
Dulaglutide	Semaglutide	0.00	0.10
Dulaglutide	Tirzepatide	0.03	0.09
Semaglutide	Exenatide	0.00	0.09
Dulaglutide	Semaglutide	NA	0.09
Retatrutide	Dulaglutide	0.00	0.09
CagriSema	Semaglutide	0.00	0.09
Tirzepatide	Semaglutide	0.00	0.09
Dulaglutide	Orforglipron	NA	0.09

Abbreviations: FPG, fasting plasma glucose.

Table S5.13: Heterogeneity score by each comparison for main model of body weight

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Dulaglutide	0.09	0.13
Placebo	Efpeglenatide	0.00	0.11
Placebo	Exenatide	0.04	0.11
Placebo	Liraglutide	0.36	0.11
Placebo	Mazdutide	0.04	0.11
Placebo	Orforglipron	0.00	0.11
Placebo	Retatrutide	0.13	0.12
Placebo	Semaglutide	0.18	0.22
Placebo	Tirzepatide	0.01	0.12
Placebo	Albiglutide	0.00	0.22
CagriSema	Semaglutide	0.00	0.11
Placebo	CagriSema	NA	0.11
Dulaglutide	Liraglutide	0.00	0.11
Dulaglutide	Mazdutide	0.00	0.16
Dulaglutide	Orforglipron	0.03	0.11
Dulaglutide	Retatrutide	0.00	0.11
Dulaglutide	Semaglutide	0.00	0.22
Dulaglutide	Tirzepatide	0.00	0.12
Efpeglenatide	Liraglutide	0.03	0.11
Exenatide	Liraglutide	0.00	0.12
Exenatide	Semaglutide	NA	0.11
Liraglutide	Semaglutide	0.06	0.12
Semaglutide	Tirzepatide	NA	0.09
Orforglipron	Placebo	0.00	0.11
Placebo	PEG-Loxenatide	0.00	0.22

Table S5.14: Heterogeneity score by each comparison for main model of BMI

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Dulaglutide	0.00	0.08
Placebo	Liraglutide	0.10	0.04
Placebo	Orforglipron	0.00	0.08
Placebo	Semaglutide	0.08	0.05
Placebo	Tirzepatide	0.03	0.08
Dulaglutide	Orforglipron	0.00	0.07
Dulaglutide	Semaglutide	0.00	0.08
Dulaglutide	Tirzepatide	0.00	0.08
Liraglutide	Tirzepatide	0.01	0.10
Exenatide	Semaglutide	0.00	0.07
Liraglutide	Semaglutide	0.08	0.05
Placebo	PEG-Loxenatide	0.00	0.10

Abbreviations: BMI, Body Mass Index.

Table S5.15: Heterogeneity score by each comparison for main model of waist circumference

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Dulaglutide	0.00	0.03
Placebo	Liraglutide	0.00	0.03
Placebo	Mazdutide	0.00	0.04
Placebo	Orforglipron	0.00	0.02
Placebo	Retatrutide	0.00	0.04
Placebo	Semaglutide	0.00	0.02
Placebo	Tirzepatide	0.00	0.04
Dulaglutide	Mazdutide	0.00	0.03
Dulaglutide	Orforglipron	0.00	0.03
Dulaglutide	Retatrutide	0.00	0.10
Dulaglutide	Semaglutide	0.00	0.03
Dulaglutide	Tirzepatide	NA	0.03
Exenatide	Semaglutide	0.00	0.04
Liraglutide	Semaglutide	0.00	0.04

Table S5.16: Heterogeneity score by each comparison for main model of HDL

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Exenatide	0.00	0.00
Placebo	Liraglutide	0.00	0.00
Placebo	Semaglutide	0.00	0.00
Exenatide	Liraglutide	0.20	0.01
Exenatide	Semaglutide	0.01	0.01
Liraglutide	Semaglutide	0.01	0.01
Semaglutide	Tirzepatide	0.00	0.00

Abbreviations: HDL, high-density lipoprotein.

Table S5.17: Heterogeneity score by each comparison for main model of LDL

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Exenatide	0.00	0.01
Placebo	Liraglutide	0.00	0.02
Placebo	Semaglutide	0.83	0.02
Exenatide	Liraglutide	0.00	0.02
Exenatide	Semaglutide	0.00	0.02
Liraglutide	Semaglutide	0.00	0.02
Semaglutide	Tirzepatide	0.10	0.02

Abbreviations: LDL, low-density lipoprotein.

Table S5.18: Heterogeneity score by each comparison for main model of TC

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Exenatide	0.00	0.05
Placebo	Liraglutide	0.00	0.11
Placebo	Semaglutide	0.10	0.06
Placebo	Dulaglutide	0.03	0.11
Placebo	PEG-Loxenatide	0.10	0.11
Exenatide	Liraglutide	0.00	0.11
Exenatide	Semaglutide	0.00	0.08
Liraglutide	Semaglutide	0.00	0.11
Semaglutide	Tirzepatide	0.00	0.10

Abbreviations: TC, total cholesterol

Table S5.19: Heterogeneity score by each comparison for main model of TG

Treatment 1	Treatment 2	τ^2 pairwise	τ^2 network
Placebo	Liraglutide	0.10	0.09
Placebo	Semaglutide	0.05	0.09
Placebo	Dulaglutide	0.05	0.09
Exenatide	Liraglutide	0.00	0.12
Exenatide	Semaglutide	0.00	0.12
Liraglutide	Semaglutide	0.00	0.10
Semaglutide	Tirzepatide	0.00	0.10

Abbreviations: TG, triglyceride.

Appendix 6: Network maps and forest plots of secondary outcomes

Figure S6.1: Network map of the effect on BMI, and forest plot of network effect sizes for compared with placebo. The size of the nodes was proportional to the number of participants included in the trial, and the thickness of lines between the interventions relates to the number of studies for that comparison.

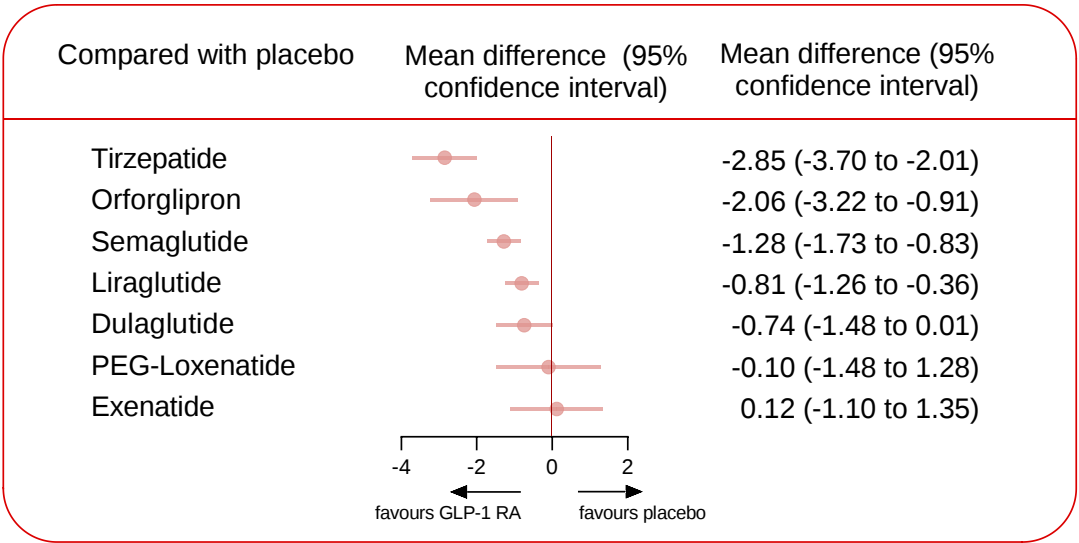
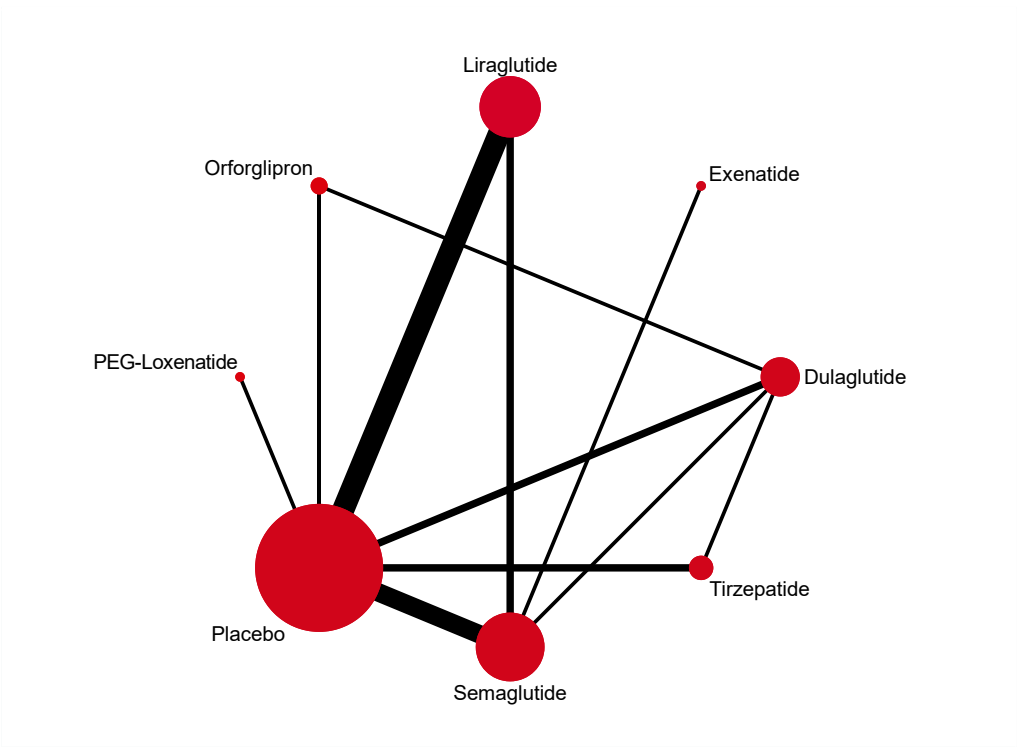


Figure S6.2: Network map of the effect on waist circumference, and forest plot of network effect sizes for compared with placebo. The size of the nodes was proportional to the number of participants included in the trial, and the thickness of lines between the interventions relates to the number of studies for that comparison.

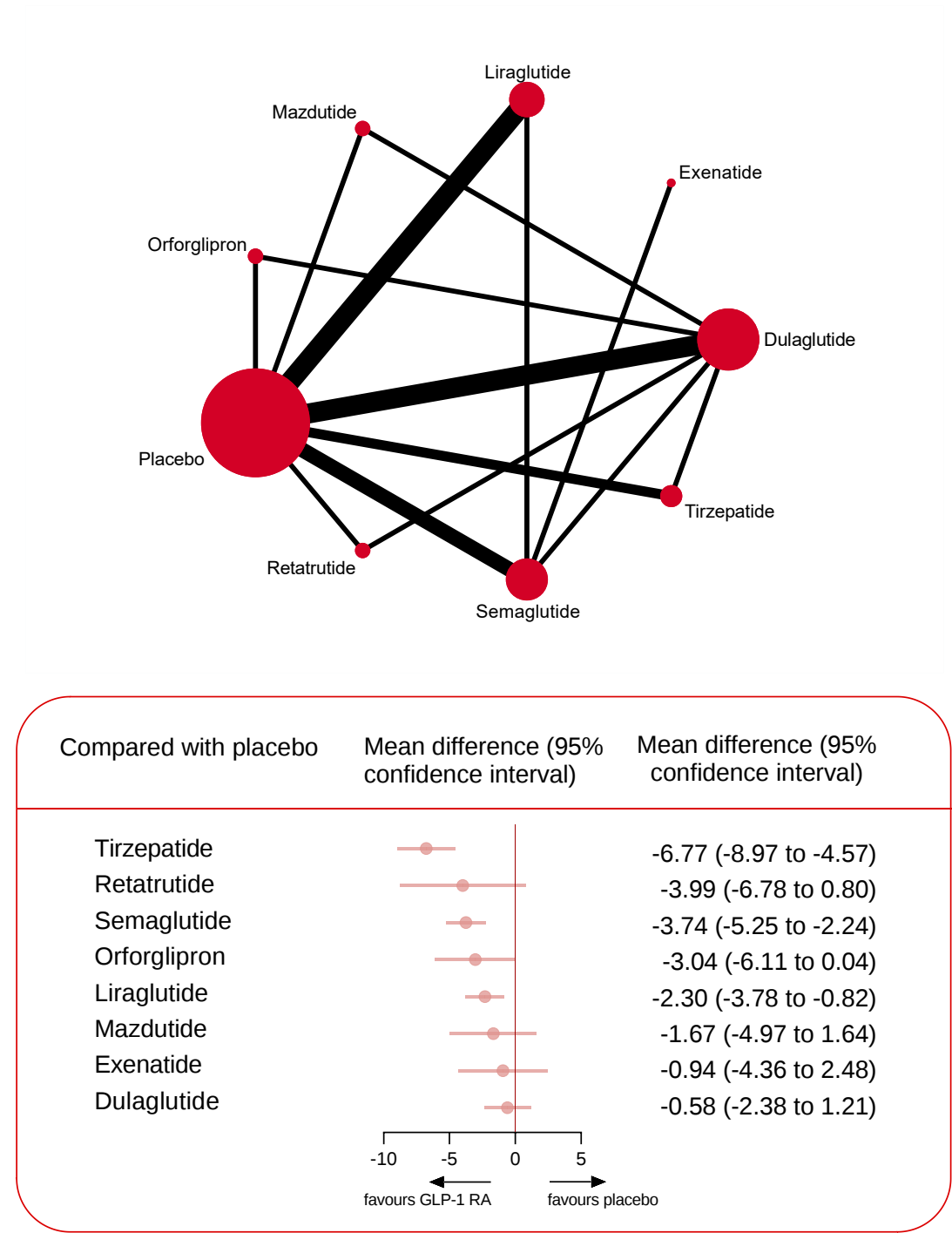


Figure S6.3: Network map of the effect on HDL, and forest plot of network effect sizes for compared with placebo. The size of the nodes was proportional to the number of participants included in the trial, and the thickness of lines between the interventions relates to the number of studies for that comparison.

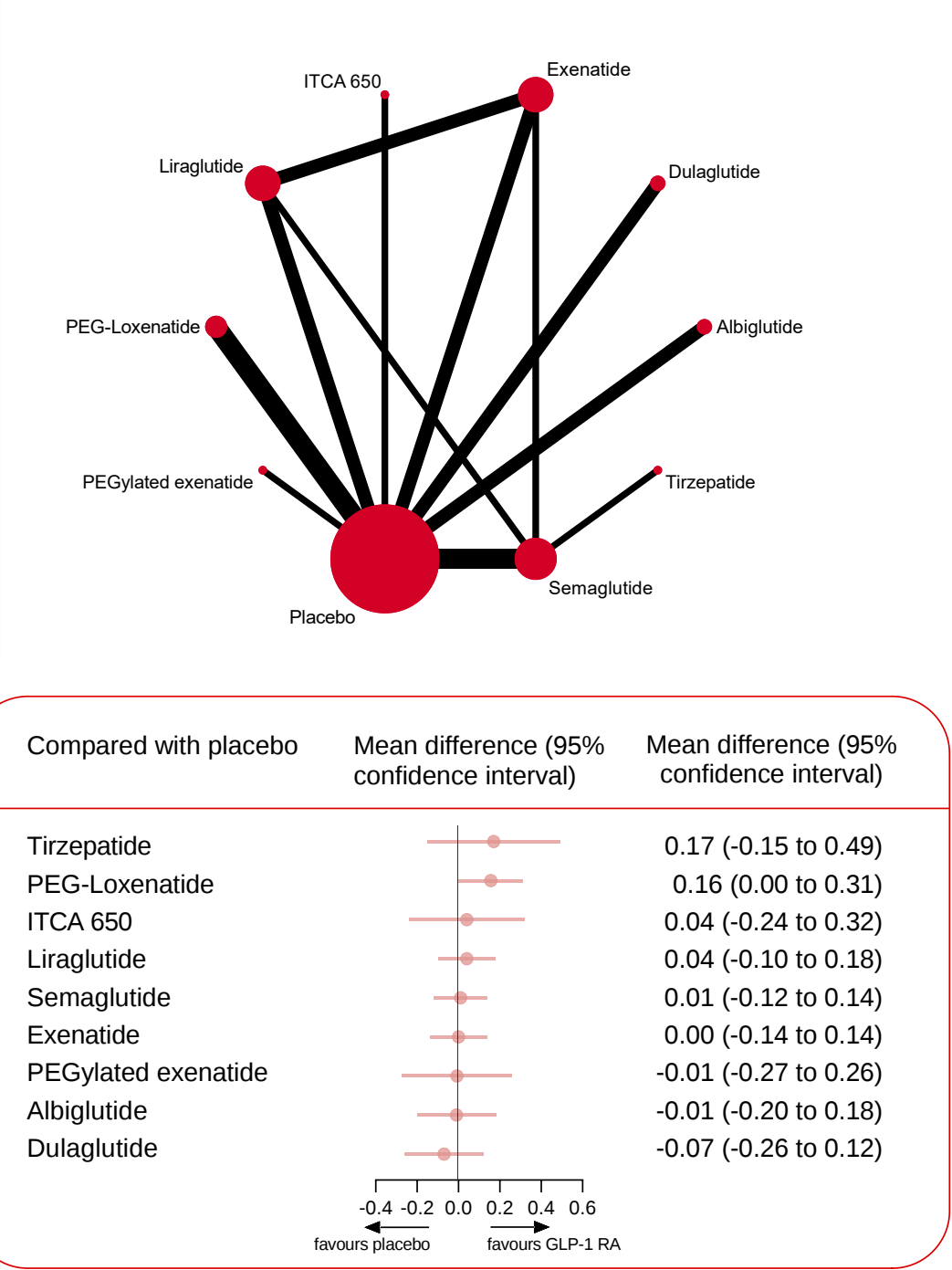


Figure S6.4: Network map of the effect on LDL, and forest plot of network effect sizes for compared with placebo. The size of the nodes was proportional to the number of participants included in the trial, and the thickness of lines between the interventions relates to the number of studies for that comparison.

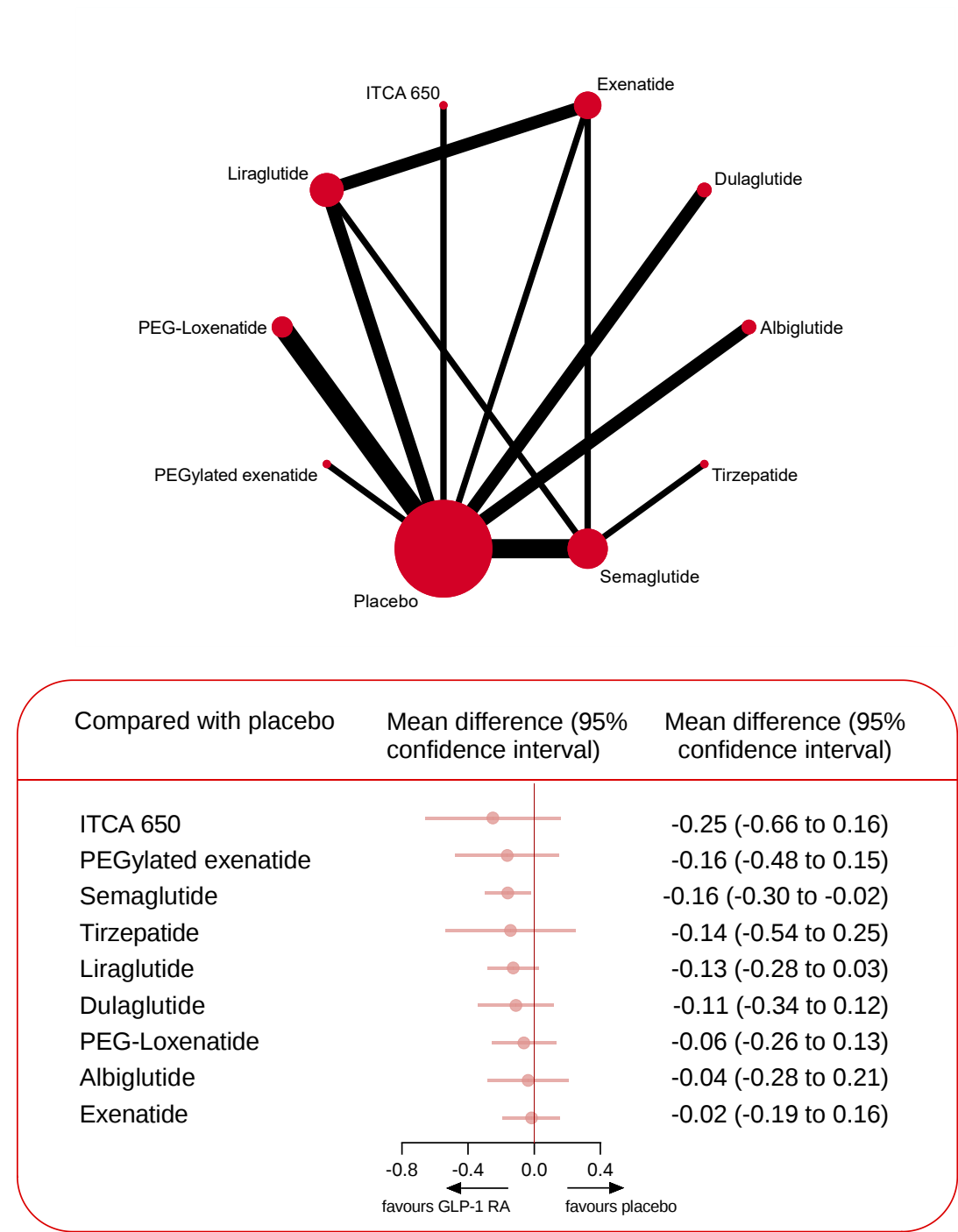


Figure S6.5: Network map of the effect on TC, and forest plot of network effect sizes for compared with placebo. The size of the nodes was proportional to the number of participants included in the trial, and the thickness of lines between the interventions relates to the number of studies for that comparison.

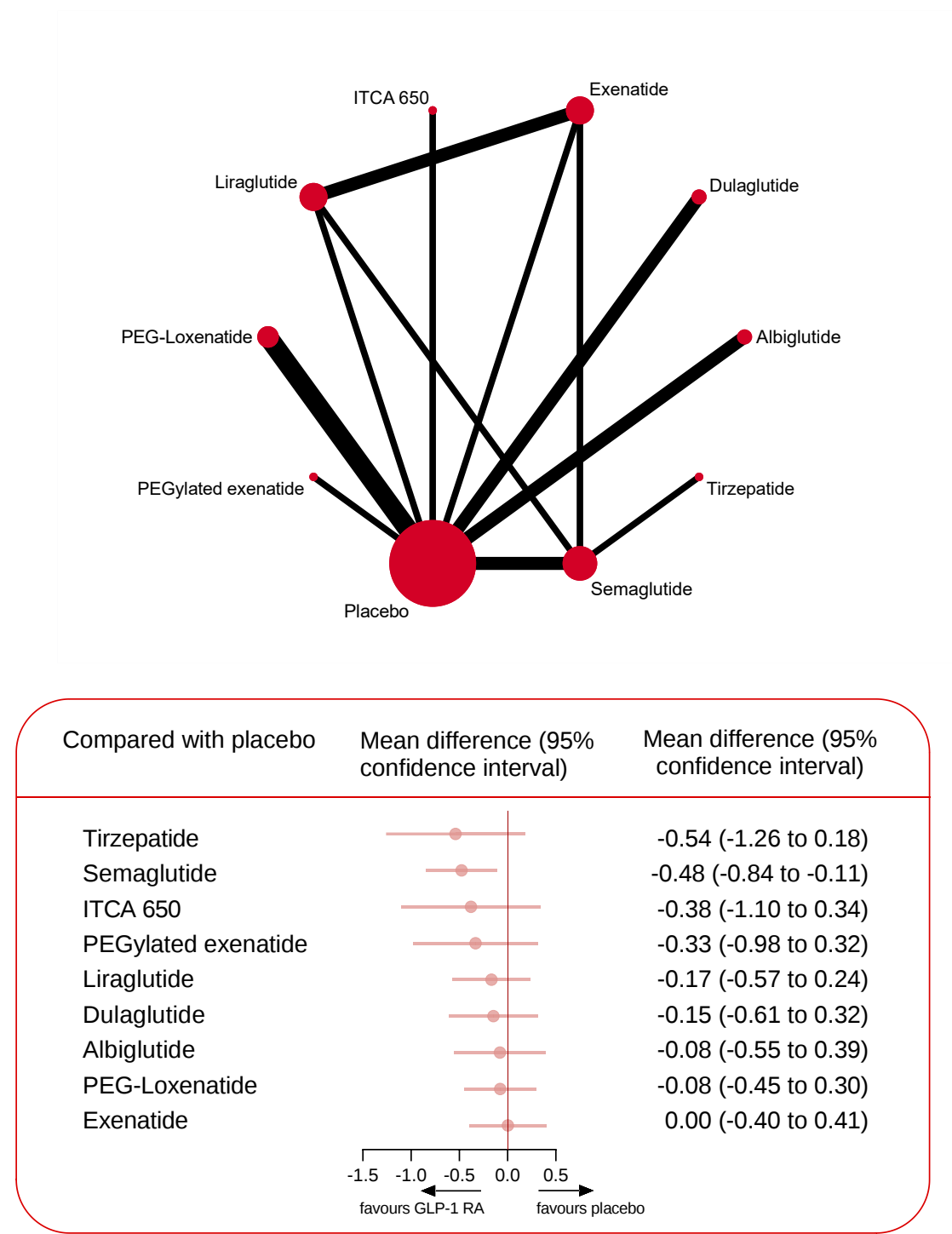
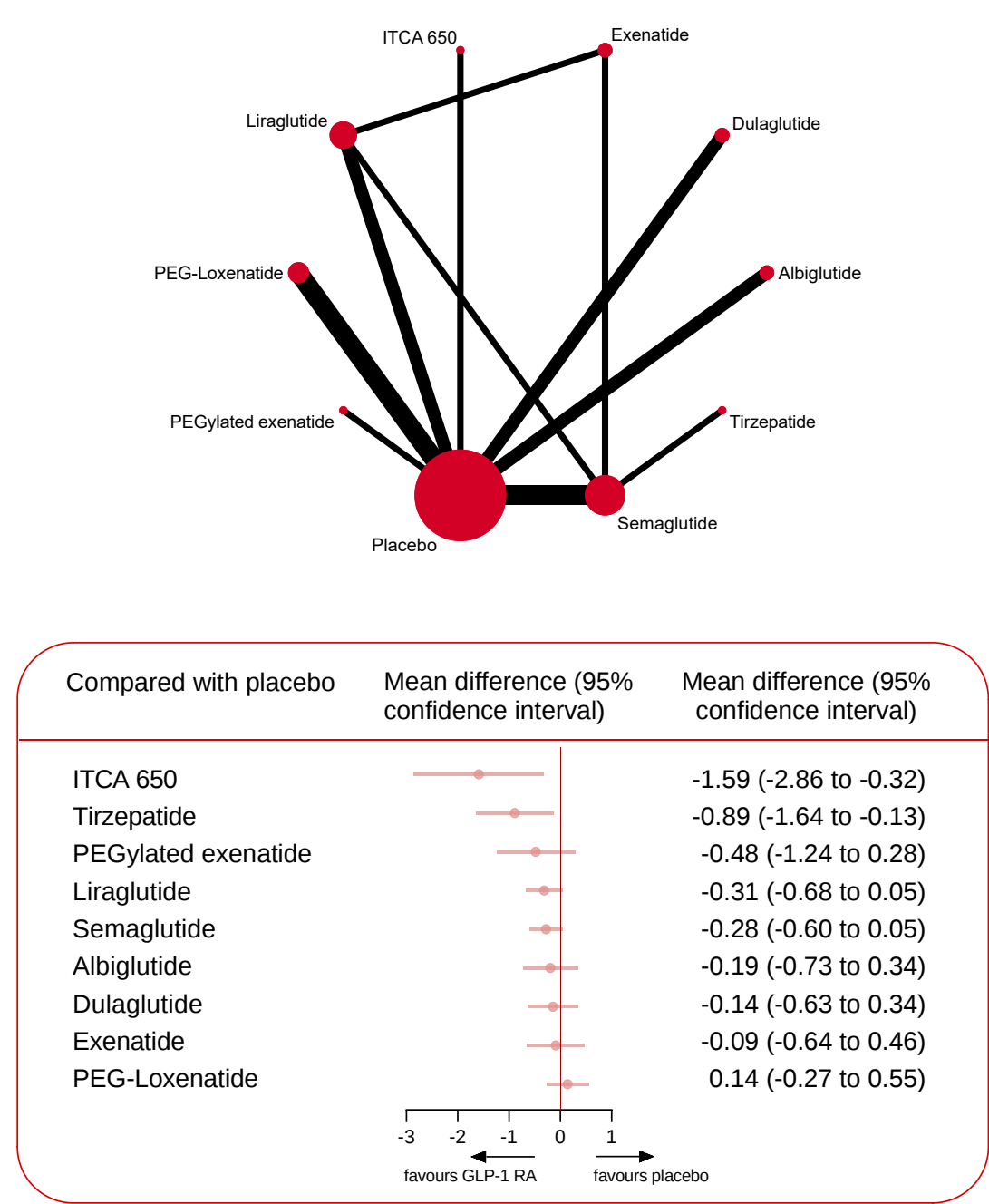


Figure S6.6: Network map of the effect on TG, and forest plot of network effect sizes for compared with placebo. The size of the nodes was proportional to the number of participants included in the trial, and the thickness of lines between the interventions relates to the number of studies for that comparison.



Appendix 7: SUCRA and cumulative probability plots

Figure S7.1: Cumulative ranking curve plots of GLP-1RAs for HbA1c in range network. Higher surface under the curve reflects higher probability of association with HbA1c.

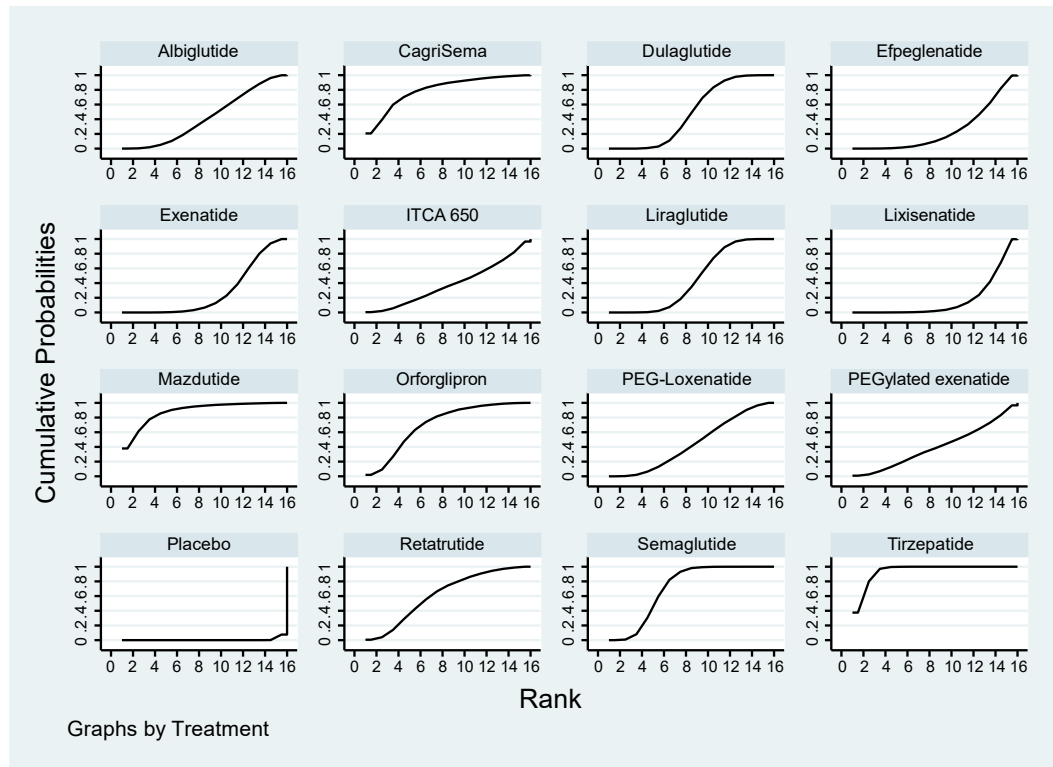


Table S7.1: SUCRA of the effects of various GLP-1RAs on HbA1c.

Treatment	SUCRA	PrBest	MeanRank
Tirzepatide	94.2	35.5	1.9
Mazdutide	90.4	40.8	2.4
CagriSema	80.9	20.9	3.9
Orforglipron	73	1.7	5.1
Semaglutide	71	0	5.4
Retatrutide	63.1	0.5	6.5
Dulaglutide	48.7	0	8.7
Liraglutide	45.1	0	9.2
PEG-Loxenatide	44.9	0	9.3
Albiglutide	43.5	0	9.5
PEGylated exenatide	40.5	0.3	9.9
ITCA 650	37.4	0.3	10.4
Exenatide	26.8	0	12
Efpeglenatide	24.3	0	12.4
Lixisenatide	16.1	0	13.6
Placebo	0.3	0	16

Abbreviations: SUCRA, surface under the cumulative ranking curve.

Figure S7.2: Cumulative ranking curve plots of GLP-1RAs for FPG in range network. Higher surface under the curve reflects higher probability of association with FPG.

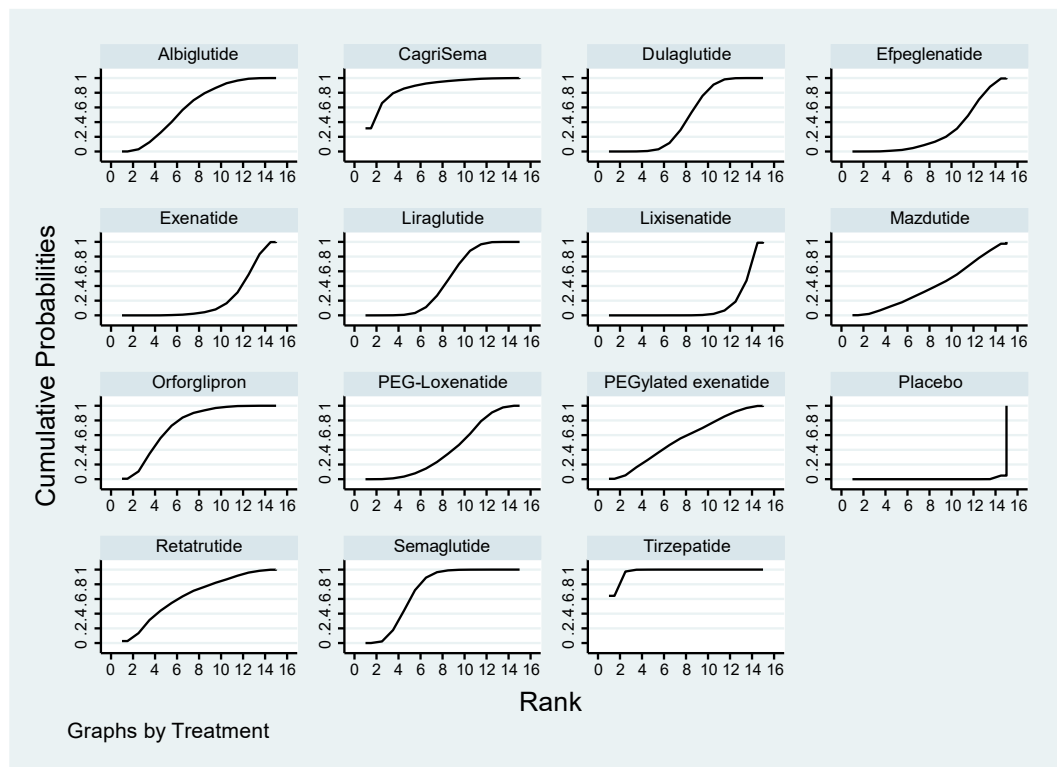


Table S7.2: SUCRA of the effects of various GLP-1RAs on FPG.

Treatment	SUCRA	PrBest	MeanRank
Tirzepatide	97.2	64.3	1.4
CagriSema	87.8	31.6	2.7
Orforglipron	74.1	0.6	4.6
Semaglutide	72.9	0	4.8
Retatrutide	65.1	2.7	5.9
Albiglutide	61.6	0.1	6.4
PEGylated exenatide	55.1	0.5	7.3
Dulaglutide	47.3	0	8.4
Liraglutide	46	0	8.6
Mazdutide	40.6	0.2	9.3
PEG-Loxenatide	40.1	0	9.4
Efpeglenatide	27.7	0	11.1
Exenatide	21.6	0	12
Lixisenatide	12.4	0	13.3
Placebo	0.4	0	14.9

Abbreviations: FPG, fasting plasma glucose; SUCRA, surface under the cumulative ranking curve.

Figure S7.3: Cumulative ranking curve plots of GLP-1RAs for weight loss in range network. Higher surface under the curve reflects higher probability of association with weight.

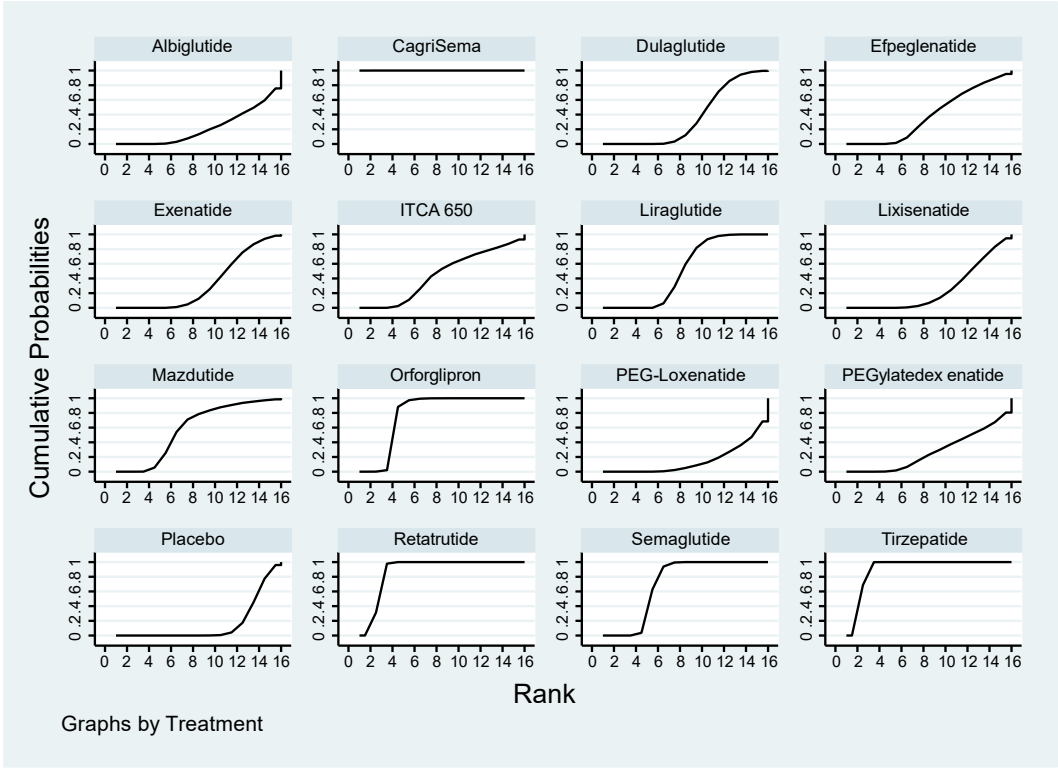


Table S7.3: SUCRA of the effects of various GLP-1RAs on body weight loss.

Treatment	SUCRA	PrBest	MeanRank
CagriSema	100	100	1
Tirzepatide	91.2	0	2.3
Retatrutide	88.6	0	2.7
Orforglipron	79.1	0	4.1
Semaglutide	70.7	0	5.4
Mazdutide	58.7	0	7.2
Liraglutide	51.1	0	8.3
ITCA 650	45	0	9.2
Efpeglenatide	39.4	0	10.1
Dulaglutide	36.2	0	10.6
Exenatide	33.3	0	11
PEGylated exenatide	27.8	0	11.8
Lixisenatide	25.7	0	12.1
Albiglutide	21.9	0	12.7
Placebo	16.1	0	13.6
PEG-Loxenatide	15.1	0	13.7

Abbreviations: SUCRA, surface under the cumulative ranking curve.

Figure S7.4: Cumulative ranking curve plots of GLP-1RAs for BMI in range network. Higher surface under the curve reflects higher probability of association with BMI.

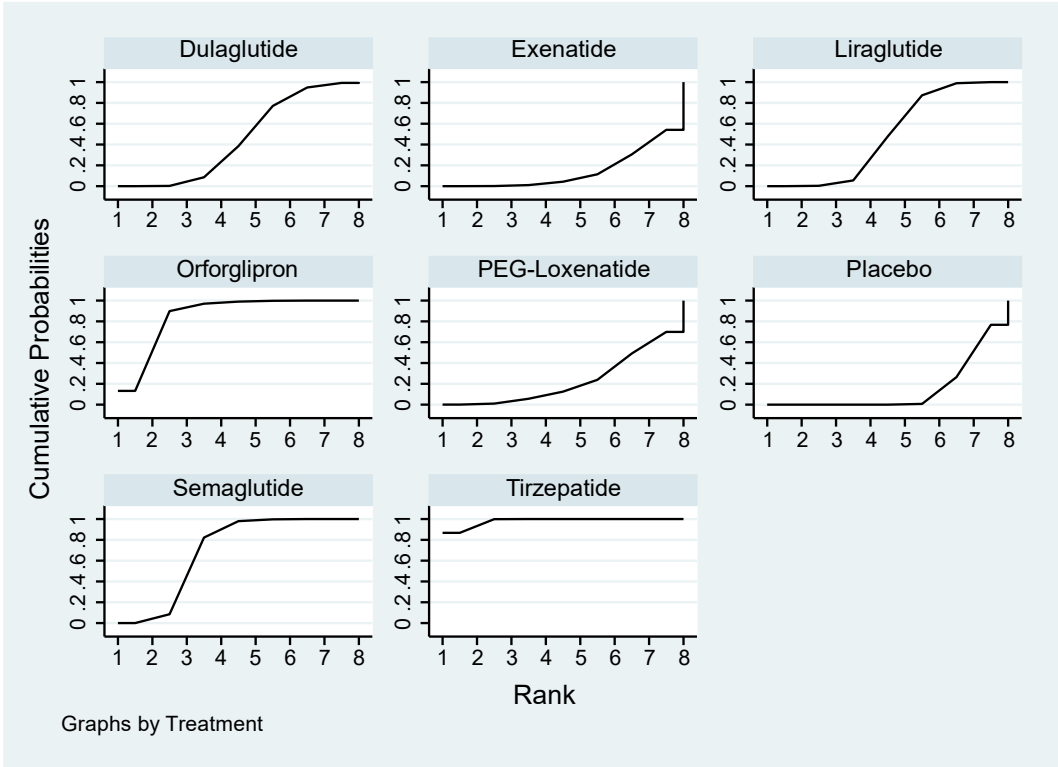


Table S7.4: SUCRA of the effects of various GLP-1RAs on BMI.

Treatment	SUCRA	PrBest	MeanRank
Tirzepatide	98.1	86.7	1.1
Orforglipron	85.6	13.2	2
Semaglutide	69.8	0	3.1
Liraglutide	48.5	0	4.6
Dulaglutide	45.5	0	4.8
PEG-Loxenatide	23.2	0	6.4
Placebo	14.8	0	7
Exenatide	14.5	0	7

Abbreviations: BMI, body mass index; SUCRA, surface under the cumulative ranking curve.

Figure S7.5: Cumulative ranking curve plots of GLP-1RAs for waist circumference in range network. Higher surface under the curve reflects higher probability of association with waist circumference.

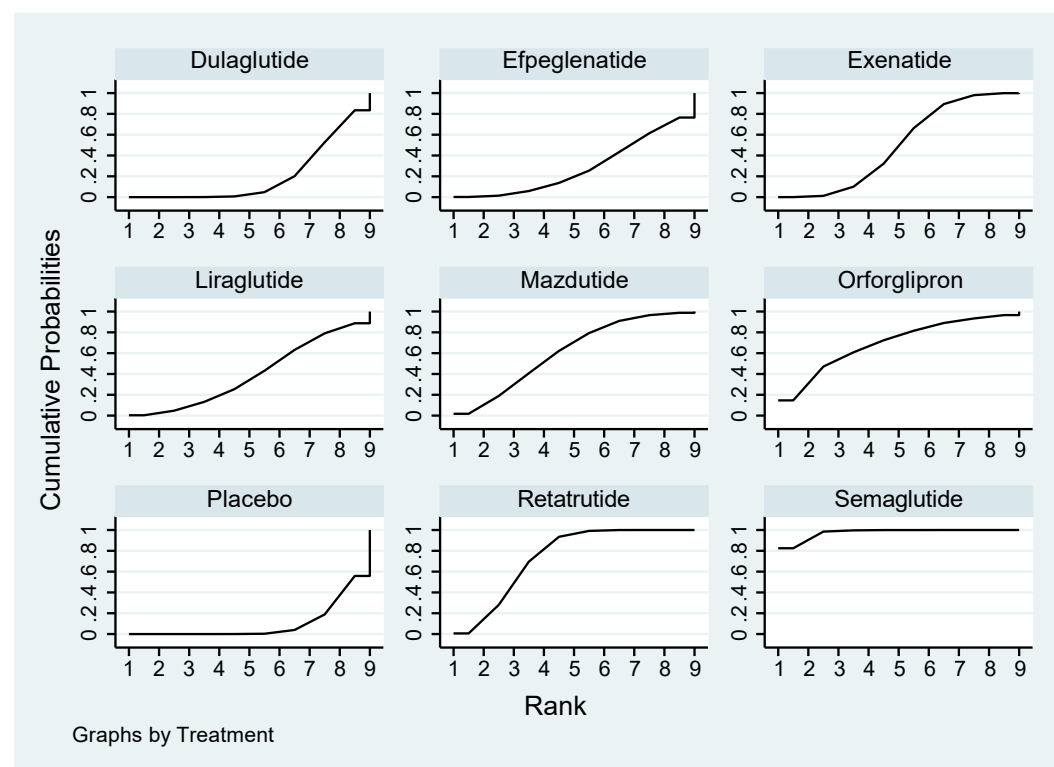


Table S7.5: SUCRA of the effects of various GLP-1RAs on waist circumference.

Treatment	SUCRA	PrBest	MeanRank
Semaglutide	97.6	82.5	1.2
Retatrutide	73.9	0.6	3.1
Orforglipron	69.4	14.6	3.4
Mazdutide	61.2	1.8	4.1
Exenatide	49.6	0	5
Liraglutide	39.7	0.3	5.8
Efpeglenatide	28.5	0.2	6.7
Dulaglutide	20.2	0	7.4
Placebo	9.9	0	8.2

Abbreviation: SUCRA, surface under the cumulative ranking curve.

Figure S7.6: Cumulative ranking curve plots of GLP-1RAs for HDL in range network. Higher surface under the curve reflects higher probability of association with HDL.

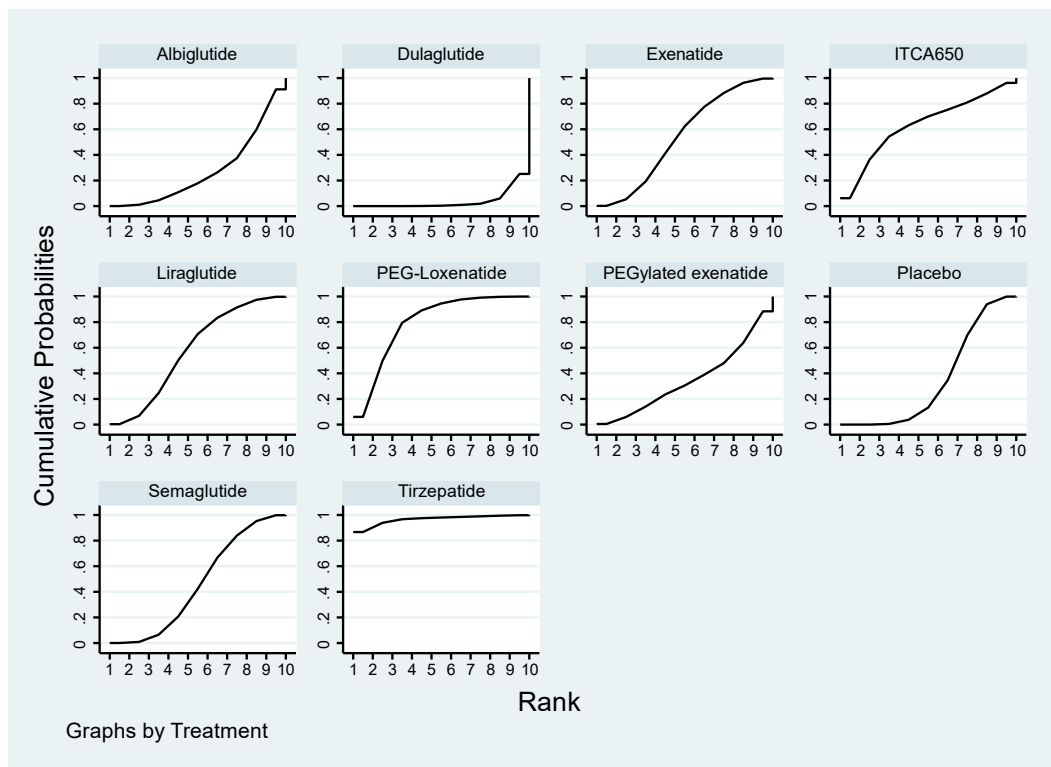


Table S7.6: SUCRA of the effects of various GLP-1RAs on HDL.

Treatment	SUCRA	PrBest	MeanRank
Tirzepatide	96.6	86.7	1.3
PEG-Loxenatide	79.5	6	2.8
ITCA 650	63.4	6.2	4.3
Liraglutide	58.3	0.3	4.8
Exenatide	54.4	0.2	5.1
Semaglutide	46.2	0	5.8
Placebo	35.1	0	6.8
PEGylated exenatide	34.9	0.5	6.9
Albiglutide	27.7	0	7.5
Dulaglutide	3.8	0	9.7

Abbreviations: HDL, high-density lipoprotein; SUCRA, surface under the cumulative ranking curve.

Figure S7.7: Cumulative ranking curve plots of GLP-1RAs for LDL in range network. Higher surface under the curve reflects higher probability of association with LDL.

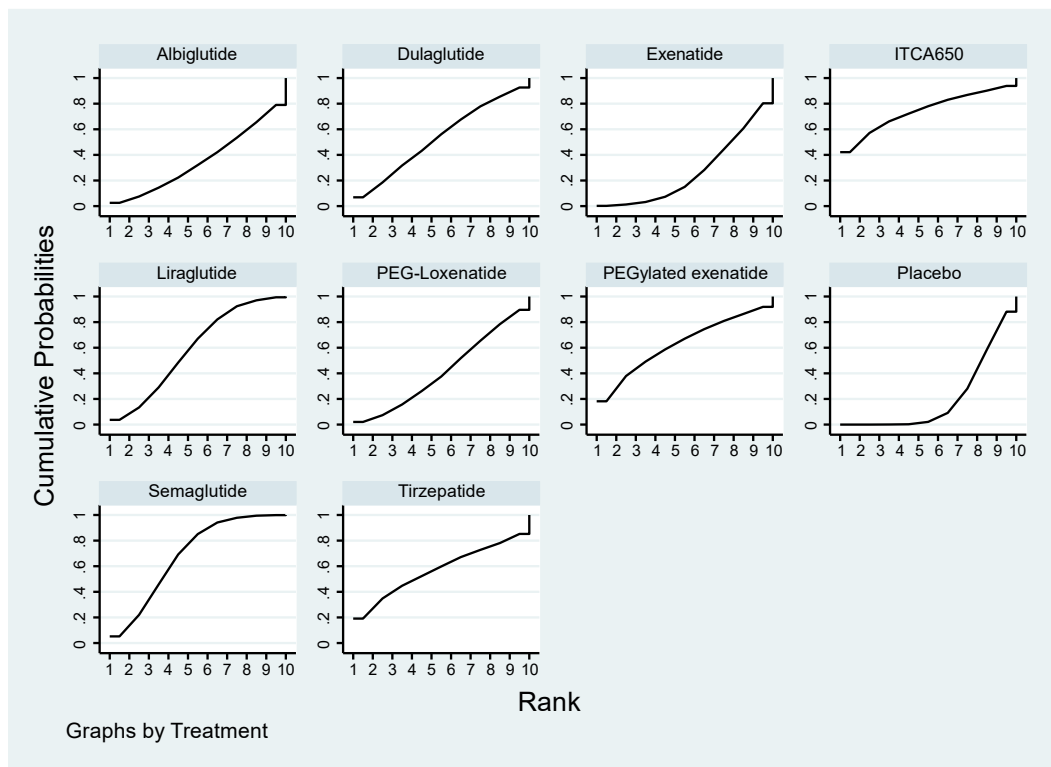


Table S7.7: SUCRA of the effects of various GLP-1RAs on LDL.

Treatment	SUCRA	PrBest	MeanRank
ITCA 650	74.4	42.1	3.3
Semaglutide	68.7	5.2	3.8
PEGylated exenatide	62.8	18.2	4.4
Liraglutide	59.2	3.7	4.7
Tirzepatide	57.1	19.1	4.9
Dulaglutide	53.3	6.9	5.2
PEG-Loxenatide	41.6	2.1	6.3
Albiglutide	35.4	2.6	6.8
Exenatide	26.7	0.2	7.6
Placebo	20.7	0	8.1

Abbreviations: LDL, low-density lipoprotein; SUCRA, surface under the cumulative ranking curve.

Figure S7.8: Cumulative ranking curve plots of GLP-1RAs for TC in range network. Higher surface under the curve reflects higher probability of association with waist circumference.

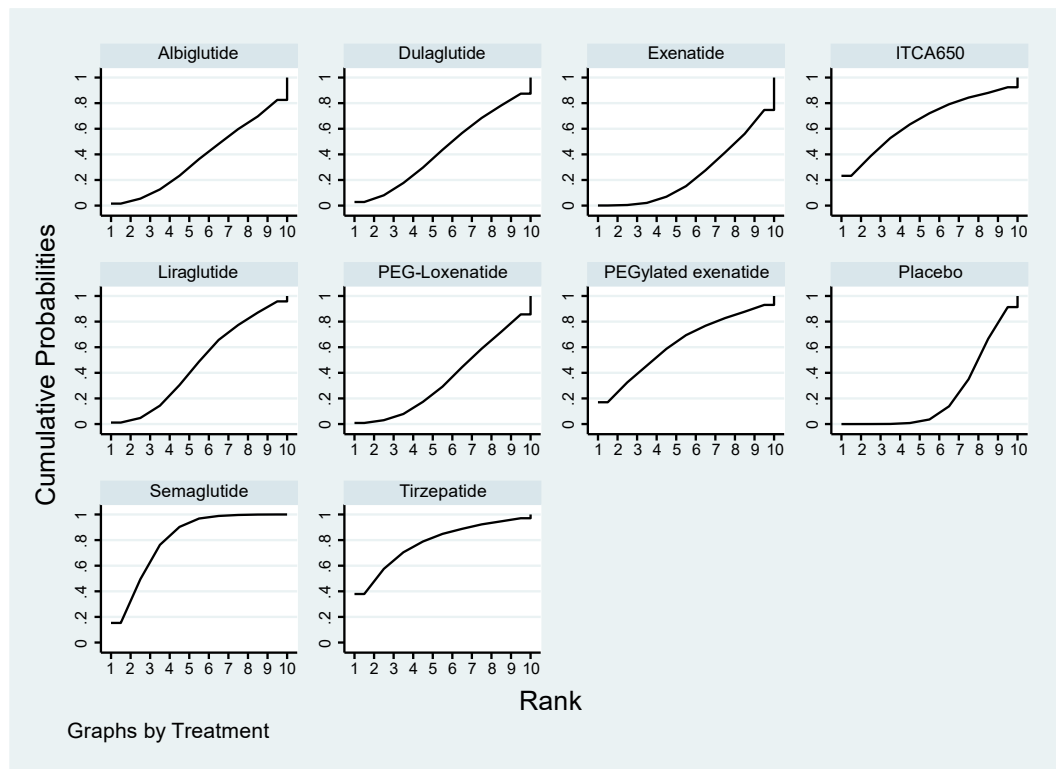


Table S7.8: SUCRA of the effects of various GLP-1RAs on TC.

Treatment	SUCRA	PrBest	MeanRank
Semaglutide	81.1	15.5	2.7
Tirzepatide	79.2	39.1	2.9
ITCA 650	65.1	21.7	4.1
PEGylated exenatide	62.9	17.3	4.3
Liraglutide	48.1	1.1	5.7
Dulaglutide	43.9	2.6	6
Albiglutide	36.7	1.6	6.7
PEG-Loxenatide	35.5	0.8	6.8
Exenatide	24.9	0.1	7.8
Placebo	22.6	0	8

Abbreviations: TC, total cholesterol; Abbreviation; SUCRA, surface under the cumulative ranking curve.

Figure S7.9: Cumulative ranking curve plots of GLP-1RAs for TG in range network. Higher surface under the curve reflects higher probability of association with TG.

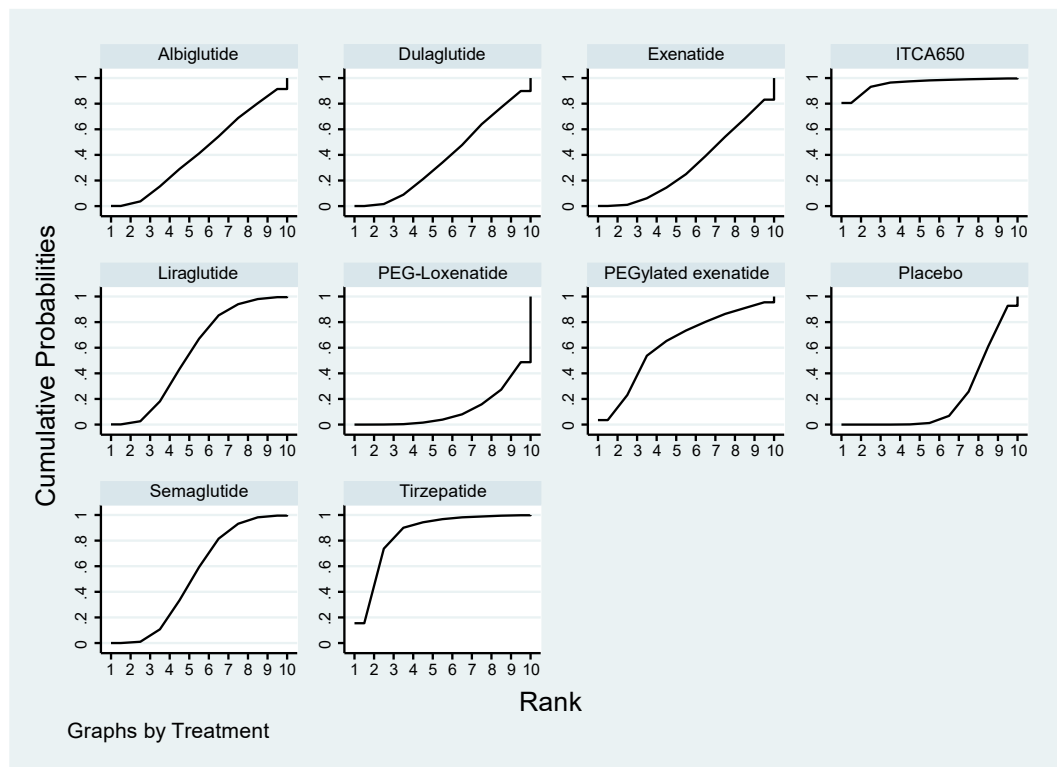


Table S7.9: SUCRA of the effects of various GLP-1RAs on TG.

Treatment	SUCRA	PrBest	MeanRank
ITCA 650	95.8	80.6	1.4
Tirzepatide	85.2	15.5	2.3
PEGylated exenatide	63.6	3.5	4.3
Liraglutide	56.5	0.2	4.9
Semaglutide	53	0	5.2
Albiglutide	42.7	0.1	6.2
Dulaglutide	38.3	0.1	6.6
Exenatide	32.4	0.1	7.1
Placebo	20.9	0	8.1
PEG-Loxenatide	11.7	0	8.9

Abbreviations: TG, triglyceride; SUCRA, surface under the cumulative ranking curve.

Appendix 8: league table of Summary Estimates for GLP-1RAs on T2D Derived from Network Meta-analysis of 75 Trials

Table S8.1: HbA1c

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in HbA1c for tirzepatide compared to mazdutide is -0.01 (95% confidence interval -1.08 to 1.05). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row. According to the network meta-analysis (CINeMA) framework, the certainty of the evidence for our comparisons of interest is included in the league table, with * as low, † as moderate, and ‡ as high confidence in the evidence. The full CINeMA assessment is shown in Appendix 9.

Tirzepatide													
-0.01* (-1.08,1.05)	Mazdutide												
-0.31* (-1.42,0.81)	-0.30* (-1.76,1.17)	CagriSema											
-0.62* (-1.34,0.11)	-0.61* (-1.79,0.58)	-0.31 (-1.55,0.93)	Orforglipron										
-0.71* (-1.14,-0.28)	-0.70* (-1.74,0.34)	-0.40‡ (-1.43,0.63)	-0.09* (-0.78,0.59)	Semaglutide									
-0.78* (-1.51,-0.05)	-0.77* (-1.96,0.41)	-0.48* (-1.72,0.77)	-0.17* (-1.06,0.73)	-0.08* (-0.77,0.62)	Retatrutide								
-1.02‡ (-1.42,-0.62)	-1.00‡ (-2.02,0.01)	-0.71* (-1.79,0.38)	-0.40‡ (-1.05,0.25)	-0.31* (-0.64,0.02)	-0.23‡ (-0.88,0.42)	Dulaglutide							
-1.06‡ (-1.49,-0.63)	-1.05* (-2.08,-0.02)	-0.75* (-1.83,0.33)	-0.44* (-1.12,0.23)	-0.35* (-0.68,-0.03)	-0.28* (-0.96,0.41)	-0.04† (-0.35,0.27)	Liraglutide						
-1.07‡ (-1.71,-0.42)	-1.05† (-2.20,0.09)	-0.76* (-1.95,0.44)	-0.45* (-1.28,0.38)	-0.36* (-0.96,0.24)	-0.28* (-1.12,0.56)	-0.05* (-0.64,0.54)	-0.01* (-0.60,0.59)	PEG-Loxenatide					
-1.09‡ (-1.74,-0.44)	-1.08‡ (-2.22,0.06)	-0.78* (-1.98,0.41)	-0.47* (-1.31,0.36)	-0.38* (-0.99,0.22)	-0.31* (-1.15,0.53)	-0.08* (-0.67,0.52)	-0.03* (-0.62,0.56)	-0.02* (-0.78,0.73)	Albiglutide				
-1.13‡ (-2.10,-0.16)	-1.12‡ (-2.47,0.23)	-0.83* (-2.22,0.57)	-0.52* (-1.62,0.58)	-0.43* (-1.37,0.51)	-0.35* (-1.46,0.76)	-0.12* (-1.05,0.82)	-0.07* (-1.01,0.86)	-0.07* (-1.12,0.98)	-0.04* (-1.09,1.01)	PEGylated exenatide			
-1.19‡ (-2.16,-0.23)	-1.18‡ (-2.53,0.17)	-0.89* (-2.28,0.51)	-0.58* (-1.68,0.52)	-0.49* (-1.43,0.45)	-0.41* (-1.52,0.69)	-0.18* (-1.11,0.75)	-0.13* (-1.07,0.80)	-0.13* (-1.17,0.92)	-0.10* (-1.15,0.94)	-0.06* (-1.33,1.21)	ITCA650		
-1.29‡ (-1.78,-0.81)	-1.28‡ (-2.34,-0.22)	-0.99* (-2.09,0.12)	-0.68† (-1.39,0.04)	-0.59* (-0.98,-0.19)	-0.51* (-1.23,0.21)	-0.28* (-0.68,0.13)	-0.23‡ (-0.61,0.14)	-0.23* (-0.86,0.40)	-0.20* (-0.84,0.43)	-0.16* (-1.12,0.80)	-0.10† (-1.06,0.86)	Exenatide	
-1.36‡ (-1.97,-0.75)	-1.35‡ (-2.47,-0.23)	-1.06* (-2.23,0.12)	-0.75‡ (-1.55,0.06)	-0.66* (-1.21,-0.10)	-0.58* (-1.39,0.23)	-0.35* (-0.89,0.20)	-0.30* (-0.83,0.23)	-0.30* (-1.02,0.43)	-0.27* (-1.00,0.46)	-0.23* (-1.25,0.80)	-0.17* (-1.19,0.85)	-0.07* (-0.66,0.52)	Efpeglenatide

-1.50‡ (-2.04,-0.96)	-1.49‡ (-2.57,-0.40)	-1.19‡ (-2.33,-0.05)	-0.88‡ (-1.64,-0.13)	-0.79‡ (-1.28,-0.31)	-0.72* (-1.48,0.04)	-0.48* (-0.96,-0.01)	-0.44* (-0.91,0.03)	-0.43* (-1.10,0.24)	-0.41* (-1.08,0.26)	-0.37* (-1.35,0.62)	-0.31* (-1.29,0.68)	-0.21* (-0.73,0.32)	-0.14* (-0.77,0.50)	Lixisenatide	
-2.10‡ (-2.47,-1.74)	-2.09‡ (-3.10,-1.09)	-1.80‡ (-2.87,-0.73)	-1.49‡ (-2.12,-0.85)	-1.40‡ (-1.67,-1.12)	-1.32‡ (-1.97,-0.68)	-1.09‡ (-1.34,-0.84)	-1.04‡ (-1.30,-0.79)	-1.04‡ (-1.57,-0.50)	-1.01‡ (-1.55,-0.48)	-0.97‡ (-1.87,-0.07)	-0.91‡ (-1.81,-0.01)	-0.81‡ (-1.15,-0.48)	-0.74‡ (-1.23,-0.25)	-0.60‡ (-1.01,-0.20)	Placebo

Table S8.2: FPG

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in FPG for Tirzepatide compared to CagriSema is -0.33 (95% confidence interval -1.90 to 1.23). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row. Abbreviation: FPG, fasting plasma glucose.

Tirzepatide															
-0.33 † (-1.90,1.23)	CagriSema														
-1.04* (-1.93,-0.15)	-0.71* (-2.40,0.99)	Orforglipron													
-1.13 * (-1.71,-0.55)	-0.80 * (-2.26,0.66)	-0.09* (-0.97,0.78)	Semaglutide												
-1.19 † (-2.54,0.16)	-0.86* (-2.83,1.12)	-0.15* (-1.63,1.33)	-0.06* (-1.39,1.28)	Retatrutide											
-1.34 * (-2.22,-0.47)	-1.01* (-2.70,0.68)	-0.30* (-1.38,0.77)	-0.21* (-1.06,0.64)	-0.15* (-1.63,1.32)	Albiglutide										
-1.44* (-2.71,-0.18)	-1.11* (-3.03,0.80)	-0.41* (-1.81,1.00)	-0.31* (-1.56,0.93)	-0.26* (-1.99,1.48)	-0.10* (-1.49,1.29)	PEGylated exenatide									
-1.63‡ (-2.16,-1.11)	-1.30‡ (-2.84,0.24)	-0.60‡ (-1.40,0.21)	-0.50‡ (-0.99,-0.01)	-0.45* (-1.72,0.83)	-0.29* (-1.11,0.53)	-0.19* (-1.42,1.04)	Dulaglutide								
-1.66‡ (-2.24,-1.09)	-1.33‡ (-2.86,0.21)	-0.62 † (-1.47,0.23)	-0.53* (-1.01,-0.04)	-0.47* (-1.79,0.84)	-0.32* (-1.15,0.51)	-0.22* (-1.45,1.02)	-0.03 † (-0.46,0.41)	Liraglutide							
-1.82* (-3.16,-0.48)	-1.49* (-3.46,0.49)	-0.78* (-2.26,0.70)	-0.69* (-2.02,0.64)	-0.63* (-2.42,1.16)	-0.48* (-1.95,1.00)	-0.37* (-2.11,1.36)	-0.18* (-1.47,1.10)	-0.16‡ (-1.47,1.16)	Mazdutide						
-1.79 † (-2.65,-0.93)	-1.46* (-3.14,0.22)	-0.75* (-1.81,0.31)	-0.66* (-1.49,0.17)	-0.60* (-2.07,0.87)	-0.45* (-1.48,0.59)	-0.35* (-1.73,1.03)	-0.16* (-0.96,0.65)	-0.13* (-0.94,0.68)	0.03* (-1.43,1.49)	PEG-Loxenatide					
-2.08‡ (-3.00,-1.16)	-1.75* (-3.45,-0.04)	-1.04* (-2.15,0.07)	-0.95* (-1.84,-0.06)	-0.89* (-2.40,0.61)	-0.74* (-1.83,0.36)	-0.64* (-2.06,0.79)	-0.45* (-1.31,0.42)	-0.42* (-1.25,0.42)	-0.26* (-1.76,1.24)	-0.29* (-1.37,0.79)	Efpeglenatide				
-2.22‡ (-3.02,-1.43)	-1.89* (-3.50,-0.28)	-1.18* (-2.20,-0.17)	-1.09* (-1.79,-0.39)	-1.03* (-2.47,0.40)	-0.88* (-1.87,0.12)	-0.78* (-2.13,0.57)	-0.59* (-1.32,0.14)	-0.56‡ (-1.26,0.14)	-0.40* (-1.83,1.02)	-0.43* (-1.41,0.55)	-0.14* (-1.17,0.88)	Exenatide			
-2.51‡ (-3.22,-1.81)	-2.18* (-3.78,-0.58)	-1.47* (-2.42,-0.53)	-1.38* (-2.06,-0.71)	-1.32* (-2.71,0.06)	-1.17* (-2.08,-0.26)	-1.07* (-2.36,0.22)	-0.88* (-1.52,-0.24)	-0.85* (-1.50,-0.20)	-0.69* (-2.07,0.68)	-0.72* (-1.62,0.17)	-0.43 † (-1.39,0.53)	-0.29* (-1.14,0.56)	Lixisenatide		
-3.12‡ (-3.59,-2.66)	-2.79‡ (-4.30,-1.28)	-2.09‡ (-2.86,-1.31)	-1.99‡ (-2.41,-1.58)	-1.94* (-3.21,-0.66)	-1.78‡ (-2.52,-1.04)	-1.68* (-2.85,-0.51)	-1.49 † (-1.84,-1.14)	-1.46 † (-1.84,-1.09)	-1.31* (-2.58,-0.03)	-1.33* (-2.05,-0.61)	-1.04* (-1.84,-0.24)	-0.90* (-1.56,-0.24)	-0.61* (-1.14,-0.08)	Placebo	

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in weight for tirzepatide compared to semaglutide is -5.35 (95% confidence interval -6.66 to -4.03). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

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Table S8.4: BMI

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in BMI for tirzepatide compared to orforglipron is -0.79 (95% confidence interval -2.16 to 0.58). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

Tirzepatide							
-0.79 (-2.16,0.58)	Orforglipron						
-1.58 (-2.51,-0.64)	-0.79 (-1.99,0.41)	Semaglutide					
-2.05 (-3.00,-1.10)	-1.26 (-2.49,-0.03)	-0.47 (-1.02,0.08)	Liraglutide				
-2.12 (-3.10,-1.13)	-1.33 (-2.46,-0.19)	-0.54 (-1.31,0.23)	-0.07 (-0.92,0.78)	Dulaglutide			
-2.75 (-4.37,-1.14)	-1.96 (-3.76,-0.17)	-1.18 (-2.63,0.27)	-0.71 (-2.15,0.74)	-0.64 (-2.20,0.93)	Loxenatide		
-2.85 (-3.70,-2.01)	-2.06 (-3.22,-0.91)	-1.28 (-1.73,-0.83)	-0.81 (-1.26,-0.36)	-0.74 (-1.48,0.01)	-0.10 (-1.48,1.28)	Placebo	
-2.98 (-4.45,-1.50)	-2.19 (-3.84,-0.53)	-1.40 (-2.54,-0.26)	-0.93 (-2.20,0.34)	-0.86 (-2.24,0.52)	-0.22 (-2.07,1.62)	-0.12 (-1.35,1.10)	Exenatide

Table S8.5: Waist circumference

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in waist circumference for semaglutide compared to retatrutide is -3.02 (95% confidence interval -5.61 to -0.43). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

Semaglutide									
-3.02 (-5.61,-0.43)	Retatrutide								
-2.78 (-8.01,2.45)	0.25 (-4.73,5.22)	Orforglipron							
-3.73 (-7.42,-0.05)	-0.71 (-4.02,2.61)	-0.95 (-6.56,4.65)	Mazdutide						
-4.47 (-7.11,-1.83)	-1.44 (-3.30,0.42)	-1.69 (-6.70,3.32)	-0.74 (-4.13,2.65)	Exenatide					
-5.10 (-8.97,-1.23)	-2.07 (-5.60,1.45)	-2.32 (-8.05,3.41)	-1.37 (-5.69,2.95)	-0.63 (-4.23,2.97)	Liraglutide				
-5.82 (-9.84,-1.81)	-2.80 (-5.87,0.27)	-3.05 (-8.89,2.80)	-2.09 (-6.61,2.43)	-1.36 (-4.95,2.23)	-0.73 (-5.40,3.95)	Efpeglenatide			
-6.19 (-8.75,-3.62)	-3.16 (-5.17,-1.16)	-3.41 (-8.32,1.51)	-2.45 (-5.52,0.62)	-1.72 (-3.97,0.54)	-1.09 (-4.37,2.19)	-0.36 (-4.03,3.31)	Dulaglutide		
-6.77 (-8.97,-4.57)	-3.74 (-5.25,-2.24)	-3.99 (-8.78,0.80)	-3.04 (-6.11,0.04)	-2.30 (-3.78,-0.82)	-1.67 (-4.97,1.64)	-0.94 (-4.36,2.48)	-0.58 (-2.38,1.21)	Placebo	

Table S8.6: HDL

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in HDL for tirzepatide compared to PEG-Loxanatide is 0.12 (95% confidence interval -0.05 to 0.28). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

Tirzepatide									
0.12 (-0.05,0.28)	PEG- Loxanatide								
0.13 (-0.06,0.33)	0.02 (-0.11,0.14)	ITCA 650							
0.15 (-0.01,0.31)	0.03 (-0.04,0.10)	0.02 (-0.10,0.14)	Liraglutide						
0.15 (-0.00,0.31)	0.04 (-0.03,0.11)	0.02 (-0.10,0.14)	0.00 (-0.04,0.05)	Exenatide					
0.16 (0.01,0.31)	0.05 (-0.02,0.11)	0.03 (-0.09,0.15)	0.01 (-0.03,0.06)	0.01 (-0.04,0.06)	Semaglutide				
0.17 (0.02,0.33)	0.06 (0.01,0.11)	0.04 (-0.07,0.15)	0.02 (-0.02,0.07)	0.02 (-0.03,0.06)	0.01 (-0.03,0.05)	Placebo			
0.18 (0.00,0.36)	0.06 (-0.04,0.16)	0.05 (-0.09,0.19)	0.03 (-0.07,0.13)	0.03 (-0.07,0.12)	0.02 (-0.08,0.11)	0.01 (- 0.08,0.09)	PEGylated exenatide		
0.19 (0.02,0.35)	0.07 (-0.01,0.15)	0.05 (-0.07,0.18)	0.04 (-0.04,0.11)	0.03 (-0.04,0.11)	0.02 (-0.05,0.09)	0.01 (-0.05,0.07)	0.01 (-0.10,0.11)	Albiglutide	
0.24 (0.07,0.40)	0.12 (0.05,0.20)	0.10 (-0.02,0.23)	0.09 (0.01,0.16)	0.08 (0.01,0.15)	0.07 (0.01,0.14)	0.06 (0.01,0.12)	0.06 (-0.04,0.16)	0.05 (-0.03,0.13)	Dulaglutide

Abbreviation: HDL, high-density lipoprotein

Table S8.7: LDL

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in LDL for ITCA 650 compared to semaglutide is -0.09 (95% confidence interval -0.52 to 0.35). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

ITCA 650										
-0.09 (-0.52,0.35)	Semaglutide									
-0.09 (-0.60,0.43)	0.00 (-0.35,0.35)	PEGylated exenatide								
-0.12 (-0.56,0.32)	-0.03 (-0.21,0.14)	-0.04 (-0.39,0.32)	Liraglutide							
-0.11 (-0.68,0.46)	-0.02 (-0.39,0.35)	-0.02 (-0.53,0.49)	0.01 (-0.39,0.42)	Tirzepatide						
-0.14 (-0.61,0.33)	-0.05 (-0.32,0.22)	-0.06 (-0.45,0.34)	-0.02 (-0.30,0.26)	-0.03 (-0.49,0.42)	Dulaglutide					
-0.19 (-0.64,0.27)	-0.10 (-0.34,0.14)	-0.10 (-0.47,0.27)	-0.06 (-0.31,0.19)	-0.08 (-0.52,0.36)	-0.04 (-0.34,0.26)	PEG- Loxenatide				
-0.21 (-0.69,0.26)	-0.13 (-0.41,0.15)	-0.13 (-0.53,0.27)	-0.09 (-0.38,0.20)	-0.11 (-0.57,0.36)	-0.07 (-0.40,0.26)	-0.03 (-0.34,0.28)	Albiglutide			
-0.23 (-0.68,0.21)	-0.14 (-0.33,0.04)	-0.15 (-0.51,0.22)	-0.11 (-0.28,0.06)	-0.12 (-0.54,0.29)	-0.09 (-0.38,0.20)	-0.05 (-0.31,0.22)	-0.02 (-0.32,0.28)	Exenatide		
-0.25 (-0.66,0.16)	-0.16 (-0.30,-0.02)	-0.16 (-0.48,0.15)	-0.13 (-0.28,0.03)	-0.14 (-0.54,0.25)	-0.11 (-0.34,0.12)	-0.06 (-0.26,0.13)	-0.04 (-0.28,0.21)	-0.02 (-0.19,0.16)	Placebo	

Abbreviation: LDL, low-density lipoprotein

Table S8.8: TC

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in TC for semaglutide compared to tirzepatide is 0.06 (95% confidence interval -0.56 to 0.69). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

Semaglutide										
0.06 (-0.56,0.69)	Tirzepatide									
-0.10 (-0.90,0.71)	-0.16 (-1.18,0.86)	ITCA 650								
-0.15 (-0.89,0.60)	-0.21 (-1.18,0.76)	-0.05 (-1.02,0.92)	PEGylated exenatide							
-0.31 (-0.71,0.09)	-0.37 (-1.12,0.37)	-0.21 (-1.04,0.61)	-0.16 (-0.92,0.60)	Liraglutide						
-0.33 (-0.92,0.26)	-0.39 (-1.25,0.46)	-0.23 (-1.09,0.62)	-0.18 (-0.98,0.61)	-0.02 (-0.63,0.59)	Dulaglutide					
-0.39 (-0.99,0.20)	-0.46 (-1.32,0.41)	-0.30 (-1.15,0.56)	-0.25 (-1.04,0.55)	-0.08 (-0.70,0.54)	-0.06 (-0.72,0.60)	Albiglutide				
-0.40 (-0.92,0.12)	-0.46 (-1.28,0.35)	-0.30 (-1.11,0.51)	-0.25 (-1.00,0.49)	-0.09 (-0.64,0.46)	-0.07 (-0.66,0.52)	-0.01 (-0.61,0.59)	PEG- Loxenatide			
-0.48 (-0.88,-0.08)	-0.54 (-1.29,0.20)	-0.38 (-1.21,0.44)	-0.33 (-1.10,0.43)	-0.17 (-0.54,0.19)	-0.15 (-0.76,0.46)	-0.09 (-0.71,0.53)	-0.08 (-0.63,0.47)	Exenatide		
-0.48 (-0.84,-0.11)	-0.54 (-1.26,0.18)	-0.38 (- 1.10,0.34)	-0.33 (-0.98,0.32)	-0.17 (-0.57,0.24)	-0.15 (-0.61,0.32)	-0.08 (-0.55,0.39)	-0.08 (-0.45,0.30)	0.00 (-0.40,0.41)	Placebo	

Abbreviation: TC, total cholesterol

Table S8.9: TG

The columns represent the comparison of the row drug class to the column drug class. The rows represent the comparison of the row drug class to the column drug class. The effect estimates are expressed as mean difference and 95% confidence interval. For example, the mean difference in TG for ITCA650 compared to tirzepatide is -0.70 (95% confidence interval -2.18 to 0.77). Mean difference <0 favors the drug in the column, and mean difference >0 favors the drug in the row.

ITCA650										
-0.70 (-2.18,0.77)	Tirzepatide									
-1.11 (-2.59,0.37)	-0.41 (-1.48,0.67)	PEGylated exenatide								
-1.28 (-2.60,0.04)	-0.57 (-1.36,0.21)	-0.17 (-1.01,0.68)	Liraglutide							
-1.31 (-2.62,-0.01)	-0.61 (-1.29,0.07)	-0.20 (-1.03,0.62)	-0.04 (-0.43,0.35)	Semaglutide						
-1.40 (-2.77,-0.02)	-0.69 (-1.62,0.23)	-0.29 (-1.22,0.64)	-0.12 (-0.77,0.53)	-0.08 (-0.71,0.54)	Albiglutide					
-1.45 (-2.80,-0.09)	-0.74 (-1.64,0.15)	-0.34 (-1.24,0.56)	-0.17 (-0.78,0.44)	-0.13 (-0.72,0.45)	-0.05 (-0.77,0.67)	Dulaglutide				
-1.50 (-2.88,-0.12)	-0.79 (-1.64,0.05)	-0.39 (-1.33,0.55)	-0.22 (-0.74,0.29)	-0.18 (-0.69,0.32)	-0.10 (-0.87,0.67)	-0.05 (-0.78,0.68)	Exenatide			
-1.59 (-2.86,-0.32)	-0.89 (-1.64,-0.13)	-0.48 (-1.24,0.28)	-0.31 (-0.68,0.05)	-0.28 (-0.60,0.05)	-0.19 (-0.73,0.34)	-0.14 (-0.63,0.34)	-0.09 (-0.64,0.46)	Placebo		
-1.73 (-3.06,-0.40)	-1.02 (-1.88,-0.16)	-0.62 (-1.48,0.25)	-0.45 (-1.01,0.10)	-0.41 (-0.94,0.11)	-0.33 (-1.00,0.34)	-0.28 (-0.92,0.35)	-0.23 (-0.92,0.46)	-0.14 (-0.55,0.27)	PEG- Loxenatide	

Abbreviation: TG, triglyceride

Appendix 9: CINeMA Assessment

We use the CINeMA framework to evidence certainty, assessing it for each network estimate based on the following criteria:

A: Within study bias: We classified the overall risk of bias for each study as low risk of bias, the risk of bias as moderate when none of the four assessed risk of bias items were rated as high risk, and the risk of bias as high when one or both items were rated as high risk. See Appendix 4 for the bias assessment. The risk of bias for a pairwise comparison of each drug is shown in figure S9.1-9.6.

Figure S9.1: Risk of bias contribution by intervention group in HbA1c

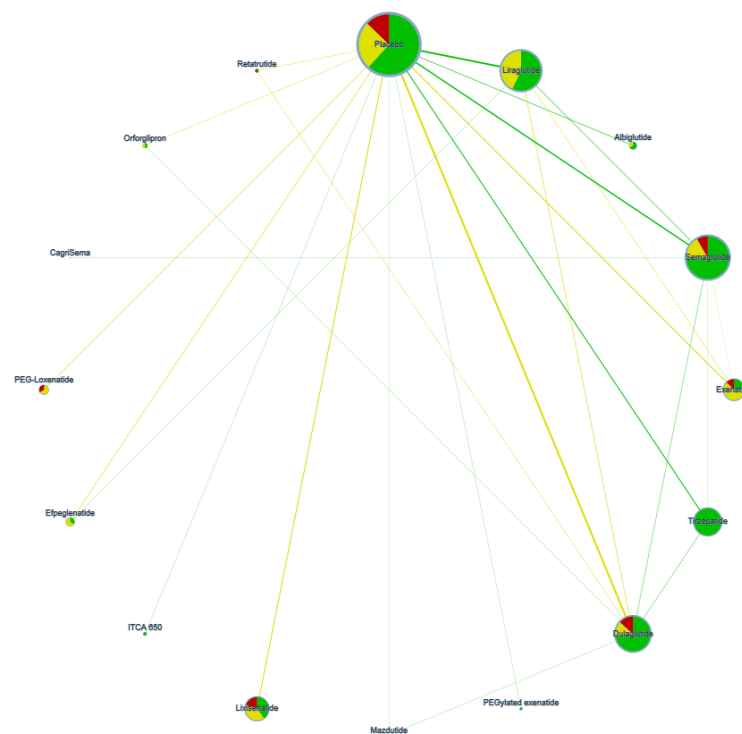


Figure S9.2: Overall risk of bias by treatment comparison in HbA1c

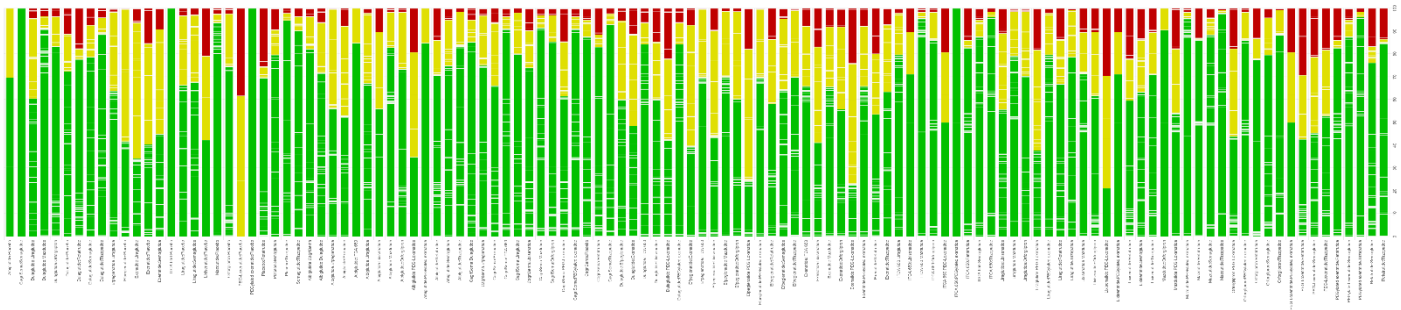


Figure S9.3: Risk of bias contribution by intervention group in FPG

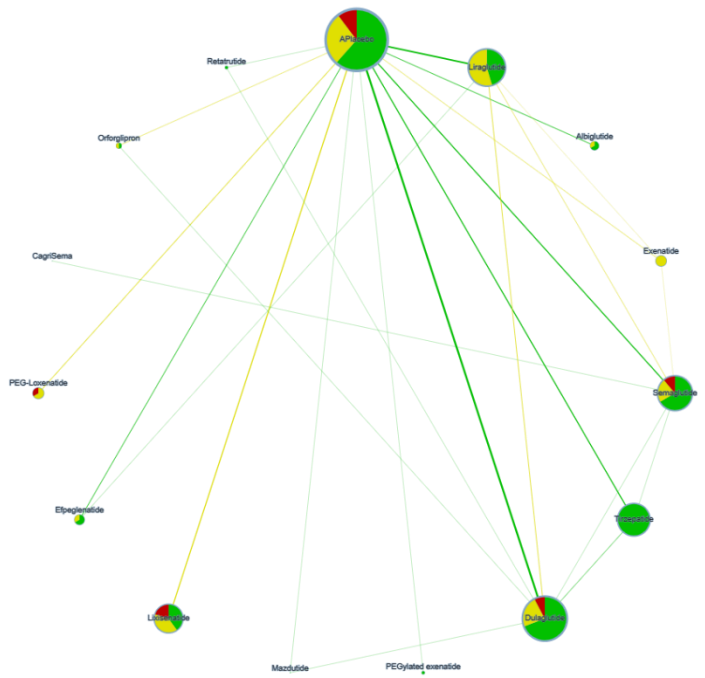


Figure S9.4: Overall risk of bias by treatment comparison in FPG

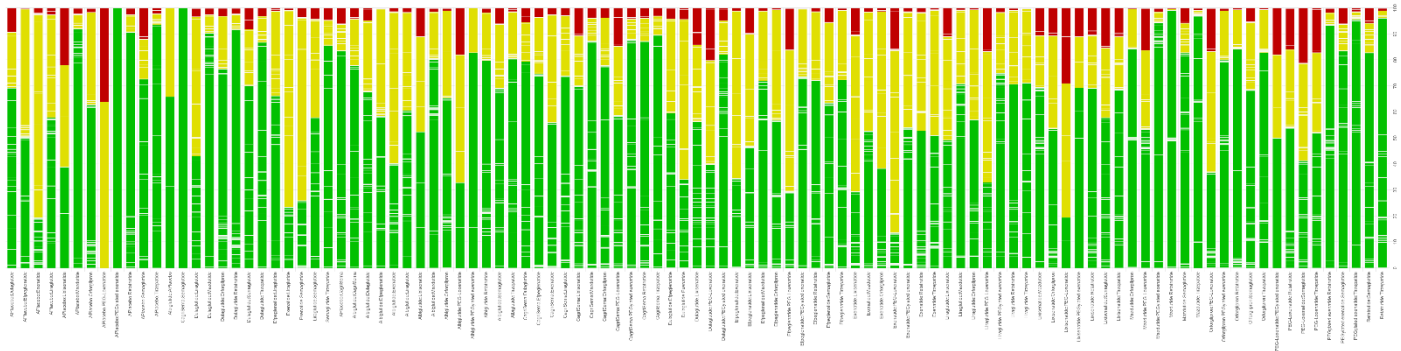
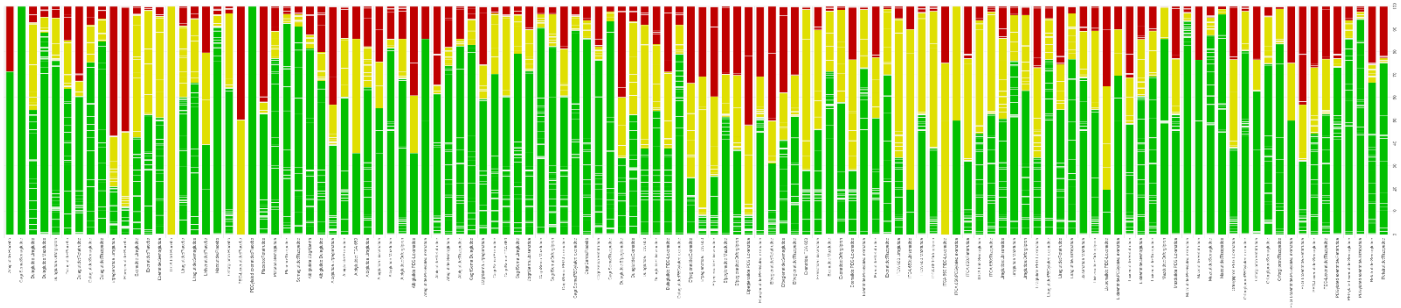


Figure S9.5: Risk of bias contribution by intervention group in weight



Figure S9.6: Overall risk of bias by treatment comparison in weight



Reporting bias: We judged it visually by a funnel plot (Appendix 10).

Indirectness: Transferability assumptions were assessed by reporting baseline glycated hemoglobin levels in the included study population and by comparing age at baseline concordance between groups.

Figure S9.7: Mean age and glycated hemoglobin plots for each intervention group

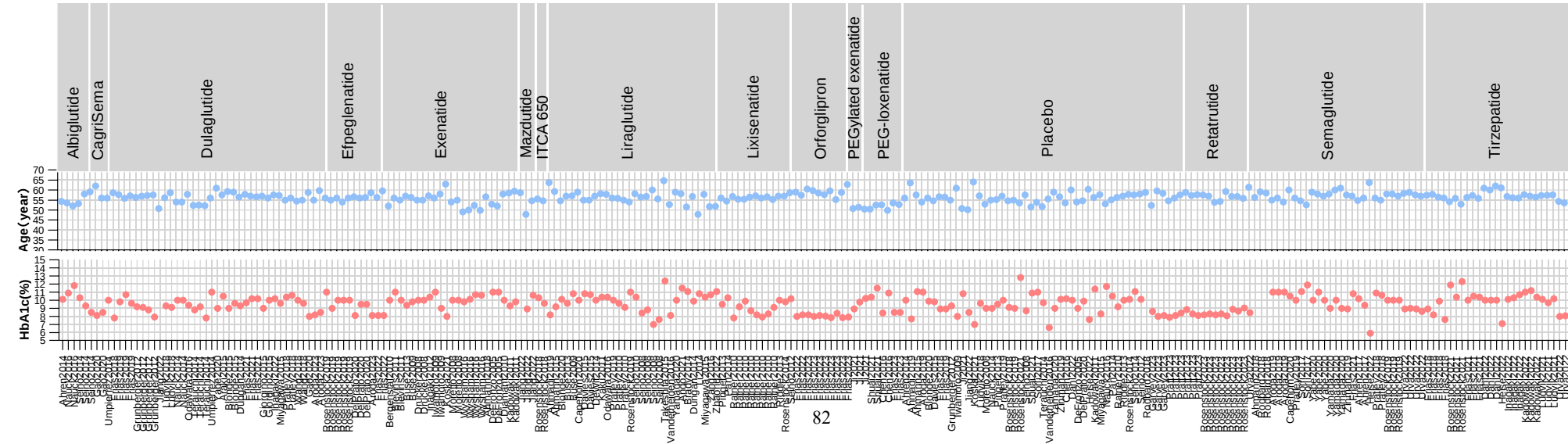


Table S9.1: Transitivity (Indirectness) Assessment

Intervention	Baseline variable (Mean $\pm$ SD)	
	Age(year)	HbA1c (%)
Albiglutide	54.60 $\pm$ 10.81	8.20 $\pm$ 0.87
Tirzepatide	56.99 $\pm$ 10.38	8.22 $\pm$ 0.95
Liraglutide	56.53 $\pm$ 10.37	8.35 $\pm$ 1.01
Exenatide	55.73 $\pm$ 10.23	8.31 $\pm$ 0.97
Semaglutide	56.81 $\pm$ 10.55	8.16 $\pm$ 0.89
Dulaglutide	56.59 $\pm$ 9.94	8.28 $\pm$ 0.99
Efpeglenatide	55.85 $\pm$ 9.51	7.80 $\pm$ 0.73
Lixisenatide	56.52 $\pm$ 9.65	8.05 $\pm$ 0.88
ITCA 650	55.10 $\pm$ 9.95	8.50 $\pm$ 0.80
Mazdutide	53.70 $\pm$ 9.34	8.73 $\pm$ 0.93
PEGylated exenatide	50.90 $\pm$ 9.62	8.66 $\pm$ 0.86
PEG-loxanatide	52.33 $\pm$ 10.62	8.47 $\pm$ 0.88
Placebo	55.88 $\pm$ 10.25	8.15 $\pm$ 0.86
CagriSema	56.00 $\pm$ 10.00	8.50 $\pm$ 0.80
Orforglipron	58.90 $\pm$ 8.86	8.09 $\pm$ 0.85
Retatrutide	56.59 $\pm$ 8.93	8.33 $\pm$ 1.09
Pooled average	56.79 $\pm$ 9.59	8.13 $\pm$ 0.93

Imprecision: We use the CINeMA website to grade the accuracy of each comparison.

Heterogeneity: We assessed the degree of worry by comparing clinical reasoning based on 95% confidence intervals (CIs) while applying the same clinical reasoning framework as for inaccuracy. In particular, we judged the consistency of our findings based on the confidence and prediction intervals associated with clinically important effect sizes. And we used the same thresholds of clinical significance as described above and followed the recommendations automatically provided by CINeMA (<https://cinema.ispm.unibe.ch/>).

Inconsistency: For inconsistency, we looked at the results for node splitting (Appendix 5) and we saw major problems when $p < 0.10$, but otherwise no problems.

Table S9.2: CINeMA Results of HbA1c

Comparison	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Albiglutide:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
CagriSema:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Liraglutide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Dulaglutide:Orforglipron	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Dulaglutide:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Dulaglutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Dulaglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Efpeglenatide:Liraglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Placebo	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Exenatide:Liraglutide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	High
Exenatide:Placebo	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Exenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
ITCA 650:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High

Liraglutide:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Liraglutide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Lixisenatide:Placebo	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Mazdutide:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Orforglipron:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
PEG-Loxenatide:Placebo	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
PEGylated exenatide:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Placebo:Semaglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Semaglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Albiglutide:CagriSema	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Dulaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Efpeglenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:ITCA 650	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Liraglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Albiglutide:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Dulaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Efpeglenatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
CagriSema:Exenatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
CagriSema:ITCA 650	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Liraglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Lixisenatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

CagriSema:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Tirzepatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Efpeglenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:ITCA 650	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Lixisenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Dulaglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:ITCA 650	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Efpeglenatide:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Efpeglenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Retatrutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Efpeglenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Exenatide:ITCA 650	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Exenatide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Exenatide:Orforglipron	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Exenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Retatrutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
ITCA 650:Liraglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Lixisenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
ITCA 650:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

ITCA 650:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Liraglutide:Lixisenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Liraglutide:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Liraglutide:Orforglipron	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Liraglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Lixisenatide:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Lixisenatide:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Lixisenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Lixisenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Lixisenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Mazdutide:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Mazdutide:PEGylated exenatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Mazdutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Mazdutide:Tirzepatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Tirzepatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:PEGylated exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:Retatrutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:Semaglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

PEG-Loxenatide:Tirzepatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
PEGylated exenatide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEGylated exenatide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEGylated exenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Retatrutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Retatrutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low

Table S9.3: CINeMA Results of FPG

Comparison	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Albiglutide:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Dulaglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Efpeglenatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Placebo:Exenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Placebo:Liraglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Placebo:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Placebo:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:PEG-Loxenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Placebo:PEGylated exenatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Placebo:Retatrutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Placebo:Semaglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Liraglutide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Orforglipron	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Semaglutide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Efpeglenatide:Liraglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Liraglutide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Exenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Liraglutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Semaglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Placebo:CagriSema	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Albiglutide:CagriSema	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Dulaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Efpeglenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Albiglutide:Liraglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Lixisenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Albiglutide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
CagriSema:Dulaglutide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
CagriSema:Efpeglenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Exenatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
CagriSema:Liraglutide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
CagriSema:Lixisenatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
CagriSema:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Tirzepatide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Efpeglenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Lixisenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Dulaglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Lixisenatide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Efpeglenatide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Efpeglenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Exenatide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Orforglipron	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Liraglutide:Lixisenatide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Liraglutide:Mazdutide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Liraglutide:Orforglipron	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Liraglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Lixisenatide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:Orforglipron	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Lixisenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Lixisenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Mazdutide:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Orforglipron:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Tirzepatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

PEG-Loxenatide:PEGylated exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:Retatrutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:Semaglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:Tirzepatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
PEGylated exenatide:Retatrutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEGylated exenatide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEGylated exenatide:Tirzepatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Retatrutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Retatrutide:Tirzepatide	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate

Table S9.4: CINeMA Results of body weight

Comparison	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Albiglutide:Placebo	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CagriSema:Semaglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Dulaglutide:Liraglutide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Dulaglutide:Placebo	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Dulaglutide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Dulaglutide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Dulaglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Efpeglenatide:Liraglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Placebo	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Liraglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Placebo	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Exenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
ITCA 650:Placebo	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Placebo	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Liraglutide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Lixisenatide:Placebo	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Placebo	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
PEG-Loxenatide:Placebo	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEGylated exenatide:Placebo	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Placebo:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Placebo:Semaglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Semaglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Albiglutide:CagriSema	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Albiglutide:Dulaglutide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Albiglutide:Efpeglenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Albiglutide:ITCA 650	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Liraglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Albiglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Albiglutide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Albiglutide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Albiglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Dulaglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Efpeglenatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
CagriSema:Exenatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:ITCA 650	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Liraglutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Lixisenatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Mazdutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:PEG-Loxenatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Low
CagriSema:PEGylated exenatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Placebo	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Retatrutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
CagriSema:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Dulaglutide:Efpeglenatide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:Exenatide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Dulaglutide:ITCA 650	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Dulaglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:ITCA 650	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Lixisenatide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Efpeglenatide:Mazdutide	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate

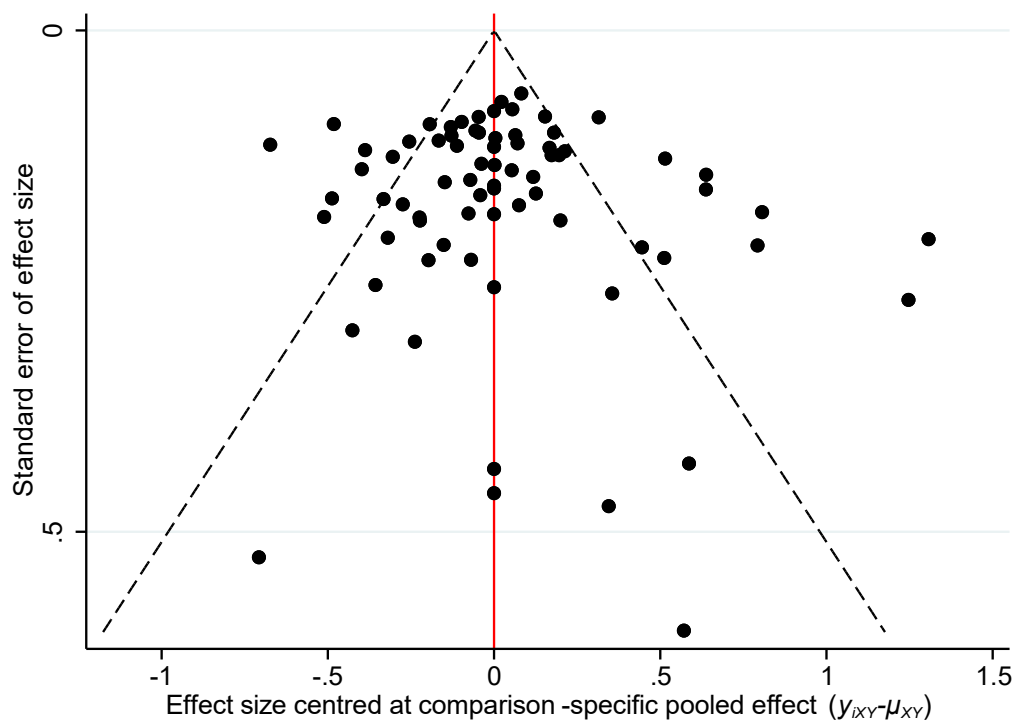
Efpeglenatide:Orforglipron	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Efpeglenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:PEGylated exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Efpeglenatide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Efpeglenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Efpeglenatide:Tirzepatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Exenatide:ITCA 650	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Exenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Exenatide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Exenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
ITCA 650:Liraglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Mazdutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Orforglipron	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
ITCA 650:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:PEGylated exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
ITCA 650:Semaglutide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ITCA 650:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Liraglutide:Lixisenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Orforglipron	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Liraglutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Liraglutide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Liraglutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Lixisenatide:Mazdutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:Orforglipron	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Lixisenatide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Lixisenatide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Lixisenatide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Lixisenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Lixisenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Mazdutide:Orforglipron	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:PEG-Loxenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:PEGylated exenatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Retatrutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Mazdutide:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Mazdutide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Orforglipron:PEG-Loxenatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Orforglipron:PEGylated exenatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Orforglipron:Retatrutide	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Orforglipron:Semaglutide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Orforglipron:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
PEG-Loxenatide:PEGylated exenatide	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
PEG-Loxenatide:Retatrutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
PEG-Loxenatide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
PEG-Loxenatide:Tirzepatide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
PEGylated exenatide:Retatrutide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
PEGylated exenatide:Semaglutide	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
PEGylated exenatide:Tirzepatide	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Retatrutide:Semaglutide	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Retatrutide:Tirzepatide	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Appendix 10: Funnel plots

The figures show the assessment of small study effect bias in studies on the effects of various GLP-1RAs on various measures of T2D. The funnel plots pertain to all trials comparing at least one GLP-1 receptor agonist versus placebo or other hypoglycemic. In the case of multi- arm trials which compared, for example, placebo vs Liraglutide vs Tizepatide, we plotted placebo vs Liraglutide as well as placebo vs Tizepatide. We also used Begg's test and Egger's test to assess the symmetry of the funnel plot, if $P > 0.05$, the funnel plot is proved to be symmetrical and may not have publication bias; and if $P < 0.05$, the results were tested for robustness using the "Metatrim" method.

Figure S10.1: Funnel plot of HbA1c



Begg's test $P=0.012$

Egger's test $t=4.87$ $P=0.002$

After metatrim $Q= 6682.780$ on 121 degrees of freedom ($p= 0.000$)

Figure S10.2: Funnel plot of FPG

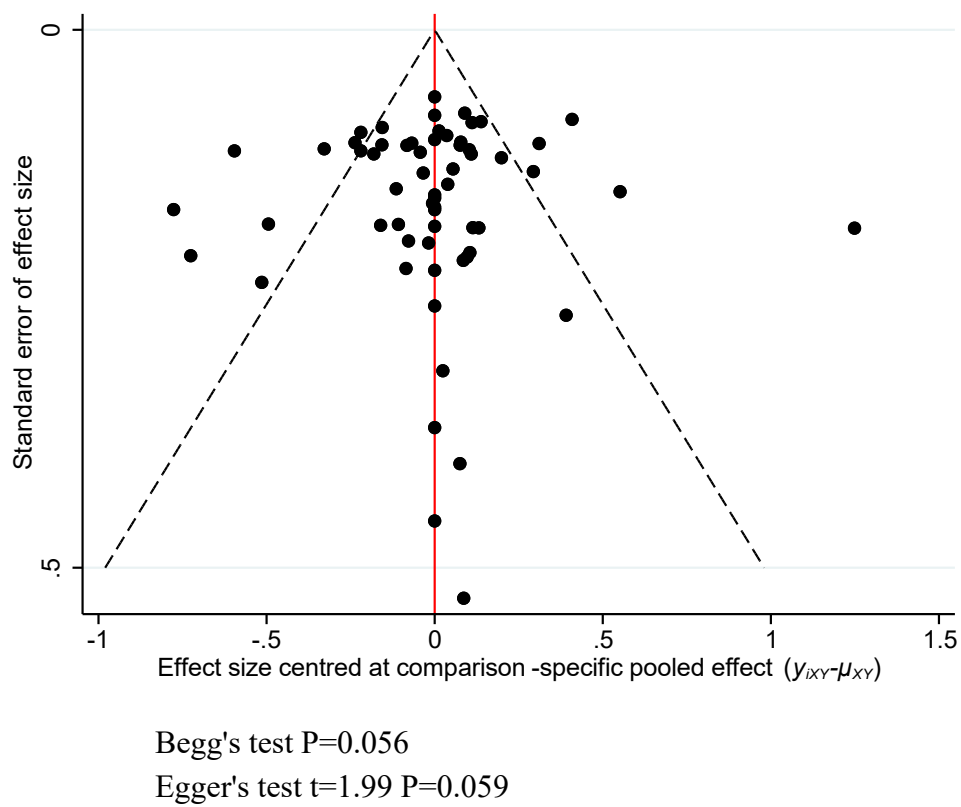


Figure S10.3: Funnel plot of weight

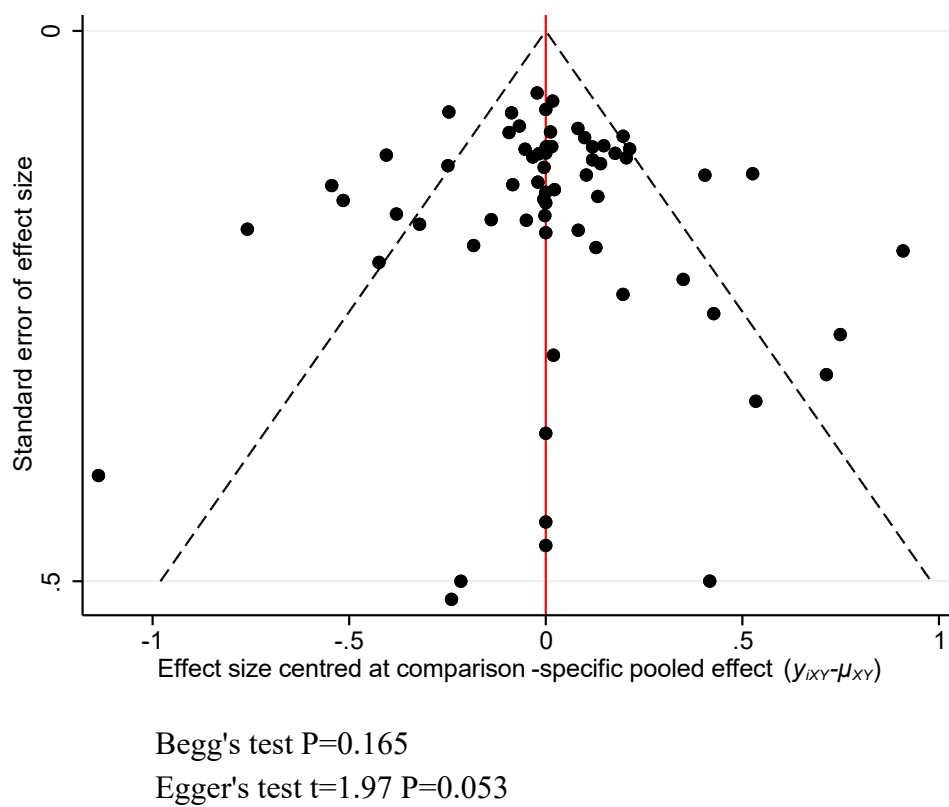
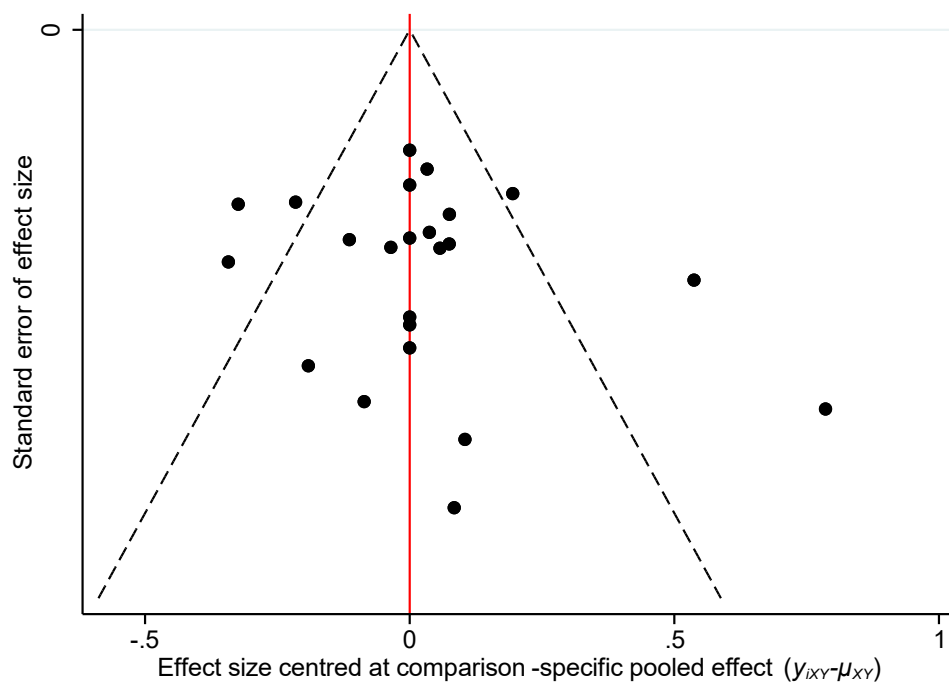


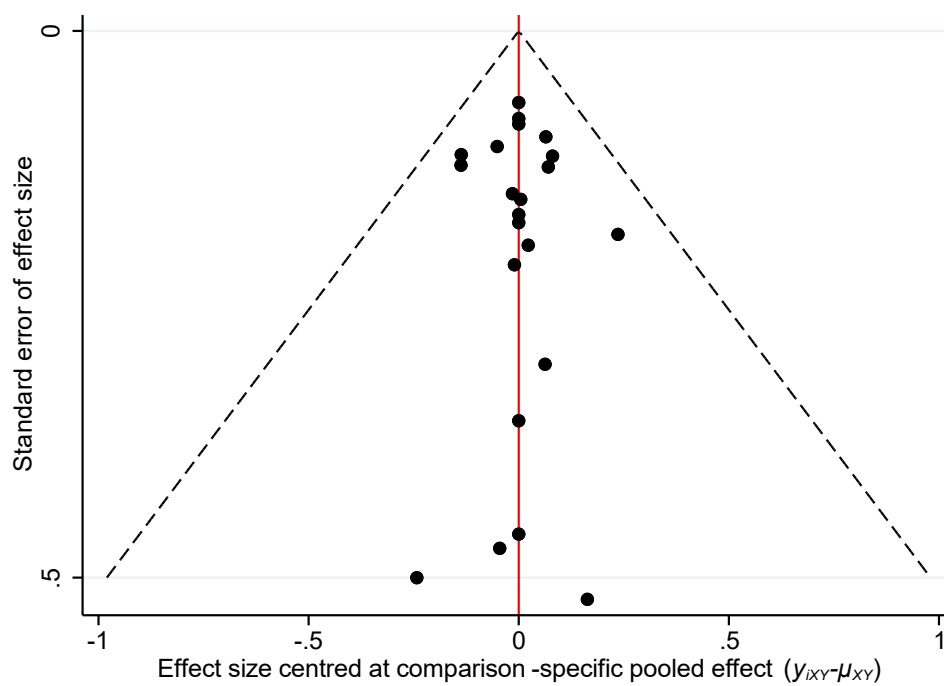
Figure S10.4: Funnel plot of BMI



Begg's test $P=0.833$

Egger's test $t=0.35$ $P=0.556$

Figure S10.5: Funnel plot of waist circumference



Begg's test $P=0.259$

Egger's test $t=0.26$ $P=0.771$

Figure S10.6: Funnel plot of HDL

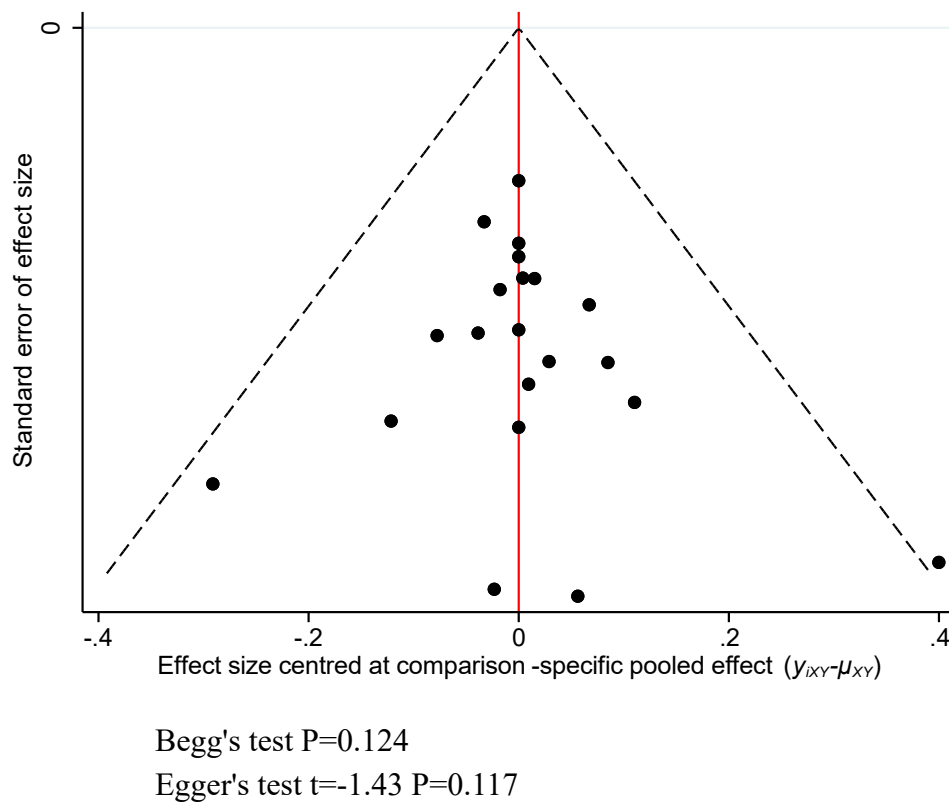


Figure S10.7: Funnel plot of LDL

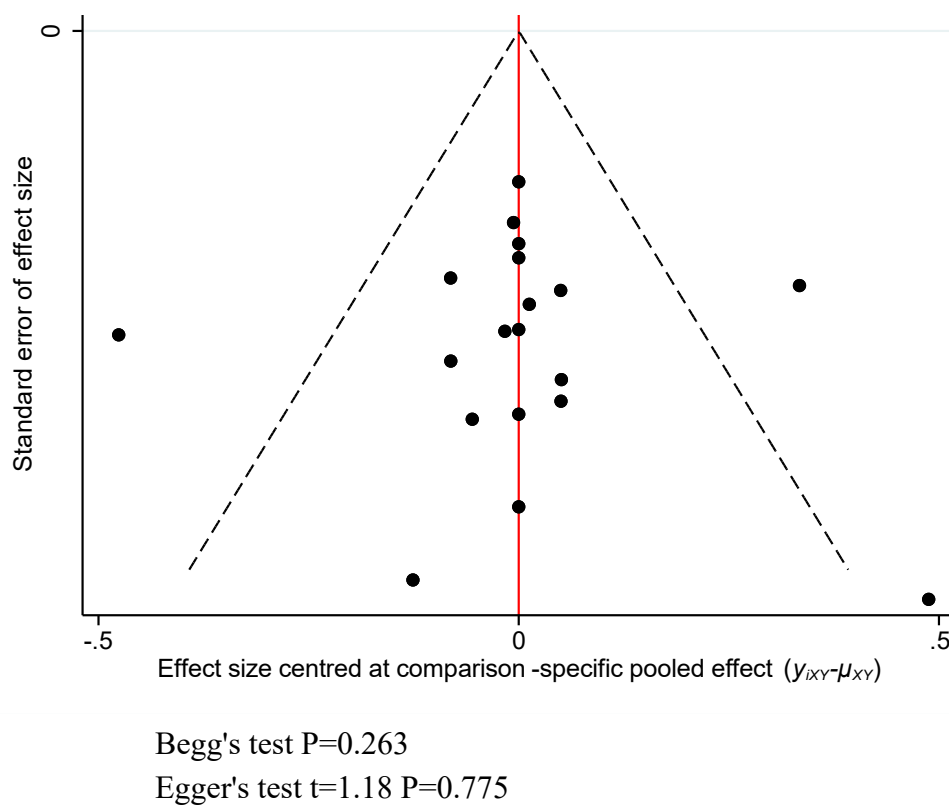


Figure S10.8: Funnel plot of TC

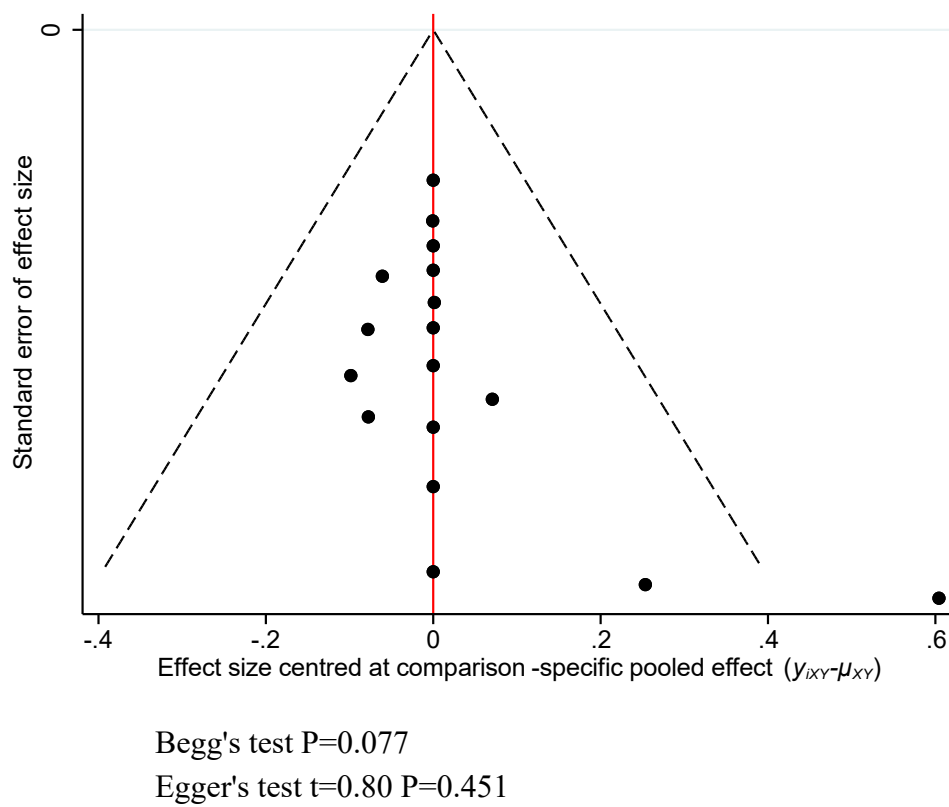
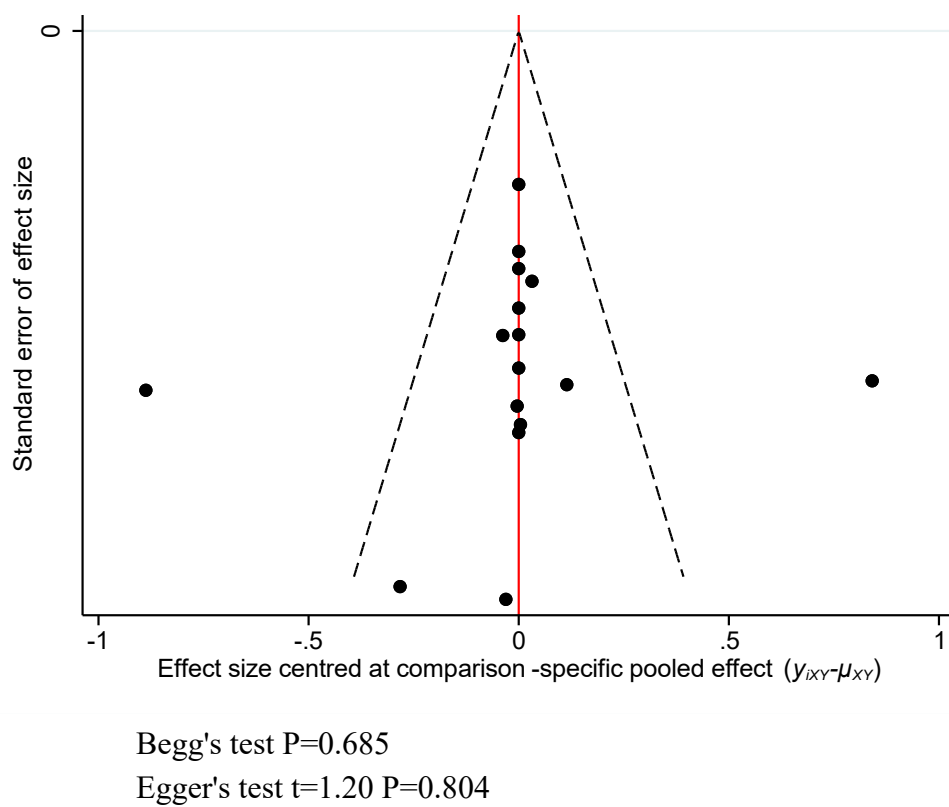


Figure S10.9: Funnel plot of TG



Appendix 11: Sensitivity analyses

Sensitivity analyses were performed by adding all trials comparing GLP-1 receptor agonists against other classes of glucose-lowering drugs.

Figure S11.1: Flow diagram of sensitivity analyses.

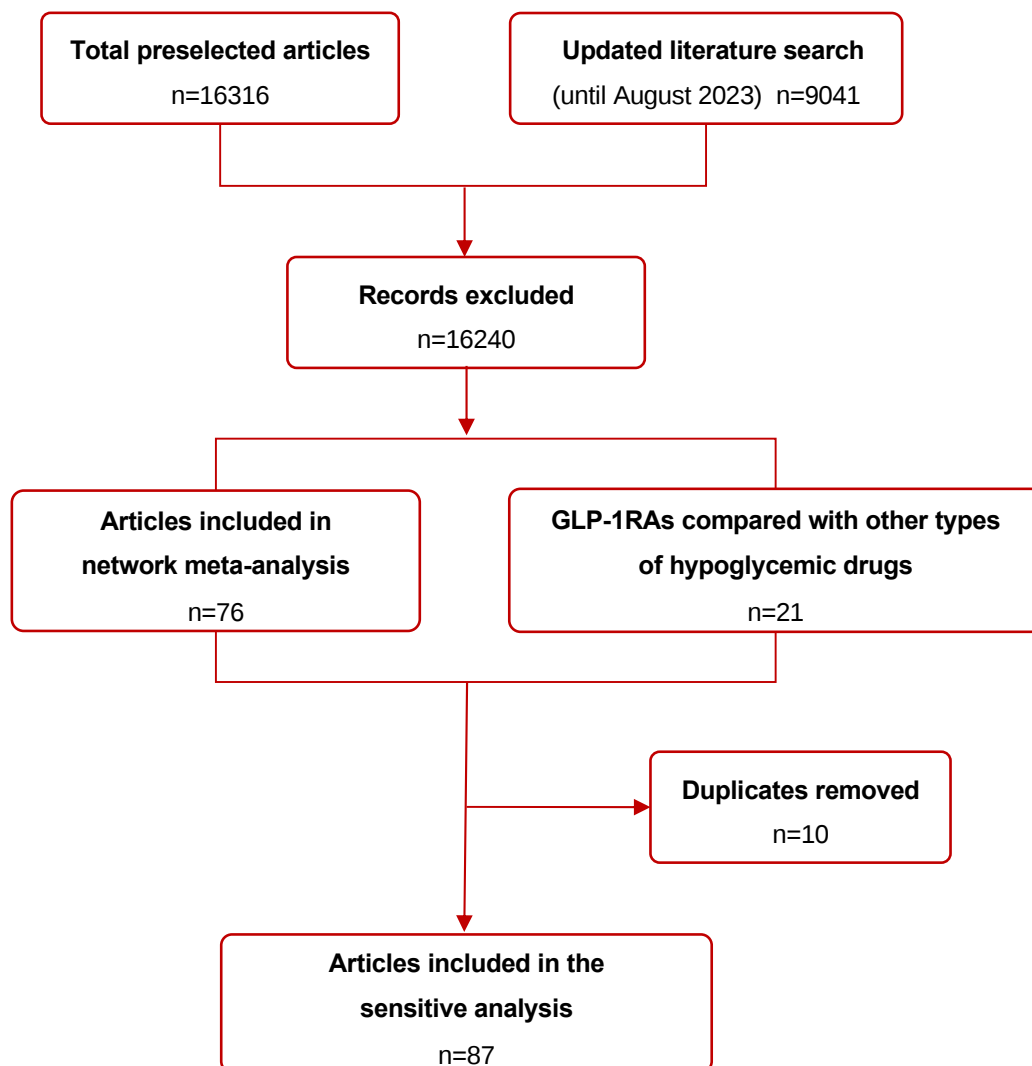


Table S11.1: Baseline characteristics of included studies supplemented in sensitivity analyses

Study	Trial registration	Country and region	Design	Follow-up duration	Number of participants	Randomised treatments	Dose and frequency	Diabetes duration (years)	Age (mean $\pm$ SD), years	Male %	BMI (mean $\pm$ SD), kg/m ²	HbA1c (mean $\pm$ SD), %	Additional glucose-lowering interventions
Brady 2014	NA	UK	RCT	12 weeks	99	Liraglutide: 47 Sulphonylurea:52	1.2 mg QD sc QD po		51.5 $\pm$ 11.1 52.2 $\pm$ 10.7	51.1% 50.0%	33.0 $\pm$ 7.3 30.1 $\pm$ 4.3	7.60 $\pm$ 1.10 7.80 $\pm$ 1.00	metformin, sulphonylurea
De Wit 2014	NCT01392898	Denmark	RCT	26 weeks	50	Liraglutide:26 Standard therapy:24	1.8 mg QD sc	8.3 $\pm$ 5.9 7.6 $\pm$ 6.2	57 $\pm$ 10 59 $\pm$ 8	61.5% 62.5%	34 $\pm$ 7 32 $\pm$ 5	7.20 $\pm$ 0.60 7.50 $\pm$ 0.70	insulin therapy and sulfonylurea or metformin
Kaku 2011	NCT00393718	Not provided	RCT	52 weeks	500	Liraglutide: 268 Glibenclamide: 132	0.9 mg QD sc 1.25–2.5 mg QD sc	8.1 $\pm$ 6.7 8.5 $\pm$ 6.8	58.2 $\pm$ 10.4 58.5 $\pm$ 10.4	68.3% 65.2%	24.9 $\pm$ 3.7 24.6 $\pm$ 3.8	9.32 $\pm$ 1.08 9.18 $\pm$ 0.97	none
Seino 2010	NCT00393718	Japan	RCT	24 weeks	411	Liraglutide: 272 Glibenclamide: 139	0.9 mg QD sc 2.5mg QD po	8.1 $\pm$ 6.7 8.5 $\pm$ 6.8	58.2 $\pm$ 10.4 58.5 $\pm$ 10.4	68.0% 65.0%	24.5 $\pm$ 3.7 24.4 $\pm$ 3.8	8.92 $\pm$ 1.08 8.78 $\pm$ 0.97	With/without oral antidiabetic drug
Zang 2016	NCT02008682	China	RCT	26 weeks	368	Liraglutide: 184 Sitagliptin: 184	1.8mg QD sc 100mg QD po	5.3 $\pm$ 4.4 5.5 $\pm$ 5.4	51.7 $\pm$ 10.7 51.4 $\pm$ 11.0	55.7% 63.6%	27.3 $\pm$ 3.4 27.2 $\pm$ 4.0	8.14 $\pm$ 0.83 8.11 $\pm$ 0.78	metformin
Zhaohu 2022	ChiCTR1800019864	China	RCT	24 weeks	309	Liraglutide: 143 Dapagliflozin: 166	1.2 mg QD sc 10 mg QD po	6.5 $\pm$ 5.8 6.1 $\pm$ 5.5	51.9 $\pm$ 11.1 51.8 $\pm$ 11.4	58.0% 64.5%	30.2 $\pm$ 4.3 29.6 $\pm$ 4.2	8.92 $\pm$ 1.49 8.80 $\pm$ 1.41	metformin with/without premixed insulin
Li 2014		China	RCT	24 weeks	203	Liraglutide: 68 Saxagliptin: 68 Vildagliptin: 67	1.2mg QD sc 5mg QD po 50mg BID po	5.8 $\pm$ 2.8 5.4 $\pm$ 2.7 5.4 $\pm$ 2.2	47.9 $\pm$ 10.8 47.0 $\pm$ 11.3 46.4 $\pm$ 9.8	59.0% 65.0% 69.6%	26.7 $\pm$ 2.4 26.3 $\pm$ 2.2 25.9 $\pm$ 1.8	8.48 $\pm$ 0.79 8.59 $\pm$ 0.87 8.56 $\pm$ 0.77	metformin, with/or sulphonylurea
Ando 2021	UMIN000019382	Japan	RCT	24 weeks	40	Liraglutide: 20 Canagliflozin: 20	0.3 mg QD sc 100 mg QD sc	7.8 $\pm$ 7.0 10.4 $\pm$ 6.9	58.2 $\pm$ 11.5 55.9 $\pm$ 13.0	76.5% 76.5%	26.8 $\pm$ 3.1 27.0 $\pm$ 3.3	6.40 $\pm$ 0.60 6.80 $\pm$ 0.70	none
Bergental 2010	NCT00637273	USA, India, and Mexico	RCT	26 weeks	514	Exanatide:170 Sitagliptin:172 Pioglitazone:172	2mg QW+ placebo QD 100 mg QD+ placebo QW 45 mg QD+ placebo QW	6.0 $\pm$ 5.0 5.0 $\pm$ 4.0 6.0 $\pm$ 5.0	52 $\pm$ 10 52 $\pm$ 11 53 $\pm$ 10	89.0% 76.0% 79.0%	32.0 $\pm$ 5.0 32.0 $\pm$ 5.0 32.0 $\pm$ 6.0	8.60 $\pm$ 1.20 8.50 $\pm$ 1.20 8.50 $\pm$ 1.10	metformin

Takeshita 2015	no. 000004953	Japan	RCT	12 weeks	112	Liraglutide: 54 Vildagliptin: 58	0.9 mg QD sc 50 mg BID po		64.7 ±12.4 64.8% 62.1%	25.4 ± 4.8 24.5 ± 4.6	8.00 ± 0.90 8.10± 1.20	sitagliptin	
Diamant 2010	NCT00641056	USA, the European Union, Russia, Australia, Korea, Taiwan China, Mexico	RCT	26 weeks	456	Exenatide: 233 Insulin Glargine: 233	2mg QW sc QD sc	8.0 ± 6.0 7.8 ± 6.0	58 ± 10 58 ± 9	52.0% 55.0%	32 ± 5 ± 5	32 8.30 ± 1.10 8.30 ± 1.00	metformin, with/or sulphonylurea
Ahren 2014	NCT00838903	Sweden	RCT	104 weeks	1049	Placebo:104 Sitagliptin:313 Glimepiride:317 Albiglutide:315	 100 mg QD po 2 mg QD po 30 mg QW sc	6.7 ± 6.6 5.8 ± 4.8 6.0 ± 4.8 6.0 ± 4.3	56.1 ± 10.0 54.3 ± 9.8 54.4 ± 10.0 54.3 ± 10.1	49.5% 46.0% 51.5% 44.7%	32.8 ± 5.4 32.5 ± 5.4 32.5 ± 5.5 32.7 ± 5.6	8.10 ± 0.50 8.10 ± 0.86 8.10 ± 0.87 8.10 ± 0.86	metformin
Nauck 2014	NCT00734474	Multinational	RCT	52 weeks	1098	Placebo: 177 Dulaglutide: 304 Dulaglutide: 302 Sitagliptin: 315	1.5 mg QW sc 0.75 mg QW sc 100 mg QD po	7 ± 5 54± 10 54 ± 10 54 ± 10	55 ± 9 54± 10 54 ± 10 54 ± 10	51.0% 48.0% 44.0% 48.0%	31± 4 31±5 31 ±4 31±4	8.10 ±1.10 8.10 ±1.10 8.10 ±1.10 8.10 ±1.10	metformin or other pre-study medications
Pratley 2010	NCT00700817	Europe, USA, Canada	RCT	26 weeks	665	Liraglutide: 225 Liraglutide: 221 Sitagliptin: 219	1.2 mg QD sc 1.8 mg QD sc 100 mg QD po	6.0 ± 4.5 6.4 ± 5.4 6.3 ± 5.4	55.9 ± 9.6 55.0 ± 9.1 55.0 ± 9.0	52.0% 52.0% 55.0%	32.6 ± 5.2 33.1 ± 5.1 32.6 ± 5.4	8.40 ± 0.80 8.40 ± 0.70 8.50 ± 0.70	metformin
Umpierrez 2014	NCT01126580	Multinational	RCT	52 weeks	807	Dulaglutid: 269 Dulaglutide: 270 Metformin: 268	1.5 mg QW sc 0.75 mg QW sc 2000mg QD po	3 ± 2 3 ± 2 3 ± 2	56 ± 10 56 ± 11 55 ± 10	42.0% 44.0% 45.0%	34 ± 6.0 33 ± 6.0 33 ± 5.0	7.60 ± 0.90 7.60 ± 0.90 7.60 ± 0.80	none
Ahren 2017	NCT01930188	Europe (Bulgaria, Czech Republic, Hungary, Norway, Portugal, Romania, Spain, Sweden, Turkey, and Ukraine), Argentina, Hong Kong China, India, Japan, Mexico, Russia, South Africa, Thailand	RCT	56 weeks	1231	Semaglutide: 410 Semaglutide: 410 Sitagliptin: 411	0.5mg QW sc 1mg QW sc 100mg QD po	6.4 ± 4.7 6.7 ± 5.6 6.6 ± 5.1	54.8 ± 10.2 56.0 ± 9.4 54.6 ± 10.4	51.0% 50.0% 51.0%	32.4 ± 6.2 32.5 ± 6.5 32.5 ± 5.8	8.00 ± 0.90 8.00 ± 0.90 8.20 ± 0.90	metformin, pioglitazone, rosiglitazone

Blonde 2015	NCT01191268	Argentina, Australia, Belgium, Brazil, Canada, Denmark, Greece, Hungary, Mexico, Poland, Russia, Spain, Sweden, Taiwan, USA	RCT	52 weeks	884	Dulaglutide: 293	0.75mg QW sc	12.4 ± 6.9	59.3 ± 9.0	50.0%	33.1 ± 5.2	8.40 ± 1.03	any combination of insulin, with/without oral antidiabetic drug
						Dulaglutide: 295	1.5mg QW sc	12.8 ± 7.2	58.9 ± 9.6	54.0%	32.0 ± 5.1	8.46 ± 1.08	
						Insulin Glargine: 296	QD sc	13.0 ± 6.8	59.9 ± 9.1	56.0%	32.4 ± 5.3	8.53 ± 1.03	
Giorgino 2015	NCT01075282	Argentina, Australia, Italy, Belgium, Canada, Croatia, Czech Republic, France, Greece, Hungary, India, Korea, Mexico, Poland, Romania, Slovakia, Spain, Sweden, China Taiwan	RCT	52 weeks	810	Dulaglutide: 272	0.75mg QW sc	9.0 ± 6.0	57.0 ± 9.0	50.0%	32.0 ± 5.0	8.10 ± 1.00	metformin, glimepiride
						Dulaglutide: 273	1.5mg QW sc	9.0 ± 6.0	56.0 ± 10.0	43.0%	31.0 ± 5.0	8.20 ± 1.00	
						Insulin glargine: 262	QD sc	9.0 ± 6.0	57.0 ± 9.0	51.0%	32.0 ± 6.0	8.10 ± 1.00	
Ludvik 2021	NCT03882970	Argentina, Austria, Italy, Greece, Hungary, Poland, Puerto Rico, USA, Romania, South Korea, Spain, China Taiwan, Ukraine	RCT	52 weeks	1437	Tirzepatide:358	5 mg QW sc	8.5 ± 5.8	57.2 ± 10.1	56.0%	33.6 ± 5.9	8.17 ± 0.89	metformin with /without SGLT2 inhibitor
						Tirzepatide:360	10 mg QW sc	8.4 ± 6.6	57.4 ± 9.7	54.0%	33.4 ± 6.2	8.18 ± 0.89	
						Tirzepatide:359	15 mg QW sc QD sc	8.5 ± 6.5	57.5 ± 10.2	54.0%	33.7 ± 6.1	8.21 ± 0.94	
						Insulin degludec: 360		8.1 ± 6.0	57.5 ± 10.1	59.0%	33.4 ± 6.1	8.12 ± 0.94	
Rosenstock 2019	NCT02607865	USA, Argentina, Mexico, France, Germany, India, Israel, Brazil, Japan, UK, Romania, Russia, South Africa, Turkey, Ukraine	RCT	78 weeks	1864	Semaglutide: 466	3 mg QD sc	8.4 ± 6.1	58 ± 10.0	54.5%	32.6 ± 6.7	8.30 ± 1.00	metformin
						Semaglutide: 465	7 mg QD sc	8.3 ± 5.8	58 ± 10.0	52.7%	32.6 ± 6.4	8.40 ± 1.00	
						Semaglutide: 465	14 mg QD sc	8.7 ± 6.1	57 ± 10.0	53.1%	32.3 ± 6.3	8.30 ± 0.90	
						Sitagliptin: 467	100 mg QD sc	8.8 ± 6.0	58 ± 10.0	51.0%	32.5 ± 6.2	8.30 ± 0.90	

Wang 2018	NCT01648582	China, Russia, Mexico RCT and South Korea	52 weeks	774	Dulaglutide: 257	0.75 mg QW sc	8.1 ± 5.3	54.5 ± 10.0	56.7%	27.0 ± 3.8	8.30 ± 1.10	insulin glargine
					Dulaglutide: 258	1.5 mg QW sc	7.9 ± 4.8	55.0 ± 9.6	53.4%	26.6 ± 3.7	8.50 ± 1.20	
					Insulin Glargine:	QD sc	8.4 ± 5.3	55.4 ± 9.2	55.6%	26.7 ± 3.5	8.30 ± 1.10	
					259							

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride. SC, subcutaneous injections; PO, oral intake; QD, once daily; QW, once weekly; BID, twice daily; BIW: twice weekly; QMS, once monthly suspension.

Table S11.2: Sensitivity analyses of primary outcomes

GLP-1 RA	HbA1c		FPG		Weight	
	Main estimate	Sensitivity analyses	Main estimate	Sensitivity analyses	Main estimate	Sensitivity analyses
Mazdutide	-2.09 (-3.10, -1.09)	-2.09 (-3.03, -1.16)	-1.31 (-2.58, -0.03)	-1.28 (-2.55, -0.01)	-2.26 (-4.99, 0.47)	-2.22 (-4.93, 0.50)
Tirzepatide	-2.10 (-2.47, -1.74)	-2.09 (-2.41, -1.77)	-3.12 (-3.59, -2.66)	-3.09 (-3.56, -2.63)	-8.47 (-9.68, -7.26)	-8.38 (-9.59, -7.18)
Retatrutide	-1.32 (-1.97, -0.68)	-1.30 (-1.89, -0.72)	-1.94 (-3.21, -0.66)	-1.90 (-3.17, -0.62)	-7.87 (-9.95, -5.79)	-7.83 (-9.90, -5.75)
Orforglipron	-1.49 (-2.12, -0.85)	-1.49 (-2.06, -0.92)	-2.09 (-2.86, -1.31)	-2.06 (-2.84, -1.29)	-4.88 (-6.93, -2.83)	-4.85 (-6.89, -2.81)
CagriSema	-1.80 (-2.87, -0.73)	-1.80 (-2.77, -0.82)	-2.79 (-4.30, -1.28)	-2.67 (-4.18, -1.17)	-14.03 (-17.05, -11.00)	-13.76 (-16.76, -10.76)
Semaglutide	-1.40 (-1.67, -1.12)	-1.40 (-1.63, -1.16)	-1.99 (-2.41, -1.58)	-1.87 (-2.25, -1.50)	-3.13(-3.95, -2.31)	-2.86 (-3.62, -2.10)
Dulaglutide	-1.09 (-1.34, -0.84)	-1.07 (-1.28, -0.86)	-1.49 (-1.84, -1.14)	-1.42 (-1.77, -1.08)	-0.73 (-1.56, 0.10)	-0.63 (-0.43, 0.16)
Liraglutide	-1.04 (-1.30, -0.79)	-1.04 (-1.26, -0.83)	-1.46 (-1.84, -1.09)	-1.54 (-1.89, -1.18)	-1.33 (-2.08, -0.59)	-1.40 (-2.11, -0.68)
Exenatide	-0.81 (-1.15, -0.48)	-0.87 (-1.14, -0.60)	-0.90 (-1.56, -0.24)	-1.25 (-1.80, -0.70)	-0.62 (-1.69, 0.45)	-0.79 (-1.75, 0.16)
Lixisenatide	-0.60 (-1.01, -0.20)	-0.60 (-0.96, -0.25)	-0.61 (-1.14, -0.08)	-0.61 (-1.14, -0.08)	-0.32 (-1.51, 0.87)	-0.32 (-1.50, 0.87)
Efpeglenatide	-0.74 (-1.23, -0.25)	-0.74 (-1.18, -0.31)	-1.04 (-1.84, -0.24)	-1.22 (-0.97, -0.47)	-0.93 (-2.89, 1.03)	-1.29 (-3.11, 0.53)
ITCA 650	-0.91 (-1.81, -0.01)	-0.91 (-1.70, -0.12)	NA	NA	-1.36 (-4.30, 1.58)	-1.36 (-4.29, 1.57)
PEG-Loxenatide	-1.04 (-1.57, -0.50)	-1.03 (-1.51, -0.56)	-1.33 (-2.05, -0.61)	-1.33 (-2.05, -0.61)	0.27 (-1.58, 2.13)	0.27 (-1.57, 2.12)
PEGylated exenatide	-0.97 (-1.87, -0.07)	-0.97 (-1.77, -0.17)	-1.68 (-2.85, -0.51)	-1.68 (-2.85, -0.51)	-0.34 (-3.01, 2.33)	-0.34 (-3.00, 2.32)
Albiglutide	-1.01 (-1.55, -0.48)	-0.97(-1.43, -0.52)	-1.78 (-2.52, -1.04)	-1.69 (-2.38, -1.00)	-0.03 (-2.27, 2.21)	-0.01 (-1.96, 1.93)

Appendix 12: The meta-regression of the factors that may lead to differences to the main outcome indicators

Factors	HbA1c			FPG			Body weight		
	Coefficient	95% confidence interval	P value	Coefficient	95% confidence interval	P value	Coefficient	95% confidence interval	P value
Diabetes duration	0.08	-0.02, -0.19	0.13	0.03	-0.02, -0.09	0.26	0.06	-0.06, -0.17	0.35
Age	0.13	0.01, -0.25	0.05	0.05	-0.03, -0.12	0.19	-0.02	-0.17, -0.25	0.76
Whether background hypoglycemic therapy was combined	-0.14	-0.93, -0.64	0.72	-0.25	-0.66, -0.17	0.24	0.03	-0.39, -0.45	0.89

Appendix 13: Comprehensive comparisons of different GLP-IRAs at various doses

Figure S13.1: HbA1c

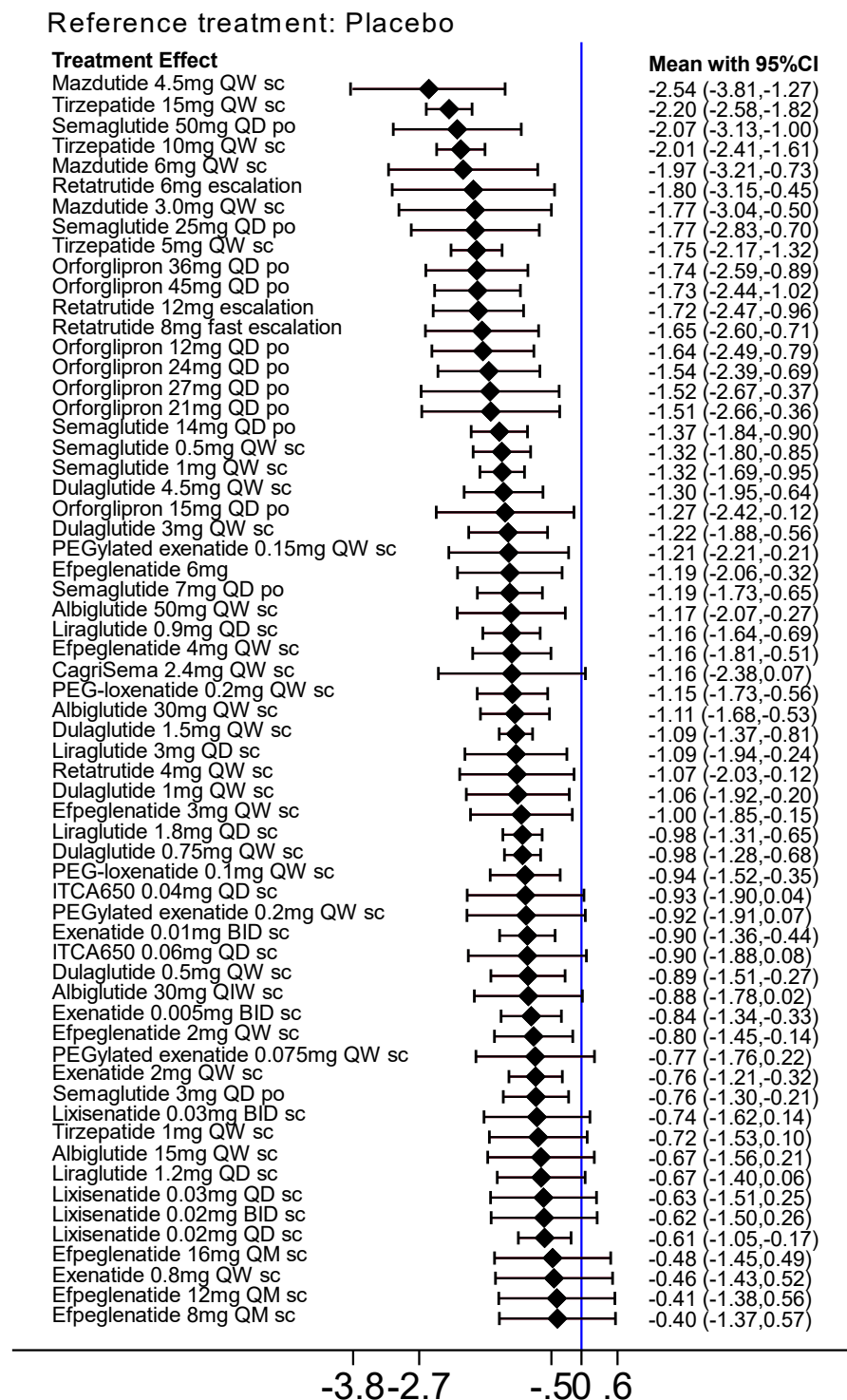


Figure S13.2: FPG

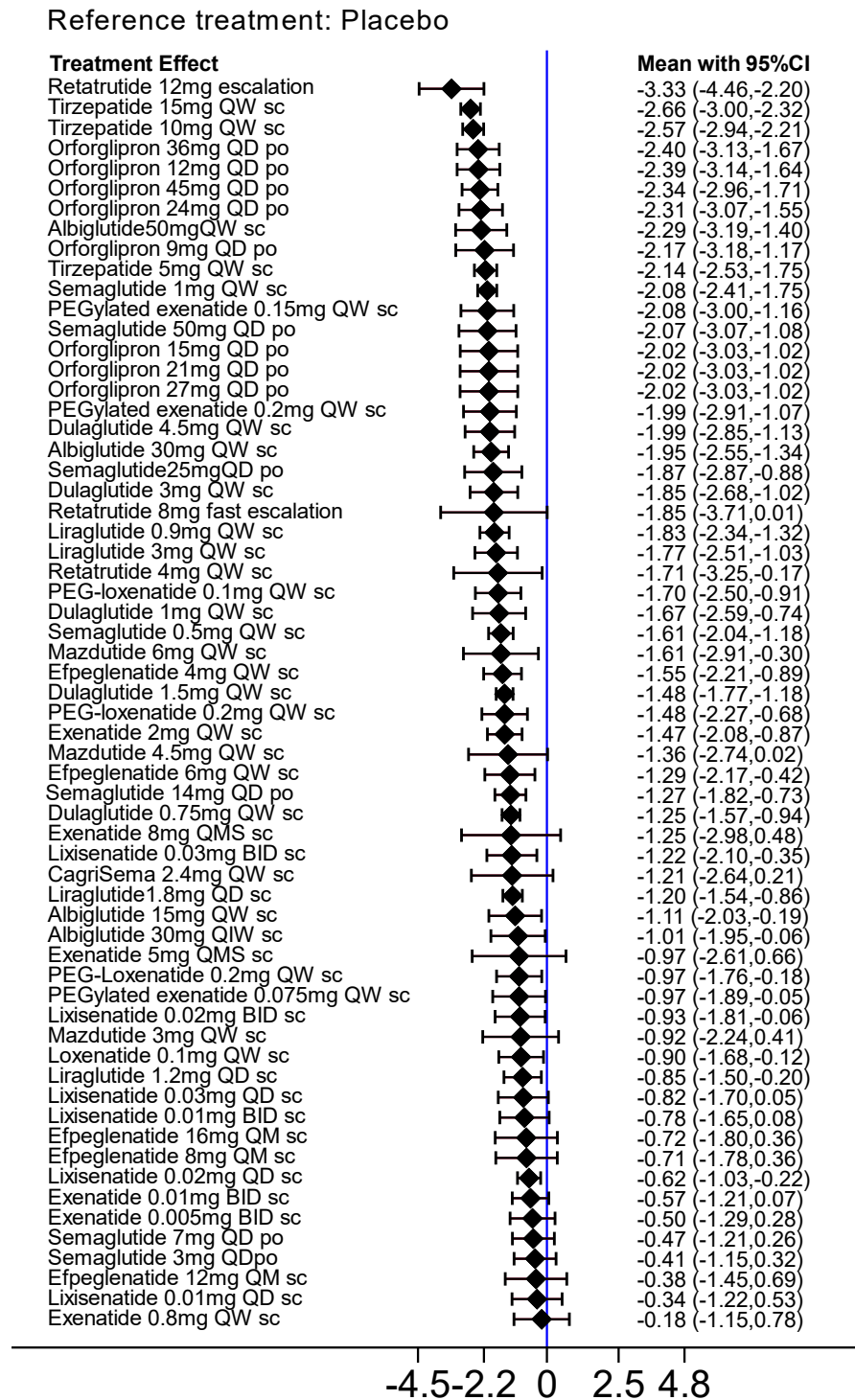


Figure S13.3: Weight

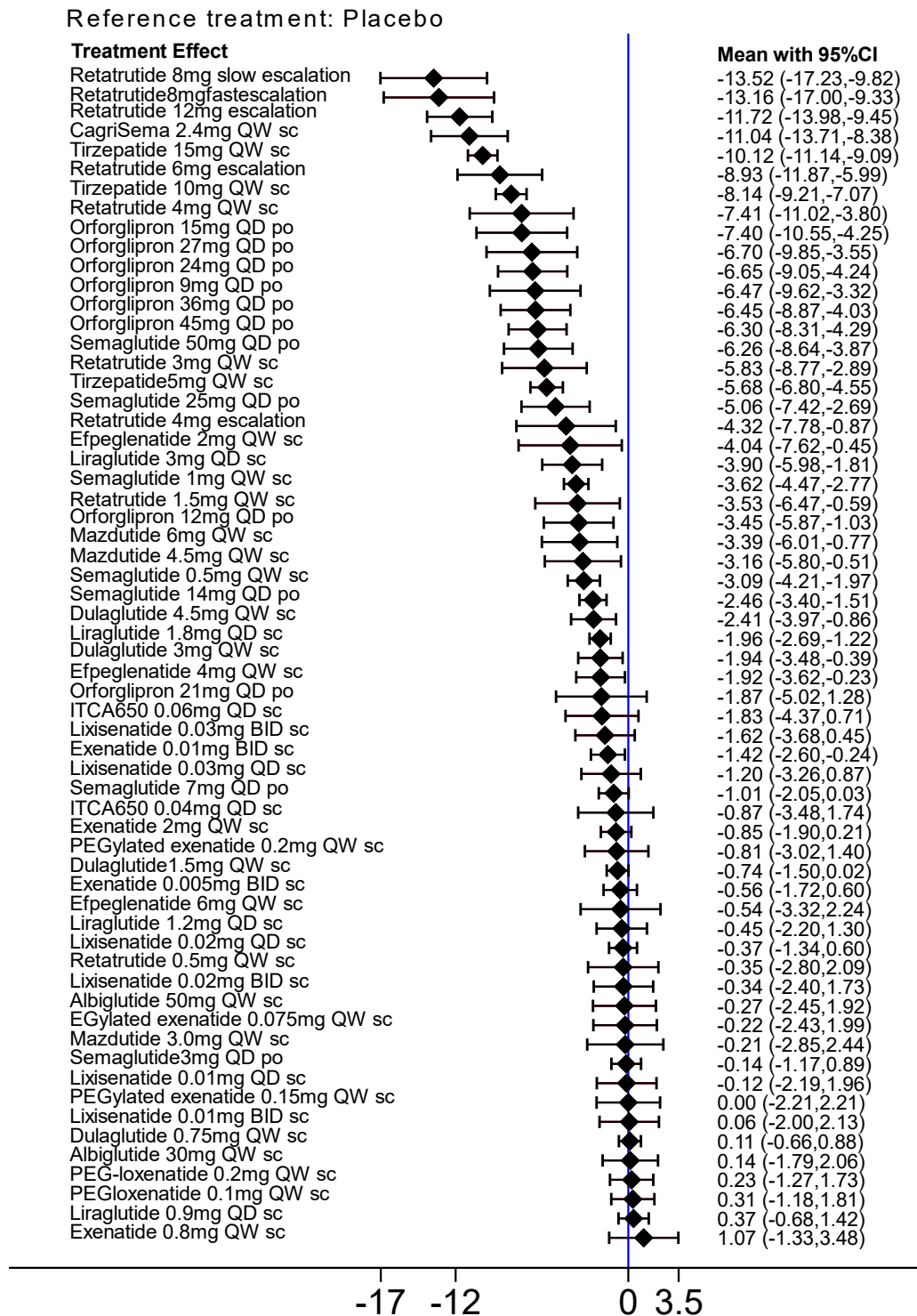


Figure S13.4: BMI

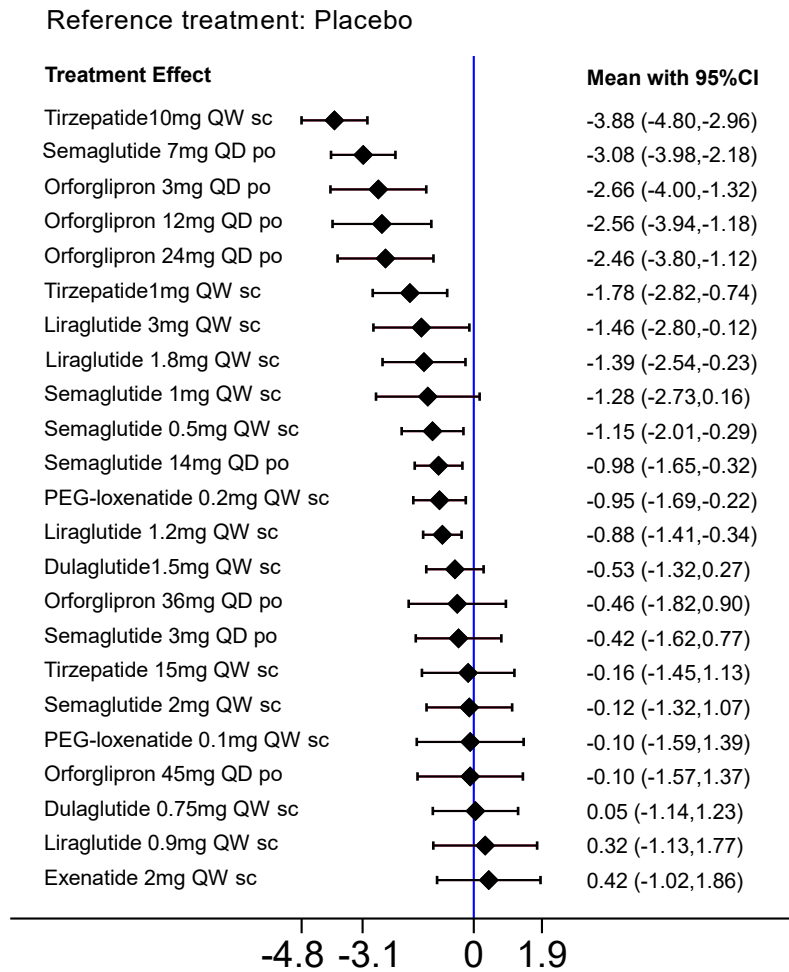


Figure S13.5: Waist circumference

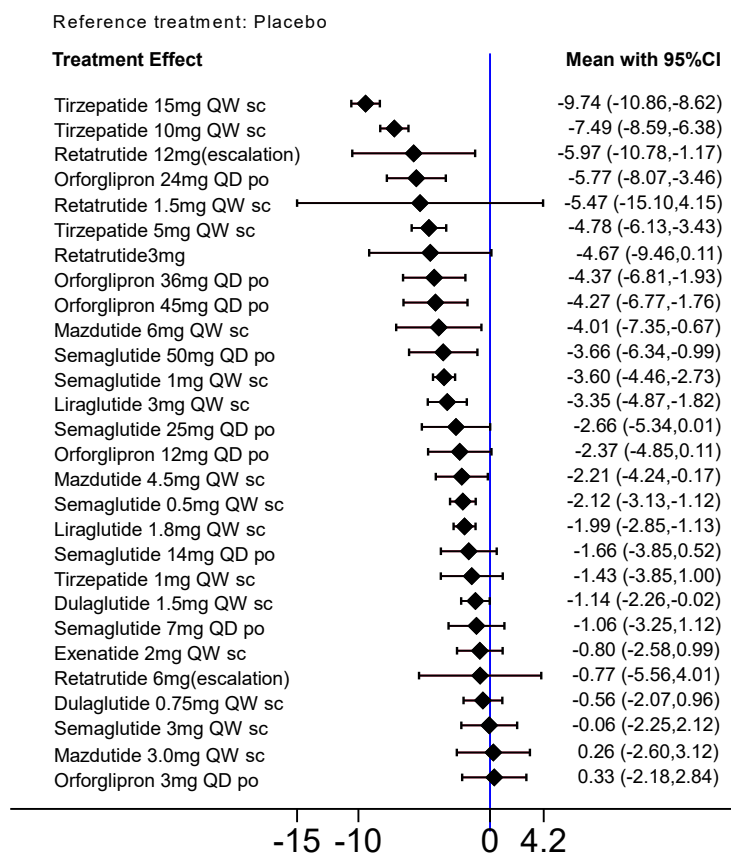


Figure S13.6: HDL

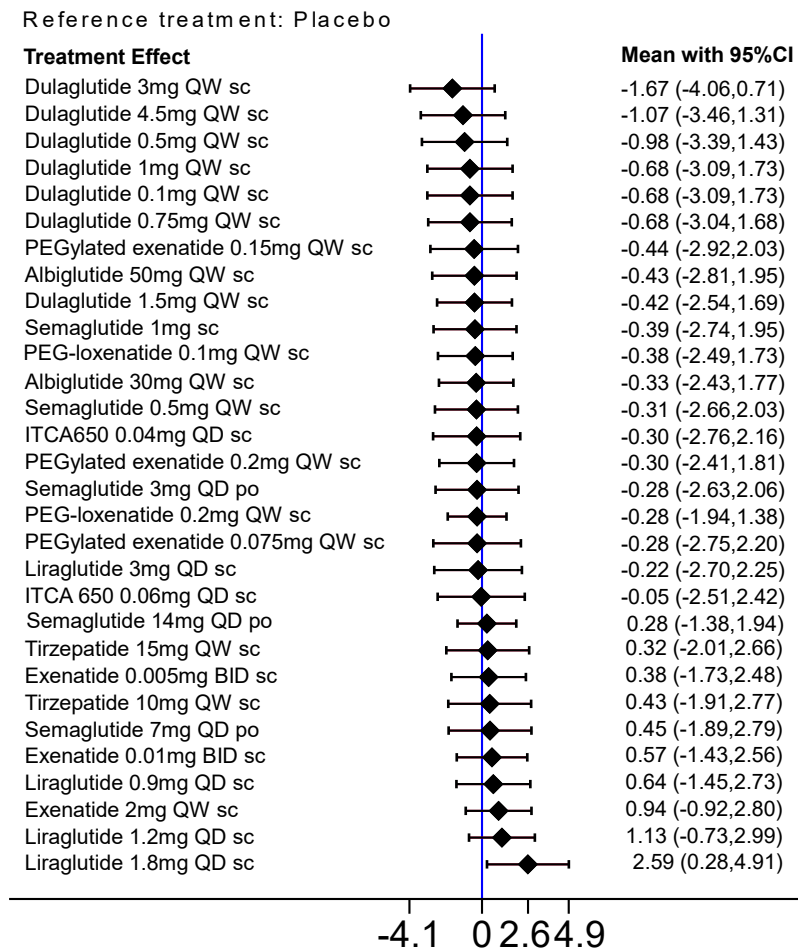


Figure S13.7: LDL

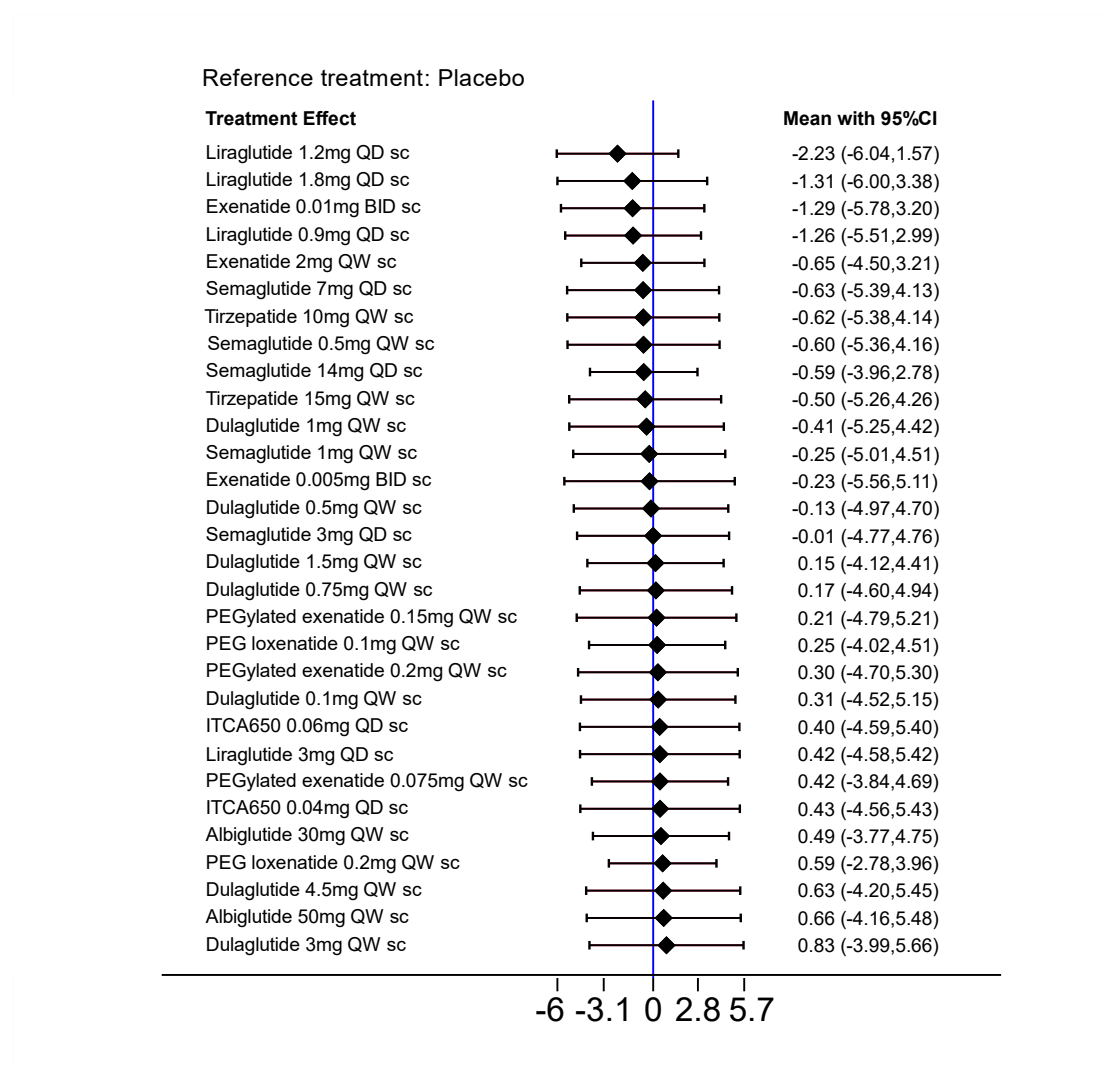


Figure S13.8: TC

Reference treatment: Placebo

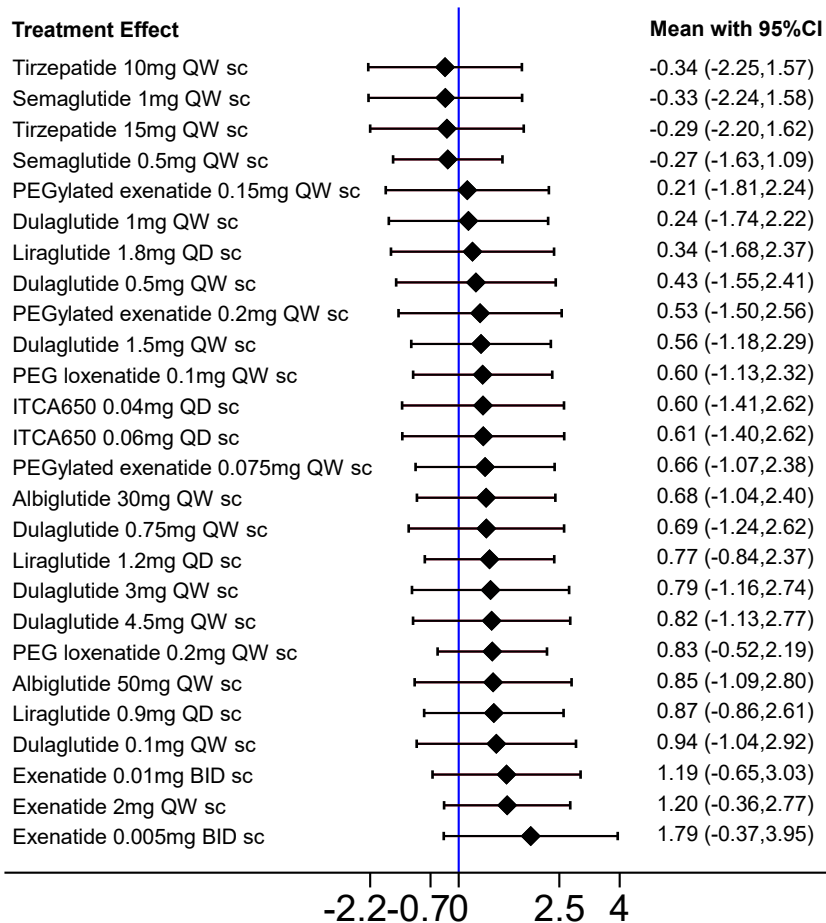


Figure S13.9: TG

Reference treatment: Placebo

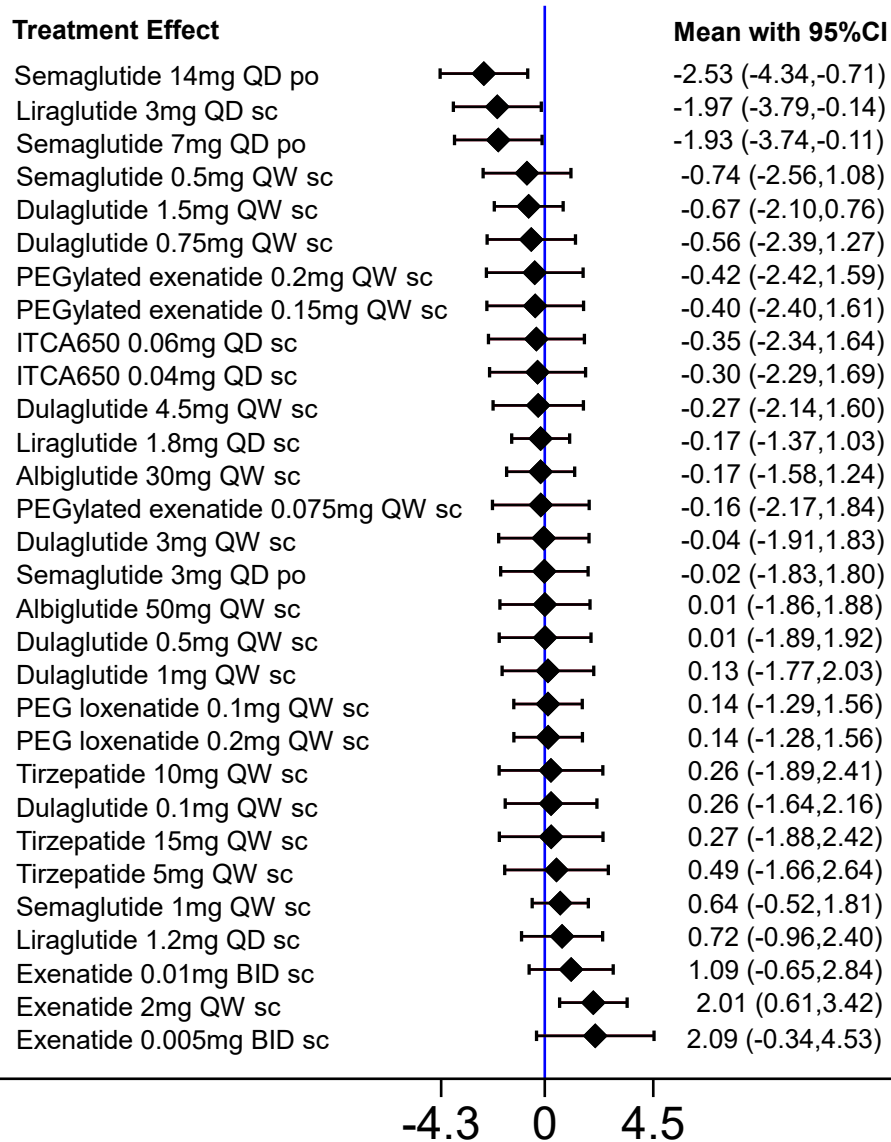


Table S13: Global consistency

Clinical outcome	Chi square	P value
HbA1c	8.92	0.7058
FPG	24.26	0.9876
weight	53.70	0.5243
BMI	5.50	0.9047
Waist circumference	11.06	0.1202
TG	3.88	0.0728
TC	24.38	0.7556
HDL	0.85	0.7690
LDL	10.05	0.1650

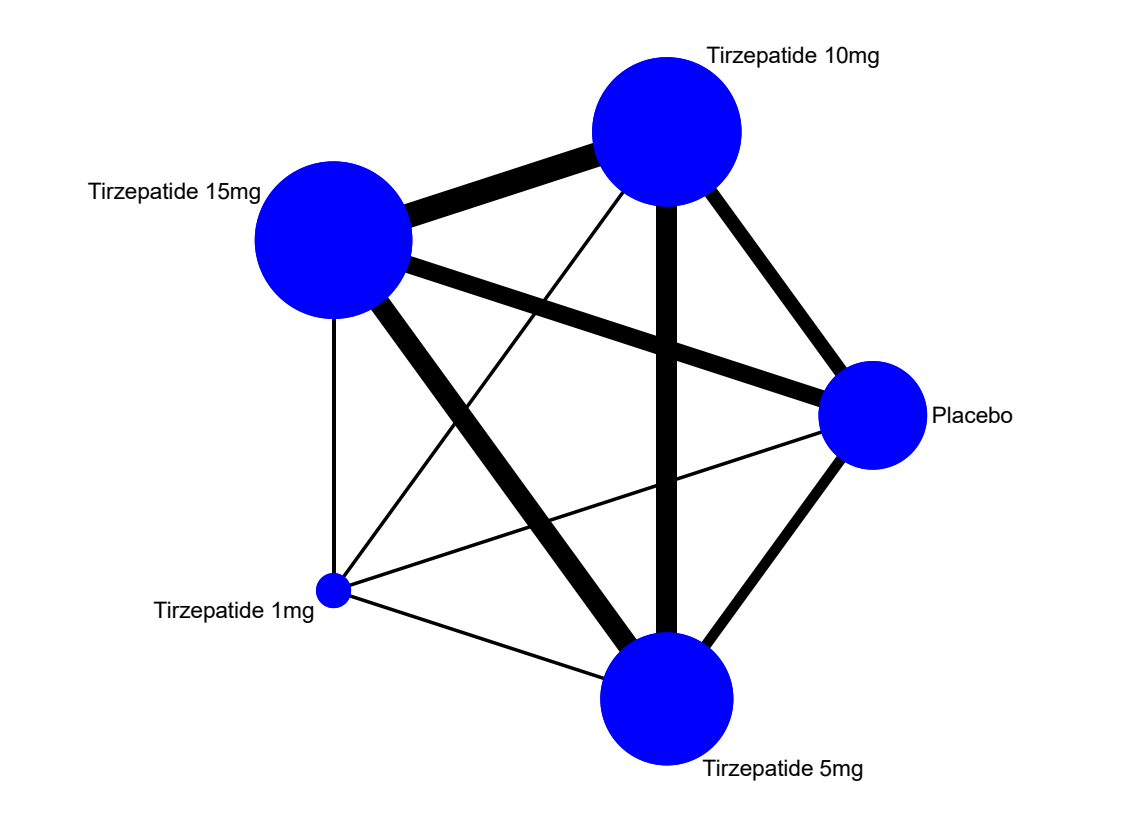
Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Appendix 14: Subgroup analysis of different doses of GLP-1RAs on T2D

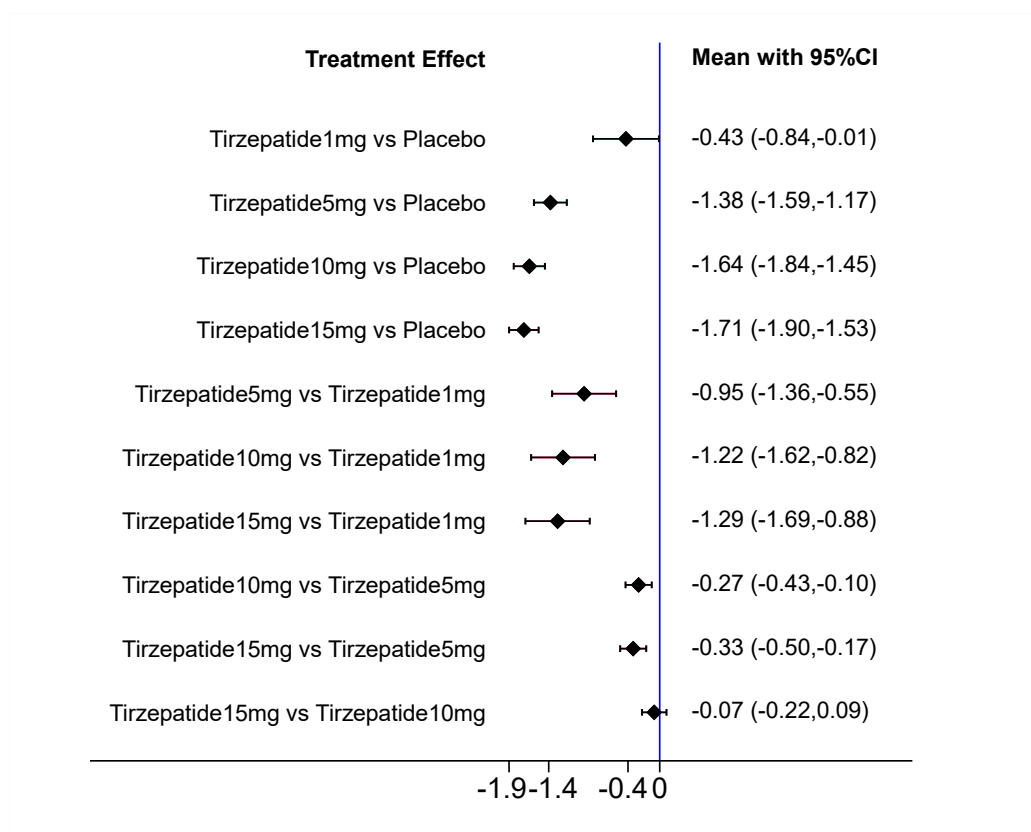
Figure S14.1: Effects of different doses of Tirzepatide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Tirzepatide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) BMI, (E) waist circumference, (F) HDL, (G) LDL, (H) TC, (I) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



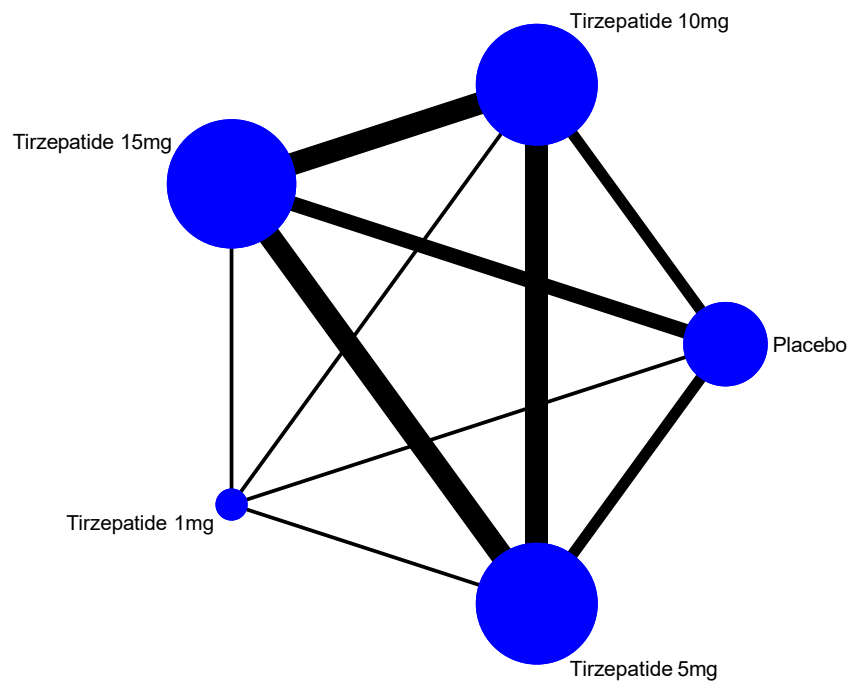
(A2) Forest plot of HbA1c



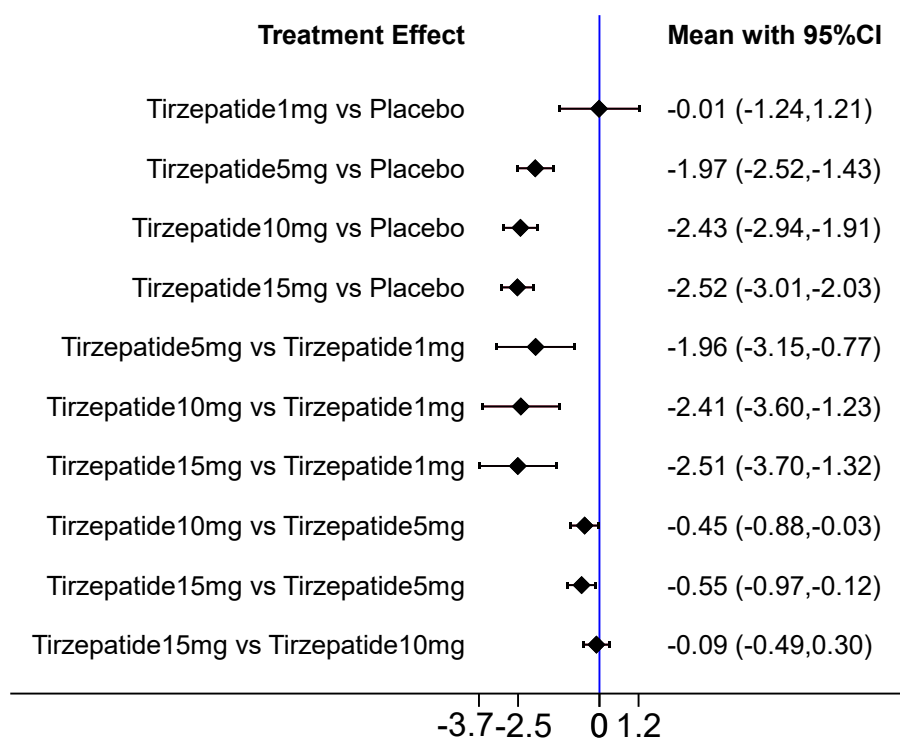
(A3) League table of HbA1c

Tirzepatide 15mg	0.07 (-0.09, 0.22)	0.33 (0.17, 0.50)	1.29 (0.88, 1.69)	1.71 (1.53, 1.90)
-0.07 (-0.22, 0.09)	Tirzepatide 10mg	0.27 (0.10, 0.43)	1.22 (0.82, 1.62)	1.64 (1.45, 1.84)
-0.33 (-0.50, -0.17)	-0.27 (-0.43, -0.10)	Tirzepatide 5mg	0.95 (0.55, 1.36)	1.38 (1.17, 1.59)
-1.29 (-1.69, -0.88)	-1.22 (-1.62, -0.82)	-0.95 (-1.36, -0.55)	Tirzepatide 1mg	0.43 (0.01, 0.84)
-1.71 (-1.90, -1.53)	-1.64 (-1.84, -1.45)	-1.38 (-1.59, -1.17)	-0.43 (-0.84, -0.01)	Placebo

(B1) Network map of FPG



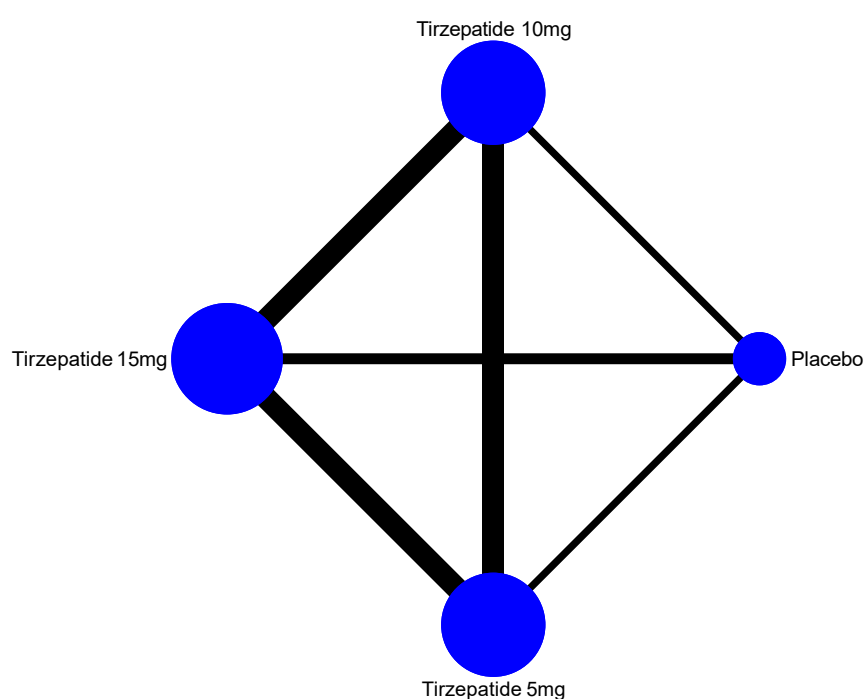
(B2) Forest plot of FPG



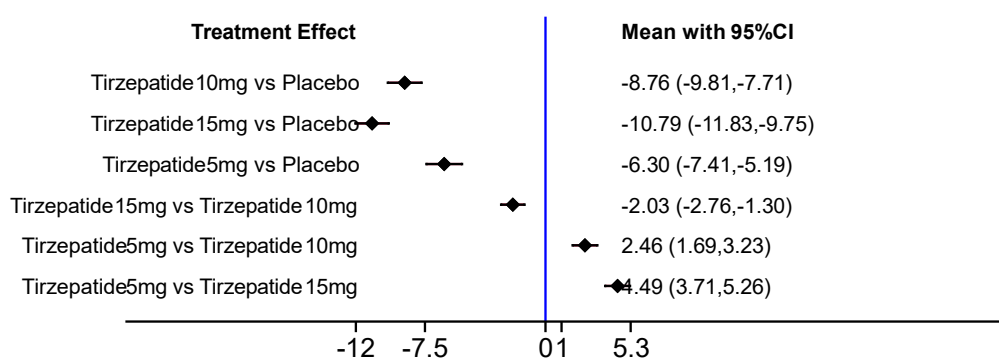
(B3) League table of FPG

Tirzepatide 15mg	0.09 (-0.30,0.49)	0.55 (0.12,0.97)	2.51 (1.32,3.70)	2.52 (2.03,3.01)
-0.09 (-0.49,0.30)	Tirzepatide 10mg	0.45 (0.03,0.88)	2.41 (1.23,3.60)	2.43 (1.91,2.94)
-0.55 (-0.97,-0.12)	-0.45 (-0.88,-0.03)	Tirzepatide 5mg	1.96 (0.77,3.15)	1.97 (1.43,2.52)
-2.51 (-3.70,-1.32)	-2.41 (-3.60,-1.23)	-1.96 (-3.15,-0.77)	Tirzepatide 1mg	0.01 (-1.21,1.24)
-2.52 (-3.01,-2.03)	-2.43 (-2.94,-1.91)	-1.97 (-2.52,-1.43)	-0.01 (-1.24,1.21)	Placebo

(C1) Network map of weight loss



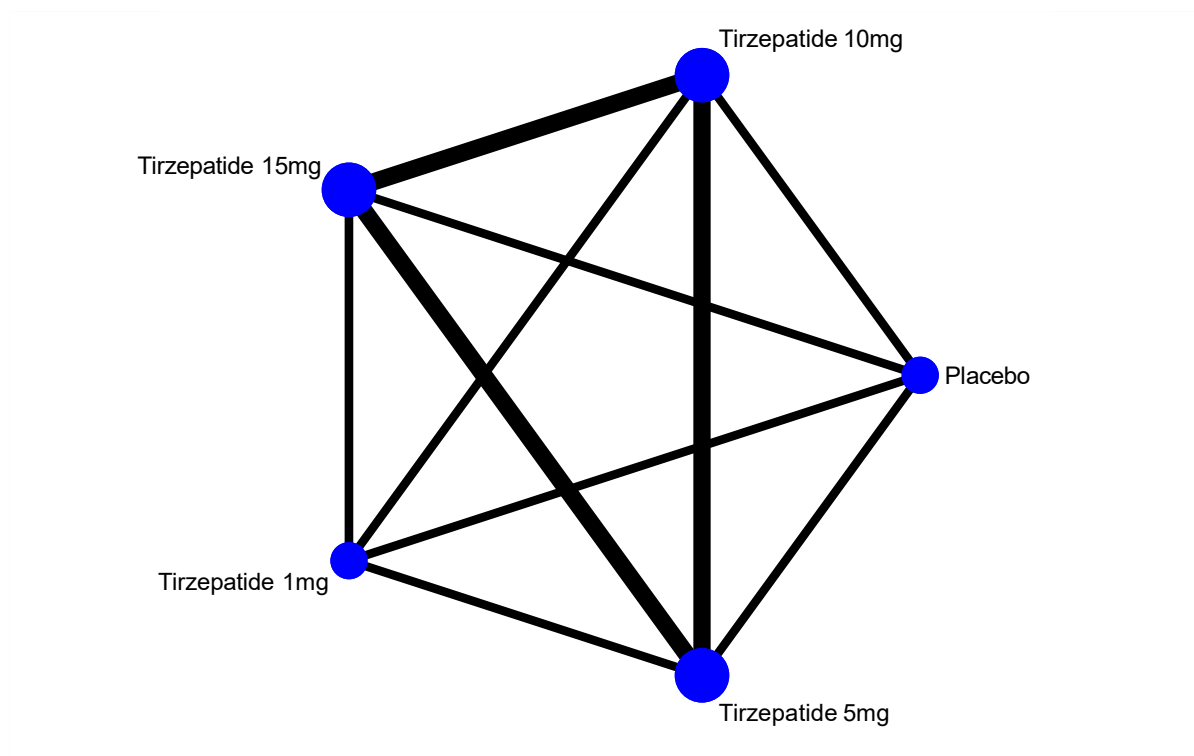
(C2) Forest plot of weight loss



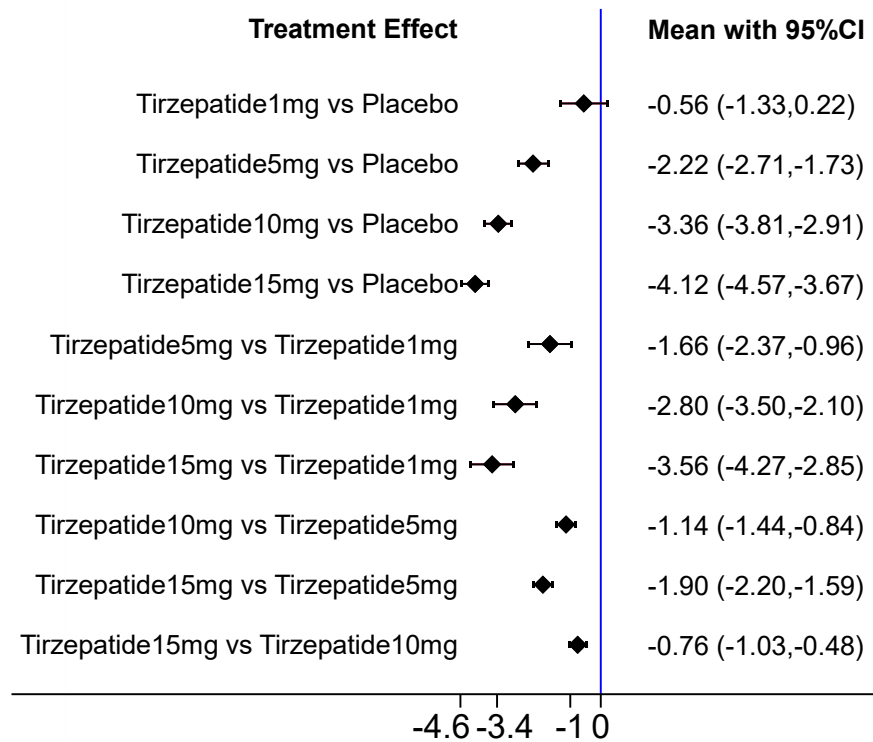
(C3) League table of weight loss

Tirzepatide 15mg	2.03 (1.30,2.76)	4.49 (3.71,5.26)	10.79 (9.75,11.83)
-2.03 (-2.76,-1.30)	Tirzepatide 10mg	2.46 (1.69,3.23)	8.76 (7.71,9.81)
-4.49 (-5.26,-3.71)	-2.46 (-3.23,-1.69)	Tirzepatide 5mg	6.30 (5.19,7.41)
-10.79 (-11.83,-9.75)	-8.76 (-9.81,-7.71)	-6.30 (-7.41,-5.19)	Placebo

(D1) Network map of BMI



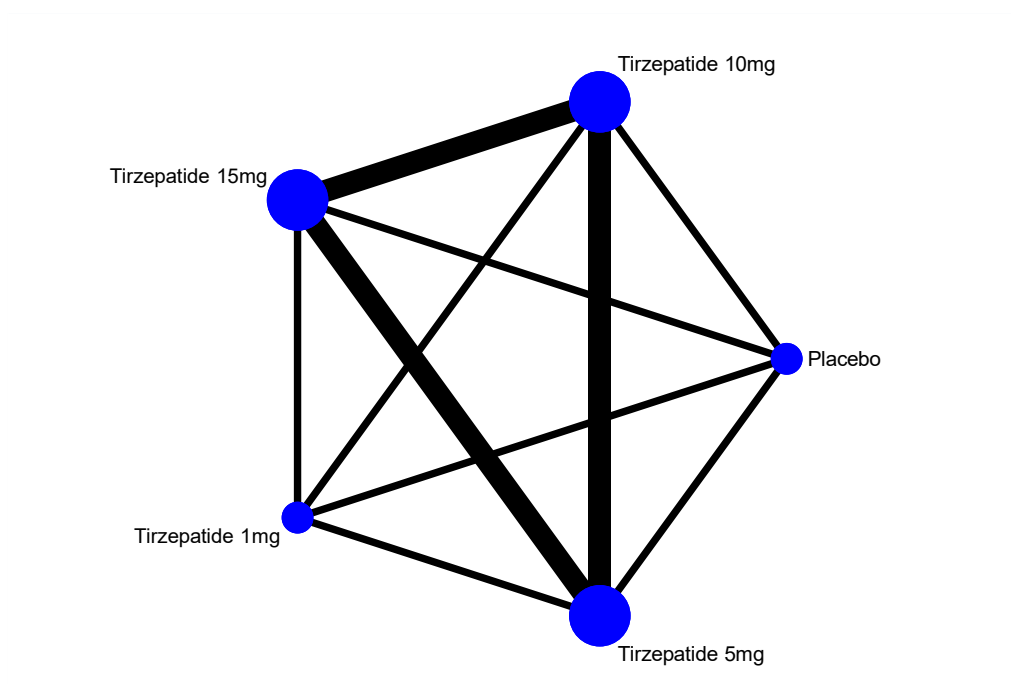
(D2) Forest plot of BMI



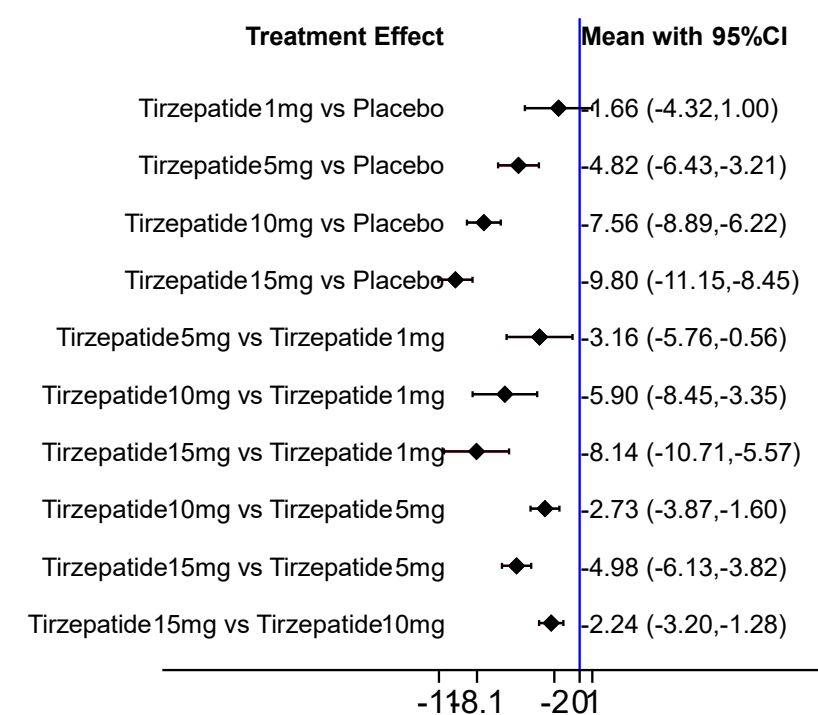
(D3) League table of BMI

Tirzepatide 15mg	0.76 (0.48, 1.03)	1.90 (1.59, 2.20)	3.56 (2.85, 4.27)	4.12 (3.67, 4.57)
-0.76 (-1.03, -0.48)	Tirzepatide 10mg	1.14 (0.84, 1.44)	2.80 (2.10, 3.50)	3.36 (2.91, 3.81)
-1.90 (-2.20, -1.59)	-1.14 (-1.44, -0.84)	Tirzepatide 5mg	1.66 (0.96, 2.37)	2.22 (1.73, 2.71)
-3.56 (-4.27, -2.85)	-2.80 (-3.50, -2.10)	-1.66 (-2.37, -0.96)	Tirzepatide 1mg	0.56 (-0.22, 1.33)
-4.12 (-4.57, -3.67)	-3.36 (-3.81, -2.91)	-2.22 (-2.71, -1.73)	-0.56 (-1.33, 0.22)	Placebo

(E1) Network map of waist circumference



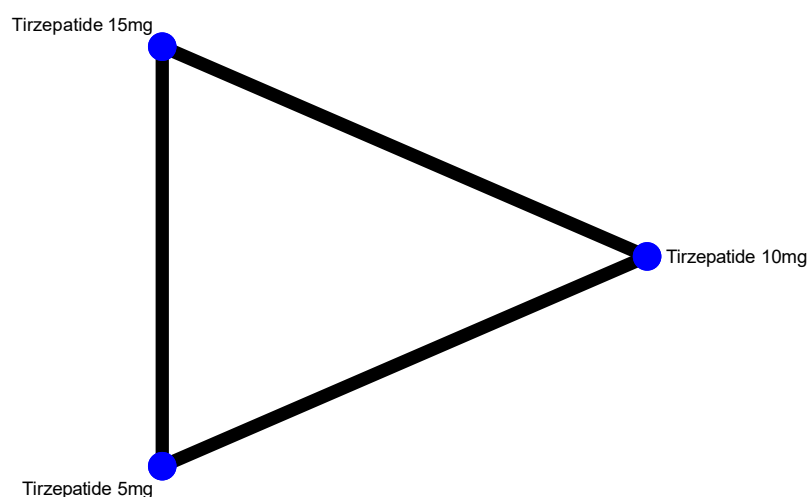
(E2) Forest plot of waist circumference



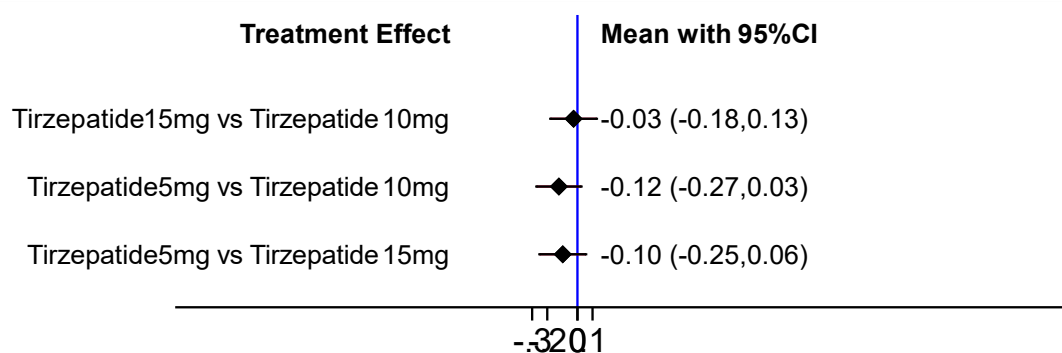
(E3) League table of waist circumference

Tirzepatide 15mg	2.24 (1.28, 3.20)	4.98 (3.82, 6.13)	8.14 (5.57, 10.71)	9.80 (8.45, 11.15)
-2.24 (-3.20, -1.28)	Tirzepatide 10mg	2.73 (1.60, 3.87)	5.90 (3.35, 8.45)	7.56 (6.22, 8.89)
-4.98 (-6.13, -3.82)	-2.73 (-3.87, -1.60)	Tirzepatide 5mg	3.16 (0.56, 5.76)	4.82 (3.21, 6.43)
-8.14 (-10.71, -5.57)	-5.90 (-8.45, -3.35)	-3.16 (-5.76, -0.56)	Tirzepatide 1mg	1.66 (-1.00, 4.32)
-9.80 (-11.15, -8.45)	-7.56 (-8.89, -6.22)	-4.82 (-6.43, -3.21)	-1.66 (-4.32, 1.00)	Placebo

(F1) Network map of HDL



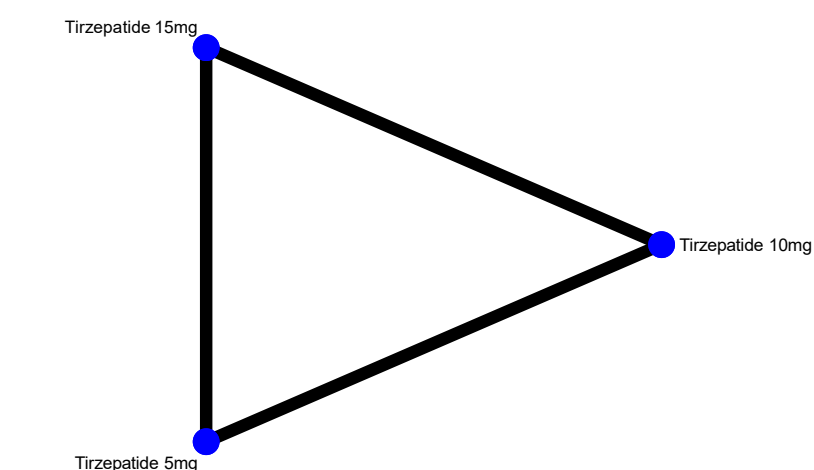
(F2) Forest plot of HDL



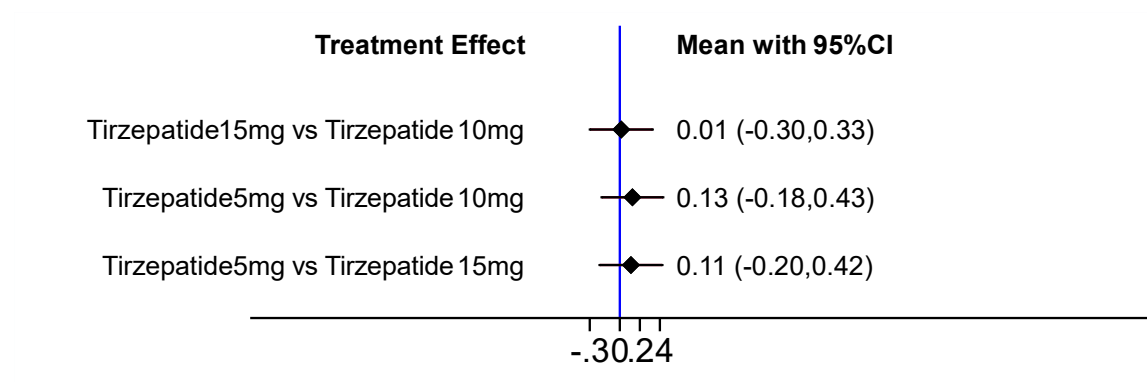
(F3) League table of HDL

Tirzepatide 10mg	-0.03 (-0.18,0.13)	-0.12 (-0.27,0.03)
0.03 (-0.13,0.18)	Tirzepatide 15mg	-0.10 (-0.25,0.06)
0.12 (-0.03,0.27)	0.10 (-0.06,0.25)	Tirzepatide 5mg

(G1) Network map of LDL



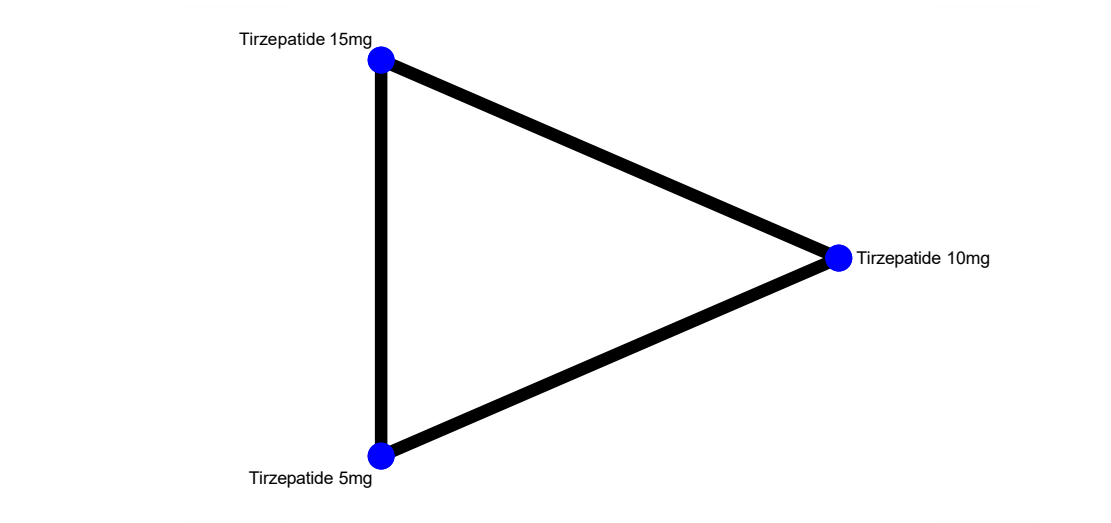
(G2) Forest plot of LDL



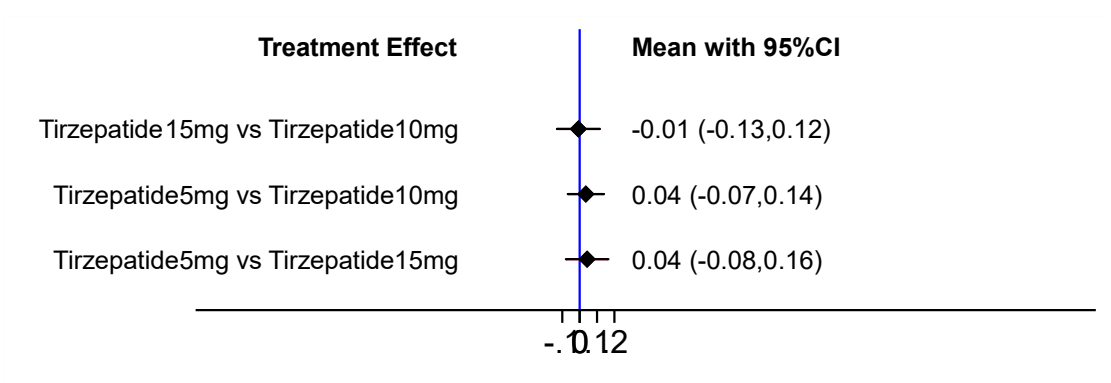
(G3) League table of LDL

Tirzepatide 10mg	0.01 (-0.30,0.33)	0.13 (-0.18,0.43)
-0.01 (-0.33,0.30)	Tirzepatide 15mg	0.11 (-0.20,0.42)
-0.13 (-0.43,0.18)	-0.11 (-0.42,0.20)	Tirzepatide 5mg

(H1) Network map of TC



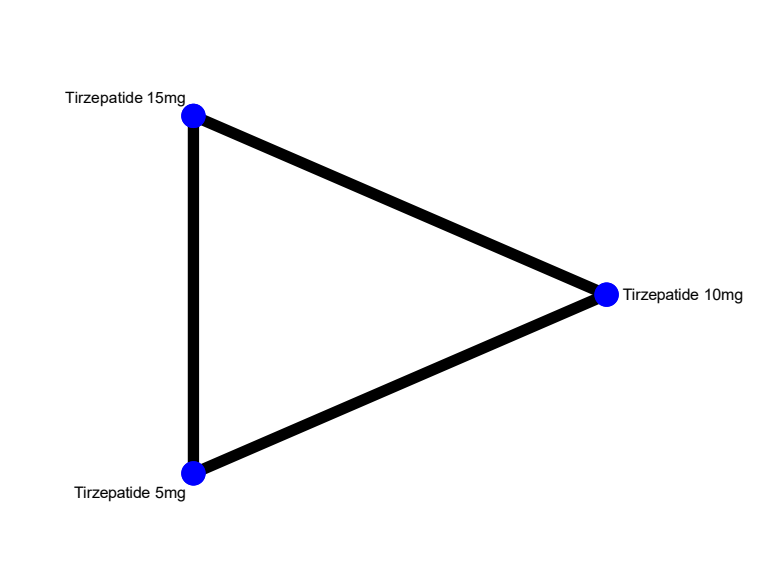
(H2) Forest plot of TC



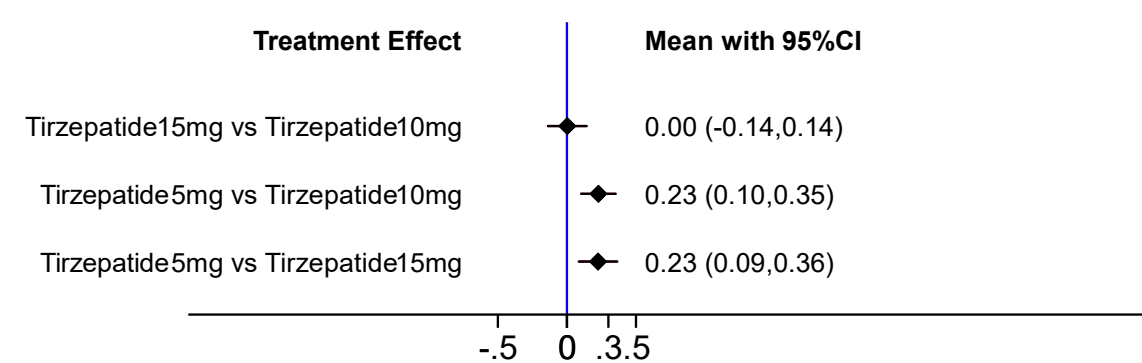
(H3) League table of TC

Tirzepatide 15mg	0.01 (-0.12,0.13)	0.04 (-0.08,0.16)
-0.01 (-0.13,0.12)	Tirzepatide 10mg	0.04 (-0.07,0.14)
-0.04 (-0.16,0.08)	-0.04 (-0.14,0.07)	Tirzepatide 5mg

(I1) Network map of TG



(I2) Forest plot of TG



(I3) League table of TG

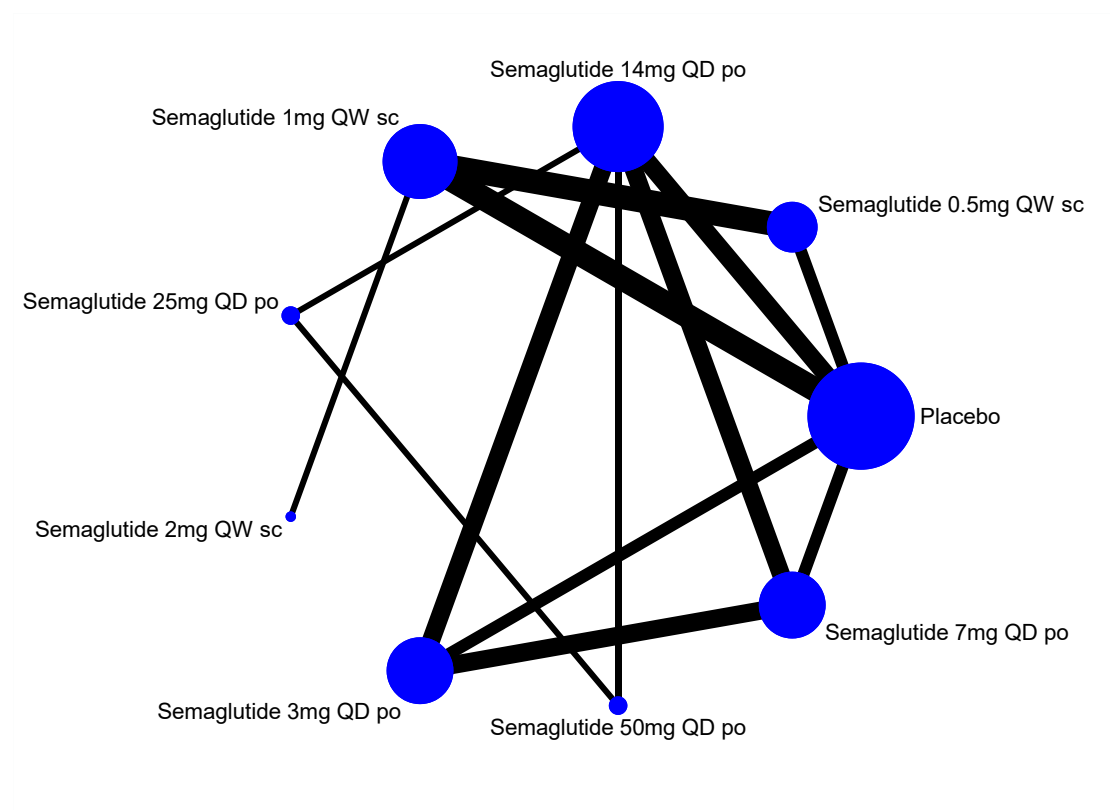
Tirzepatide 10mg	0.00 (-0.14,0.14)	0.23 (0.10,0.35)
-0.00 (-0.14,0.14)	Tirzepatide 15mg	0.23 (0.09,0.36)
-0.23 (-0.35,-0.10)	-0.23 (-0.36,-0.09)	Tirzepatide 5mg

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

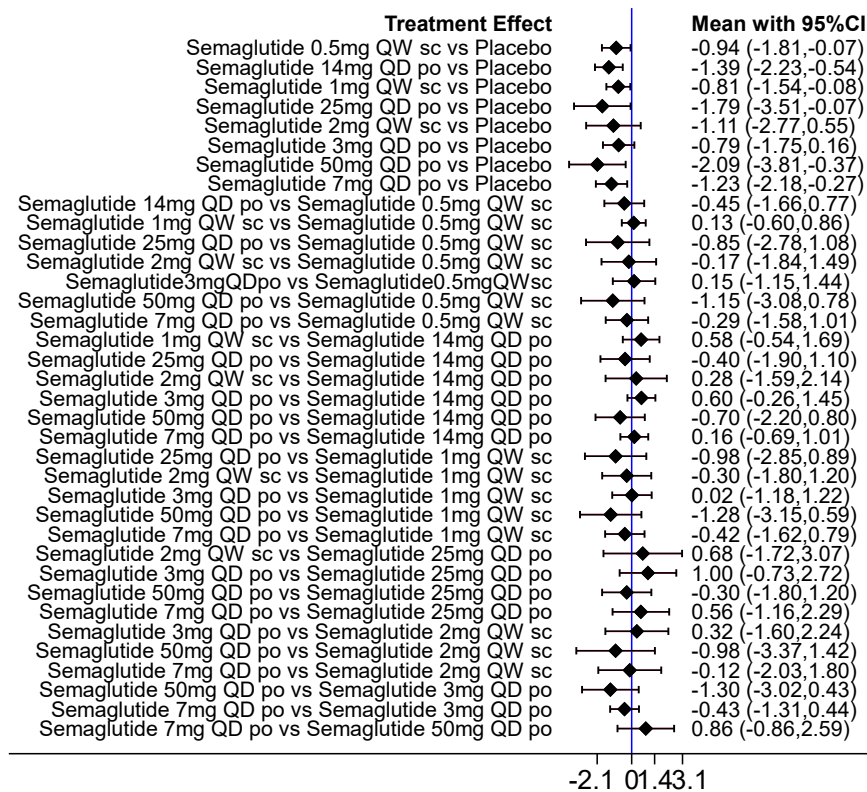
Figure S14.2: Effects of different doses of Semaglutide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Semaglutide 0.5mg, 1mg, 2mg subcutaneous injection once weekly and 3mg, 7mg, 14mg oral consumption once daily on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) BMI, (E) waist circumference, (F) HDL, (G) LDL, (H) TC, (I) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



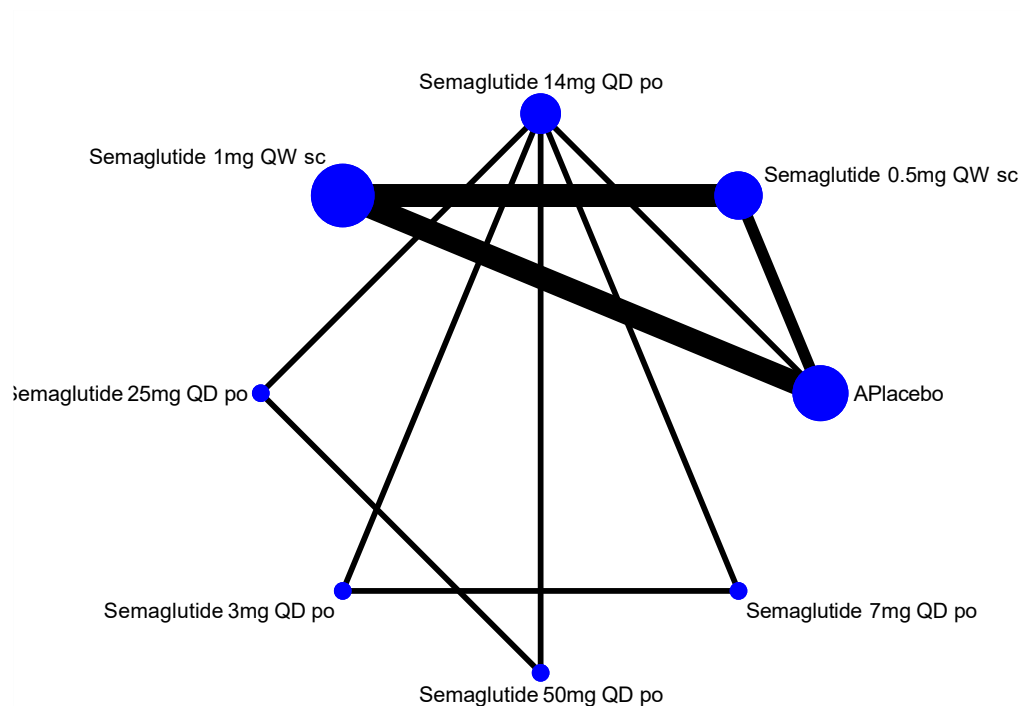
(A2) Forest plot of HbA1c



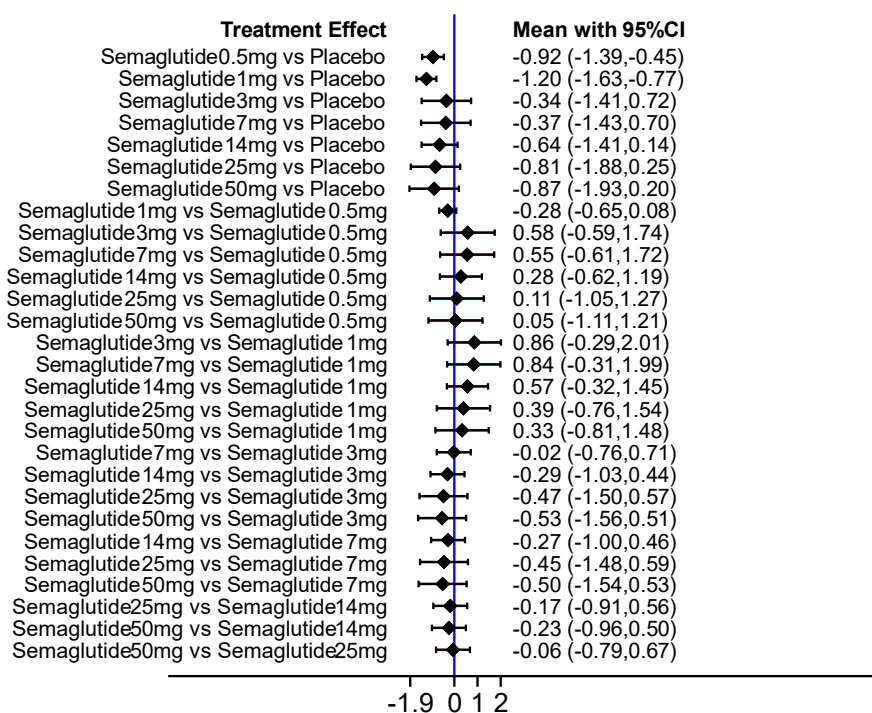
(A3) League table of HbA1c

Semaglutide 50mg QD po	0.30 (-1.20,1.80)	0.70 (-0.80,2.20)	0.86 (-0.86,2.59)	0.98 (-1.42,3.37)	1.15 (-0.78,3.08)	1.28 (-0.59,3.15)	1.30 (-0.43,3.02)	2.09 (0.37,3.81)
-0.30 (-1.80,1.20)	Semaglutide 25mg QD po	0.40 (-1.10,1.90)	0.56 (-1.16,2.29)	0.68 (-1.72,3.07)	0.85 (-1.08,2.78)	0.98 (-0.89,2.85)	1.00 (-0.73,2.72)	1.79 (0.07,3.51)
-0.70 (-2.20,0.80)	-0.40 (-1.90,1.10)	Semaglutide 14mg QD po	0.16 (-0.69,1.01)	0.28 (-1.59,2.14)	0.45 (-0.77,1.66)	0.58 (-0.54,1.69)	0.60 (-0.26,1.45)	1.39 (0.54,2.23)
-0.86 (-2.59,0.86)	-0.56 (-2.29,1.16)	-0.16 (-1.01,0.69)	Semaglutide 7mg QD po	0.12 (-1.80,2.03)	0.29 (-1.01,1.58)	0.42 (-0.79,1.62)	0.43 (-0.44,1.31)	1.23 (0.27,2.18)
-0.98 (-3.37,1.42)	-0.68 (-3.07,1.72)	-0.28 (-2.14,1.59)	-0.12 (-2.03,1.80)	Semaglutide 2mg QW sc	0.17 (-1.49,1.84)	0.30 (-1.20,1.80)	0.32 (-1.60,2.24)	1.11 (-0.55,2.77)
-1.15 (-3.08,0.78)	-0.85 (-2.78,1.08)	-0.45 (-1.66,0.77)	-0.29 (-1.58,1.01)	-0.17 (-1.84,1.49)	Semaglutide 0.5mg QW sc	0.13 (-0.60,0.86)	0.15 (-1.15,1.44)	0.94 (0.07,1.81)
-1.28 (-3.15,0.59)	-0.98 (-2.85,0.89)	-0.58 (-1.69,0.54)	-0.42 (-1.62,0.79)	-0.30 (-1.80,1.20)	-0.13 (-0.86,0.60)	Semaglutide 1mg QW sc	0.02 (-1.18,1.22)	0.81 (0.08,1.54)
-1.30 (-3.02,0.43)	-1.00 (-2.72,0.73)	-0.60 (-1.45,0.26)	-0.43 (-1.31,0.44)	-0.32 (-2.24,1.60)	-0.15 (-1.44,1.15)	-0.02 (-1.22,1.18)	Semaglutide 3mg QD po	0.79 (-0.16,1.75)
-2.09 (-3.81,-0.37)	-1.79 (-3.51,-0.07)	-1.39 (-2.23,-0.54)	-1.23 (-2.18,-0.27)	-1.11 (-2.77,0.55)	-0.94 (-1.81,-0.07)	-0.81 (-1.54,-0.08)	-0.79 (-1.75,0.16)	Placebo

(B1) Network map of FPG



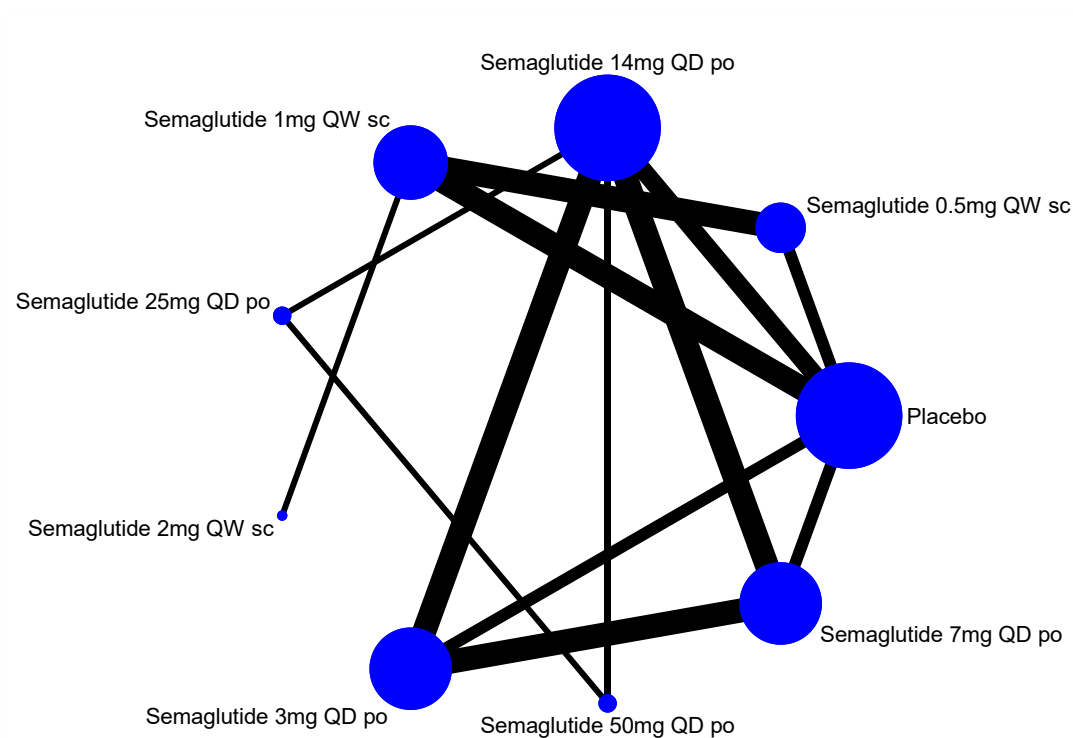
(B2) Forest plot of FPG



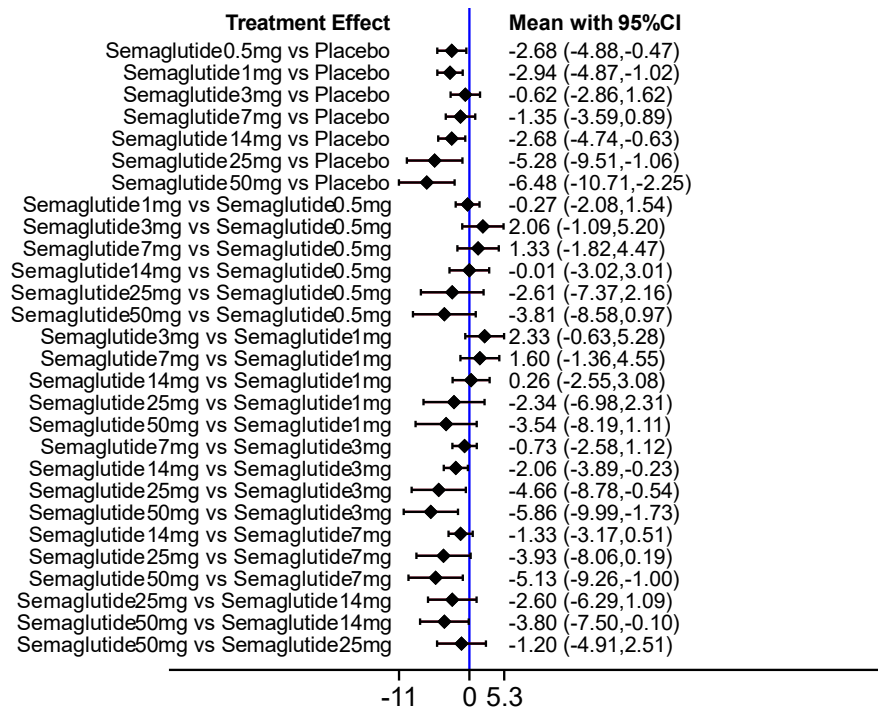
(B3) League table of FPG

Semaglutide 1mg QW sc	0.33 (-0.81,1.48)	0.28 (-0.08,0.65)	0.39 (-0.76,1.54)	0.57 (-0.32,1.45)	0.84 (-0.31,1.99)	0.86 (-0.29,2.01)	1.20 (0.77,1.63)
-0.33 (-1.48,0.81)	Semaglutide 50mg QD po	-0.05 (-1.21,1.11)	0.06 (-0.67,0.79)	0.23 (-0.50,0.96)	0.50 (-0.53,1.54)	0.53 (-0.51,1.56)	0.87 (-0.20,1.93)
-0.28 (-0.65,0.08)	0.05 (-1.11,1.21)	Semaglutide 0.5mg QW sc	0.11 (-1.05,1.27)	0.28 (-0.62,1.19)	0.55 (-0.61,1.72)	0.58 (-0.59,1.74)	0.92 (0.45,1.39)
-0.39 (-1.54,0.76)	-0.06 (-0.79,0.67)	-0.11 (-1.27,1.05)	Semaglutide 25mg QD po	0.17 (-0.56,0.91)	0.45 (-0.59,1.48)	0.47 (-0.57,1.50)	0.81 (-0.25,1.88)
-0.57 (-1.45,0.32)	-0.23 (-0.96,0.50)	-0.28 (-1.19,0.62)	-0.17 (-0.91,0.56)	Semaglutide 14mg QD po	0.27 (-0.46,1.00)	0.29 (-0.44,1.03)	0.64 (-0.14,1.41)
-0.84 (-1.99,0.31)	-0.50 (-1.54,0.53)	-0.55 (-1.72,0.61)	-0.45 (-1.48,0.59)	-0.27 (-1.00,0.46)	Semaglutide 7mg QD po	0.02 (-0.71,0.76)	0.37 (-0.70,1.43)
-0.86 (-2.01,0.29)	-0.53 (-1.56,0.51)	-0.58 (-1.74,0.59)	-0.47 (-1.50,0.57)	-0.29 (-1.03,0.44)	-0.02 (-0.76,0.71)	Semaglutide 3mg QD po	0.34 (-0.72,1.41)
-1.20 (-1.63,-0.77)	-0.87 (-1.93,0.20)	-0.92 (-1.39,-0.45)	-0.81 (-1.88,0.25)	-0.64 (-1.41,0.14)	-0.37 (-1.43,0.70)	-0.34 (-1.41,0.72)	Placebo

(C1) Network map of weight loss



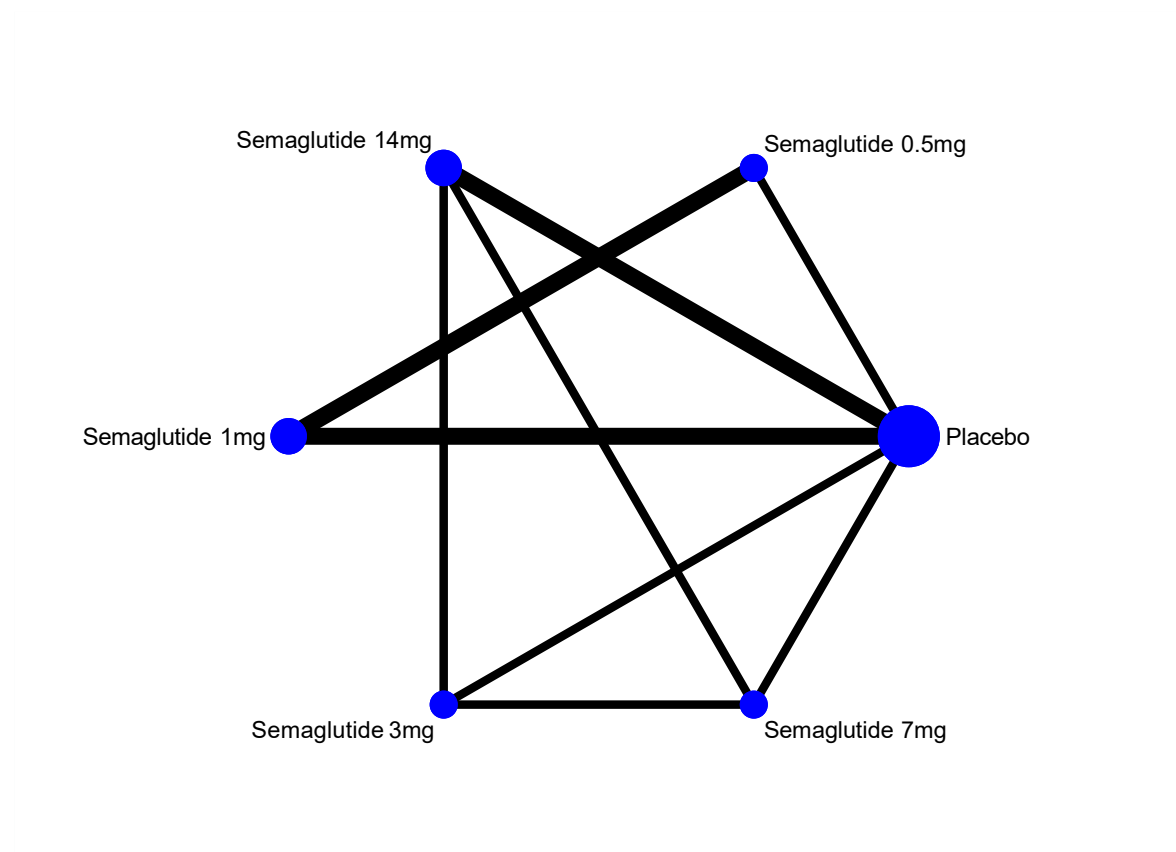
(C2) Forest plot of weight loss



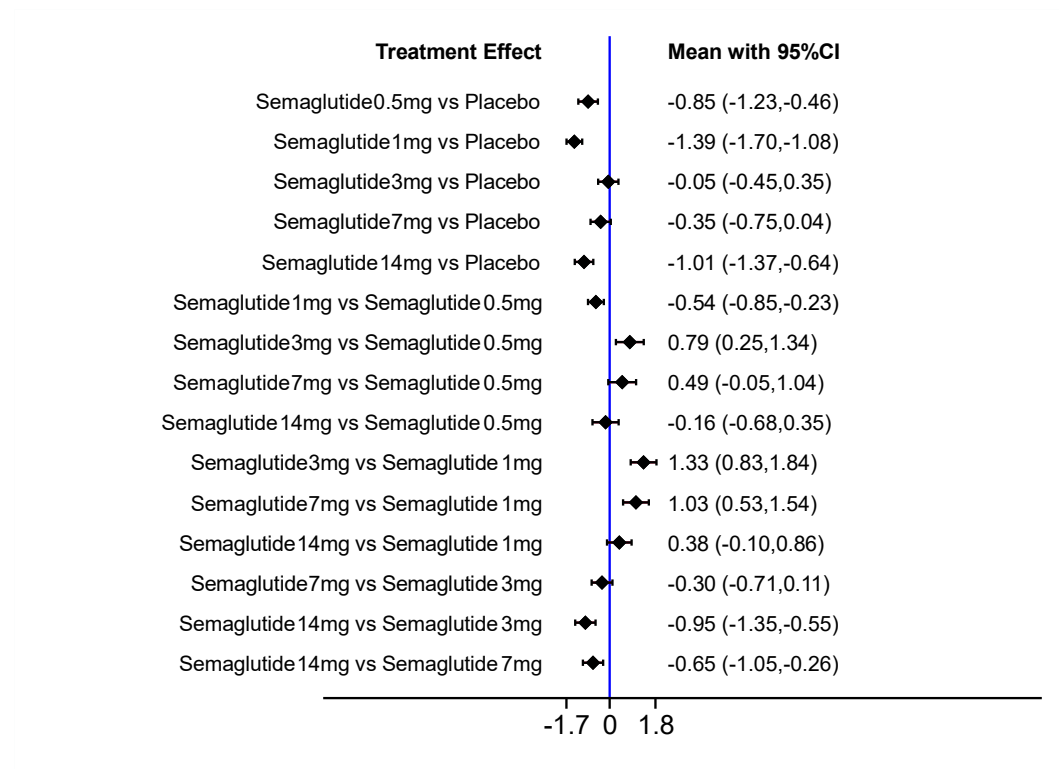
(C3) League table of weight loss

Semaglutide 50mg	1.20 (-2.51,4.91)	3.54 (-1.11,8.19)	3.80 (0.10,7.50)	3.81 (-0.97,8.58)	5.13 (1.00,9.26)	5.86 (1.73,9.99)	6.48 (2.25,10.71)	Semaglutide 50mg
-1.20 (-4.91,2.51)	Semaglutide 25mg	2.34 (-2.31,6.98)	2.60 (-1.09,6.29)	2.61 (-2.16,7.37)	3.93 (-0.19,8.06)	4.66 (0.54,8.78)	5.28 (1.06,9.51)	-1.20 (-4.91,2.51)
-3.54 (-8.19,1.11)	-2.34 (-6.98,2.31)	Semaglutide 1mg	0.26 (-2.55,3.08)	0.27 (-1.54,2.08)	1.60 (-1.36,4.55)	2.33 (-0.63,5.28)	2.94 (1.02,4.87)	-3.54 (-8.19,1.11)
-3.80 (-7.50,-0.10)	-2.60 (-6.29,1.09)	-0.26 (-3.08,2.55)	Semaglutide 14mg	0.01 (-3.01,3.02)	1.33 (-0.51,3.17)	2.06 (0.23,3.89)	2.68 (0.63,4.74)	-3.80 (-7.50,-0.10)
-3.81 (-8.58,0.97)	-2.61 (-7.37,2.16)	-0.27 (-2.08,1.54)	-0.01 (-3.02,3.01)	Semaglutide 0.5mg	1.33 (-1.82,4.47)	2.06 (-1.09,5.20)	2.68 (0.47,4.88)	-3.81 (-8.58,0.97)
-5.13 (-9.26,-1.00)	-3.93 (-8.06,0.19)	-1.60 (-4.55,1.36)	-1.33 (-3.17,0.51)	-1.33 (-4.47,1.82)	Semaglutide 7mg	0.73 (-1.12,2.58)	1.35 (-0.89,3.59)	-5.13 (-9.26,-1.00)
-5.86 (-9.99,-1.73)	-4.66 (-8.78,-0.54)	-2.33 (-5.28,0.63)	-2.06 (-3.89,-0.23)	-2.06 (-5.20,1.09)	-0.73 (-2.58,1.12)	Semaglutide 3mg	0.62 (-1.62,2.86)	-5.86 (-9.99,-1.73)
-6.48 (-10.71,-2.25)	-5.28 (-9.51,-1.06)	-2.94 (-4.87,-1.02)	-2.68 (-4.74,-0.63)	-2.68 (-4.88,-0.47)	-1.35 (-3.59,0.89)	-0.62 (-2.86,1.62)	Placebo	-6.48 (-10.71,-2.25)
Semaglutide 50mg	1.20 (-2.51,4.91)	3.54 (-1.11,8.19)	3.80 (0.10,7.50)	3.81 (-0.97,8.58)	5.13 (1.00,9.26)	5.86 (1.73,9.99)	6.48 (2.25,10.71)	Semaglutide 50mg

(D1) Network map of BMI



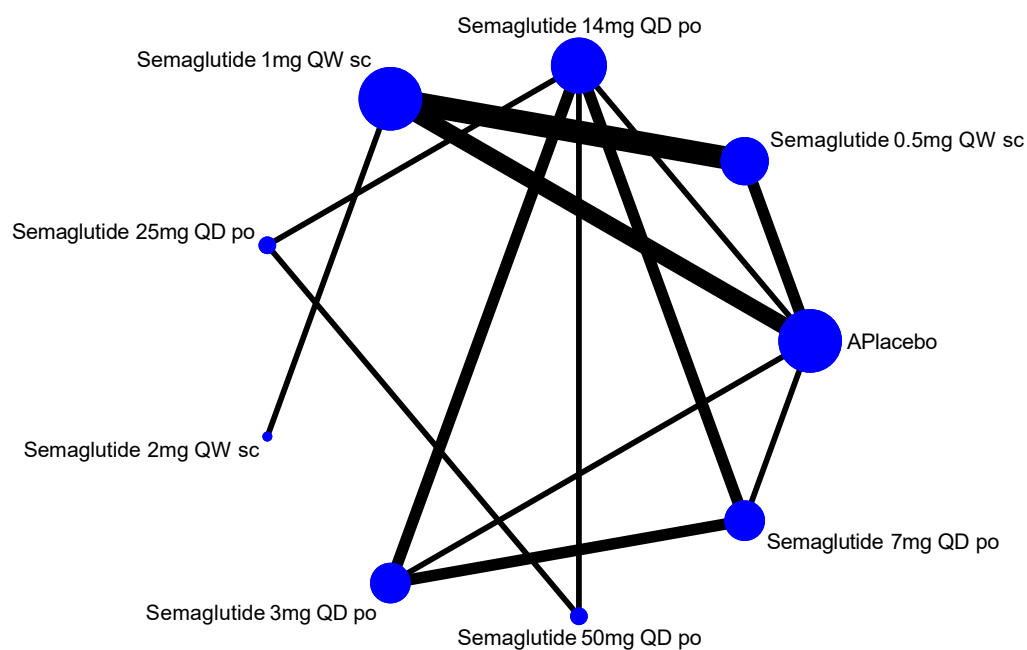
(D2) Forest plot of BMI



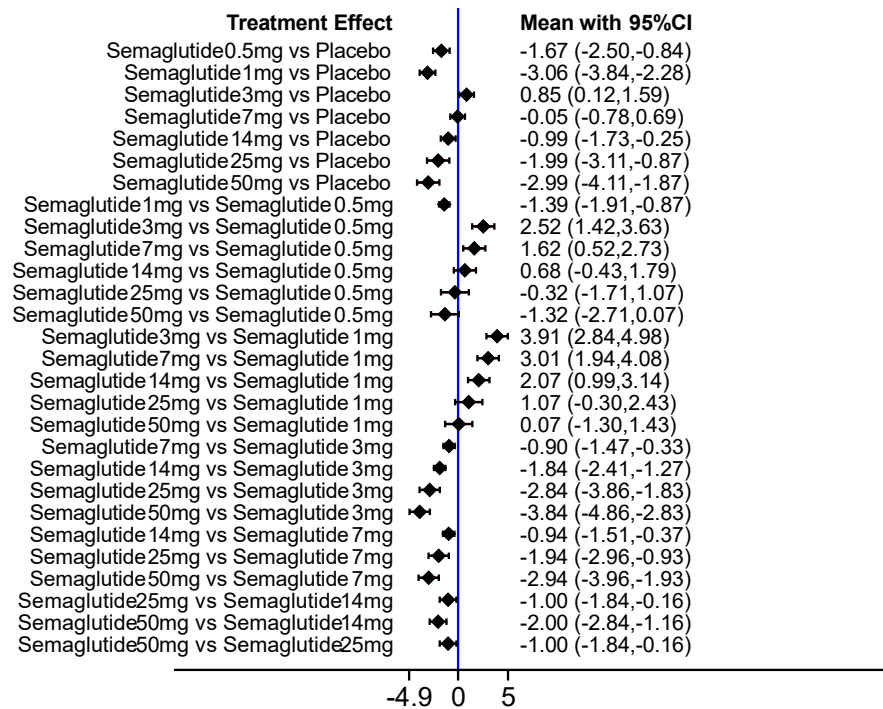
(D3) League table of BMI

Semaglutide 1mg	0.38 (-0.10,0.86)	0.54 (0.23,0.85)	1.03 (0.53,1.54)	1.33 (0.83,1.84)	1.39 (1.08,1.70)
-0.38 (-0.86,0.10)	Semaglutide 14mg	0.16 (-0.35,0.68)	0.65 (0.26,1.05)	0.95 (0.55,1.35)	1.01 (0.64,1.37)
-0.54 (-0.85,-0.23)	-0.16 (-0.68,0.35)	Semaglutide 0.5mg	0.49 (-0.05,1.04)	0.79 (0.25,1.34)	0.85 (0.46,1.23)
-1.03 (-1.54,-0.53)	-0.65 (-1.05,-0.26)	-0.49 (-1.04,0.05)	Semaglutide 7mg	0.30 (-0.11,0.71)	0.35 (-0.04,0.75)
-1.33 (-1.84,-0.83)	-0.95 (-1.35,-0.55)	-0.79 (-1.34,-0.25)	-0.30 (-0.71,0.11)	Semaglutide 3mg	0.05 (-0.35,0.45)
-1.39 (-1.70,-1.08)	-1.01 (-1.37,-0.64)	-0.85 (-1.23,-0.46)	-0.35 (-0.75,0.04)	-0.05 (-0.45,0.35)	Placebo

(E1) Network map of waist circumference



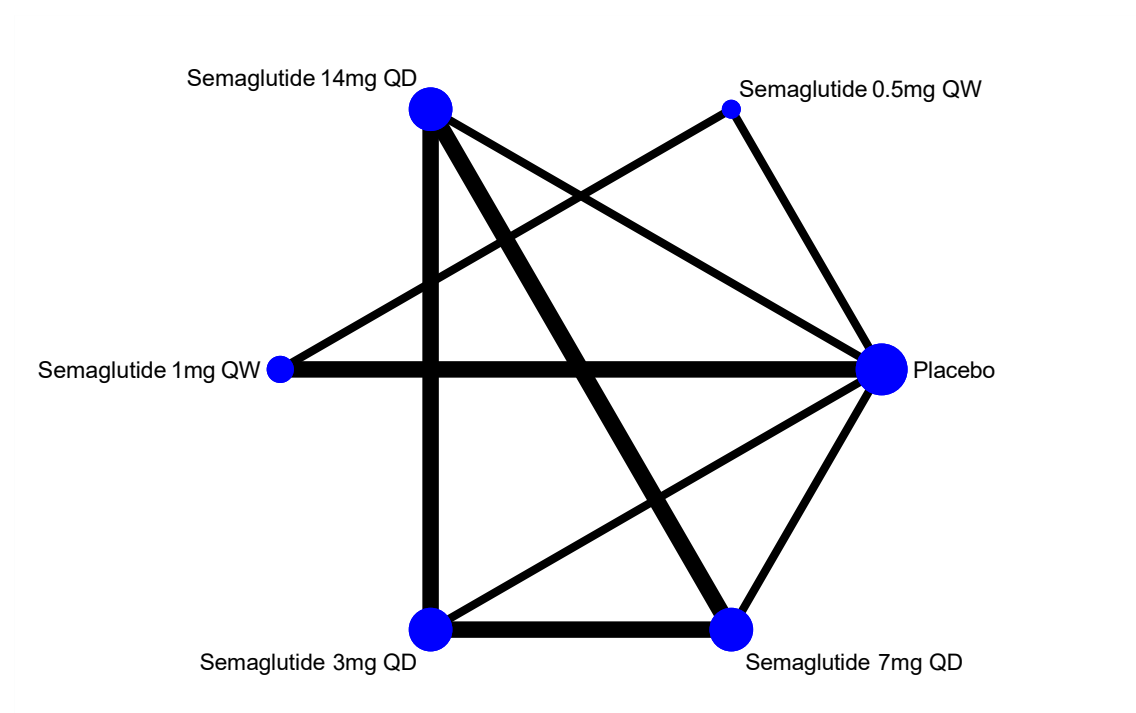
(E2) Forest plot of waist circumference



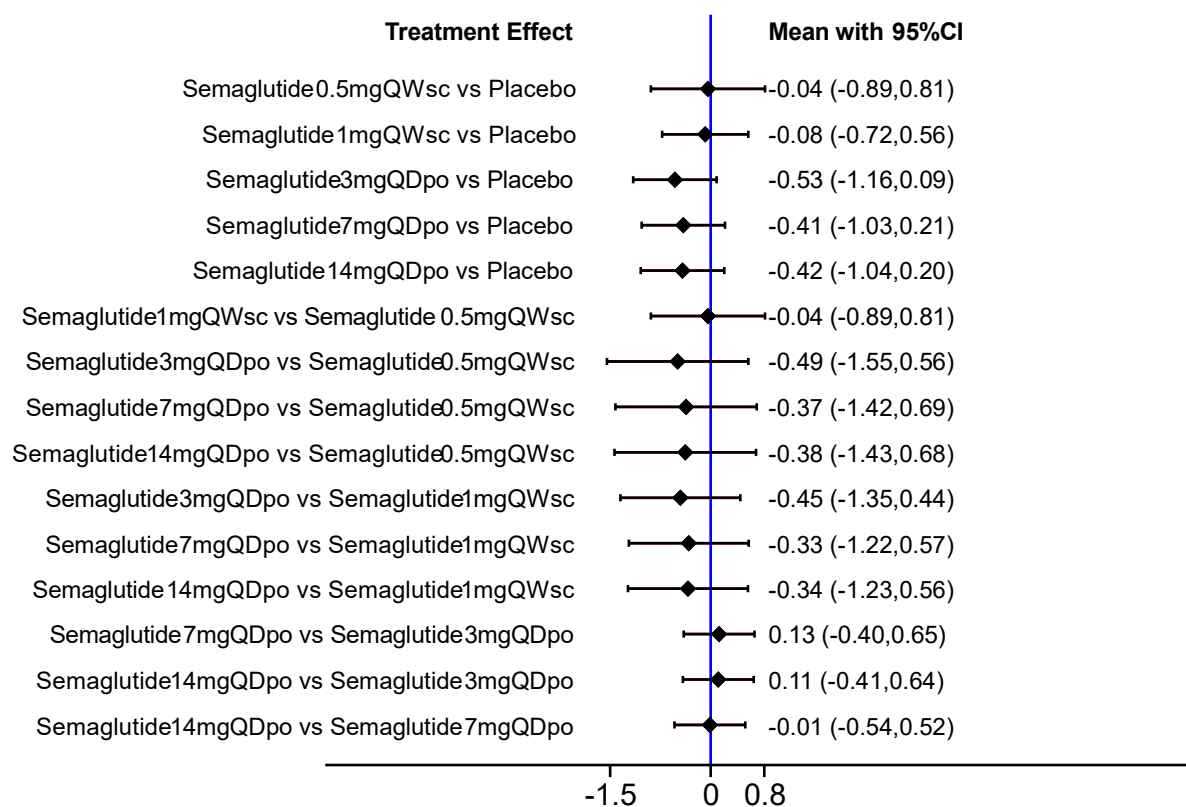
(E3) League table of waist circumference

Semaglutide 1mg	0.07 (-1.30,1.43)	1.07 (-0.30,2.43)	1.39 (0.87,1.91)	2.07 (0.99,3.14)	3.01 (1.94,4.08)	3.06 (2.28,3.84)	3.91 (2.84,4.98)
-0.07 (-1.43,1.30)	Semaglutide 50mg	1.00 (0.16,1.84)	1.32 (-0.07,2.71)	2.00 (1.16,2.84)	2.94 (1.93,3.96)	2.99 (1.87,4.11)	3.84 (2.83,4.86)
-1.07 (-2.43,0.30)	-1.00 (-1.84,-0.16)	Semaglutide 25mg	0.32 (-1.07,1.71)	1.00 (0.16,1.84)	1.94 (0.93,2.96)	1.99 (0.87,3.11)	2.84 (1.83,3.86)
-1.39 (-1.91,-0.87)	-1.32 (-2.71,0.07)	-0.32 (-1.71,1.07)	Semaglutide 0.5mg	0.68 (-0.43,1.79)	1.62 (0.52,2.73)	1.67 (0.84,2.50)	2.52 (1.42,3.63)
-2.07 (-3.14,-0.99)	-2.00 (-2.84,-1.16)	-1.00 (-1.84,-0.16)	-0.68 (-1.79,0.43)	Semaglutide 14mg	0.94 (0.37,1.51)	0.99 (0.25,1.73)	1.84 (1.27,2.41)
-3.01 (-4.08,-1.94)	-2.94 (-3.96,-1.93)	-1.94 (-2.96,-0.93)	-1.62 (-2.73,-0.52)	-0.94 (-1.51,-0.37)	Semaglutide 7mg	0.05 (-0.69,0.78)	0.90 (0.33,1.47)
-3.06 (-3.84,-2.28)	-2.99 (-4.11,-1.87)	-1.99 (-3.11,-0.87)	-1.67 (-2.50,-0.84)	-0.99 (-1.73,-0.25)	-0.05 (-0.78,0.69)	Placebo	0.85 (0.12,1.59)
-3.91 (-4.98,-2.84)	-3.84 (-4.86,-2.83)	-2.84 (-3.86,-1.83)	-2.52 (-3.63,-1.42)	-1.84 (-2.41,-1.27)	-0.90 (-1.47,-0.33)	-0.85 (-1.59,-0.12)	Semaglutide 3mg

(F1) Network map of HDL



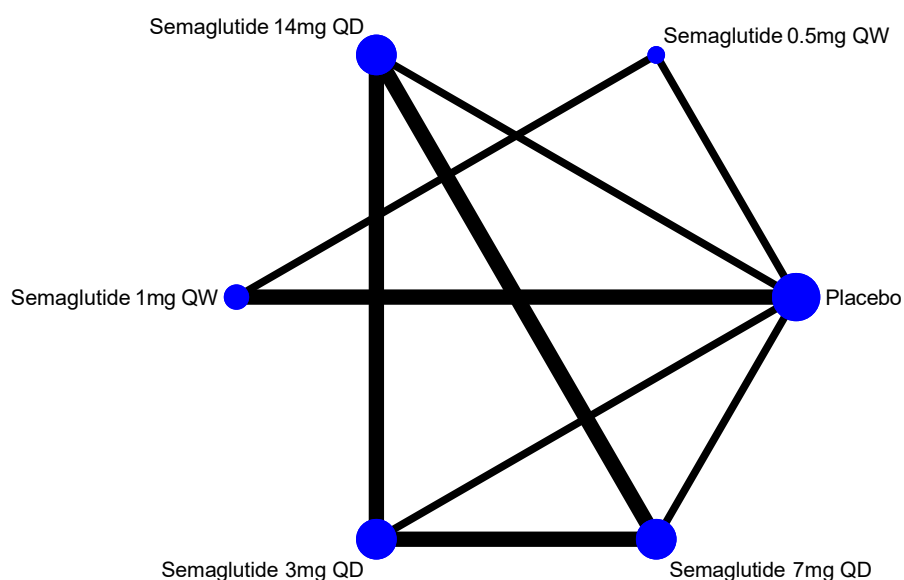
(F2) Forest plot of HDL



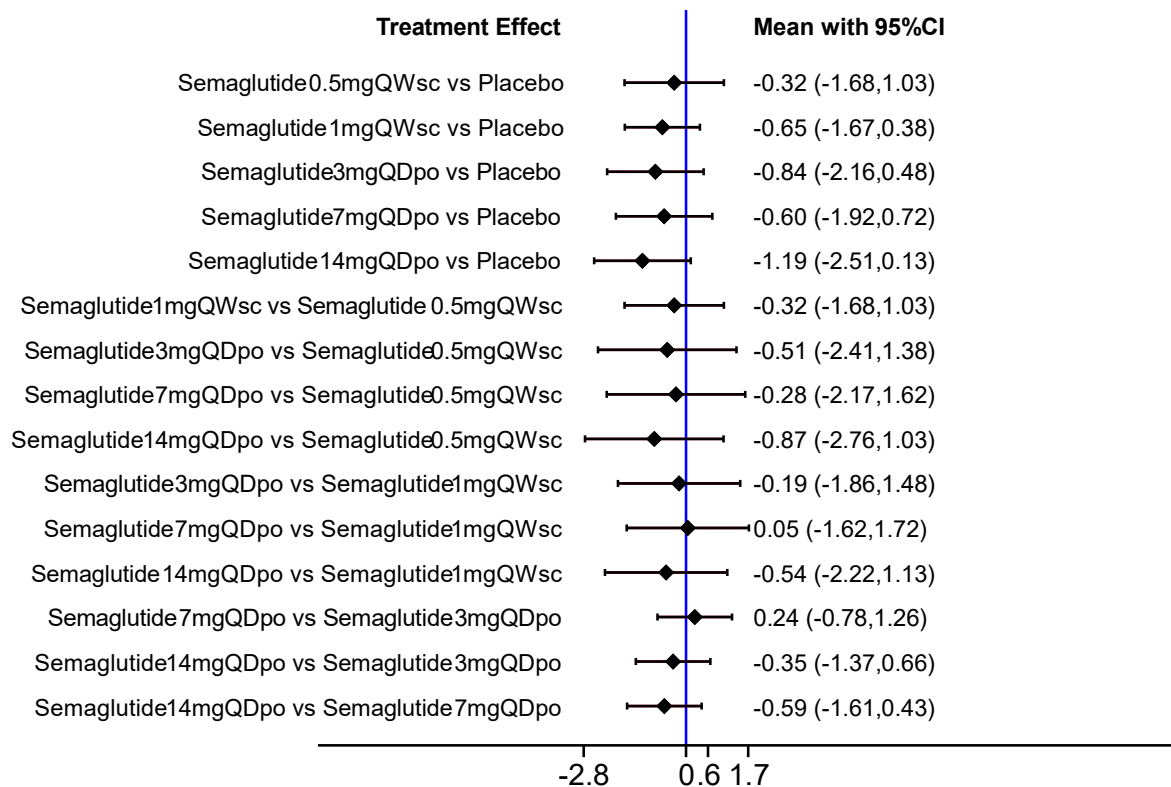
(F3) League table of HDL

Semaglutide 3mg QD po	0.11 (-0.41,0.64)	0.13 (-0.40,0.65)	0.45 (-0.44,1.35)	0.49 (-0.56,1.55)	0.53 (-0.09,1.16)
-0.11 (-0.64,0.41)	Semaglutide 14mg QD po	0.01 (-0.52,0.54)	0.34 (-0.56,1.23)	0.38 (-0.68,1.43)	0.42 (-0.20,1.04)
-0.13 (-0.65,0.40)	-0.01 (-0.54,0.52)	Semaglutide 7mg QD po	0.33 (-0.57,1.22)	0.37 (-0.69,1.42)	0.41 (-0.21,1.03)
-0.45 (-1.35,0.44)	-0.34 (-1.23,0.56)	-0.33 (-1.22,0.57)	Semaglutide 1mg QW sc	0.04 (-0.81,0.89)	0.08 (-0.56,0.72)
-0.49 (-1.55,0.56)	-0.38 (-1.43,0.68)	-0.37 (-1.42,0.69)	-0.04 (-0.89,0.81)	Semaglutide 0.5mg QW sc	0.04 (-0.81,0.89)
-0.53 (-1.16,0.09)	-0.42 (-1.04,0.20)	-0.41 (-1.03,0.21)	-0.08 (-0.72,0.56)	-0.04 (-0.89,0.81)	Placebo

(G1) Network map of LDL



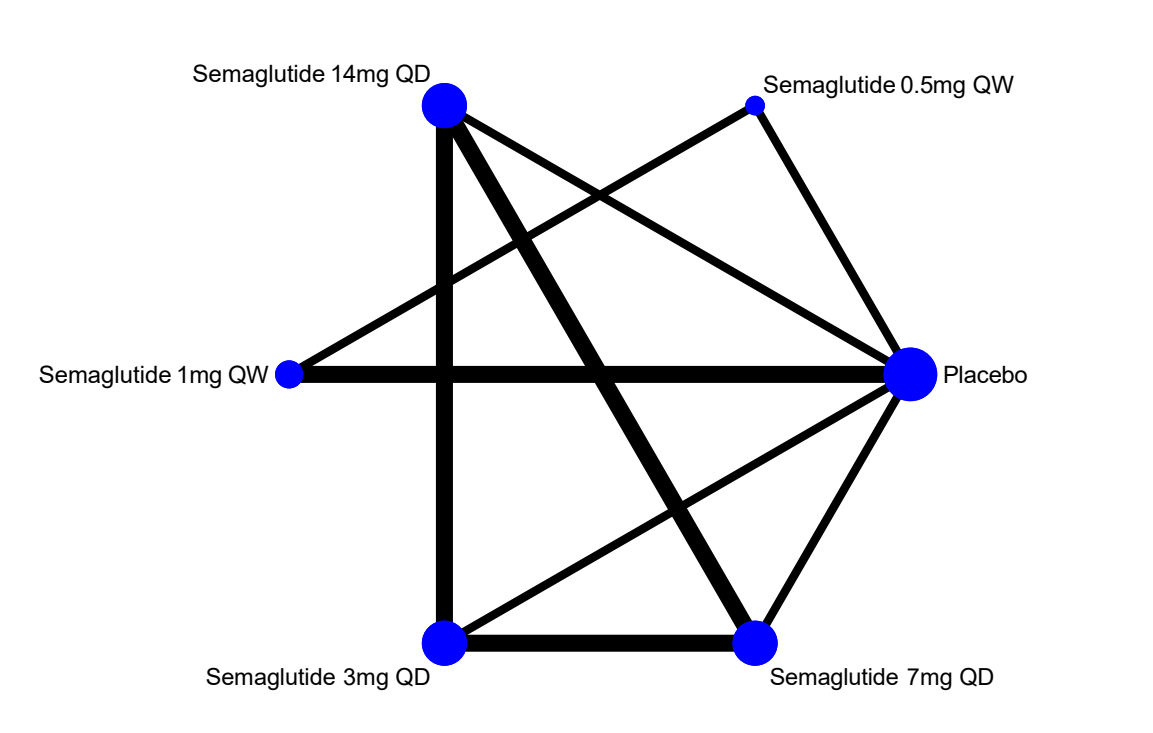
(G2) Forest plot of LDL



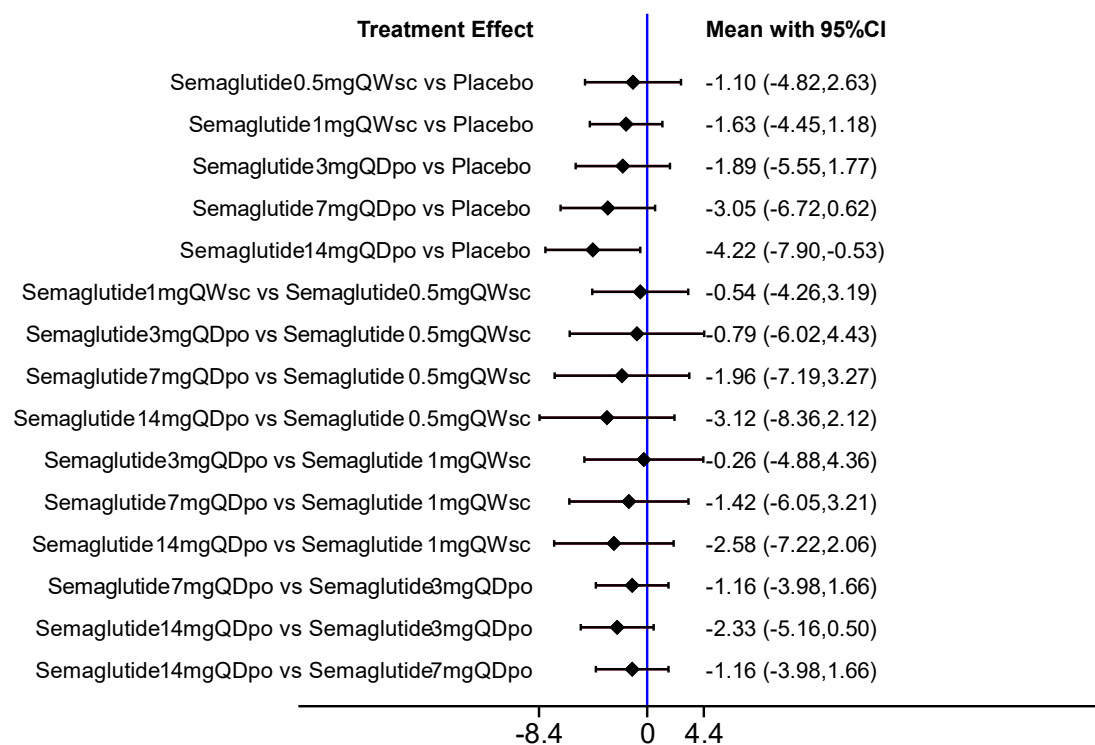
(G3) League table of LDL

Semaglutide 14mg QD po	0.35 (-0.66, 1.37)	0.54 (-1.13, 2.22)	0.59 (-0.43, 1.61)	0.87 (-1.03, 2.76)	1.19 (-0.13, 2.51)
-0.35 (-1.37, 0.66)	Semaglutide 3mg QD po	0.19 (-1.48, 1.86)	0.24 (-0.78, 1.26)	0.51 (-1.38, 2.41)	0.84 (-0.48, 2.16)
-0.54 (-2.22, 1.13)	-0.19 (-1.86, 1.48)	Semaglutide 1mg QW sc	0.05 (-1.62, 1.72)	0.32 (-1.03, 1.68)	0.65 (-0.38, 1.67)
-0.59 (-1.61, 0.43)	-0.24 (-1.26, 0.78)	-0.05 (-1.72, 1.62)	Semaglutide 7mg QD po	0.28 (-1.62, 2.17)	0.60 (-0.72, 1.92)
-0.87 (-2.76, 1.03)	-0.51 (-2.41, 1.38)	-0.32 (-1.68, 1.03)	-0.28 (-2.17, 1.62)	Semaglutide 0.5mg QW sc	0.32 (-1.03, 1.68)
-1.19 (-2.51, 0.13)	-0.84 (-2.16, 0.48)	-0.65 (-1.67, 0.38)	-0.60 (-1.92, 0.72)	-0.32 (-1.68, 1.03)	Placebo

(H1) Network map of TC



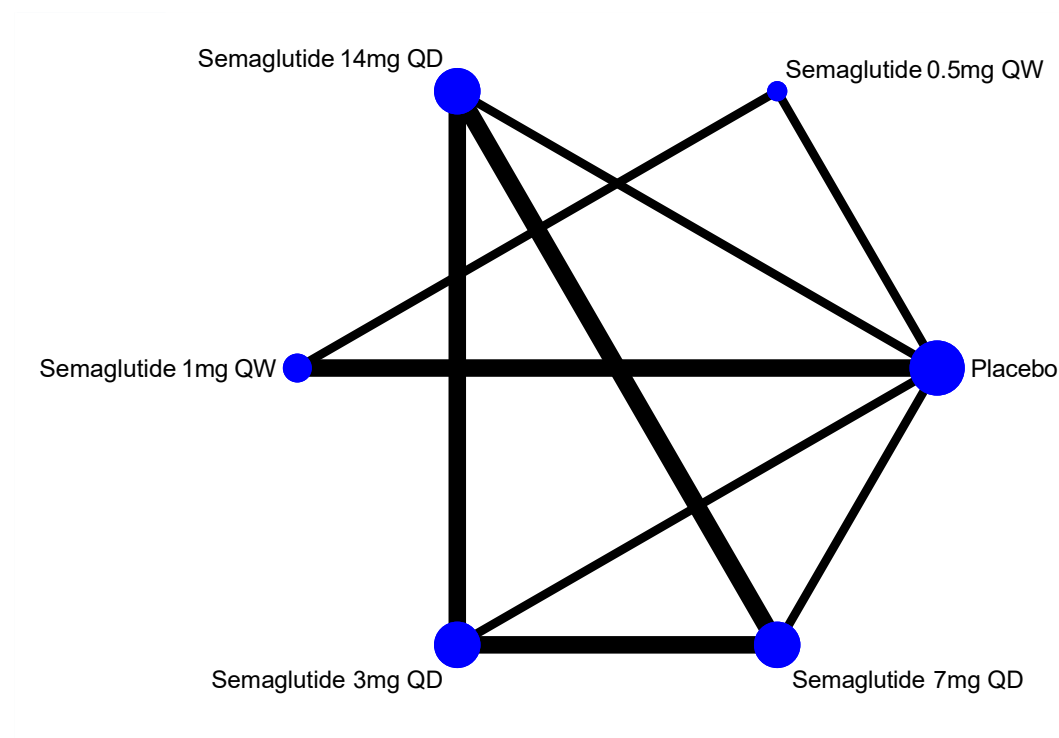
(H2) Forest plot of TC



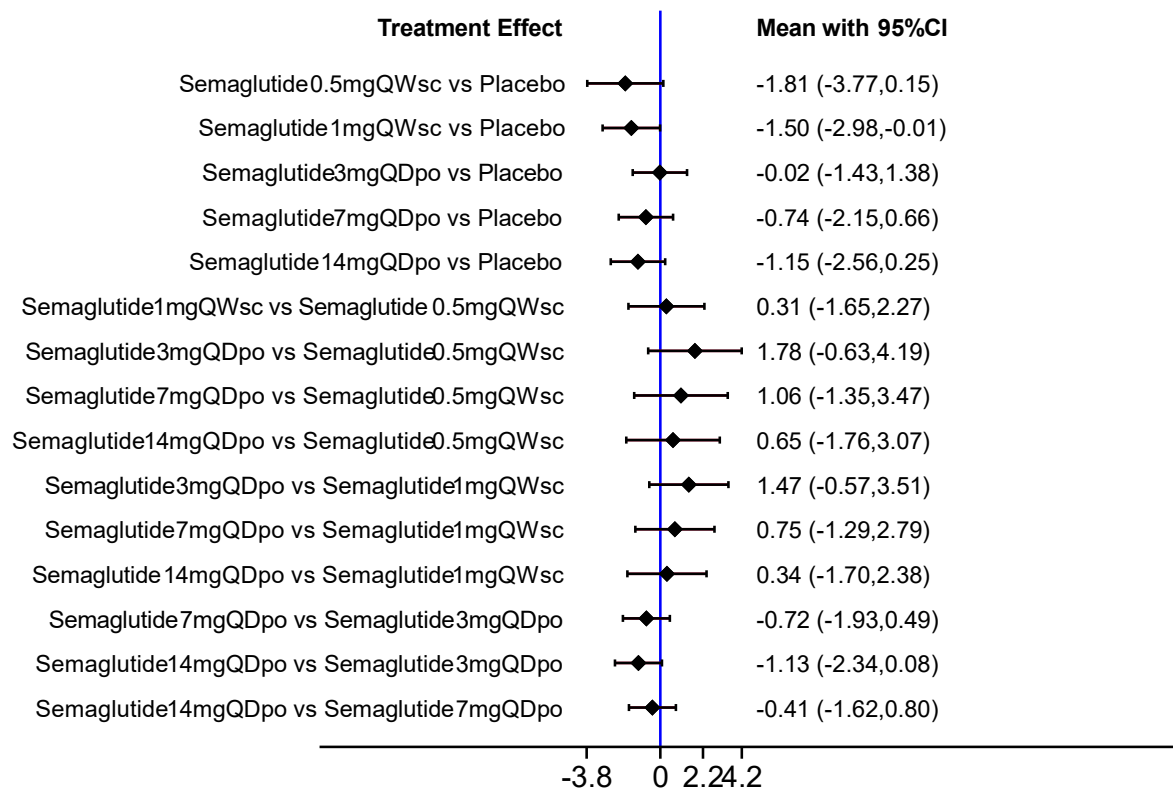
(H3) League table of TC

Semaglutide 14mg QD po	1.16 (-1.66,3.98)	2.57 (-2.06,7.21)	2.33 (-0.50,5.15)	3.11 (-2.12,8.34)	4.21 (0.53,7.89)
-1.16 (-3.98,1.66)	Semaglutide 7mg QD po	1.41 (-3.21,6.03)	1.16 (-1.66,3.98)	1.95 (-3.28,7.17)	3.05 (-0.62,6.71)
-2.57 (-7.21,2.06)	-1.41 (-6.03,3.21)	Semaglutide 1mg QW sc	-0.25 (-4.86,4.36)	0.54 (-3.19,4.26)	1.63 (-1.18,4.45)
-2.33 (-5.15,0.50)	-1.16 (-3.98,1.66)	0.25 (-4.36,4.86)	Semaglutide 3mg QD po	0.78 (-4.43,6.00)	1.88 (-1.77,5.54)
-3.11 (-8.34,2.12)	-1.95 (-7.17,3.28)	-0.54 (-4.26,3.19)	-0.78 (-6.00,4.43)	Semaglutide 0.5mg QW sc	1.10 (-2.62,4.82)
-4.21 (-7.89,-0.53)	-3.05 (-6.71,0.62)	-1.63 (-4.45,1.18)	-1.88 (-5.54,1.77)	-1.10 (-4.82,2.62)	Placebo

(I1) Network map of TG



(I2) Forest plot of TG



(I3) League table of TG

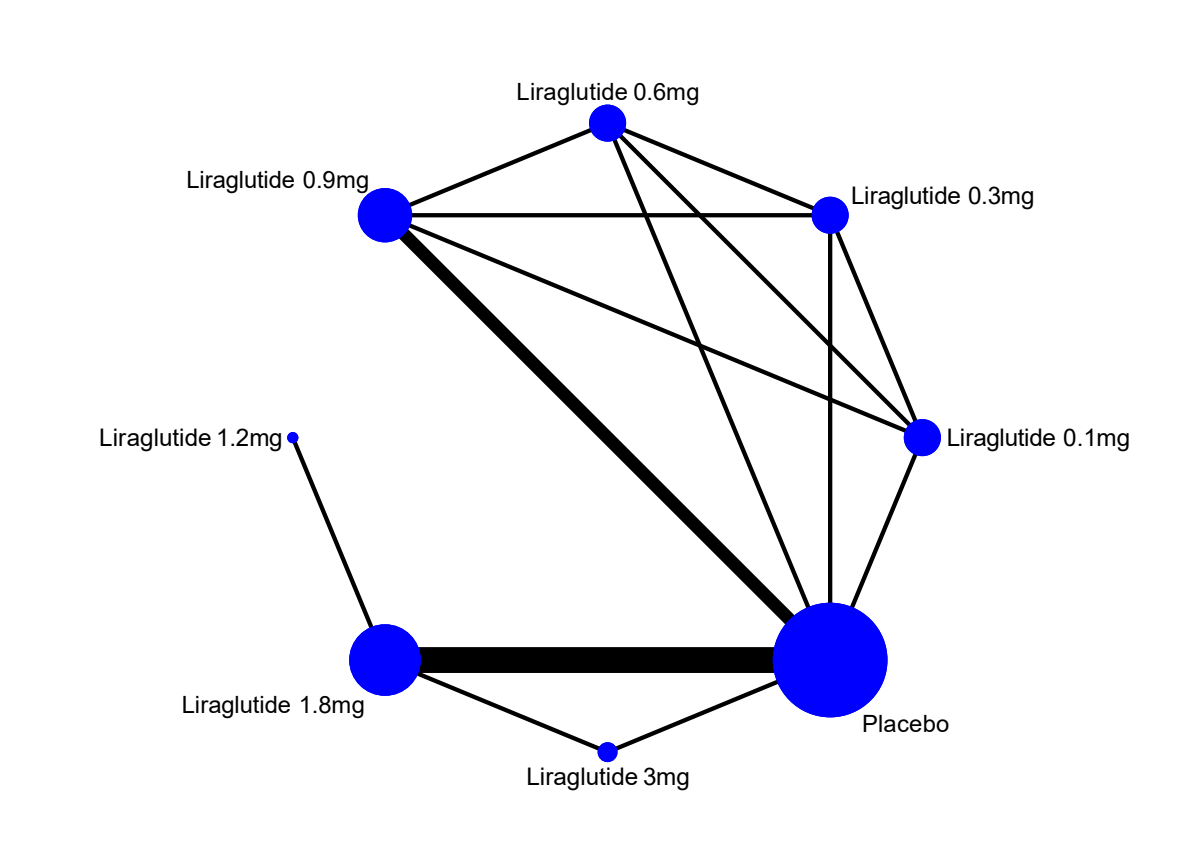
Semaglutide 0.5mg QW sc	0.31 (-1.65, 2.27)	0.65 (-1.76, 3.07)	1.06 (-1.35, 3.47)	1.78 (-0.63, 4.19)	1.81 (-0.15, 3.77)
-0.31 (-2.27, 1.65)	Semaglutide 1mg QW sc	0.34 (-1.70, 2.38)	0.75 (-1.29, 2.79)	1.47 (-0.57, 3.51)	1.50 (0.01, 2.98)
-0.65 (-3.07, 1.76)	-0.34 (-2.38, 1.70)	Semaglutide 14mg QD po	0.41 (-0.80, 1.62)	1.13 (-0.08, 2.34)	1.15 (-0.25, 2.56)
-1.06 (-3.47, 1.35)	-0.75 (-2.79, 1.29)	-0.41 (-1.62, 0.80)	Semaglutide 7mg QD po	0.72 (-0.49, 1.93)	0.74 (-0.66, 2.15)
-1.78 (-4.19, 0.63)	-1.47 (-3.51, 0.57)	-1.13 (-2.34, 0.08)	-0.72 (-1.93, 0.49)	Semaglutide 3mg QD po	0.02 (-1.38, 1.43)
-1.81 (-3.77, 0.15)	-1.50 (-2.98, -0.01)	-1.15 (-2.56, 0.25)	-0.74 (-2.15, 0.66)	-0.02 (-1.43, 1.38)	Placebo

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; QW, once weekly; QD, once daily; po, oral consumption; sc, subcutaneous injection.

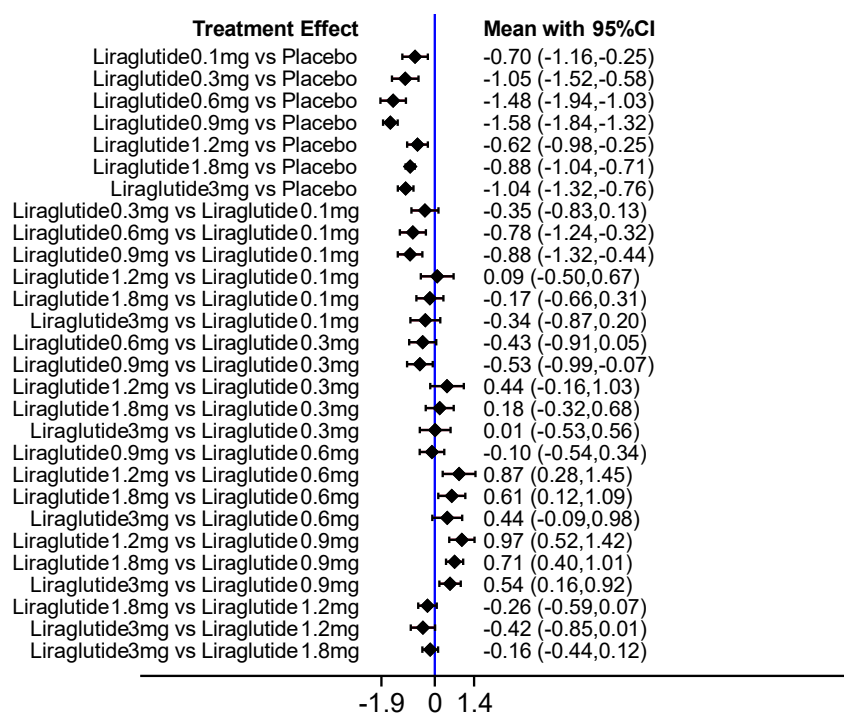
Figure S14.3: Effects of different doses of Liraglutide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Liraglutide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) BMI, (E) waist circumference, (F) HDL, (G) LDL, (H) TC, (I) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



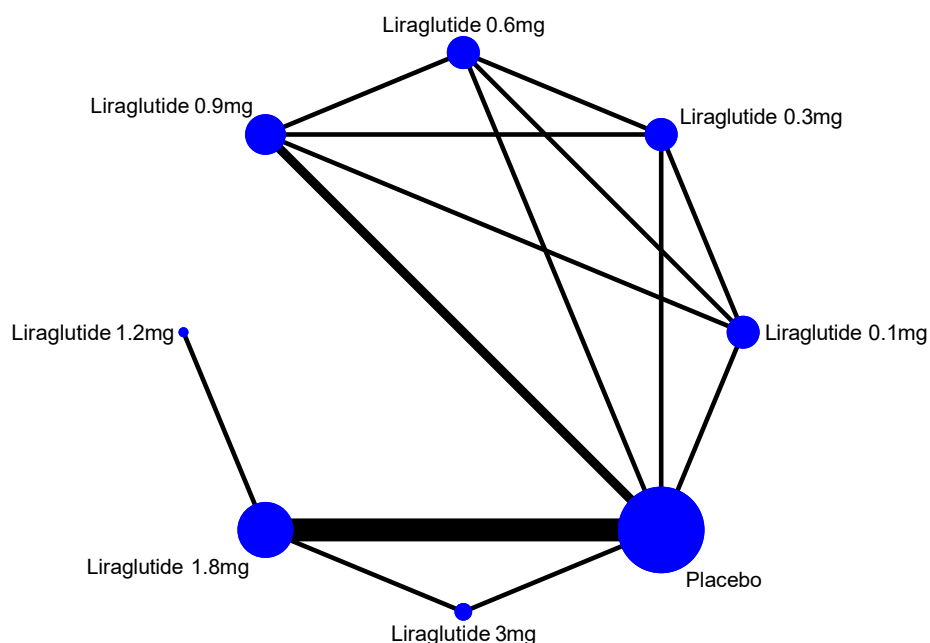
(A2) Forest plot of HbA1c



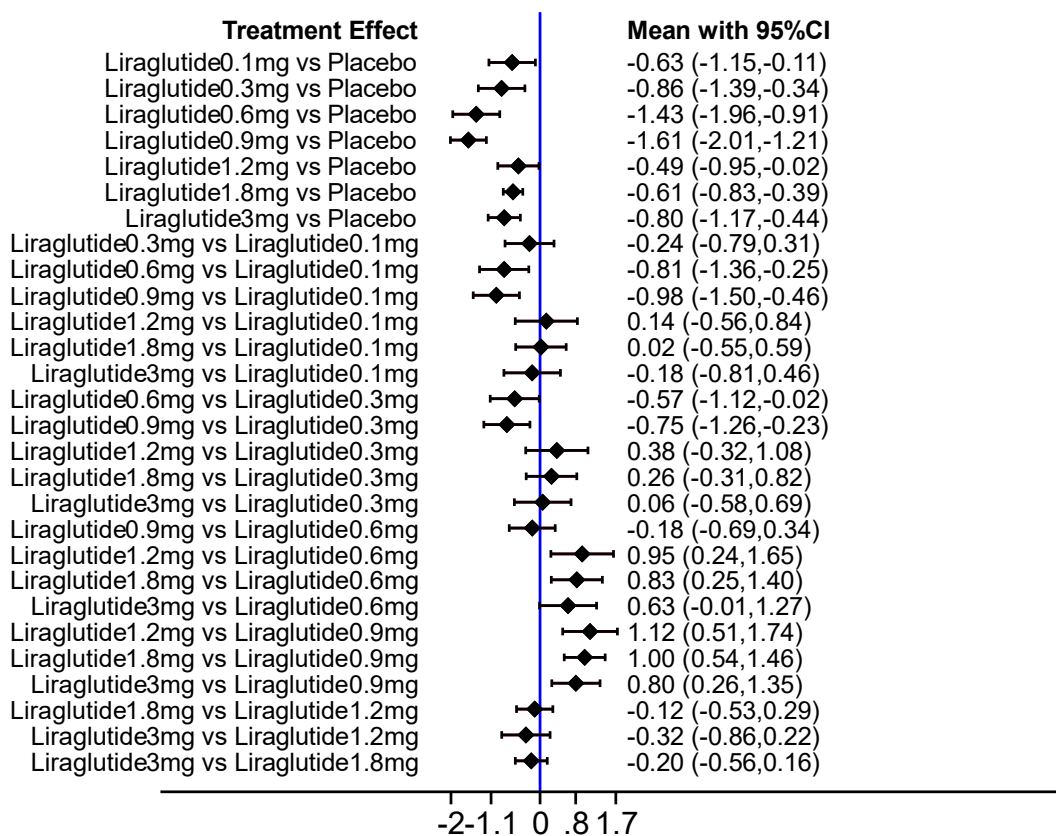
(A3) League table of HbA1c

Liraglutide 0.9mg	0.10 (-0.34,0.54)	0.54 (0.16,0.92)	0.53 (0.07,0.99)	0.71 (0.40,1.01)	0.88 (0.44,1.32)	0.97 (0.52,1.42)	1.58 (1.32,1.84)
-0.10 (-0.54,0.34)	Liraglutide 0.6mg	0.44 (-0.09,0.98)	0.43 (-0.05,0.91)	0.61 (0.12,1.09)	0.78 (0.32,1.24)	0.87 (0.28,1.45)	1.48 (1.03,1.94)
-0.54 (-0.92,-0.16)	-0.44 (-0.98,0.09)	Liraglutide 3mg	-0.01 (-0.56,0.53)	0.16 (-0.12,0.44)	0.34 (-0.20,0.87)	0.42 (-0.01,0.85)	1.04 (0.76,1.32)
-0.53 (-0.99,-0.07)	-0.43 (-0.91,0.05)	0.01 (-0.53,0.56)	Liraglutide 0.3mg	0.18 (-0.32,0.68)	0.35 (-0.13,0.83)	0.44 (-0.16,1.03)	1.05 (0.58,1.52)
-0.71 (-1.01,-0.40)	-0.61 (-1.09,-0.12)	-0.16 (-0.44,0.12)	-0.18 (-0.68,0.32)	Liraglutide 1.8mg	0.17 (-0.31,0.66)	0.26 (-0.07,0.59)	0.88 (0.71,1.04)
-0.88 (-1.32,-0.44)	-0.78 (-1.24,-0.32)	-0.34 (-0.87,0.20)	-0.35 (-0.83,0.13)	-0.17 (-0.66,0.31)	Liraglutide 0.1mg	0.09 (-0.50,0.67)	0.70 (0.25,1.16)
-0.97 (-1.42,-0.52)	-0.87 (-1.45,-0.28)	-0.42 (-0.85,0.01)	-0.44 (-1.03,0.16)	-0.26 (-0.59,0.07)	-0.09 (-0.67,0.50)	Liraglutide 1.2mg	0.62 (0.25,0.98)
-1.58 (-1.84,-1.32)	-1.48 (-1.94,-1.03)	-1.04 (-1.32,-0.76)	-1.05 (-1.52,-0.58)	-0.88 (-1.04,-0.71)	-0.70 (-1.16,-0.25)	-0.62 (-0.98,-0.25)	Placebo

(B1) Network map of FPG



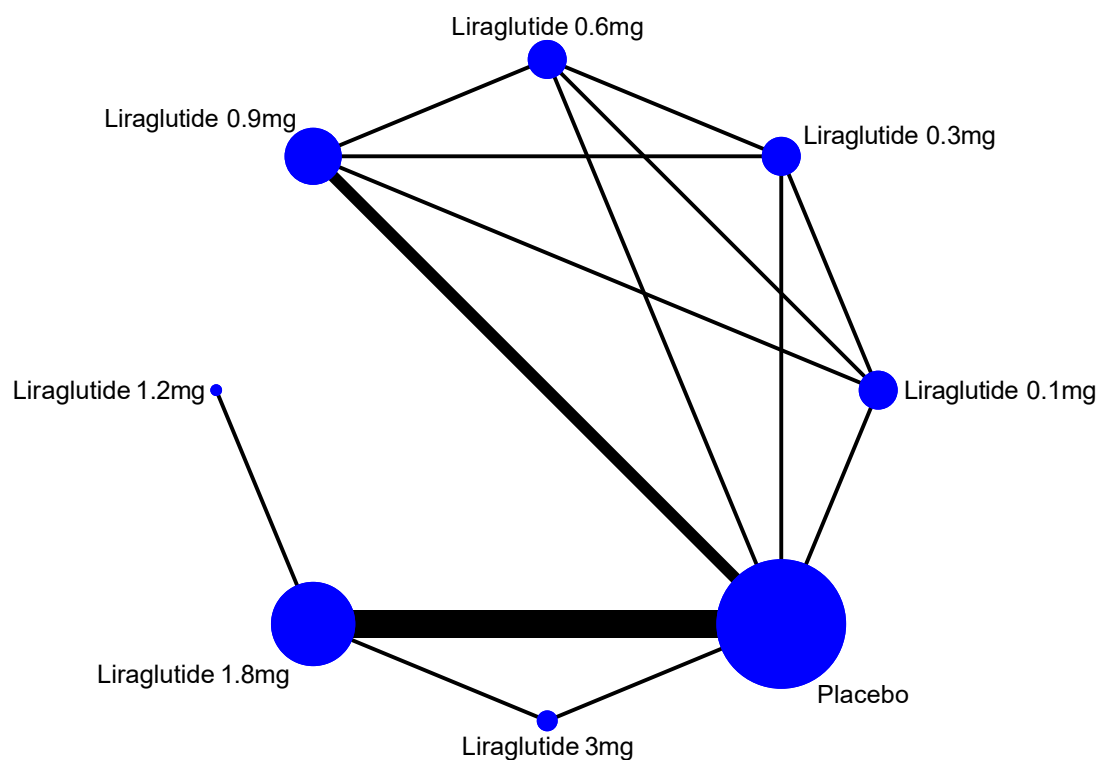
(B2) Forest plot of FPG



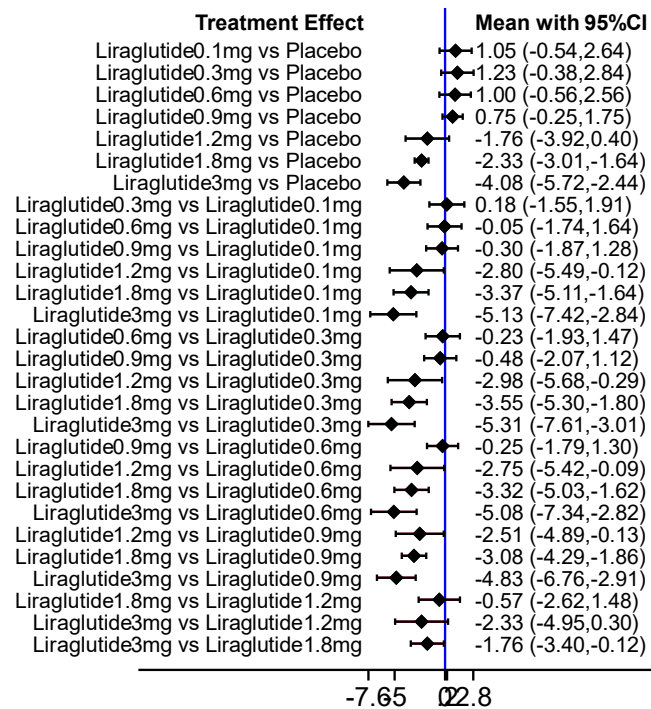
(B3) League table of FPG

Liraglutide 0.9mg	0.18 (-0.34,0.69)	0.75 (0.23,1.26)	0.80 (0.26,1.35)	0.98 (0.46,1.50)	1.00 (0.54,1.46)	1.12 (0.51,1.74)	1.61 (1.21,2.01)
-0.18 (-0.69,0.34)	Liraglutide 0.6mg	0.57 (0.02,1.12)	0.63 (-0.01,1.27)	0.81 (0.25,1.36)	0.83 (0.25,1.40)	0.95 (0.24,1.65)	1.43 (0.91,1.96)
-0.75 (-1.26,-0.23)	-0.57 (-1.12,-0.02)	Liraglutide 0.3mg	0.06 (-0.58,0.69)	0.24 (-0.31,0.79)	0.26 (-0.31,0.82)	0.38 (-0.32,1.08)	0.86 (0.34,1.39)
-0.80 (-1.35,-0.26)	-0.63 (-1.27,0.01)	-0.06 (-0.69,0.58)	Liraglutide 3mg	0.18 (-0.46,0.81)	0.20 (-0.16,0.56)	0.32 (-0.22,0.86)	0.80 (0.44,1.17)
-0.98 (-1.50,-0.46)	-0.81 (-1.36,-0.25)	-0.24 (-0.79,0.31)	-0.18 (-0.81,0.46)	Liraglutide 0.1mg	0.02 (-0.55,0.59)	0.14 (-0.56,0.84)	0.63 (0.11,1.15)
-1.00 (-1.46,-0.54)	-0.83 (-1.40,-0.25)	-0.26 (-0.82,0.31)	-0.20 (-0.56,0.16)	-0.02 (-0.59,0.55)	Liraglutide 1.8mg	0.12 (-0.29,0.53)	0.61 (0.39,0.83)
-1.12 (-1.74,-0.51)	-0.95 (-1.65,-0.24)	-0.38 (-1.08,0.32)	-0.32 (-0.86,0.22)	-0.14 (-0.84,0.56)	-0.12 (-0.53,0.29)	Liraglutide 1.2mg	0.49 (0.02,0.95)
-1.61 (-2.01,-1.21)	-1.43 (-1.96,-0.91)	-0.86 (-1.39,-0.34)	-0.80 (-1.17,-0.44)	-0.63 (-1.15,-0.11)	-0.61 (-0.83,-0.39)	-0.49 (-0.95,-0.02)	Placebo

(C1) Network map of weight loss



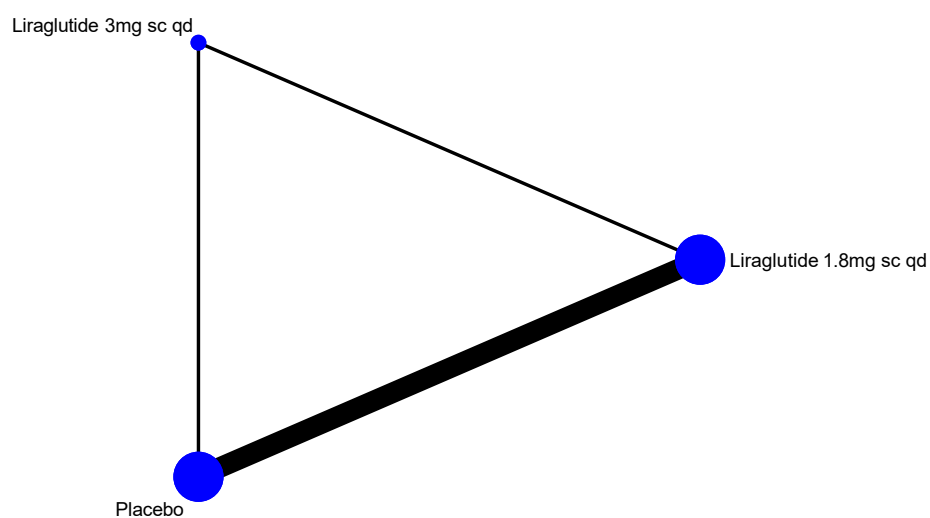
(C2) Forest plot of weight loss



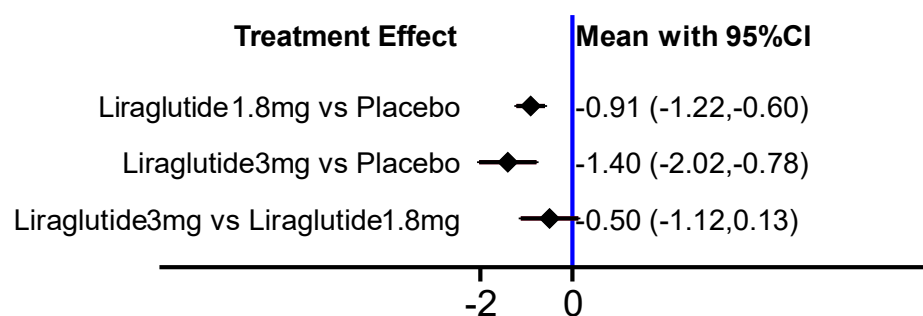
(C3) League table of weight loss

Liraglutide 3mg	1.76 (0.12,3.40)	2.33 (-0.30,4.95)	4.08 (2.44,5.72)	4.83 (2.91,6.76)	5.08 (2.82,7.34)	5.13 (2.84,7.42)	5.31 (3.01,7.61)
-1.76 (-3.40,-0.12)	Liraglutide 1.8mg	0.57 (-1.48,2.62)	2.33 (1.64,3.01)	3.08 (1.86,4.29)	3.32 (1.62,5.03)	3.37 (1.64,5.11)	3.55 (1.80,5.30)
-2.33 (-4.95,0.30)	-0.57 (-2.62,1.48)	Liraglutide 1.2mg	1.76 (-0.40,3.92)	2.51 (0.13,4.89)	2.75 (0.09,5.42)	2.80 (0.12,5.49)	2.98 (0.29,5.68)
-4.08 (-5.72,-2.44)	-2.33 (-3.01,-1.64)	-1.76 (-3.92,0.40)	Placebo	0.75 (-0.25,1.75)	1.00 (-0.56,2.56)	1.05 (-0.54,2.64)	1.23 (-0.38,2.84)
-4.83 (-6.76,-2.91)	-3.08 (-4.29,-1.86)	-2.51 (-4.89,-0.13)	-0.75 (-1.75,0.25)	Liraglutide 0.9mg	0.25 (-1.30,1.79)	0.30 (-1.28,1.87)	0.48 (-1.12,2.07)
-5.08 (-7.34,-2.82)	-3.32 (-5.03,-1.62)	-2.75 (-5.42,-0.09)	-1.00 (-2.56,0.56)	-0.25 (-1.79,1.30)	Liraglutide 0.6mg	0.05 (-1.64,1.74)	0.23 (-1.47,1.93)
-5.13 (-7.42,-2.84)	-3.37 (-5.11,-1.64)	-2.80 (-5.49,-0.12)	-1.05 (-2.64,0.54)	-0.30 (-1.87,1.28)	-0.05 (-1.74,1.64)	Liraglutide 0.1mg	0.18 (-1.55,1.91)
-5.31 (-7.61,-3.01)	-3.55 (-5.30,-1.80)	-2.98 (-5.68,-0.29)	-1.23 (-2.84,0.38)	-0.48 (-2.07,1.12)	-0.23 (-1.93,1.47)	-0.18 (-1.91,1.55)	Liraglutide 0.3mg

(D1) Network map of BMI



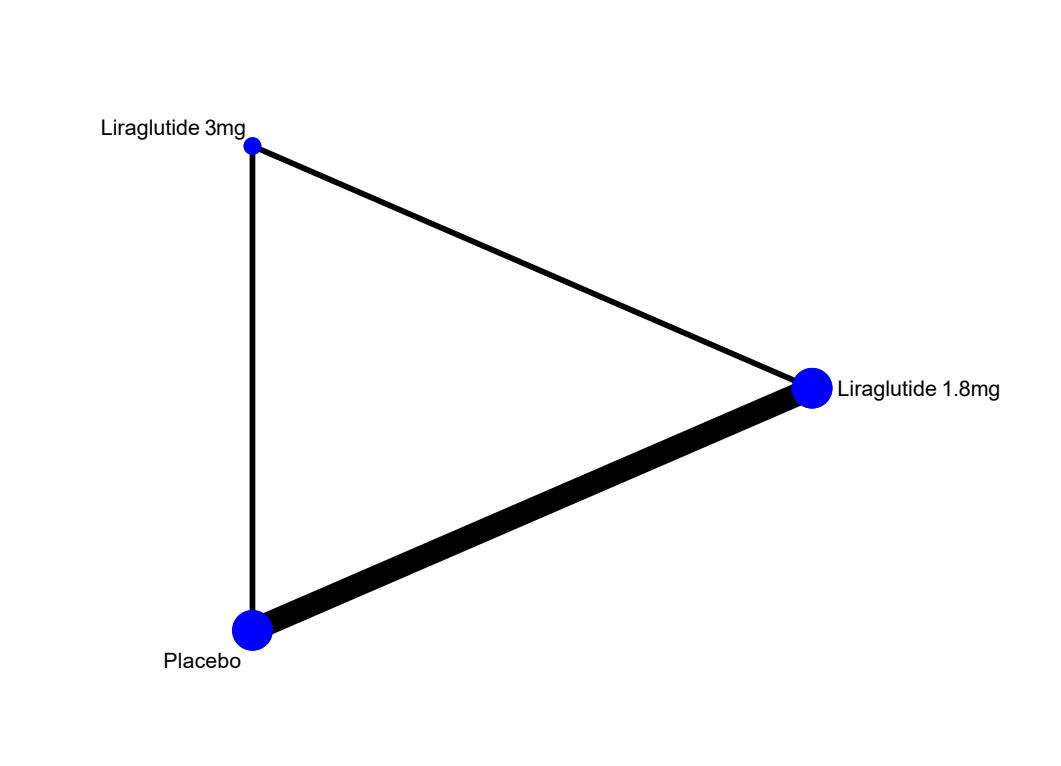
(D2) Forest plot of BMI



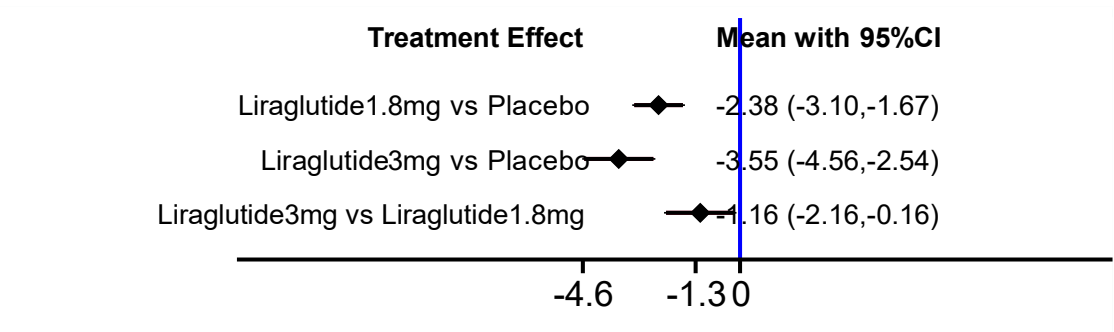
(D3) League table of BMI

Liraglutide 3mg	0.50 (-0.13, 1.12)	1.40 (0.78, 2.02)
-0.50 (-1.12, 0.13)	Liraglutide 1.8mg	0.91 (0.60, 1.22)
-1.40 (-2.02, -0.78)	-0.91 (-1.22, -0.60)	Placebo

(E1) Network map of waist circumference



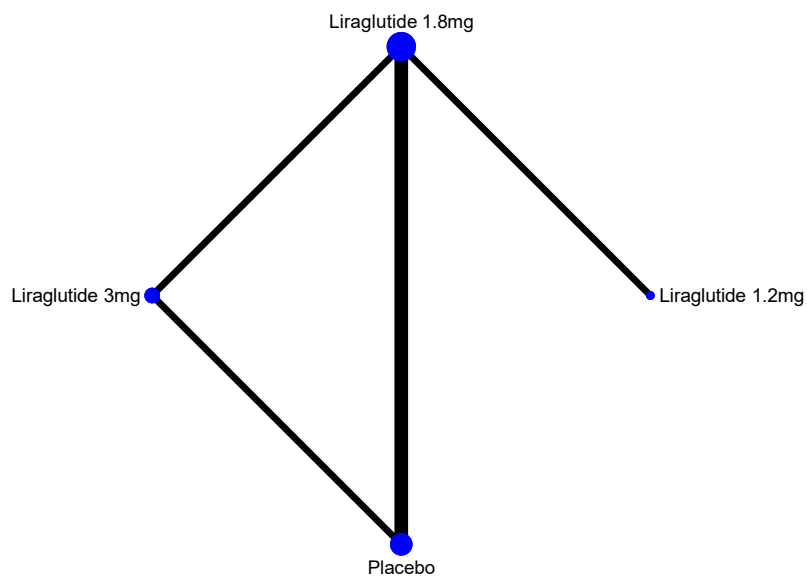
(E2) Forest plot of waist circumference



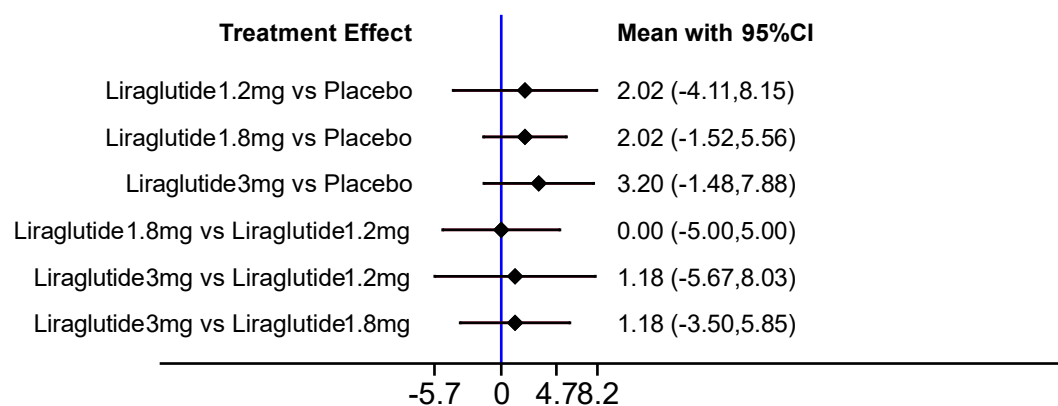
(E3) League table of waist circumference

Liraglutide 3mg	1.16 (0.16,2.16)	3.55 (2.54,4.56)
-1.16 (-2.16,-0.16)	Liraglutide 1.8mg	2.38 (1.67,3.10)
-3.55 (-4.56,-2.54)	-2.38 (-3.10,-1.67)	Placebo

(F1) Network map of HDL



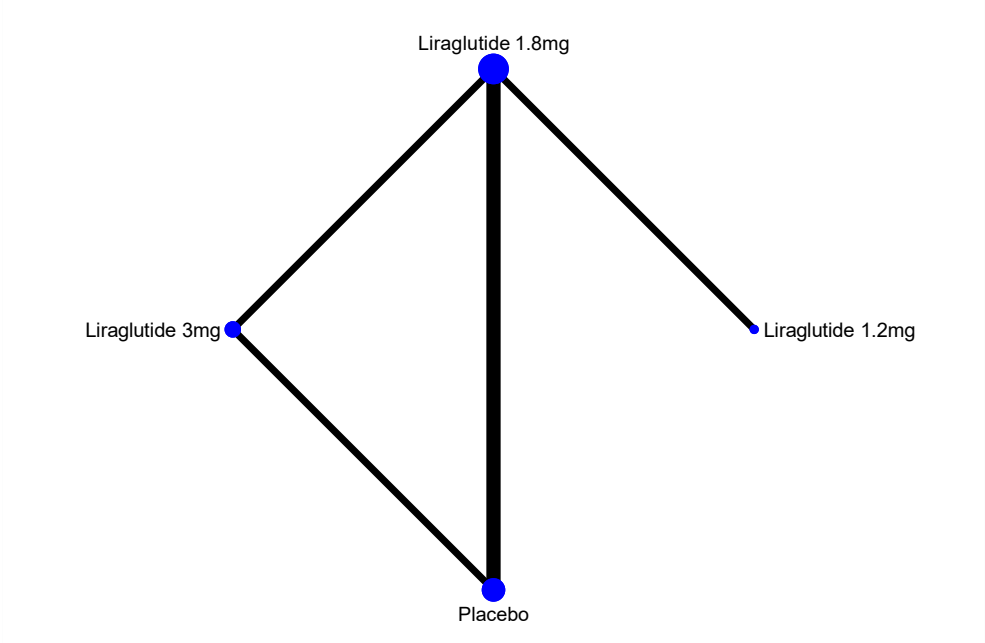
(F2) Forest plot of HDL



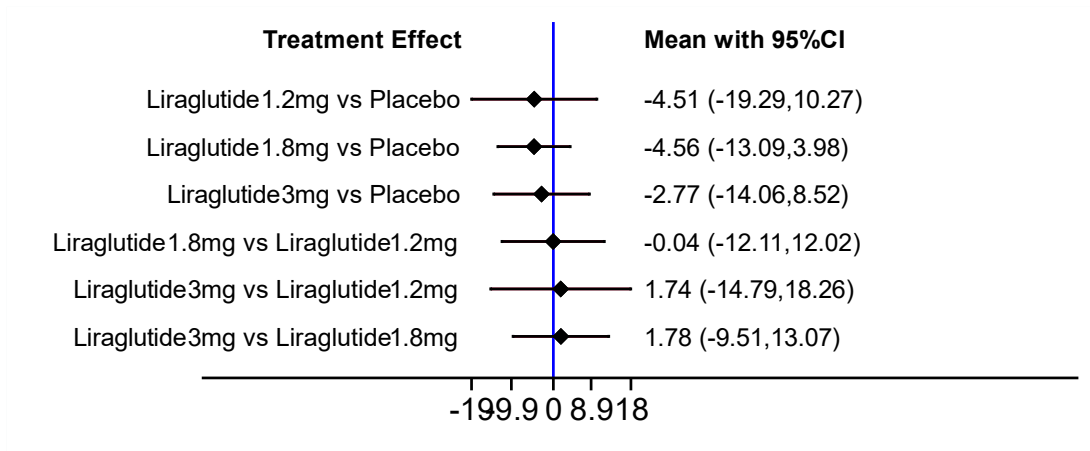
(F3) League table of HDL

Liraglutide 3mg	-1.18 (-5.80, 3.45)	-1.18 (-7.92, 5.55)	-3.20 (-7.82, 1.43)
1.18 (-3.45, 5.80)	Liraglutide 1.8mg	-0.00 (-4.92, 4.91)	-2.02 (-5.52, 1.48)
1.18 (-5.55, 7.92)	0.00 (-4.91, 4.92)	Liraglutide 1.2mg	-2.02 (-8.03, 4.00)
3.20 (-1.43, 7.82)	2.02 (-1.48, 5.52)	2.02 (-4.00, 8.03)	Placebo

(G1) Network map of LDL



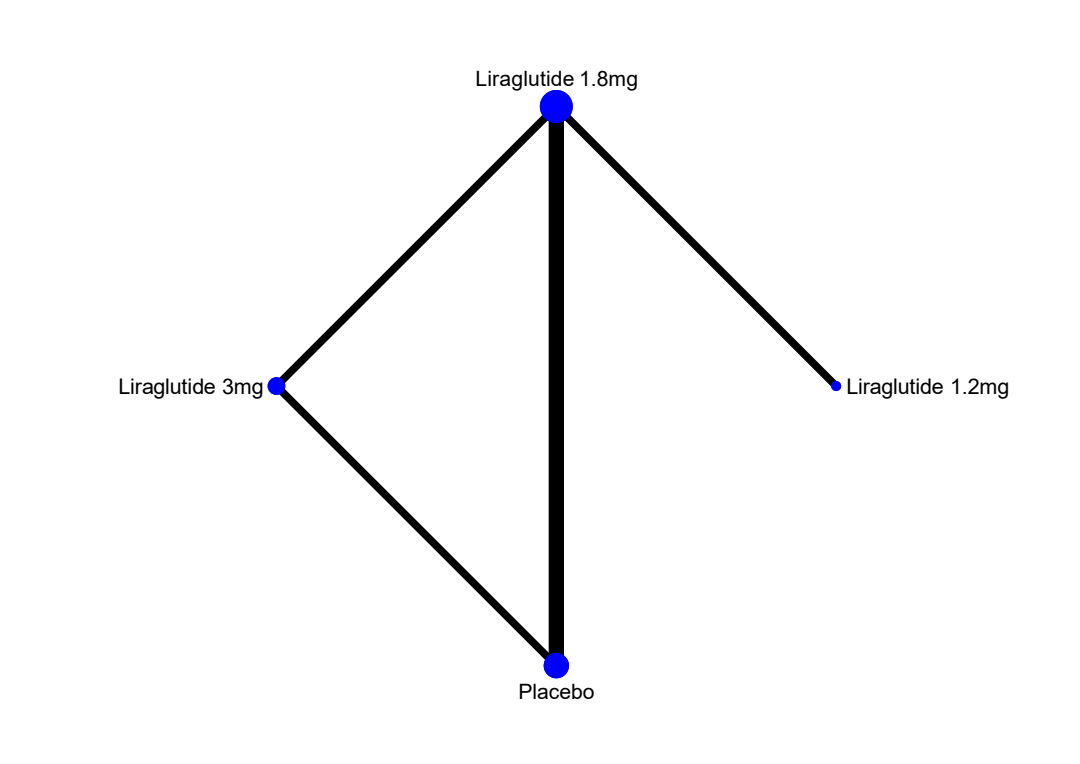
(G2) Forest plot of LDL



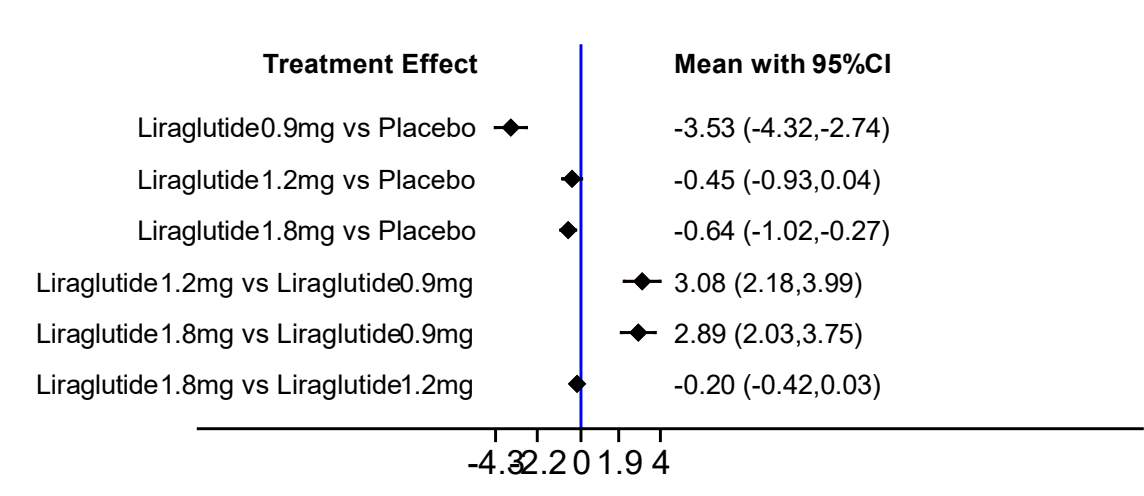
(G3) League table of LDL

Liraglutide 1.8mg	0.17 (-10.90,11.24)	1.75 (-8.90,12.41)	4.52 (-3.53,12.57)
-0.17 (-11.24,10.90)	Liraglutide 1.2mg	1.59 (-13.65,16.82)	4.36 (-9.18,17.90)
-1.75 (-12.41,8.90)	-1.59 (-16.82,13.65)	Liraglutide 3mg	2.77 (-7.91,13.45)
-4.52 (-12.57,3.53)	-4.36 (-17.90,9.18)	-2.77 (-13.45,7.91)	Placebo

(H1) Network map of TC



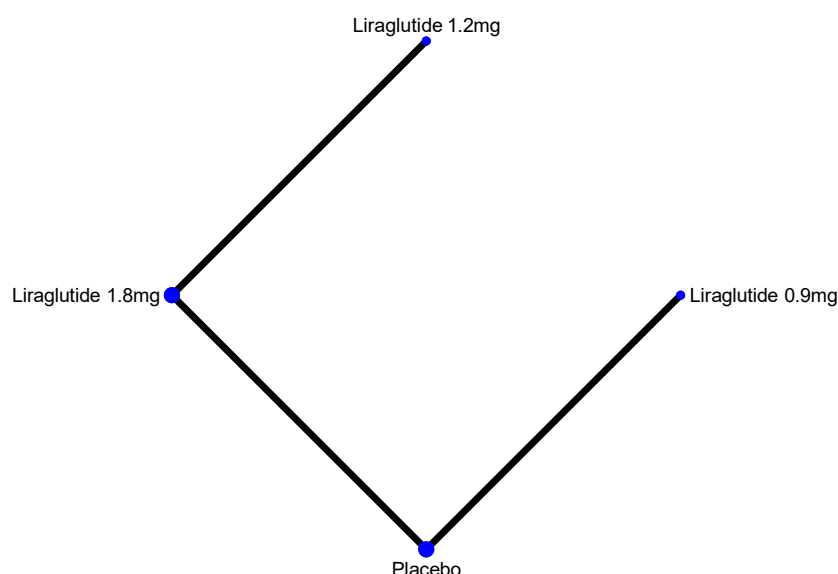
(H2) Forest plot of TC



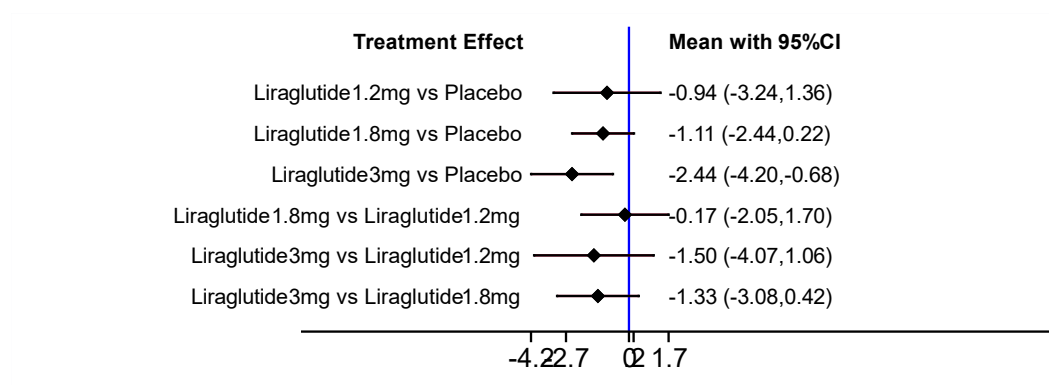
(H3) League table of TC

Liraglutide 1.8mg	0.20 (-0.01,0.40)	0.64 (0.40,0.89)
-0.20 (-0.40,0.01)	Liraglutide 1.2mg	0.45 (0.13,0.77)
-0.64 (-0.89,-0.40)	-0.45 (-0.77,-0.13)	Placebo

(I1) Network map of TG



(I2) Forest plot of TG



(I3) League table of TG

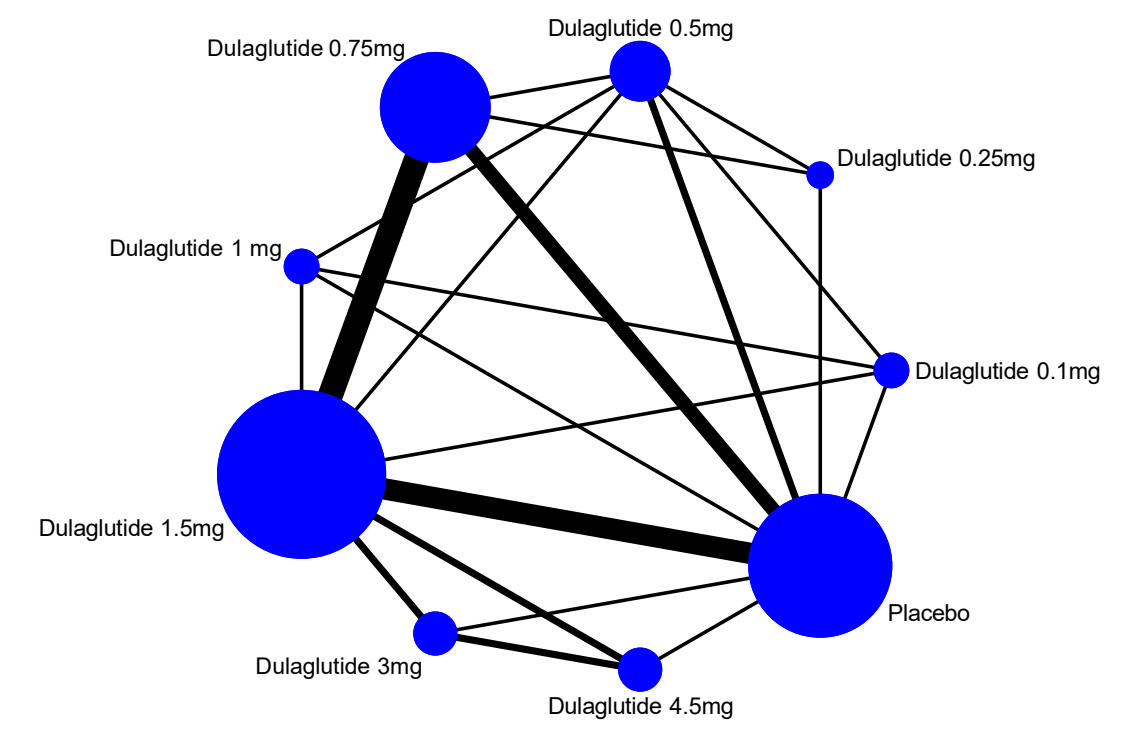
Liraglutide 3mg	1.33 (-0.42, 3.08)	1.50 (-1.06, 4.06)	2.44 (0.69, 4.19)
-1.33 (-3.08, 0.42)	Liraglutide 1.8mg	0.17 (-1.70, 2.04)	1.11 (-0.22, 2.44)
-1.50 (-4.06, 1.06)	-0.17 (-2.04, 1.70)	Liraglutide 1.2mg	0.94 (-1.35, 3.23)
-2.44 (-4.19, -0.69)	-1.11 (-2.44, 0.22)	-0.94 (-3.23, 1.35)	Placebo

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

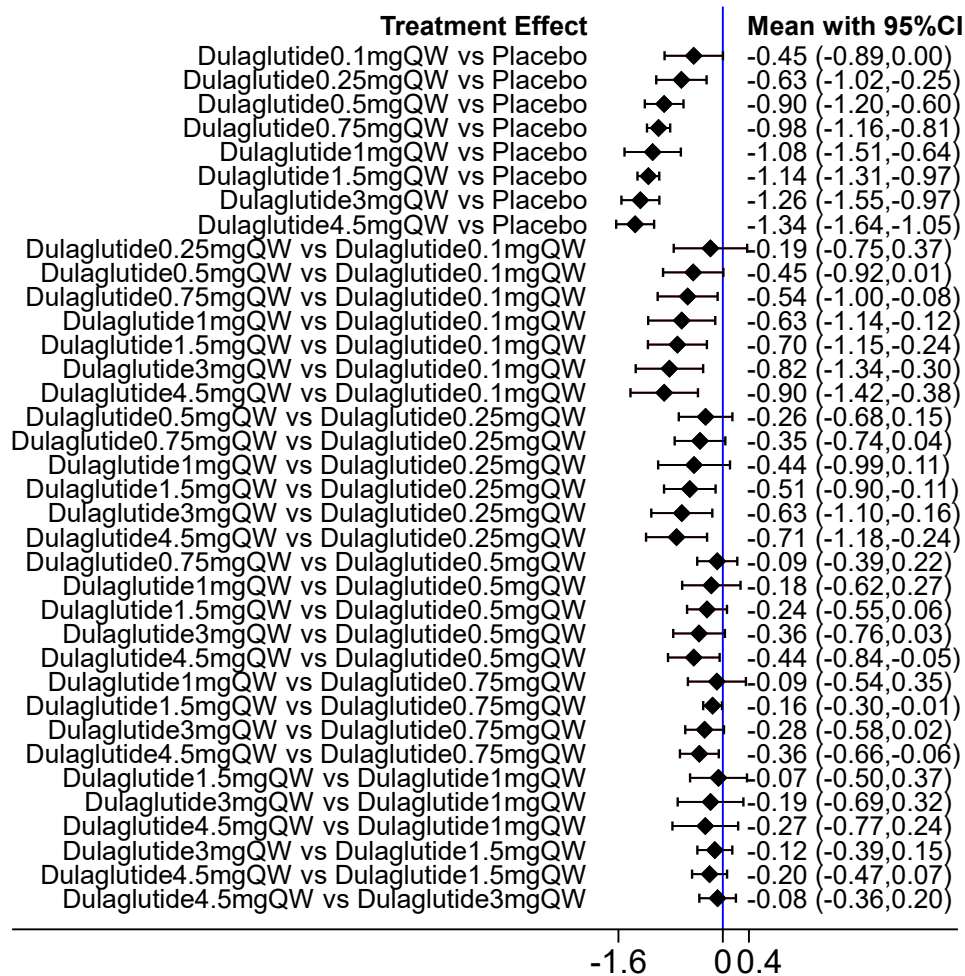
Figure S14.4: Effects of different doses of Dulaglutide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Dulaglutide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) BMI, (E) waist circumference, (F) HDL, (G) LDL, (H) TC, (I) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



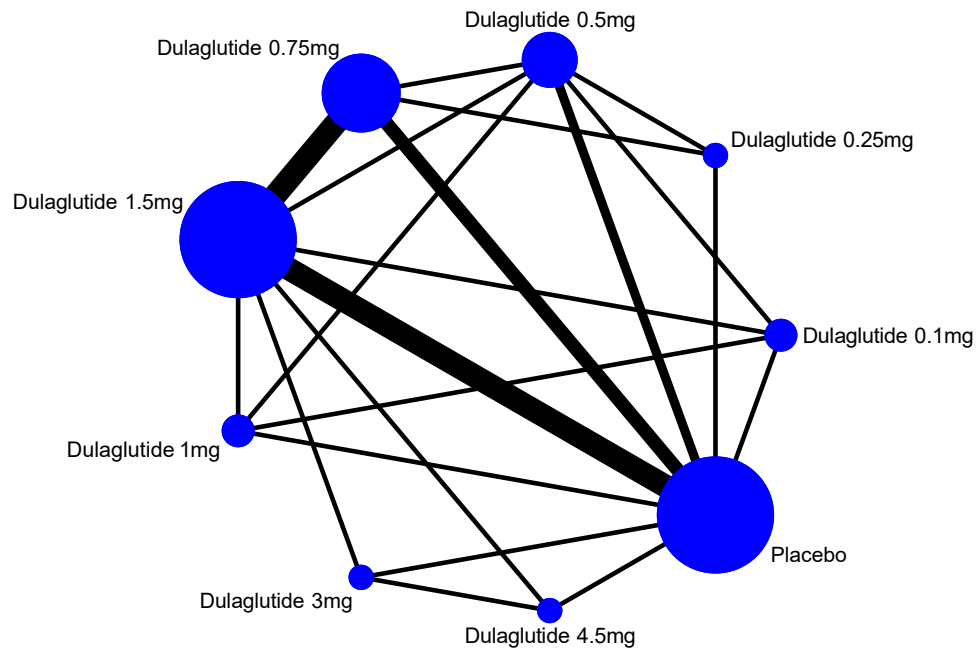
(A2) Forest plot of HbA1c



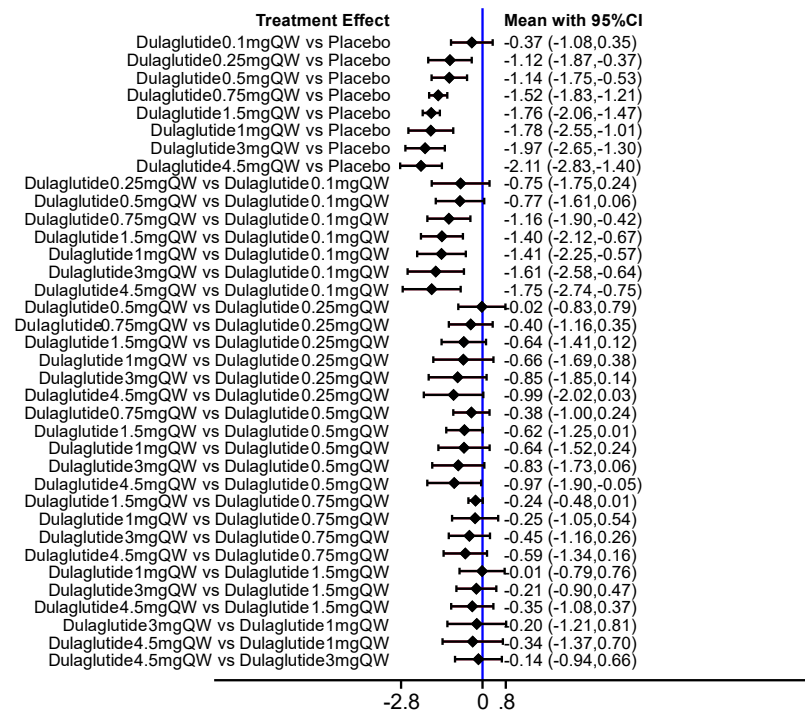
(A3) League table of HbA1c

Dulaglutide 4.5mg QW	0.08 (-0.20,0.36)	0.20 (-0.07,0.47)	0.27 (-0.24,0.77)	0.36 (0.06,0.66)	0.44 (0.05,0.84)	0.71 (0.24,1.18)	0.90 (0.38,1.42)	1.34 (1.05,1.64)
-0.08 (-0.36,0.20)	Dulaglutide 3mg QW	0.12 (-0.15,0.39)	0.19 (-0.32,0.69)	0.28 (-0.02,0.58)	0.36 (-0.03,0.76)	0.63 (0.16,1.10)	0.82 (0.30,1.34)	1.26 (0.97,1.55)
-0.20 (-0.47,0.07)	-0.12 (-0.39,0.15)	Dulaglutide 1.5mg QW	0.07 (-0.37,0.50)	0.16 (0.01,0.30)	0.24 (-0.06,0.55)	0.51 (0.11,0.90)	0.70 (0.24,1.15)	1.14 (0.97,1.31)
-0.27 (-0.77,0.24)	-0.19 (-0.69,0.32)	-0.07 (-0.50,0.37)	Dulaglutide 1 mg QW	0.09 (-0.35,0.54)	0.18 (-0.27,0.62)	0.44 (-0.11,0.99)	0.63 (0.12,1.14)	1.08 (0.64,1.51)
-0.36 (-0.66,-0.06)	-0.28 (-0.58,0.02)	-0.16 (-0.30,-0.01)	-0.09 (-0.54,0.35)	Dulaglutide 0.75mg QW	0.09 (-0.22,0.39)	0.35 (-0.04,0.74)	0.54 (0.08,1.00)	0.98 (0.81,1.16)
-0.44 (-0.84,-0.05)	-0.36 (-0.76,0.03)	-0.24 (-0.55,0.06)	-0.18 (-0.62,0.27)	-0.09 (-0.39,0.22)	Dulaglutide 0.5mg QW	0.26 (-0.15,0.68)	0.45 (-0.01,0.92)	0.90 (0.60,1.20)
-0.71 (-1.18,-0.24)	-0.63 (-1.10,-0.16)	-0.51 (-0.90,-0.11)	-0.44 (-0.99,0.11)	-0.35 (-0.74,0.04)	-0.26 (-0.68,0.15)	Dulaglutide 0.25mg QW	0.19 (-0.37,0.75)	0.63 (0.25,1.02)
-0.90 (-1.42,-0.38)	-0.82 (-1.34,-0.30)	-0.70 (-1.15,-0.24)	-0.63 (-1.14,-0.12)	-0.54 (-1.00,-0.08)	-0.45 (-0.92,0.01)	-0.19 (-0.75,0.37)	Dulaglutide 0.1mg QW	0.45 (-0.00,0.89)
-1.34 (-1.64,-1.05)	-1.26 (-1.55,-0.97)	-1.14 (-1.31,-0.97)	-1.08 (-1.51,-0.64)	-0.98 (-1.16,-0.81)	-0.90 (-1.20,-0.60)	-0.63 (-1.02,-0.25)	-0.45 (-0.89,0.00)	Placebo

(B1) Network map of FPG



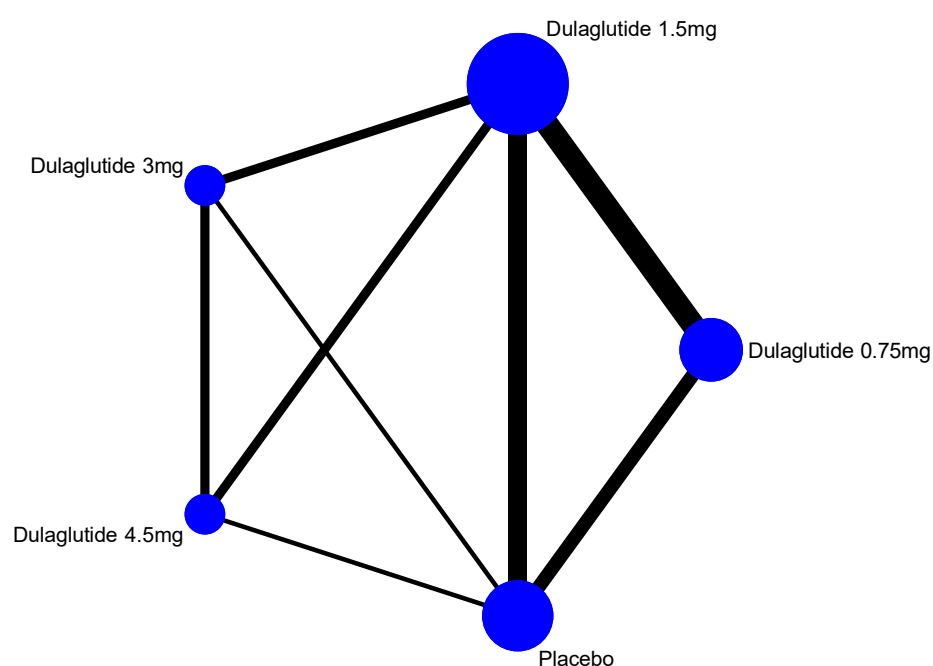
(B2) Forest plot of FPG



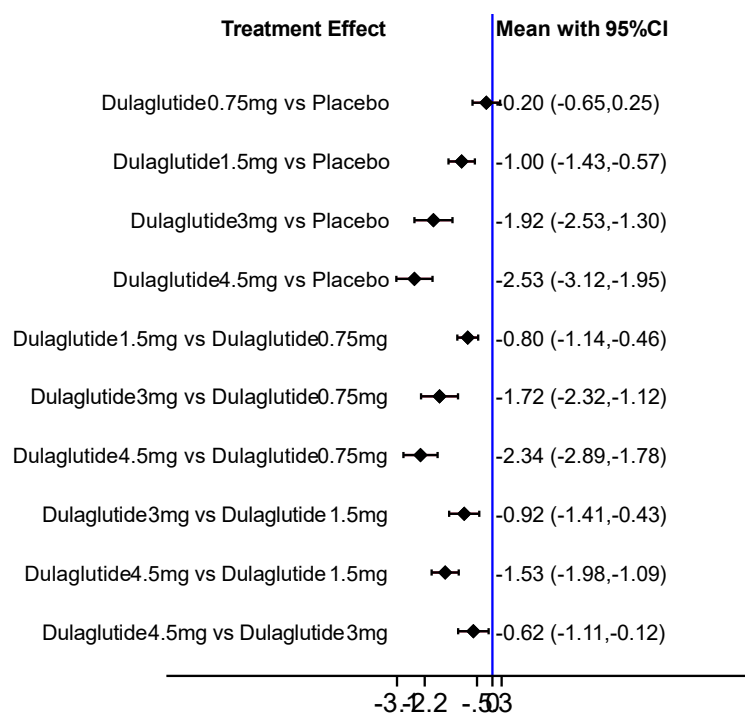
(B3) League table of FPG

Dulaglutide 4.5mg QW	0.14 (-0.66,0.94)	0.35 (-0.37,1.08)	0.34 (-0.70,1.37)	0.59 (-0.16,1.34)	0.99 (-0.03,2.02)	0.97 (0.05,1.90)	1.75 (0.75,2.74)	2.11 (1.40,2.83)
-0.14 (-0.94,0.66)	Dulaglutide 3mg QW	0.21 (-0.47,0.90)	0.20 (-0.81,1.21)	0.45 (-0.26,1.16)	0.85 (-0.14,1.85)	0.83 (-0.06,1.73)	1.61 (0.64,2.58)	1.97 (1.30,2.65)
-0.35 (-1.08,0.37)	-0.21 (-0.90,0.47)	Dulaglutide 1.5mg QW	-0.01 (-0.79,0.76)	0.24 (-0.01,0.48)	0.64 (-0.12,1.41)	0.62 (-0.01,1.25)	1.40 (0.67,2.12)	1.76 (1.47,2.06)
-0.34 (-1.37,0.70)	-0.20 (-1.21,0.81)	0.01 (-0.76,0.79)	Dulaglutide 1 mg QW	0.25 (-0.54,1.05)	0.66 (-0.38,1.69)	0.64 (-0.24,1.52)	1.41 (0.57,2.25)	1.78 (1.01,2.55)
-0.59 (-1.34,0.16)	-0.45 (-1.16,0.26)	-0.24 (-0.48,0.01)	-0.25 (-1.05,0.54)	Dulaglutide 0.75mg QW	0.40 (-0.35,1.16)	0.38 (-0.24,1.00)	1.16 (0.42,1.90)	1.52 (1.21,1.83)
-0.99 (-2.02,0.03)	-0.85 (-1.85,0.14)	-0.64 (-1.41,0.12)	-0.66 (-1.69,0.38)	-0.40 (-1.16,0.35)	Dulaglutide 0.25mg QW	-0.02 (-0.83,0.79)	0.75 (-0.24,1.75)	1.12 (0.37,1.87)
-0.97 (-1.90,-0.05)	-0.83 (-1.73,0.06)	-0.62 (-1.25,0.01)	-0.64 (-1.52,0.24)	-0.38 (-1.00,0.24)	0.02 (-0.79,0.83)	Dulaglutide 0.5mg QW	0.77 (-0.06,1.61)	1.14 (0.53,1.75)
-1.75 (-2.74,-0.75)	-1.61 (-2.58,-0.64)	-1.40 (-2.12,-0.67)	-1.41 (-2.25,-0.57)	-1.16 (-1.90,-0.42)	-0.75 (-1.75,0.24)	-0.77 (-1.61,0.06)	Dulaglutide 0.1mg QW	0.37 (-0.35,1.08)
-2.11 (-2.83,-1.40)	-1.97 (-2.65,-1.30)	-1.76 (-2.06,-1.47)	-1.78 (-2.55,-1.01)	-1.52 (-1.83,-1.21)	-1.12 (-1.87,-0.37)	-1.14 (-1.75,-0.53)	-0.37 (-1.08,0.35)	Placebo

(C1) Network map of weight loss



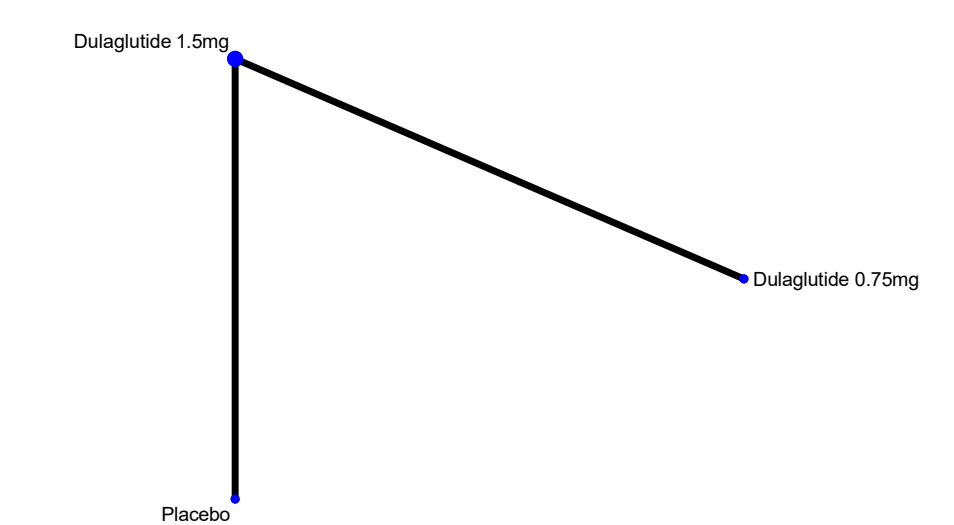
(C2) Forest plot of weight loss



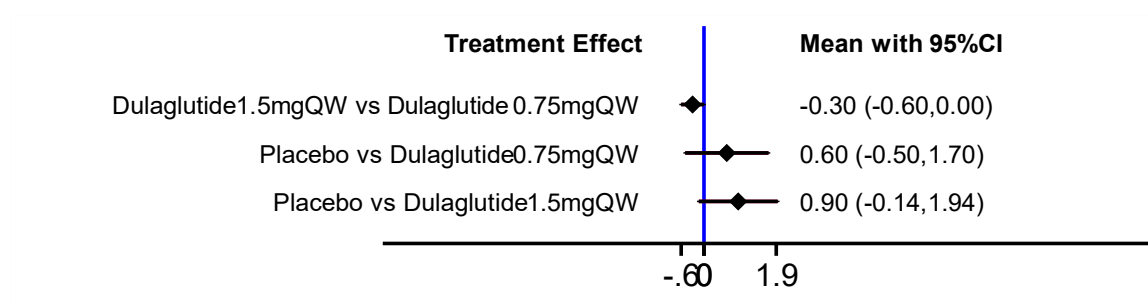
(C3) League table of weight loss

Dulaglutide 4.5mg	0.62 (0.12, 1.11)	1.53 (1.09, 1.98)	2.34 (1.78, 2.89)	2.53 (1.95, 3.12)
-0.62 (-1.11, -0.12)	Dulaglutide 3mg	0.92 (0.43, 1.40)	1.72 (1.12, 2.32)	1.92 (1.30, 2.53)
-1.53 (-1.98, -1.09)	-0.92 (-1.40, -0.43)	Dulaglutide 1.5mg	0.80 (0.46, 1.14)	1.00 (0.57, 1.43)
-2.34 (-2.89, -1.78)	-1.72 (-2.32, -1.12)	-0.80 (-1.14, -0.46)	Dulaglutide 0.75mg	0.20 (-0.25, 0.65)
-2.53 (-3.12, -1.95)	-1.92 (-2.53, -1.30)	-1.00 (-1.43, -0.57)	-0.20 (-0.65, 0.25)	Placebo

(D1) Network map of BMI



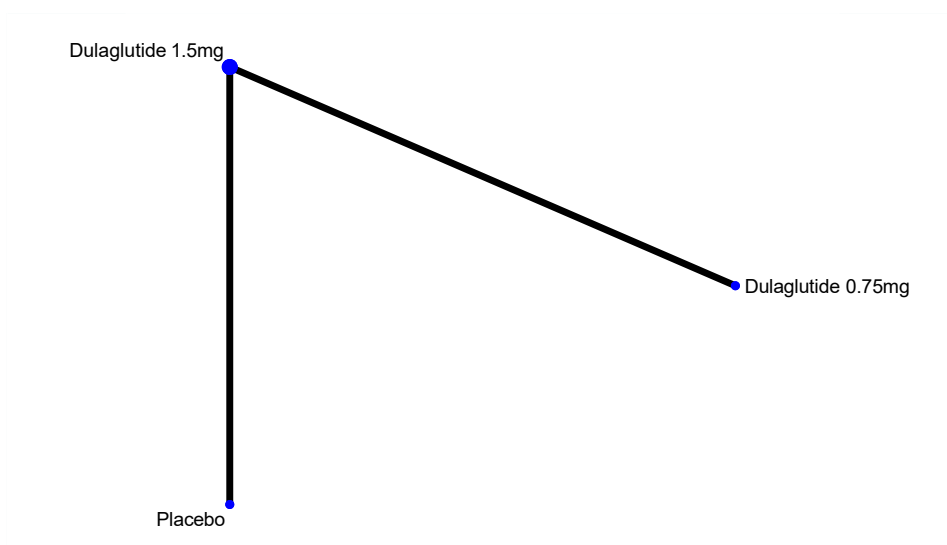
(D2) Forest plot of BMI



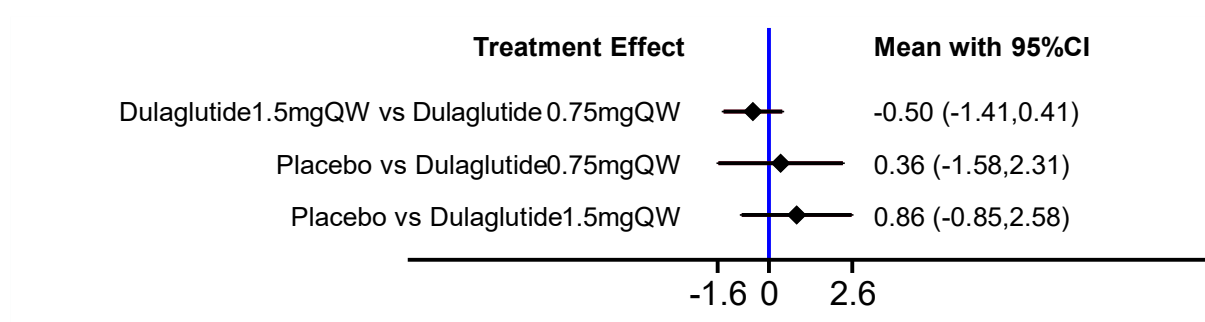
(D3) League table of BMI

Dulaglutide 1.5mg QW	0.30 (-0.00,0.60)	0.90 (-0.14,1.94)
-0.30 (-0.60,0.00)	Dulaglutide 0.75mg QW	0.60 (-0.50,1.70)
-0.90 (-1.94,0.14)	-0.60 (-1.70,0.50)	Placebo

(E1) Network map of waist circumference



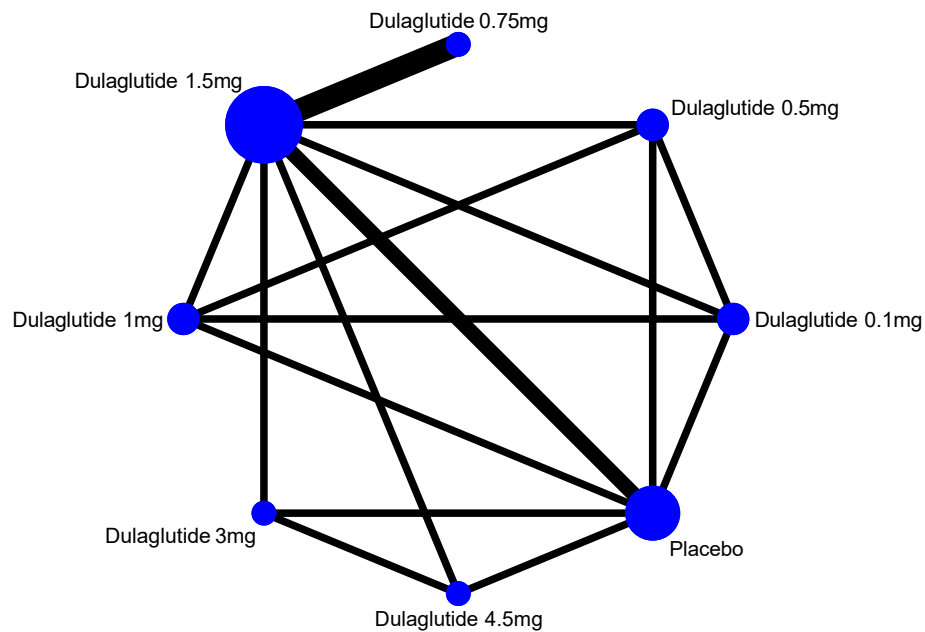
(E2) Forest plot of waist circumference



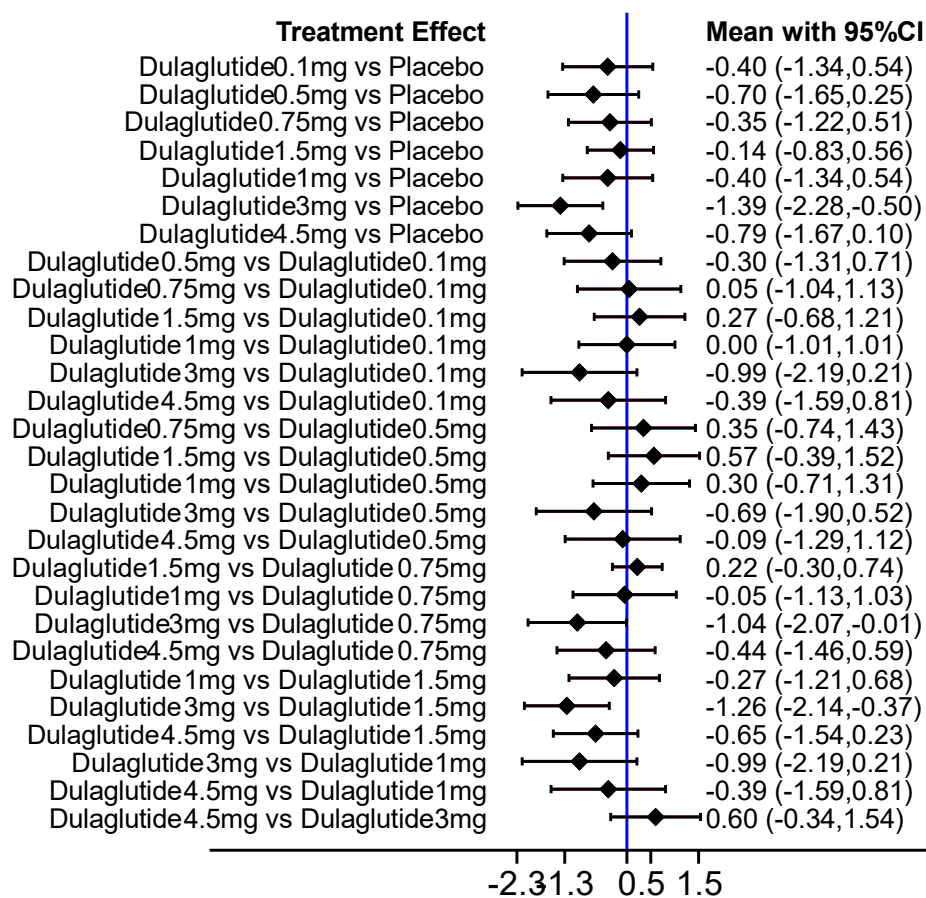
(E3) League table of waist circumference

Dulaglutide 1.5mg QW	0.50 (-0.41, 1.41)	0.86 (-0.85, 2.58)
-0.50 (-1.41, 0.41)	-0.60 (-1.70, 0.50)	0.36 (-1.58, 2.31)
-0.86 (-2.58, 0.85)	-0.36 (-2.31, 1.58)	Placebo

(F1) Network map of HDL



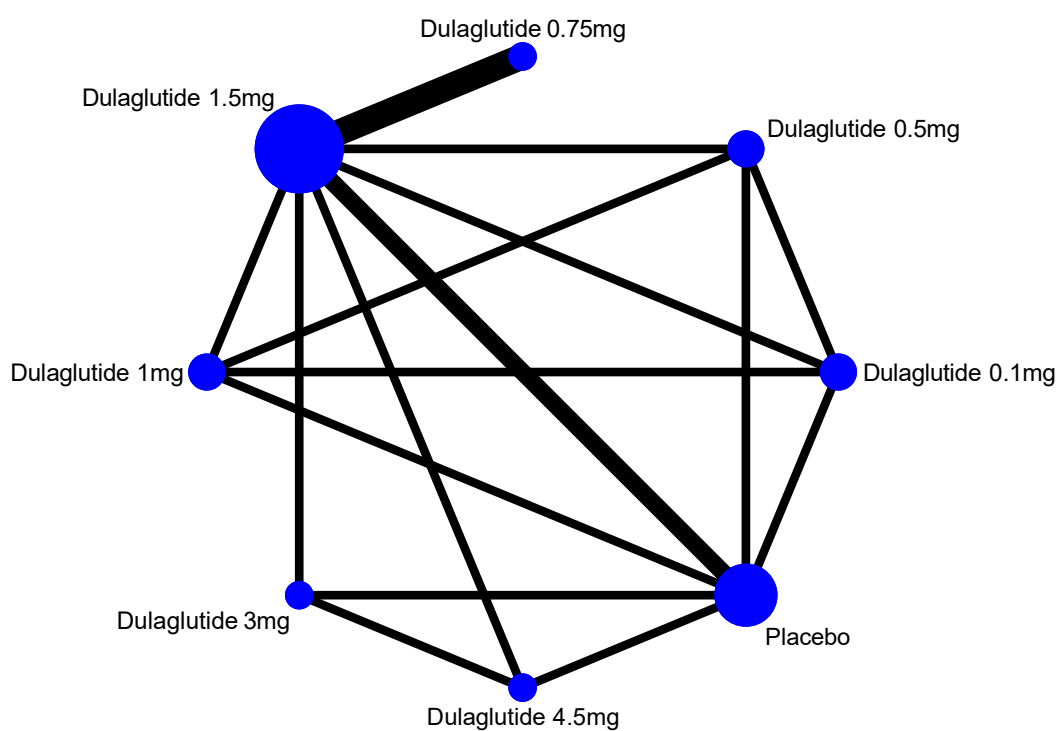
(F2) Forest plot of HDL



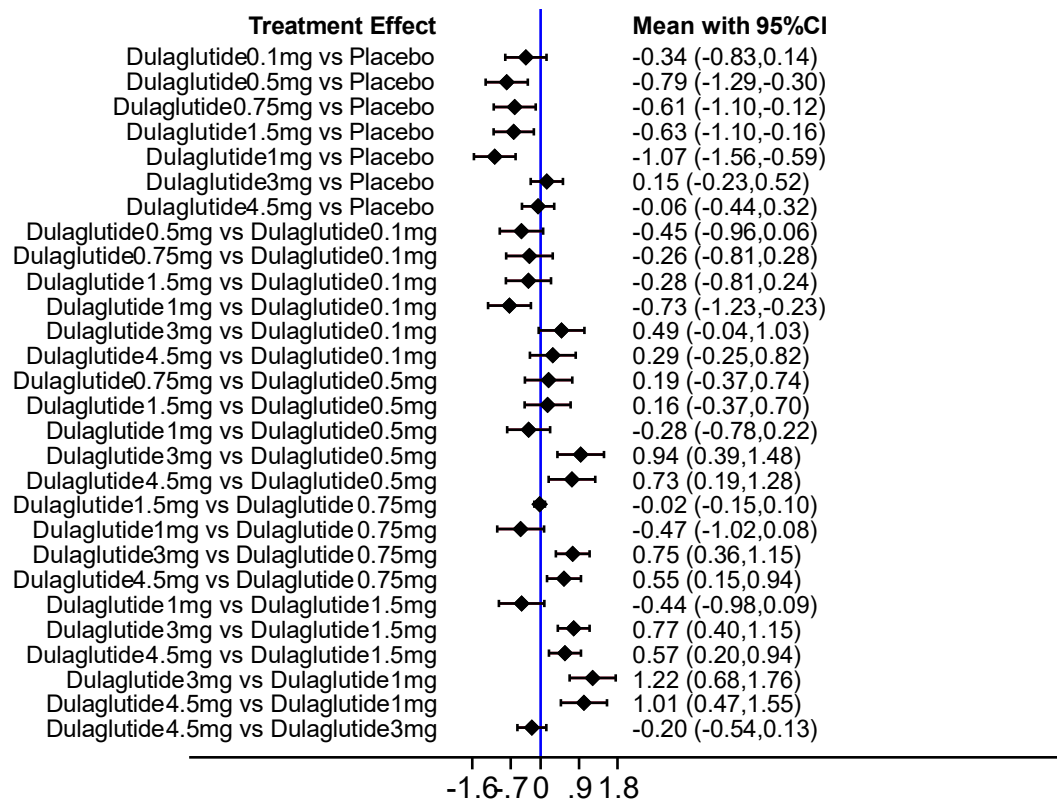
(F3) League table of HDL

Placebo	-0.14 (-0.83,0.56)	-0.35 (-1.22,0.51)	-0.40 (-1.34,0.54)	-0.40 (-1.34,0.54)	-0.70 (-1.65,0.25)	-0.79 (-1.67,0.09)	-1.39 (-2.28,-0.50)
0.14 (-0.56,0.83)	Dulaglutide 1.5mg	-0.22 (-0.74,0.30)	-0.27 (-1.21,0.68)	-0.27 (-1.21,0.68)	-0.57 (-1.52,0.39)	-0.65 (-1.54,0.23)	-1.26 (-2.14,-0.37)
0.35 (-0.51,1.22)	0.22 (-0.30,0.74)	Dulaglutide 0.75mg	-0.05 (-1.13,1.03)	-0.05 (-1.13,1.03)	-0.35 (-1.43,0.74)	-0.44 (-1.46,0.59)	-1.04 (-2.07,-0.01)
0.40 (-0.54,1.34)	0.27 (-0.68,1.21)	0.05 (-1.03,1.13)	Dulaglutide 0.1mg	-0.00 (-1.00,1.00)	-0.30 (-1.31,0.71)	-0.39 (-1.59,0.81)	-0.99 (-2.19,0.21)
0.40 (-0.54,1.34)	0.27 (-0.68,1.21)	0.05 (-1.03,1.13)	0.00 (-1.00,1.00)	Dulaglutide 1mg	-0.30 (-1.31,0.71)	-0.39 (-1.59,0.81)	-0.99 (-2.19,0.21)
0.70 (-0.25,1.65)	0.57 (-0.39,1.52)	0.35 (-0.74,1.43)	0.30 (-0.71,1.31)	0.30 (-0.71,1.31)	Dulaglutide 0.5mg	-0.09 (-1.29,1.12)	-0.69 (-1.89,0.52)
0.79 (-0.09,1.67)	0.65 (-0.23,1.54)	0.44 (-0.59,1.46)	0.39 (-0.81,1.59)	0.39 (-0.81,1.59)	0.09 (-1.12,1.29)	Dulaglutide 4.5mg	-0.60 (-1.54,0.34)
1.39 (0.50,2.28)	1.26 (0.37,2.14)	1.04 (0.01,2.07)	0.99 (-0.21,2.19)	0.99 (-0.21,2.19)	0.69 (-0.52,1.89)	0.60 (-0.34,1.54)	Dulaglutide 3mg

(G1) Network map of LDL



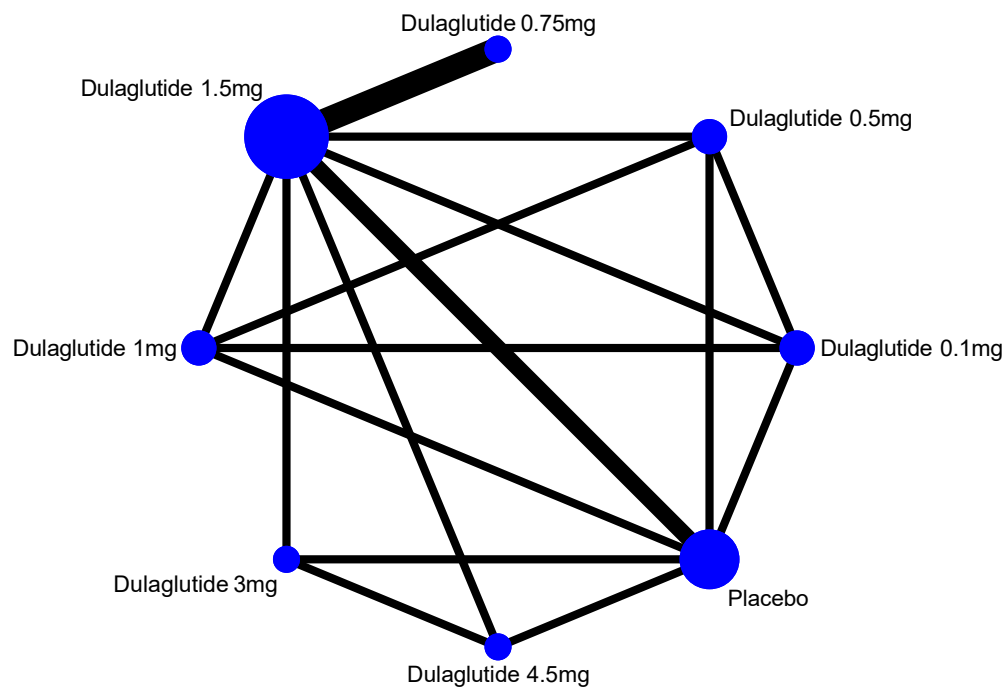
(G2) Forest plot of LDL



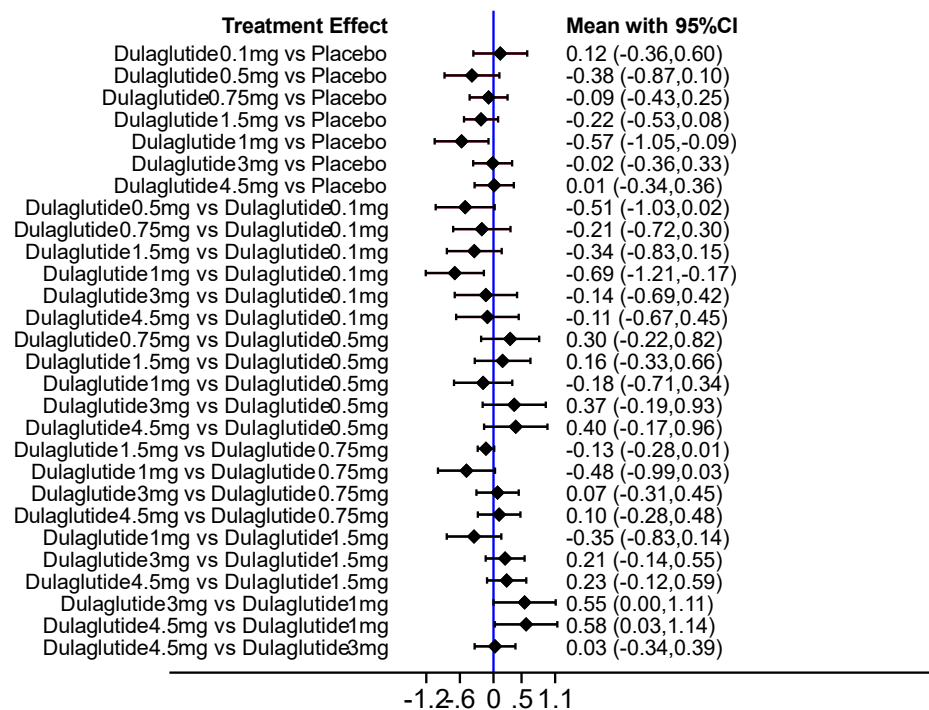
(G3) League table of LDL

Dulaglutide 1mg	0.28 (- 0.22,0.78)	0.44 (- 0.09,0.98)	0.47 (- 0.08,1.02)	0.73 (0.23,1.23)	1.01 (0.47,1.55)	1.07 (0.59,1.56)	1.22 (0.68,1.76)
-0.28 (- 0.78,0.22)	Dulaglutide 0.5mg	0.16 (- 0.37,0.70)	0.19 (- 0.37,0.74)	0.45 (- 0.06,0.96)	0.73 (0.19,1.28)	0.79 (0.30,1.29)	0.94 (0.39,1.48)
-0.44 (- 0.98,0.09)	-0.16 (- 0.70,0.37)	Dulaglutide 1.5mg	0.02 (- 0.10,0.15)	0.28 (- 0.24,0.81)	0.57 (0.20,0.94)	0.63 (0.16,1.10)	0.77 (0.40,1.15)
-0.47 (- 1.02,0.08)	-0.19 (- 0.74,0.37)	-0.02 (- 0.15,0.10)	Dulaglutide 0.75mg	0.26 (- 0.28,0.81)	0.55 (0.15,0.94)	0.61 (0.12,1.10)	0.75 (0.36,1.15)
-0.73 (- 1.23,-0.23)	-0.45 (- 0.96,0.06)	-0.28 (- 0.81,0.24)	-0.26 (- 0.81,0.28)	Dulaglutide 0.1mg	0.29 (- 0.25,0.82)	0.34 (- 0.14,0.83)	0.49 (- 0.04,1.02)
-1.01 (- 1.55,-0.47)	-0.73 (- 1.28,-0.19)	-0.57 (- 0.94,-0.20)	-0.55 (- 0.94,-0.15)	-0.29 (- 0.82,0.25)	Dulaglutide 4.5mg	0.06 (- 0.32,0.44)	0.20 (- 0.13,0.54)
-1.07 (- 1.56,-0.59)	-0.79 (- 1.29,-0.30)	-0.63 (- 1.10,-0.16)	-0.61 (- 1.10,-0.12)	-0.34 (- 0.83,0.14)	-0.06 (- 0.44,0.32)	Placebo	0.15 (- 0.23,0.52)
-1.22 (- 1.76,-0.68)	-0.94 (- 1.48,-0.39)	-0.77 (- 1.15,-0.40)	-0.75 (- 1.15,-0.36)	-0.49 (- 1.02,0.04)	-0.20 (- 0.54,0.13)	-0.15 (- 0.52,0.23)	Dulaglutide 3mg

(H1) Network map of TC



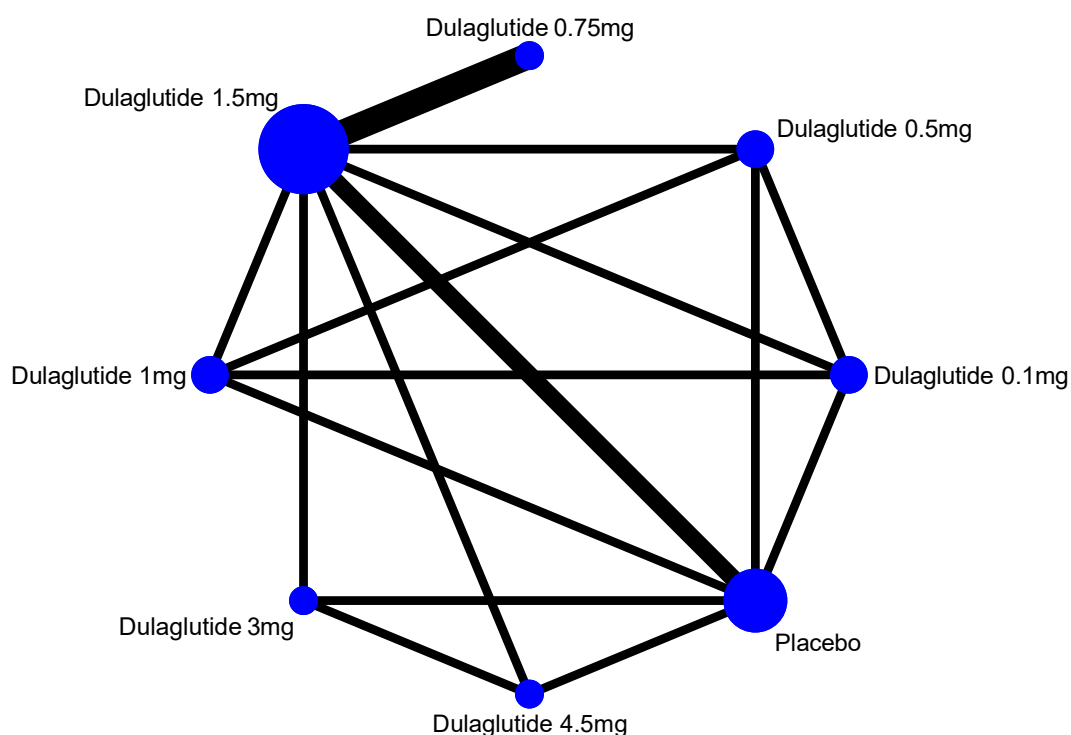
(H2) Forest plot of TC



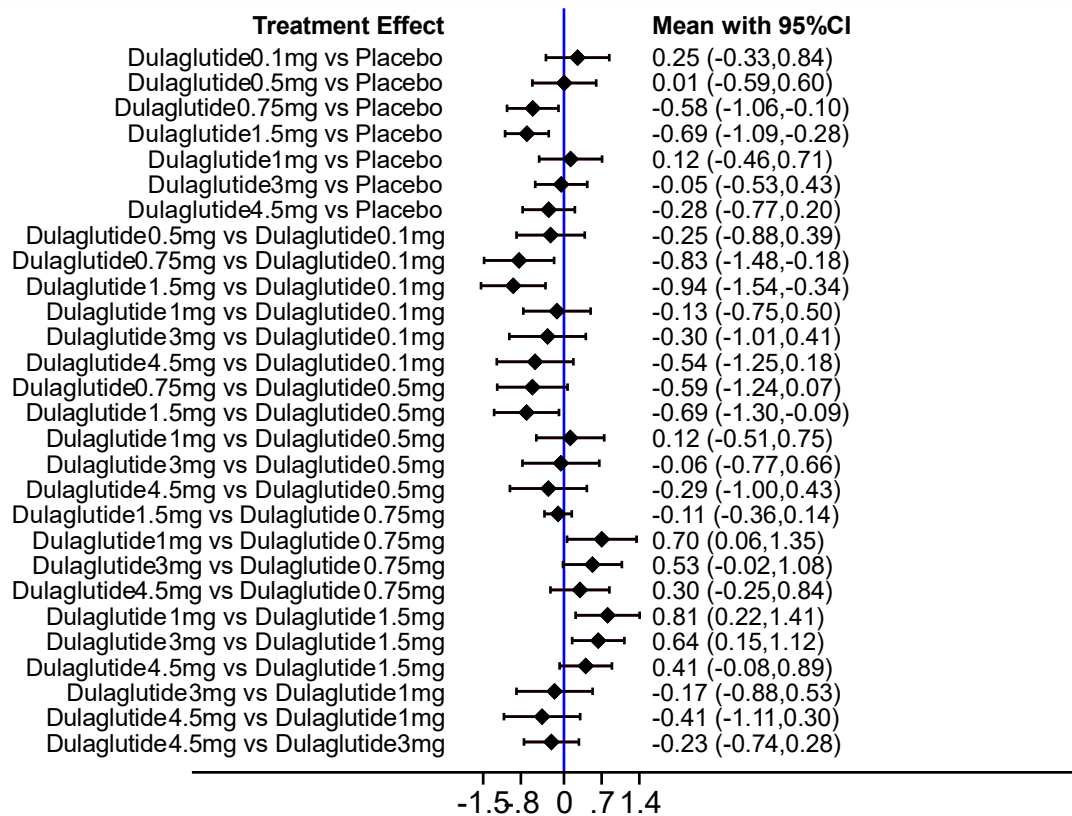
(H3) League table of TC

Dulaglutide 1mg	0.18 (-0.34,0.71)	0.35 (-0.14,0.83)	0.48 (-0.03,0.99)	0.55 (-0.00,1.11)	0.57 (0.09,1.05)	0.58 (0.03,1.14)	0.69 (0.17,1.21)
-0.18 (-0.71,0.34)	Dulaglutide 0.5mg	0.16 (-0.33,0.66)	0.30 (-0.22,0.82)	0.37 (-0.19,0.93)	0.38 (-0.10,0.87)	0.40 (-0.17,0.96)	0.51 (-0.02,1.03)
-0.35 (-0.83,0.14)	-0.16 (-0.66,0.33)	Dulaglutide 1.5mg	0.13 (-0.01,0.28)	0.21 (-0.14,0.55)	0.22 (-0.08,0.53)	0.23 (-0.12,0.59)	0.34 (-0.15,0.83)
-0.48 (-0.99,0.03)	-0.30 (-0.82,0.22)	-0.13 (-0.28,0.01)	Dulaglutide 0.75mg	0.07 (-0.31,0.45)	0.09 (-0.25,0.43)	0.10 (-0.28,0.48)	0.21 (-0.30,0.72)
-0.55 (-1.11,0.00)	-0.37 (-0.93,0.19)	-0.21 (-0.55,0.14)	-0.07 (-0.45,0.31)	Dulaglutide 3mg	0.02 (-0.33,0.36)	0.03 (-0.34,0.39)	0.14 (-0.42,0.69)
-0.57 (-1.05,-0.09)	-0.38 (-0.87,0.10)	-0.22 (-0.53,0.08)	-0.09 (-0.43,0.25)	-0.02 (-0.36,0.33)	Placebo	0.01 (-0.34,0.36)	0.12 (-0.36,0.60)
-0.58 (-1.14,-0.03)	-0.40 (-0.96,0.17)	-0.23 (-0.59,0.12)	-0.10 (-0.48,0.28)	-0.03 (-0.39,0.34)	-0.01 (-0.36,0.34)	Dulaglutide 4.5mg	0.11 (-0.45,0.67)
-0.69 (-1.21,-0.17)	-0.51 (-1.03,0.02)	-0.34 (-0.83,0.15)	-0.21 (-0.72,0.30)	-0.14 (-0.69,0.42)	-0.12 (-0.60,0.36)	-0.11 (-0.67,0.45)	Dulaglutide 0.1mg

(II) Network map of TG



(I2) Forest plot of TG



(I3) League table of TG

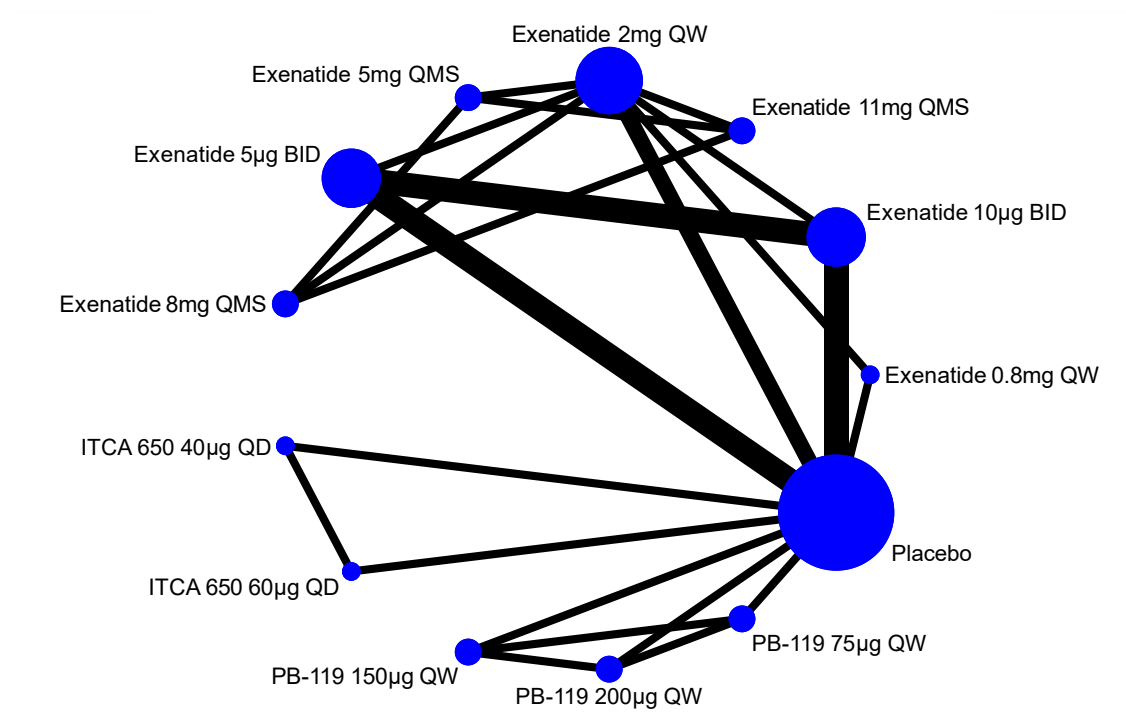
Dulaglutide 1.5mg	0.11 (-0.14,0.36)	0.41 (-0.08,0.89)	0.64 (0.15,1.12)	0.69 (0.09,1.30)	0.69 (0.28,1.09)	0.81 (0.22,1.41)	0.94 (0.34,1.54)
-0.11 (-0.36,0.14)	Dulaglutide 0.75mg	0.30 (-0.25,0.84)	0.53 (-0.02,1.08)	0.59 (-0.07,1.24)	0.58 (0.10,1.06)	0.70 (0.06,1.35)	0.83 (0.18,1.48)
-0.41 (-0.89,0.08)	-0.30 (-0.84,0.25)	Dulaglutide 4.5mg	0.23 (-0.28,0.74)	0.29 (-0.43,1.00)	0.28 (-0.20,0.77)	0.41 (-0.30,1.11)	0.54 (-0.18,1.25)
-0.64 (-1.12,-0.15)	-0.53 (-1.08,0.02)	-0.23 (-0.74,0.28)	Dulaglutide 3mg	0.06 (-0.66,0.77)	0.05 (-0.43,0.53)	0.17 (-0.53,0.88)	0.30 (-0.41,1.01)
-0.69 (-1.30,-0.09)	-0.59 (-1.24,0.07)	-0.29 (-1.00,0.43)	-0.06 (-0.77,0.66)	Dulaglutide 0.5mg	-0.01 (-0.60,0.59)	0.12 (-0.51,0.75)	0.25 (-0.39,0.88)
-0.69 (-1.09,-0.28)	-0.58 (-1.06,-0.10)	-0.28 (-0.77,0.20)	-0.05 (-0.53,0.43)	0.01 (-0.59,0.60)	Placebo	0.12 (-0.46,0.71)	0.25 (-0.33,0.84)
-0.81 (-1.41,-0.22)	-0.70 (-1.35,-0.06)	-0.41 (-1.11,0.30)	-0.17 (-0.88,0.53)	-0.12 (-0.75,0.51)	-0.12 (-0.71,0.46)	Dulaglutide 1mg	0.13 (-0.50,0.75)
-0.94 (-1.54,-0.34)	-0.83 (-1.48,-0.18)	-0.54 (-1.25,0.18)	-0.30 (-1.01,0.41)	-0.25 (-0.88,0.39)	-0.25 (-0.84,0.33)	-0.13 (-0.75,0.50)	Dulaglutide 0.1mg

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

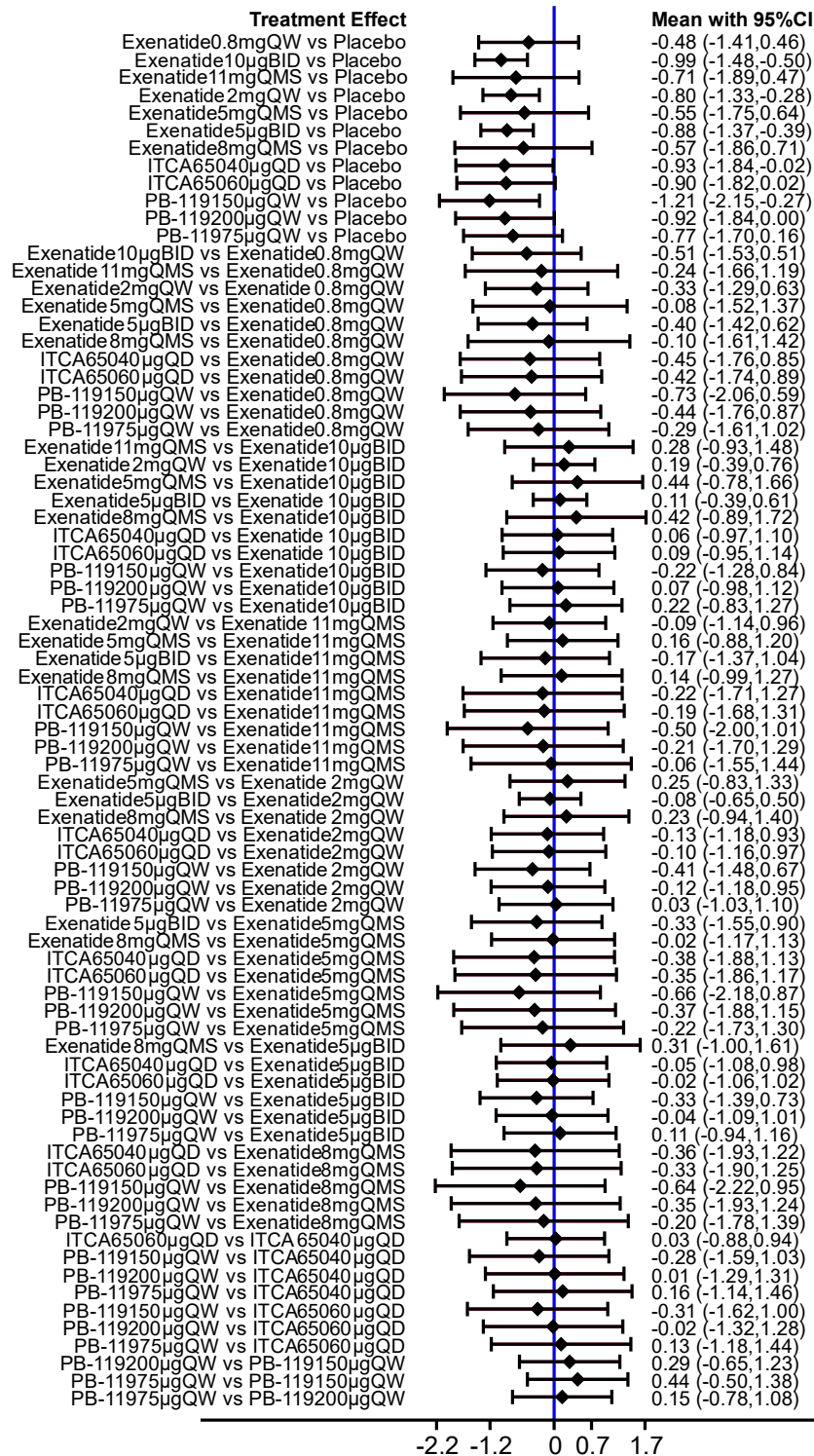
Figure S14.5: Effects of different doses of Exenatide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Exenatide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) HDL, (E) LDL, (F) TC, (G) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



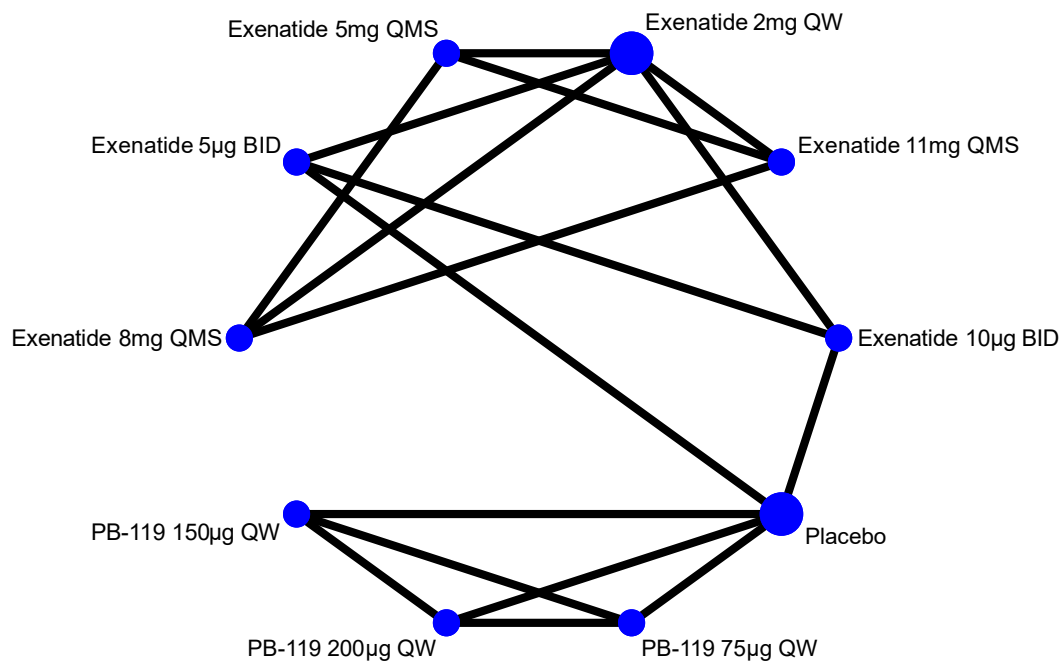
(A2) Forest plot of HbA1c



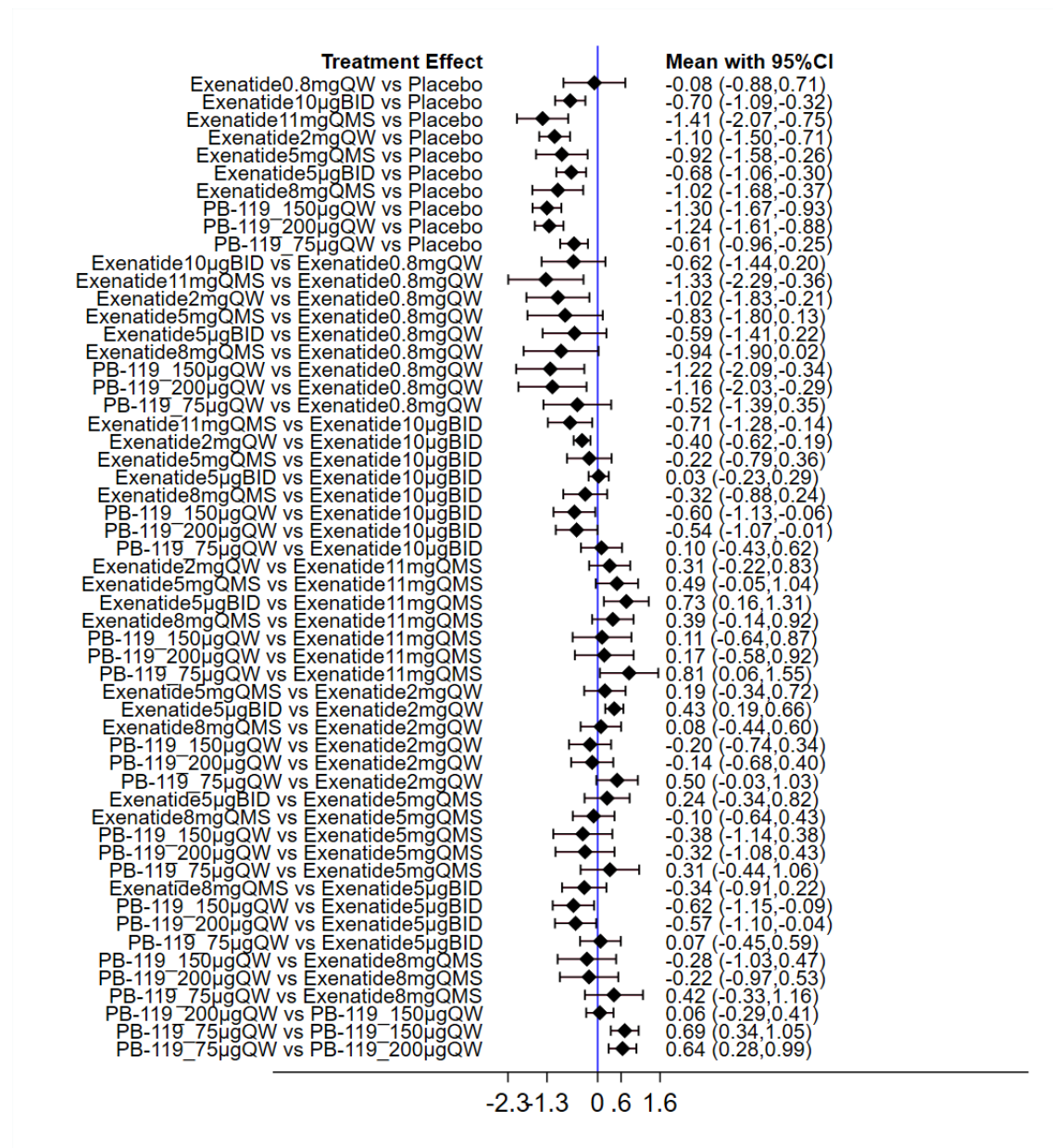
(A3) League table of HbA1c

PB-119 150µg QW	0.22 (- 0.84,1.28)	0.28 (- 1.03,1.59)	0.29 (- 0.65,1.23)	0.33 (- 0.73,1.39)	0.31 (- 1.00,1.62)	0.41 (- 0.67,1.48)	0.44 (- 0.50,1.38)	0.50 (- 1.01,2.00)	0.64 (- 0.95,2.22)	0.66 (- 0.87,2.18)	0.73 (- 0.59,2.06)	1.21 (0.27,2.15)
-0.22 (- 1.28,0.84)	Exenatide 10µg BID	0.06 (- 0.97,1.10)	0.07 (- 0.98,1.12)	0.11 (- 0.39,0.61)	0.09 (- 0.95,1.14)	0.19 (- 0.39,0.76)	0.22 (- 0.83,1.27)	0.28 (- 0.93,1.48)	0.42 (- 0.89,1.72)	0.44 (- 0.78,1.66)	0.51 (- 0.51,1.53)	0.99 (0.50,1.48)
-0.28 (- 1.59,1.03)	-0.06 (- 1.10,0.97)	ITCA650 40µg QD	0.01 (- 1.29,1.31)	0.05 (- 0.98,1.08)	0.03 (- 0.88,0.94)	0.13 (- 0.93,1.18)	0.16 (- 1.14,1.46)	0.22 (- 1.27,1.71)	0.36 (- 1.22,1.93)	0.38 (- 1.13,1.88)	0.45 (- 0.85,1.76)	0.93 (0.02,1.84)
-0.29 (- 1.23,0.65)	-0.07 (- 1.12,0.98)	-0.01 (- 1.31,1.29)	PB-119 200µgQW	0.04 (- 1.01,1.09)	0.02 (- 1.28,1.32)	0.12 (- 0.95,1.18)	0.15 (- 0.78,1.08)	0.21 (- 1.29,1.70)	0.35 (- 1.24,1.93)	0.37 (- 1.15,1.88)	0.44 (- 0.87,1.76)	0.92 (- 0.00,1.84)
-0.33 (- 1.39,0.73)	-0.11 (- 0.61,0.39)	-0.05 (- 1.08,0.98)	-0.04 (- 1.09,1.01)	Exenatide 5µg BID	-0.02 (- 1.06,1.02)	0.08 (- 0.50,0.65)	0.11 (- 0.94,1.16)	0.17 (- 1.04,1.37)	0.31 (- 1.00,1.61)	0.33 (- 0.90,1.55)	0.40 (- 0.62,1.42)	0.88 (0.39,1.37)
-0.31 (- 1.62,1.00)	-0.09 (- 1.14,0.95)	-0.03 (- 0.94,0.88)	-0.02 (- 1.32,1.28)	0.02 (- 1.02,1.06)	ITCA650 60µg QD	0.10 (- 0.97,1.16)	0.13 (- 1.18,1.44)	0.19 (- 1.31,1.68)	0.33 (- 1.25,1.90)	0.35 (- 1.17,1.86)	0.42 (- 0.89,1.74)	0.90 (- 0.02,1.82)
-0.41 (- 1.48,0.67)	-0.19 (- 0.76,0.39)	-0.13 (- 1.18,0.93)	-0.12 (- 1.18,0.95)	-0.08 (- 0.65,0.50)	-0.10 (- 1.16,0.97)	Exenatide 2mg QW	0.03 (- 1.03,1.10)	0.09 (- 0.96,1.14)	0.23 (- 0.94,1.40)	0.25 (- 0.83,1.33)	0.33 (- 0.63,1.29)	0.80 (0.28,1.33)
-0.44 (- 1.38,0.50)	-0.22 (- 1.27,0.83)	-0.16 (- 1.46,1.14)	-0.15 (- 1.08,0.78)	-0.11 (- 1.16,0.94)	-0.13 (- 1.44,1.18)	-0.03 (- 1.10,1.03)	PB-119 75µg QW	0.06 (- 1.44,1.55)	0.20 (- 1.39,1.78)	0.22 (- 1.30,1.73)	0.29 (- 1.02,1.61)	0.77 (- 0.16,1.70)
-0.50 (- 2.00,1.01)	-0.28 (- 1.48,0.93)	-0.22 (- 1.71,1.27)	-0.21 (- 1.70,1.29)	-0.17 (- 1.37,1.04)	-0.19 (- 1.68,1.31)	-0.09 (- 1.14,0.96)	-0.06 (- 1.55,1.44)	Exenatide 11mg QMS	0.14 (- 0.99,1.27)	0.16 (- 0.88,1.20)	0.24 (- 1.19,1.66)	0.71 (- 0.47,1.89)
-0.64 (- 2.22,0.95)	-0.42 (- 1.72,0.89)	-0.36 (- 1.93,1.22)	-0.35 (- 1.93,1.24)	-0.31 (- 1.61,1.00)	-0.33 (- 1.90,1.25)	-0.23 (- 1.40,0.94)	-0.20 (- 1.78,1.39)	-0.14 (- 1.27,0.99)	Exenatide 8mg QMS	0.02 (- 1.13,1.17)	0.10 (- 1.42,1.61)	0.57 (- 0.71,1.86)
-0.66 (- 2.18,0.87)	-0.44 (- 1.66,0.78)	-0.38 (- 1.88,1.13)	-0.37 (- 1.88,1.15)	-0.33 (- 1.55,0.90)	-0.35 (- 1.86,1.17)	-0.25 (- 1.33,0.83)	-0.22 (- 1.73,1.30)	-0.16 (- 1.20,0.88)	-0.02 (- 1.17,1.13)	Exenatide 5mg QMS	0.08 (- 1.37,1.52)	0.55 (- 0.64,1.75)
-0.73 (- 2.06,0.59)	-0.51 (- 1.53,0.51)	-0.45 (- 1.76,0.85)	-0.44 (- 1.76,0.87)	-0.40 (- 1.42,0.62)	-0.42 (- 1.74,0.89)	-0.33 (- 1.29,0.63)	-0.29 (- 1.61,1.02)	-0.24 (- 1.66,1.19)	-0.10 (- 1.61,1.42)	-0.08 (- 1.52,1.37)	Exenatide0. 8mgQW	0.48 (- 0.46,1.41)
-1.21 (- 2.15,-0.27)	-0.99 (- 1.48,-0.50)	-0.93 (- 1.84,-0.02)	-0.92 (- 1.84,0.00)	-0.88 (- 1.37,-0.39)	-0.90 (- 1.82,0.02)	-0.80 (- 1.33,-0.28)	-0.77 (- 1.70,0.16)	-0.71 (- 1.89,0.47)	-0.57 (- 1.86,0.71)	-0.55 (- 1.75,0.64)	-0.48 (- 1.41,0.46)	Placebo

(B1) Network map of FPG



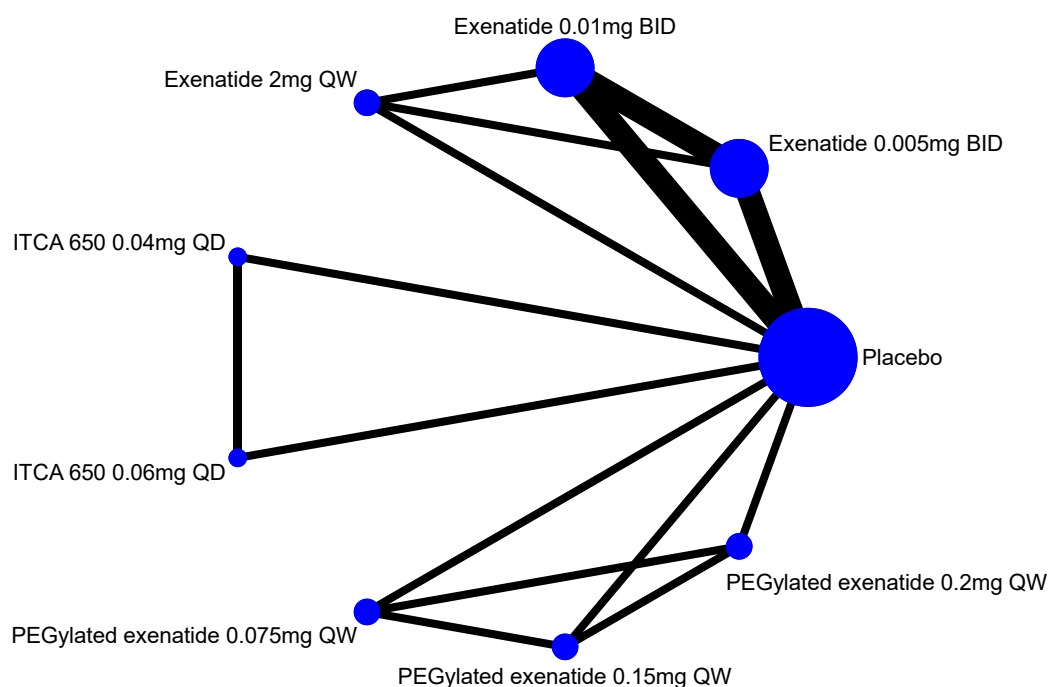
(B2) Forest plot of FPG



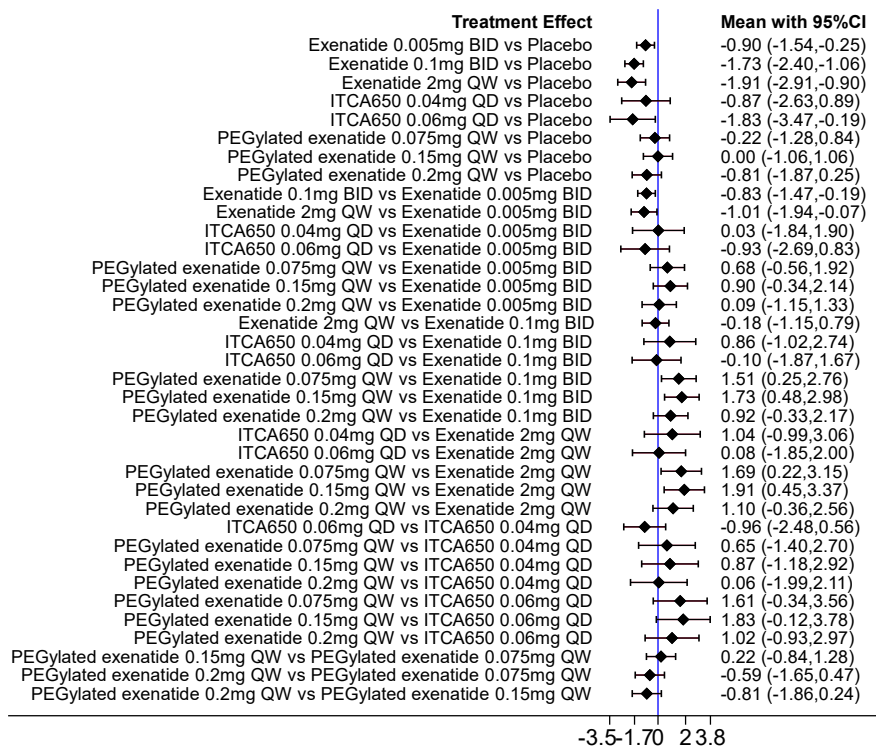
(B3) League table of FPG

Exenatide 11mg QMS	0.11 (-0.64,0.87)	0.17 (-0.58,0.92)	0.31 (-0.22,0.83)	0.39 (-0.14,0.92)	0.49 (-0.05,1.04)	0.71 (0.14,1.28)	0.73 (0.16,1.31)	0.81 (0.06,1.55)	1.33 (0.36,2.29)	1.41 (0.75,2.07)
-0.11 (-0.87,0.64)	PB-119 150µg QW	0.06 (-0.29,0.41)	0.20 (-0.34,0.74)	0.28 (-0.47,1.03)	0.38 (-0.38,1.14)	0.60 (0.06,1.13)	0.62 (0.09,1.15)	0.69 (0.34,1.05)	1.22 (0.34,2.09)	1.30 (0.93,1.67)
-0.17 (-0.92,0.58)	-0.06 (-0.41,0.29)	PB-119 200µg QW	0.14 (-0.40,0.68)	0.22 (-0.53,0.97)	0.32 (-0.43,1.08)	0.54 (0.01,1.07)	0.57 (0.04,1.10)	0.64 (0.28,0.99)	1.16 (0.29,2.03)	1.24 (0.88,1.61)
-0.31 (-0.83,0.22)	-0.20 (-0.74,0.34)	-0.14 (-0.68,0.40)	Exenatide 2mg QW	0.08 (-0.44,0.60)	0.19 (-0.34,0.72)	0.40 (0.19,0.62)	0.43 (0.19,0.66)	0.50 (-0.03,1.03)	1.02 (0.21,1.83)	1.10 (0.71,1.50)
-0.39 (-0.92,0.14)	-0.28 (-1.03,0.47)	-0.22 (-0.97,0.53)	-0.08 (-0.60,0.44)	Exenatide 8mg QMS	0.10 (-0.43,0.64)	0.32 (-0.24,0.88)	0.34 (-0.22,0.91)	0.42 (-0.33,1.16)	0.94 (0.02,1.90)	1.02 (0.37,1.68)
-0.49 (-1.04,0.05)	-0.38 (-1.14,0.38)	-0.32 (-1.08,0.43)	-0.19 (-0.72,0.34)	-0.10 (-0.64,0.43)	Exenatide 5mg QMS	0.22 (-0.36,0.79)	0.24 (-0.34,0.82)	0.31 (-0.44,1.06)	0.83 (0.13,1.80)	0.92 (0.26,1.58)
-0.71 (-1.28,-0.14)	-0.60 (-1.13,-0.06)	-0.54 (-1.07,-0.01)	-0.40 (-0.62,-0.19)	-0.32 (-0.88,0.24)	-0.22 (-0.79,0.36)	Exenatide 10µg BID	0.03 (-0.23,0.29)	0.10 (-0.43,0.62)	0.62 (0.20,1.44)	0.70 (0.32,1.09)
-0.73 (-1.31,-0.16)	-0.62 (-1.15,-0.09)	-0.57 (-1.10,-0.04)	-0.43 (-0.66,-0.19)	-0.34 (-0.91,0.22)	-0.24 (-0.82,0.34)	-0.03 (-0.29,0.23)	Exenatide 5µg BID	0.07 (-0.45,0.59)	0.59 (0.22,1.41)	0.68 (0.30,1.06)
-0.81 (-1.55,-0.06)	-0.69 (-1.05,-0.34)	-0.64 (-0.99,-0.28)	-0.50 (-1.03,0.03)	-0.42 (-1.16,0.33)	-0.31 (-1.06,0.44)	-0.10 (-0.62,0.43)	-0.07 (-0.59,0.45)	PB-119 75µg QW	0.52 (0.35,1.39)	0.61 (0.25,0.96)
-1.33 (-2.29,-0.36)	-1.22 (-2.09,-0.34)	-1.16 (-2.03,-0.29)	-1.02 (-1.83,-0.21)	-0.94 (-1.90,0.02)	-0.83 (-1.80,0.13)	-0.62 (-1.44,0.20)	-0.59 (-1.41,0.22)	-0.52 (-1.39,0.35)	Exenatide 0.8mg QW	0.08 (-0.71,0.88)
-1.41 (-2.07,-0.75)	-1.30 (-1.67,-0.93)	-1.24 (-1.61,-0.88)	-1.10 (-1.50,-0.71)	-1.02 (-1.68,-0.37)	-0.92 (-1.58,-0.26)	-0.70 (-1.09,-0.32)	-0.68 (-1.06,-0.30)	-0.61 (-0.96,-0.25)	-0.08 (-0.88,0.71)	Placebo

(C1) Network map of weight loss



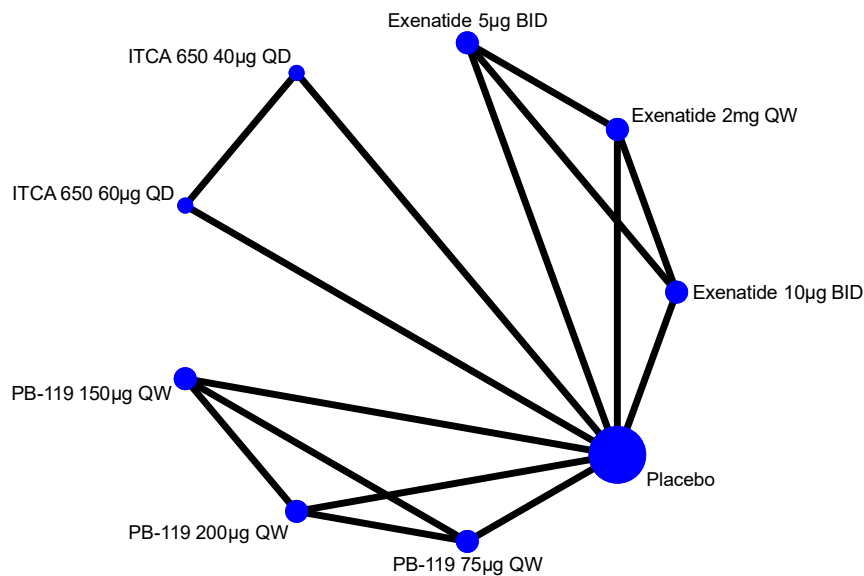
(C2) Forest plot of weight loss



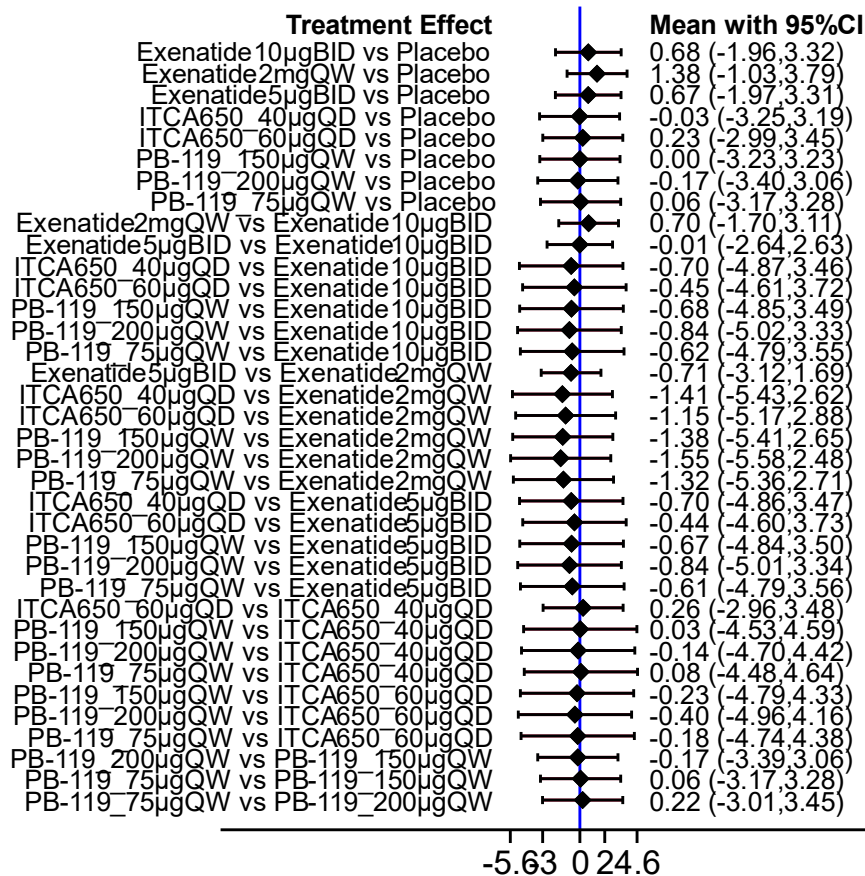
(C3) League table of weight loss

Exenatide 2mg QW	0.18 (-0.79,1.15)	0.08 (-1.85,2.00)	1.01 (0.07,1.94)	1.10 (-0.36,2.56)	1.04 (-0.99,3.06)	1.69 (0.22,3.15)	1.91 (0.45,3.37)	1.91 (0.90,2.91)
-0.18 (-1.15,0.79)	Exenatide 10µg BID	-0.10 (-1.87,1.67)	0.83 (0.19,1.47)	0.92 (-0.33,2.17)	0.86 (-1.02,2.74)	1.51 (0.25,2.76)	1.73 (0.48,2.98)	1.73 (1.06,2.40)
-0.08 (-2.00,1.85)	0.10 (-1.67,1.87)	ITCA 650 60µg QD	0.93 (-0.83,2.69)	1.02 (-0.93,2.97)	0.96 (-0.56,2.48)	1.61 (-0.34,3.56)	1.83 (-0.12,3.78)	1.83 (0.19,3.47)
-1.01 (-1.94,-0.07)	-0.83 (-1.47,-0.19)	-0.93 (-2.69,0.83)	Exenatide 5µg BID	0.09 (-1.15,1.33)	0.03 (-1.84,1.90)	0.68 (-0.56,1.92)	0.90 (-0.34,2.14)	0.90 (0.25,1.54)
-1.10 (-2.56,0.36)	-0.92 (-2.17,0.33)	-1.02 (-2.97,0.93)	-0.09 (-1.33,1.15)	PB-119 200µg QW	-0.06 (-2.11,1.99)	0.59 (-0.47,1.65)	0.81 (-0.24,1.86)	0.81 (-0.25,1.87)
-1.04 (-3.06,0.99)	-0.86 (-2.74,1.02)	-0.96 (-2.48,0.56)	-0.03 (-1.90,1.84)	0.06 (-1.99,2.11)	ITCA 650 40µg QD	0.65 (-1.40,2.70)	0.87 (-1.18,2.92)	0.87 (-0.89,2.63)
-1.69 (-3.15,-0.22)	-1.51 (-2.76,-0.25)	-1.61 (-3.56,0.34)	-0.68 (-1.92,0.56)	-0.59 (-1.65,0.47)	-0.65 (-2.70,1.40)	PB-119 75µg QW	0.22 (-0.84,1.28)	0.22 (-0.84,1.28)
-1.91 (-3.37,-0.45)	-1.73 (-2.98,-0.48)	-1.83 (-3.78,0.12)	-0.90 (-2.14,0.34)	-0.81 (-1.86,0.24)	-0.87 (-2.92,1.18)	-0.22 (-1.28,0.84)	PB-119 150µg QW	-0.00 (-1.06,1.06)
-1.91 (-2.91,-0.90)	-1.73 (-2.40,-1.06)	-1.83 (-3.47,-0.19)	-0.90 (-1.54,-0.25)	-0.81 (-1.87,0.25)	-0.87 (-2.63,0.89)	-0.22 (-1.28,0.84)	0.00 (-1.06,1.06)	Placebo

(D1) Network map of HDL



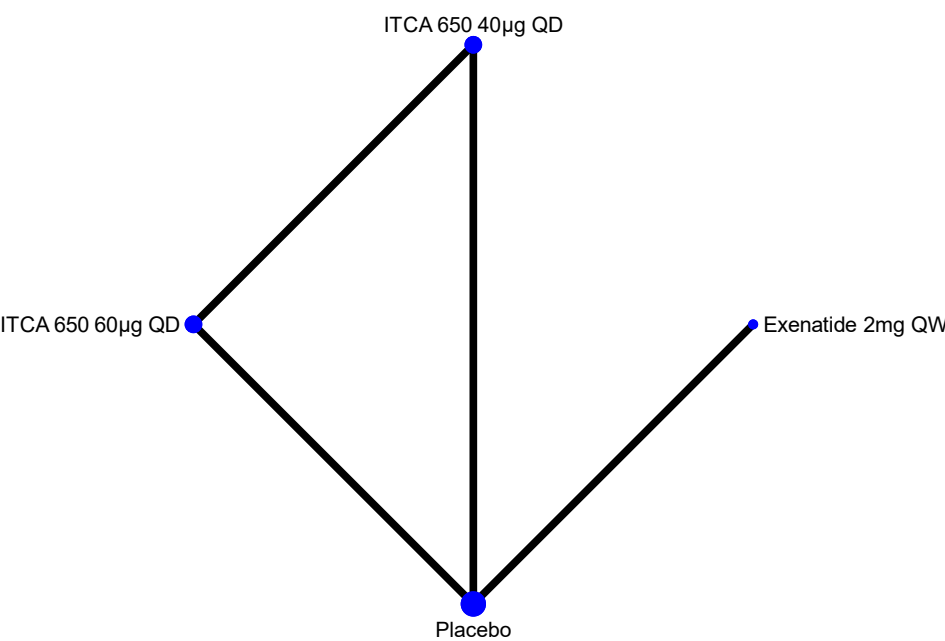
(D2) Forest plot of HDL



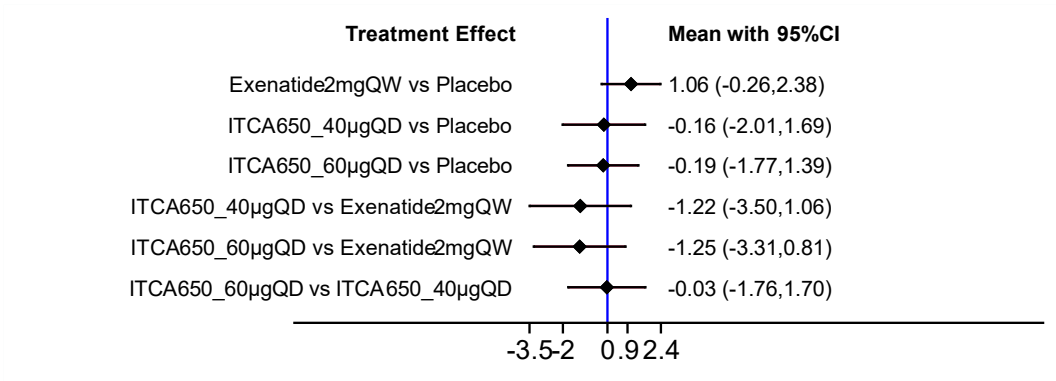
(D3) League table of HDL

Exenatide 2mg QW	-0.71 (- 3.11,1.68)	-0.70 (- 3.09,1.69)	-1.15 (- 5.15,2.86)	-1.32 (- 5.33,2.69)	-1.38 (- 5.39,2.63)	-1.40 (- 5.41,2.60)	-1.38 (- 3.78,1.02)	-1.54 (- 5.56,2.47)
0.71 (- 1.68,3.11)	Exenatide 5µg BID	0.01 (- 2.61,2.63)	-0.44 (- 4.58,3.71)	-0.61 (- 4.76,3.54)	-0.67 (- 4.82,3.49)	-0.69 (- 4.84,3.45)	-0.67 (- 3.30,1.96)	-0.83 (- 4.99,3.32)
0.70 (- 1.69,3.09)	-0.01 (- 2.63,2.61)	Exenatide 10µg BID	-0.44 (- 4.58,3.70)	-0.62 (- 4.77,3.53)	-0.67 (- 4.82,3.47)	-0.70 (- 4.84,3.44)	-0.68 (- 3.30,1.95)	-0.84 (- 4.99,3.31)
1.15 (- 2.86,5.15)	0.44 (- 3.71,4.58)	0.44 (- 3.70,4.58)	ITCA 650 60µg QD	-0.18 (- 4.72,4.36)	-0.23 (- 4.77,4.31)	-0.26 (- 3.46,2.95)	-0.23 (- 3.44,2.97)	-0.40 (- 4.94,4.14)
1.32 (- 2.69,5.33)	0.61 (- 3.54,4.76)	0.62 (- 3.53,4.77)	0.18 (- 4.36,4.72)	PB-119 75µg QW	-0.06 (- 3.27,3.16)	-0.08 (- 4.62,4.46)	-0.06 (- 3.27,3.16)	-0.22 (- 3.44,2.99)
1.38 (- 2.63,5.39)	0.67 (- 3.49,4.82)	0.67 (- 3.47,4.82)	0.23 (- 4.31,4.77)	0.06 (- 3.16,3.27)	PB-119 150µg QW	-0.03 (- 4.57,4.51)	-0.00 (- 3.22,3.21)	-0.17 (- 3.38,3.05)
1.40 (- 2.60,5.41)	0.69 (- 3.45,4.84)	0.70 (- 3.44,4.84)	0.26 (- 2.95,3.46)	0.08 (- 4.46,4.62)	0.03 (- 4.51,4.57)	ITCA 650 40µg QD	0.02 (- 3.18,3.23)	-0.14 (- 4.68,4.40)
1.38 (- 1.02,3.78)	0.67 (- 1.96,3.30)	0.68 (- 1.95,3.30)	0.23 (- 2.97,3.44)	0.06 (- 3.16,3.27)	0.00 (- 3.21,3.22)	-0.02 (- 3.23,3.18)	Placebo	-0.17 (- 3.38,3.05)
1.54 (- 2.47,5.56)	0.83 (- 3.32,4.99)	0.84 (- 3.31,4.99)	0.40 (- 4.14,4.94)	0.22 (- 2.99,3.44)	0.17 (- 3.05,3.38)	0.14 (- 4.40,4.68)	0.17 (- 3.05,3.38)	PB-119 200µg QW

(E1) Network map of LDL



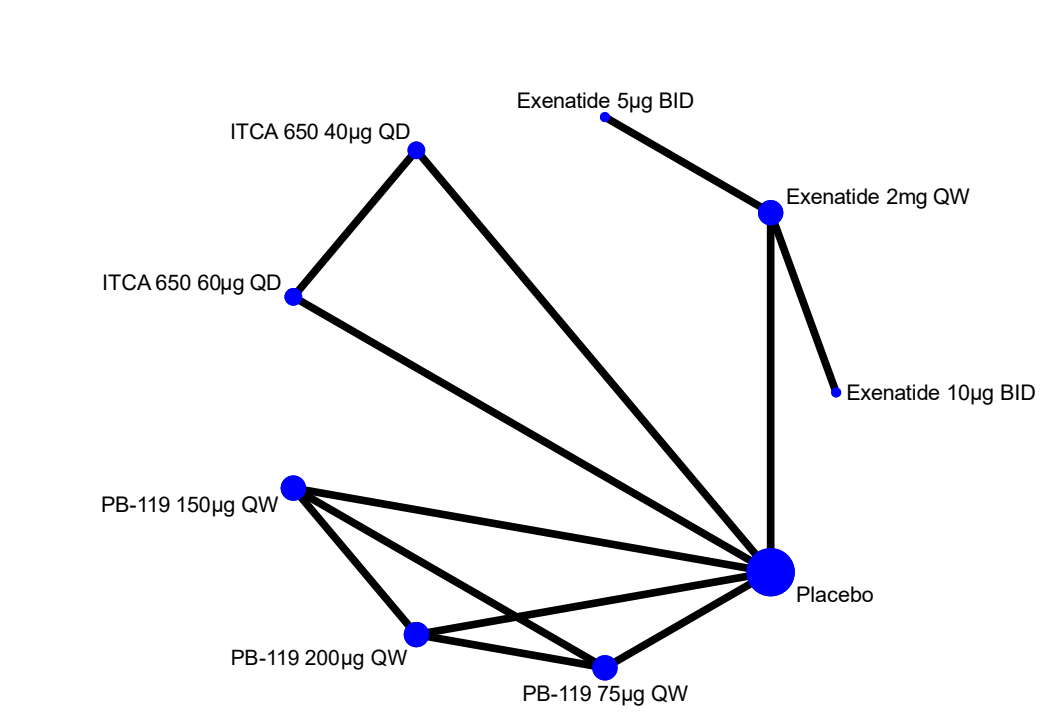
(E2) Forest plot of LDL



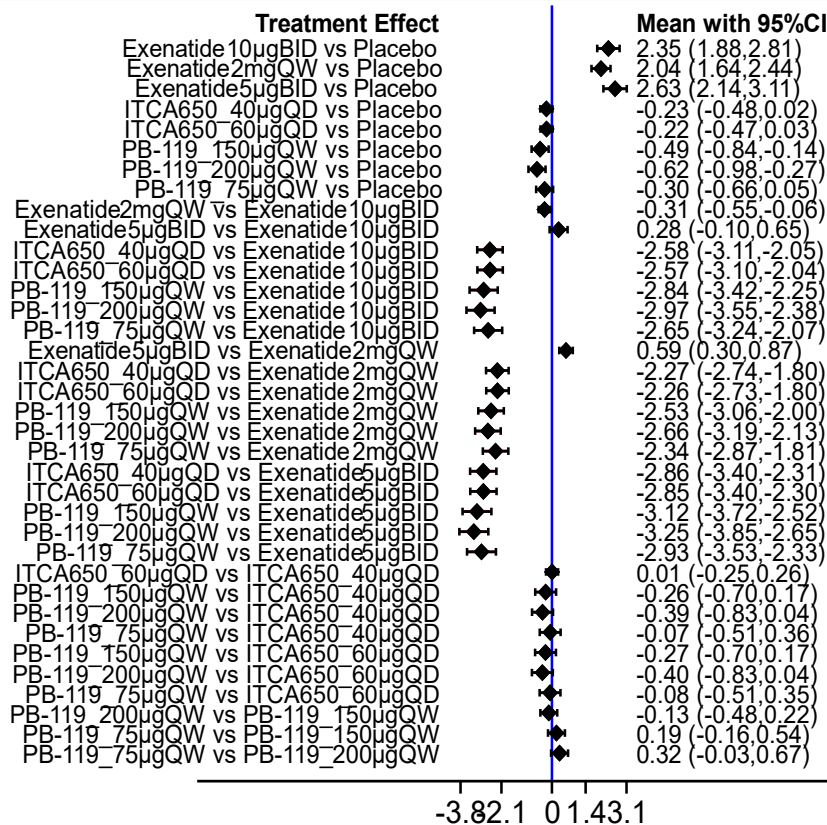
(E3) League table of LDL

ITCA 650 60µg QD	0.03 (- 0.22,0.28)	0.19 (- 0.06,0.44)	1.25 (0.82,1.67)
-0.03 (- 0.28,0.22)	ITCA 650 40µg QD	0.16 (- 0.09,0.41)	1.22 (0.79,1.65)
-0.19 (- 0.44,0.06)	-0.16 (- 0.41,0.09)	Placebo	1.06 (0.71,1.41)
-1.25 (- 1.67,-0.82)	-1.22 (- 1.65,-0.79)	-1.06 (- 1.41,-0.71)	Exenatide 2mg QW

(F1) Network map of TC



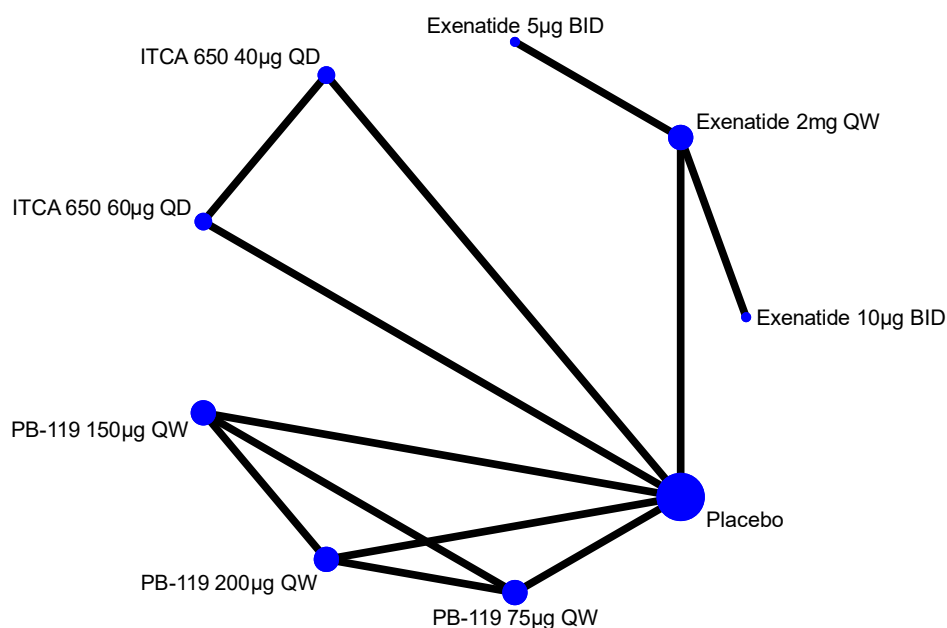
(F2) Forest plot of TC



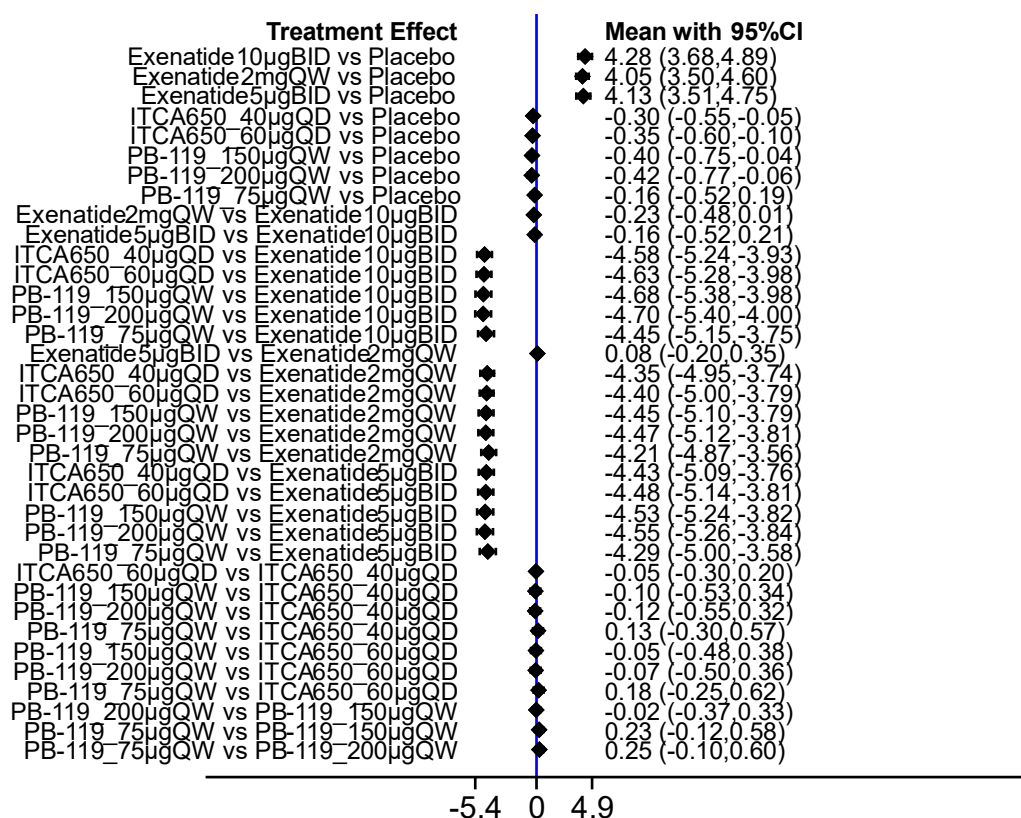
(F3) League table of TC

PB-119 200µg QW	0.13 (- 0.22,0.48)	0.32 (- 0.03,0.67)	0.39 (- 0.04,0.83)	0.40 (- 0.04,0.83)	0.62 (0.27,0.98)	2.66 (2.13,3.19)	2.97 (2.38,3.55)	3.25 (2.64,3.85)
-0.13 (- 0.48,0.22)	PB-119 150µg QW	0.19 (- 0.16,0.54)	0.26 (- 0.17,0.70)	0.27 (- 0.17,0.70)	0.49 (0.14,0.84)	2.53 (2.00,3.06)	2.84 (2.25,3.42)	3.12 (2.51,3.72)
-0.32 (- 0.67,0.03)	-0.19 (- 0.54,0.16)	PB-119 75µg QW	0.07 (- 0.36,0.51)	0.08 (- 0.35,0.51)	0.30 (- 0.05,0.66)	2.34 (1.81,2.87)	2.65 (2.07,3.23)	2.93 (2.33,3.53)
-0.39 (- 0.83,0.04)	-0.26 (- 0.70,0.17)	-0.07 (- 0.51,0.36)	ITCA 650 40µg QD	0.01 (- 0.25,0.26)	0.23 (- 0.02,0.48)	2.27 (1.80,2.74)	2.58 (2.05,3.11)	2.85 (2.31,3.40)
-0.40 (- 0.83,0.04)	-0.27 (- 0.70,0.17)	-0.08 (- 0.51,0.35)	-0.01 (- 0.26,0.25)	ITCA 650 60µg QD	0.22 (- 0.03,0.47)	2.26 (1.79,2.73)	2.57 (2.04,3.10)	2.85 (2.30,3.40)
-0.62 (- 0.98,-0.27)	-0.49 (- 0.84,-0.14)	-0.30 (- 0.66,0.05)	-0.23 (- 0.48,0.02)	-0.22 (- 0.47,0.03)	Placebo	2.04 (1.64,2.44)	2.35 (1.88,2.81)	2.62 (2.14,3.11)
-2.66 (- 3.19,-2.13)	-2.53 (- 3.06,-2.00)	-2.34 (- 2.87,-1.81)	-2.27 (- 2.74,-1.80)	-2.26 (- 2.73,-1.79)	-2.04 (- 2.44,-1.64)	Exenatide 2mg QW	0.31 (0.06,0.55)	0.59 (0.30,0.87)
-2.97 (- 3.55,-2.38)	-2.84 (- 3.42,-2.25)	-2.65 (- 3.23,-2.07)	-2.58 (- 3.11,-2.05)	-2.57 (- 3.10,-2.04)	-2.35 (- 2.81,-1.88)	-0.31 (- 0.55,-0.06)	Exenatide 10µg BID	0.28 (- 0.10,0.65)
-3.25 (- 3.85,-2.64)	-3.12 (- 3.72,-2.51)	-2.93 (- 3.53,-2.33)	-2.85 (- 3.40,-2.31)	-2.85 (- 3.40,-2.30)	-2.62 (- 3.11,-2.14)	-0.59 (- 0.87,-0.30)	-0.28 (- 0.65,0.10)	Exenatide 5µg BID

(G1) Network map of TG



(G2) Forest plot of TG



(G3) League table of TG

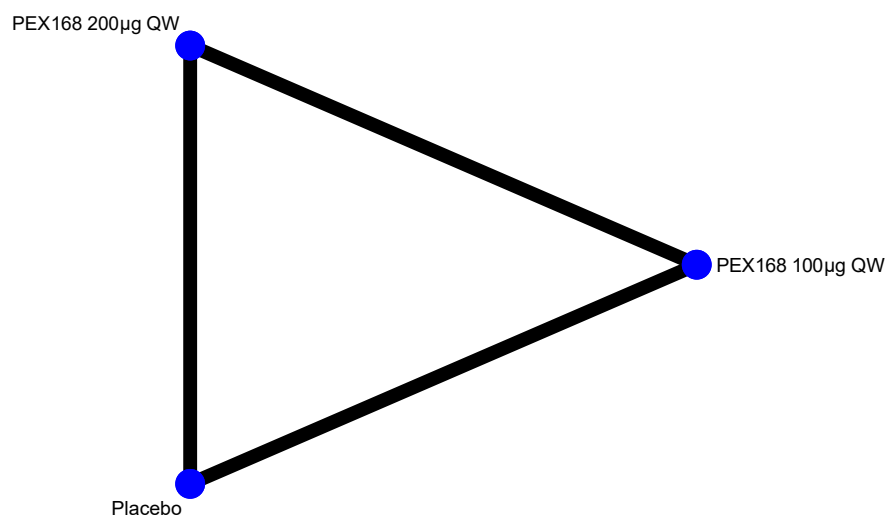
PB-119 200µg QW	0.02 (- 0.33,0.37)	0.07 (- 0.36,0.50)	0.12 (- 0.32,0.55)	0.25 (- 0.10,0.60)	0.42 (0.06,0.77)	4.47 (3.81,5.12)	4.54 (3.83,5.26)	4.70 (4.00,5.40)
-0.02 (- 0.37,0.33)	PB-119 150µg QW	0.05 (- 0.38,0.48)	0.10 (- 0.34,0.53)	0.23 (- 0.12,0.58)	0.40 (0.04,0.75)	4.44 (3.79,5.10)	4.52 (3.81,5.24)	4.68 (3.98,5.38)
-0.07 (- 0.50,0.36)	-0.05 (- 0.48,0.38)	ITCA 650 60µg QD	0.05 (- 0.20,0.30)	0.18 (- 0.25,0.62)	0.35 (0.10,0.60)	4.40 (3.79,5.00)	4.48 (3.81,5.14)	4.63 (3.98,5.28)
-0.12 (- 0.55,0.32)	-0.10 (- 0.53,0.34)	-0.05 (- 0.30,0.20)	ITCA 650 40µg QD	0.13 (- 0.30,0.57)	0.30 (0.05,0.55)	4.35 (3.74,4.95)	4.43 (3.76,5.09)	4.58 (3.93,5.24)
-0.25 (- 0.60,0.10)	-0.23 (- 0.58,0.12)	-0.18 (- 0.62,0.25)	-0.13 (- 0.57,0.30)	PB-119 75µg QW	0.16 (- 0.19,0.52)	4.21 (3.56,4.87)	4.29 (3.58,5.00)	4.45 (3.75,5.15)
-0.42 (-0.77,- 0.06)	-0.40 (-0.75,- 0.04)	-0.35 (-0.60,- 0.10)	-0.30 (-0.55,- 0.05)	-0.16 (- 0.52,0.19)	Placebo	4.05 (3.50,4.60)	4.13 (3.51,4.75)	4.28 (3.68,4.89)
-4.47 (-5.12,- 3.81)	-4.44 (-5.10,- 3.79)	-4.40 (-5.00,- 3.79)	-4.35 (-4.95,- 3.74)	-4.21 (-4.87,- 3.56)	-4.05 (-4.60,- 3.50)	Exenatide 2mg QW	0.08 (- 0.20,0.35)	0.23 (- 0.01,0.48)
-4.54 (-5.26,- 3.83)	-4.52 (-5.24,- 3.81)	-4.48 (-5.14,- 3.81)	-4.43 (-5.09,- 3.76)	-4.29 (-5.00,- 3.58)	-4.13 (-4.75,- 3.51)	-0.08 (- 0.35,0.20)	Exenatide 5µg BID	0.15 (- 0.21,0.52)
-4.70 (-5.40,- 4.00)	-4.68 (-5.38,- 3.98)	-4.63 (-5.28,- 3.98)	-4.58 (-5.24,- 3.93)	-4.45 (-5.15,- 3.75)	-4.28 (-4.89,- 3.68)	-0.23 (- 0.48,0.01)	-0.15 (- 0.52,0.21)	Exenatide 10µg BID

Abbreviations: FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

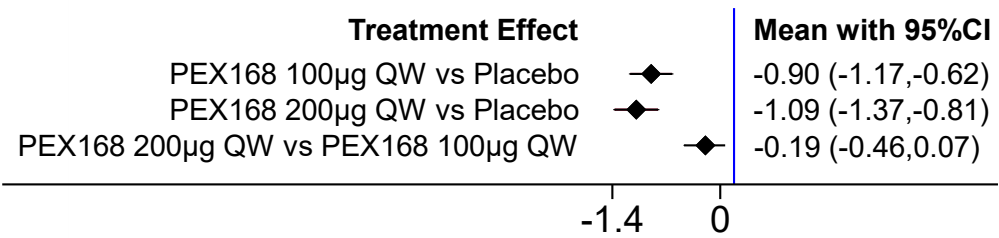
Figure S14.6: Effects of different doses of PEX168 on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of PEX168 on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) HDL, (E) LDL, (F) TC, (G) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



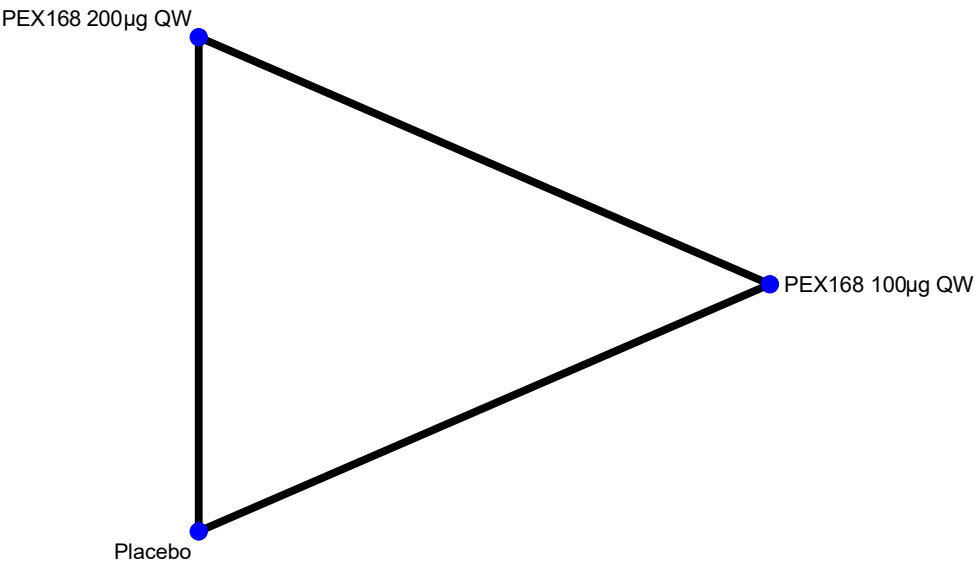
(A2) Forest plot of HbA1c



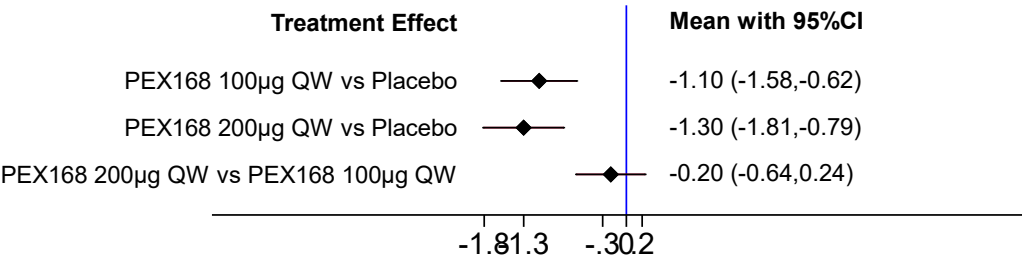
(A3) League table of HbA1c

PEX168 200µg QW	0.19 (-0.07,0.46)	1.09 (0.81,1.37)
-0.19 (-0.46,0.07)	PEX168 100µg QW	0.90 (0.62,1.17)
-1.09 (-1.37,-0.81)	-0.90 (-1.17,-0.62)	Placebo

(B1) Network map of FPG



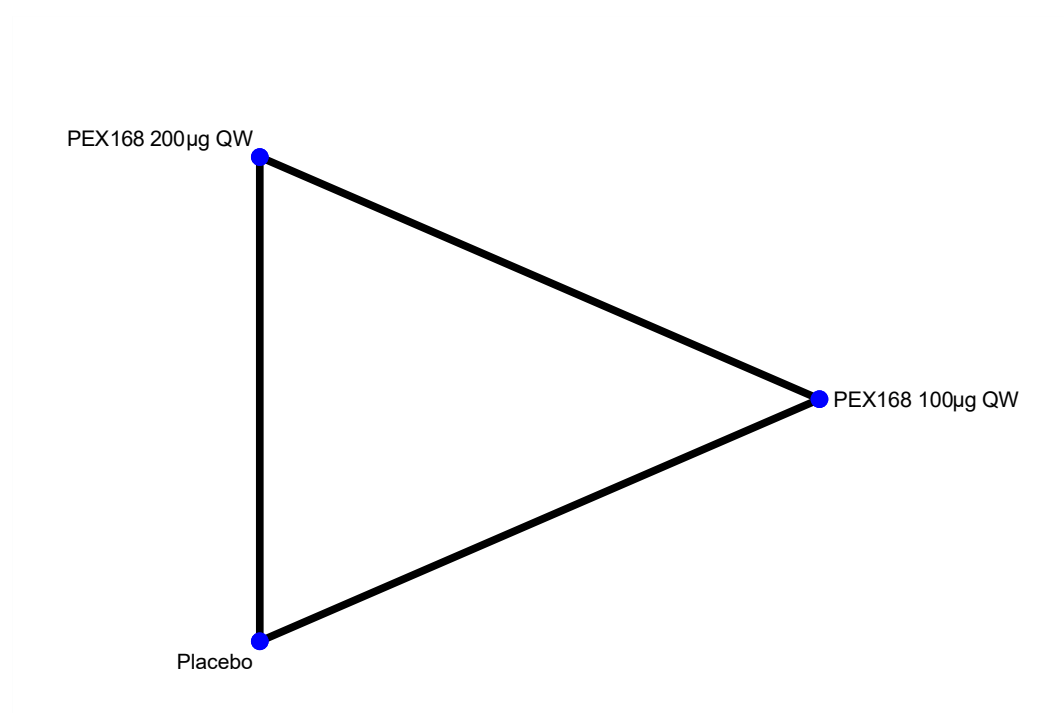
(B2) Forest plot of FPG



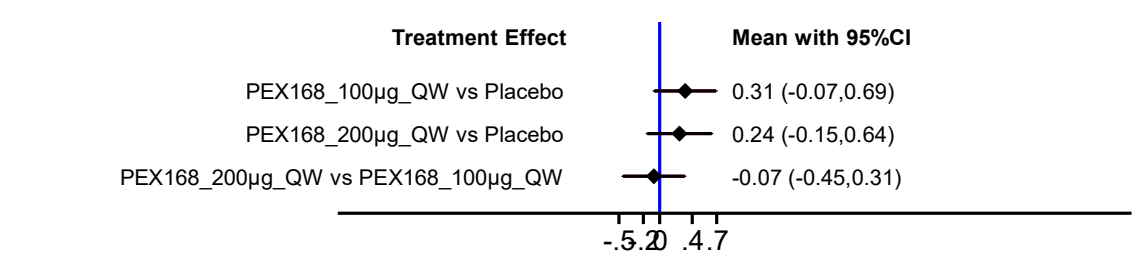
(B3) League table of FPG

PEX168 200µg QW	0.20 (-0.24,0.64)	1.30 (0.79,1.81)
-0.20 (-0.64,0.24)	PEX168 100µg QW	1.10 (0.62,1.58)
-1.30 (-1.81,-0.79)	-1.10 (-1.58,-0.62)	Placebo

(C1) Network map of weight loss



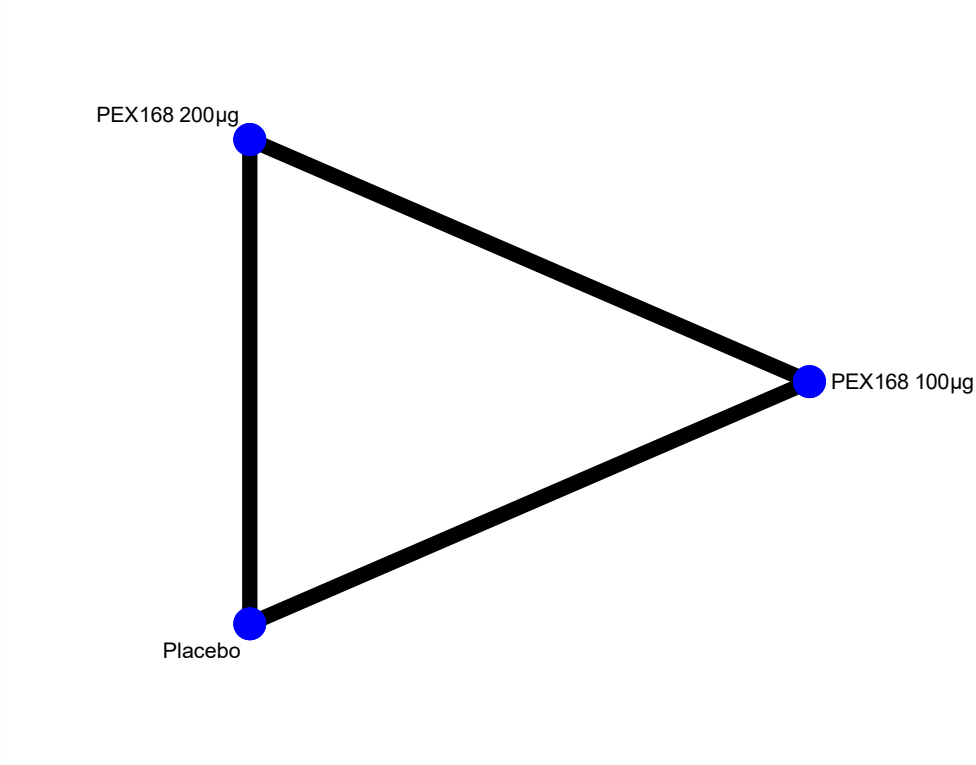
(C2) Forest plot of weight loss



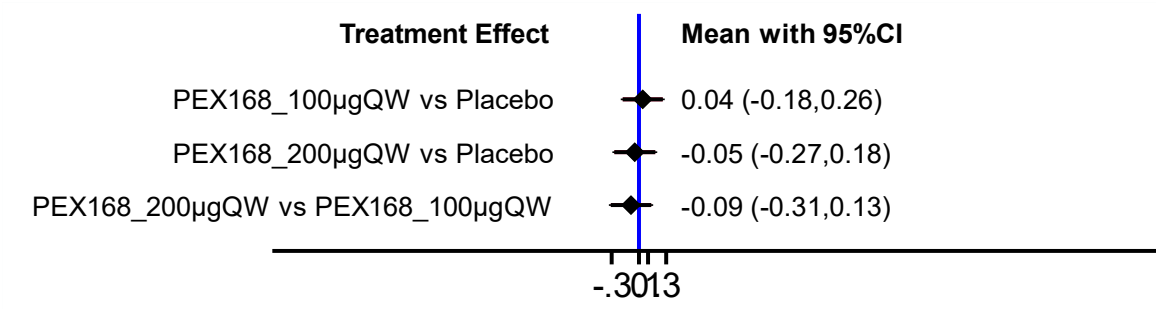
(C3) League table of weight loss

Placebo	0.24 (-0.15,0.64)	0.31 (-0.07,0.69)
-0.24 (-0.64,0.15)	PEX168 200µg QW	0.07 (-0.31,0.45)
-0.31 (-0.69,0.07)	-0.07 (-0.45,0.31)	PEX168 100µg QW

(D1) Network map of HDL



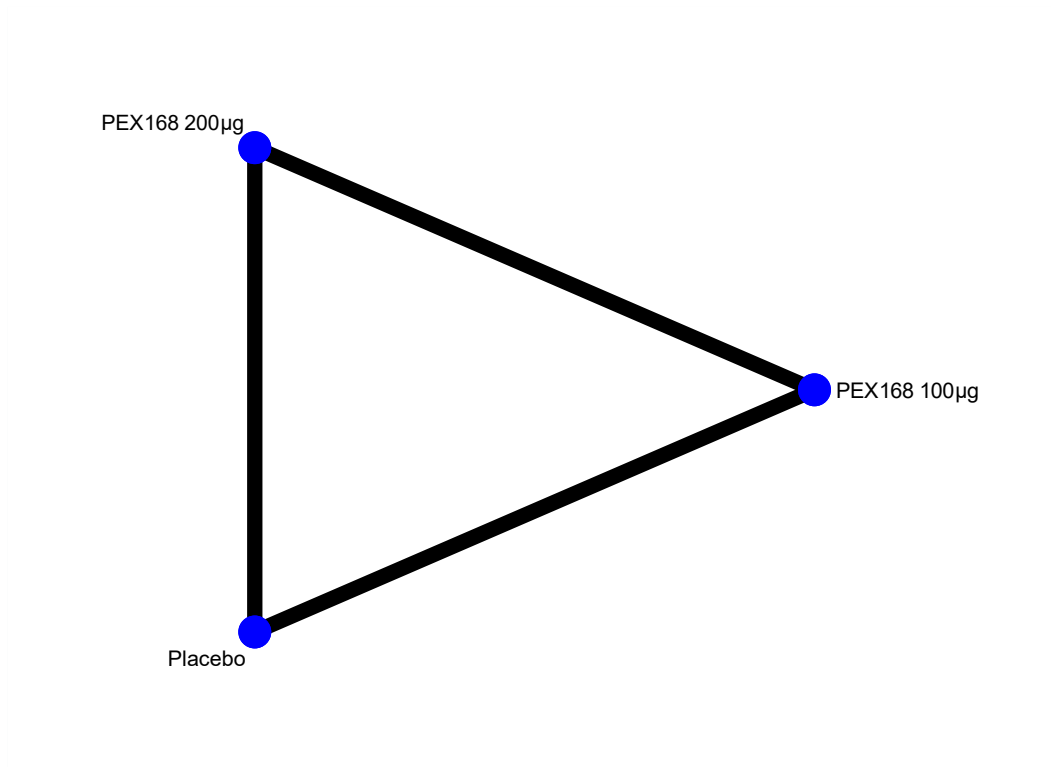
(D2) Forest plot of HDL



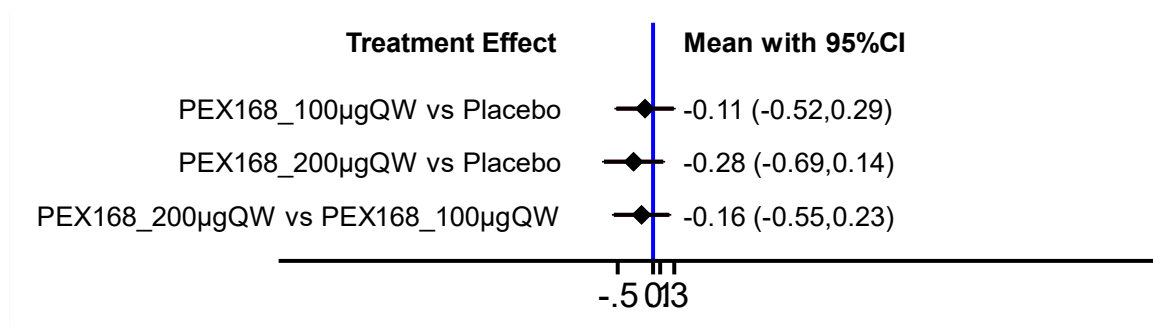
(D3) League table of HDL

PEX168 100µg QW	-0.04 (- 0.26,0.18)	-0.09 (- 0.31,0.13)
0.04 (- 0.18,0.26)	Placebo	-0.05 (- 0.27,0.18)
0.09 (- 0.13,0.31)	0.05 (- 0.18,0.27)	PEX168 200µg QW

(E1) Network map of LDL



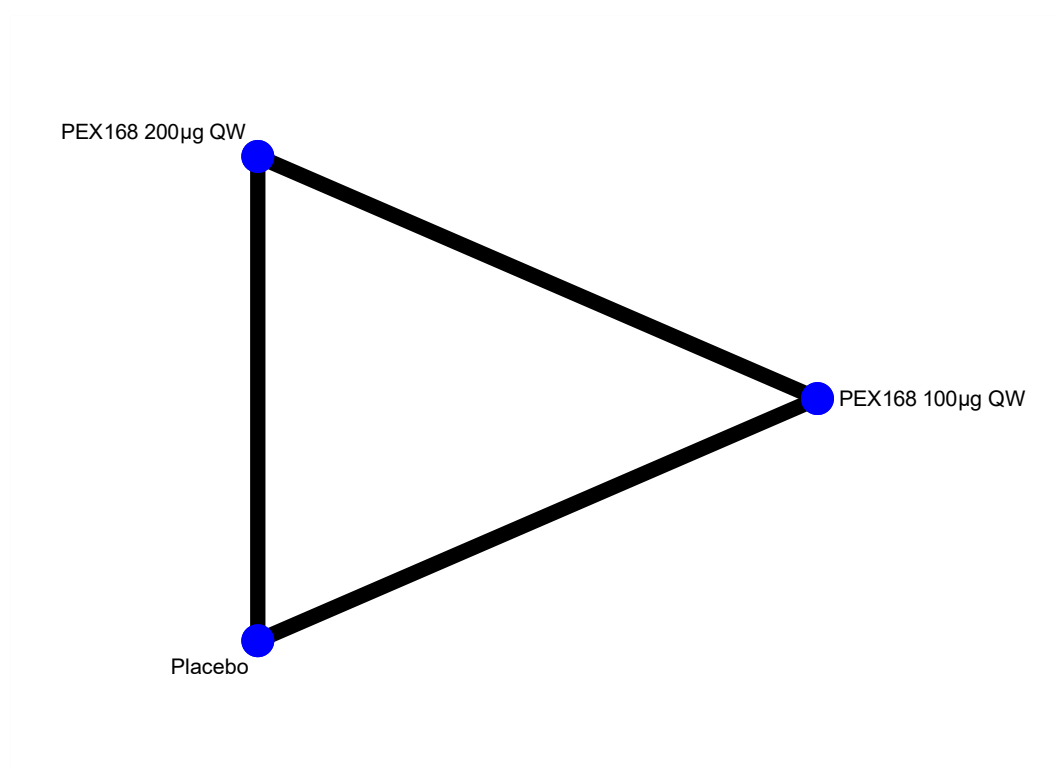
(E2) Forest plot of LDL



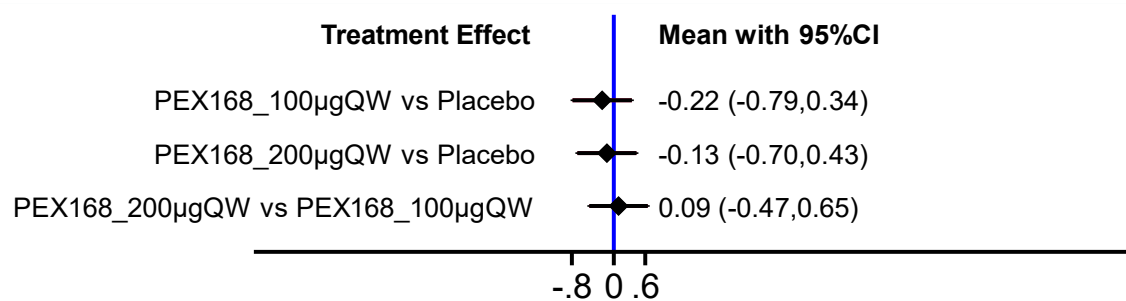
(E3) League table of LDL

PEX168 200µg QW	0.16 (- 0.23,0.55)	0.28 (- 0.14,0.69)
-0.16 (- 0.55,0.23)	PEX168 100µg QW	0.11 (- 0.29,0.52)
-0.28 (- 0.69,0.14)	-0.11 (- 0.52,0.29)	Placebo

(F1) Network map of TC



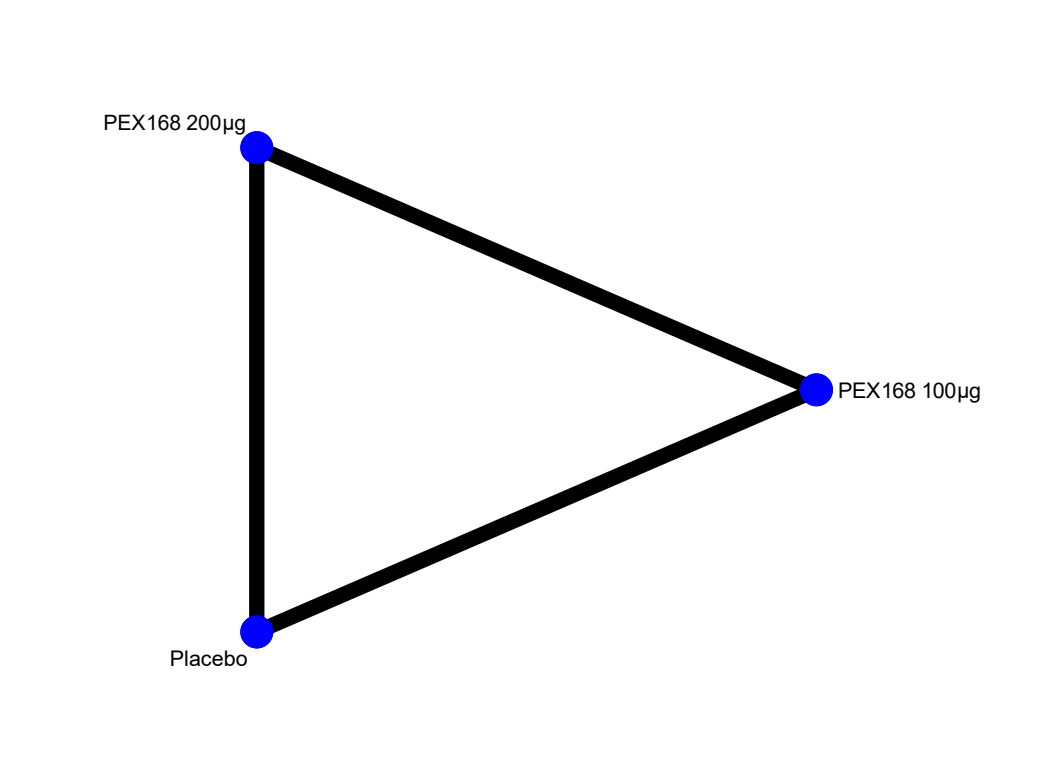
(F2) Forest plot of TC



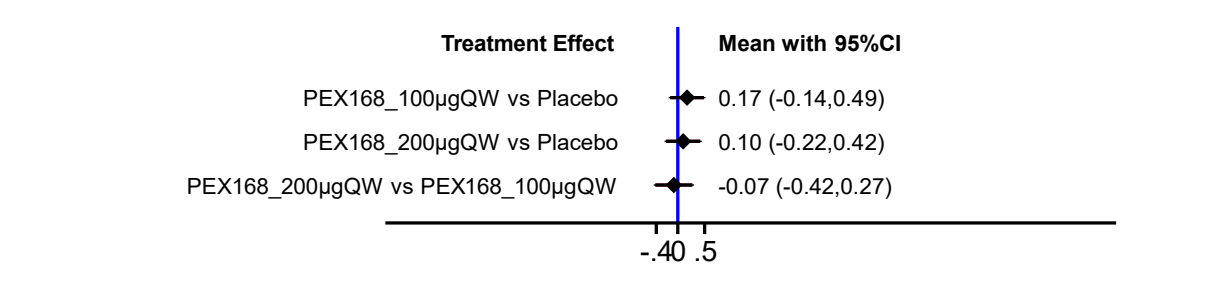
(F3) League table of TC

PEX168 100µg QW	0.09 (- 0.47,0.65)	0.22 (- 0.34,0.79)
-0.09 (- 0.65,0.47)	PEX168 200µg QW	0.13 (- 0.43,0.70)
-0.22 (- 0.79,0.34)	-0.13 (- 0.70,0.43)	Placebo

(G1) Network map of TG



(G2) Forest plot of TG



(G3) League table of TG

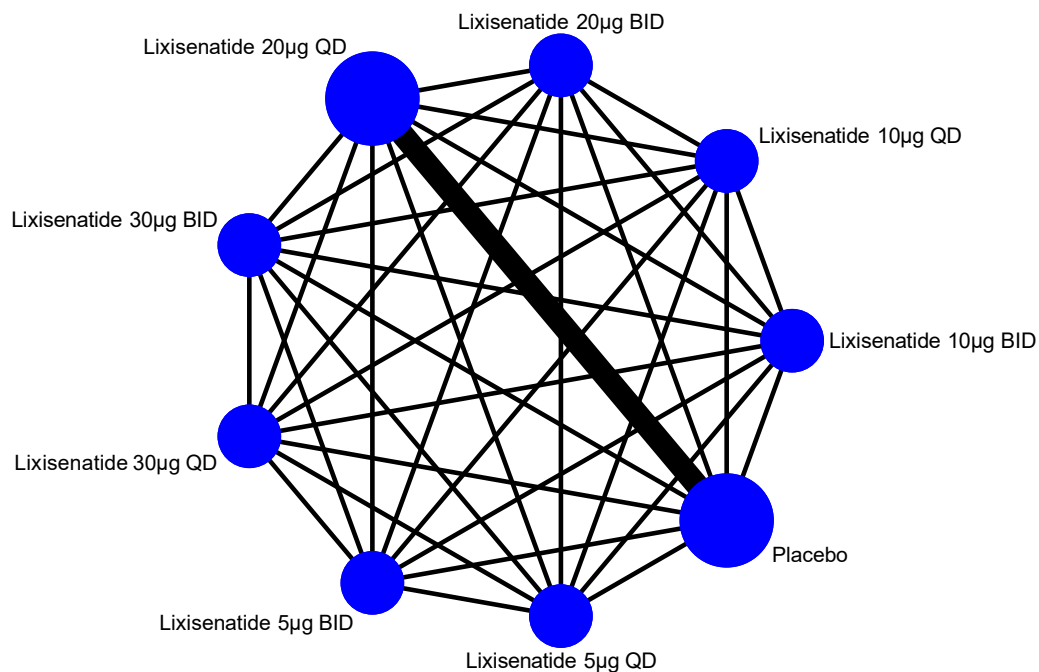
Placebo	0.10 (-0.22,0.42)	0.17 (-0.14,0.49)
-0.10 (-0.42,0.22)	PEX168Q W200µg	0.07 (-0.27,0.42)
-0.17 (-0.49,0.14)	-0.07 (-0.42,0.27)	PEX168Q W100µg

Abbreviations: FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

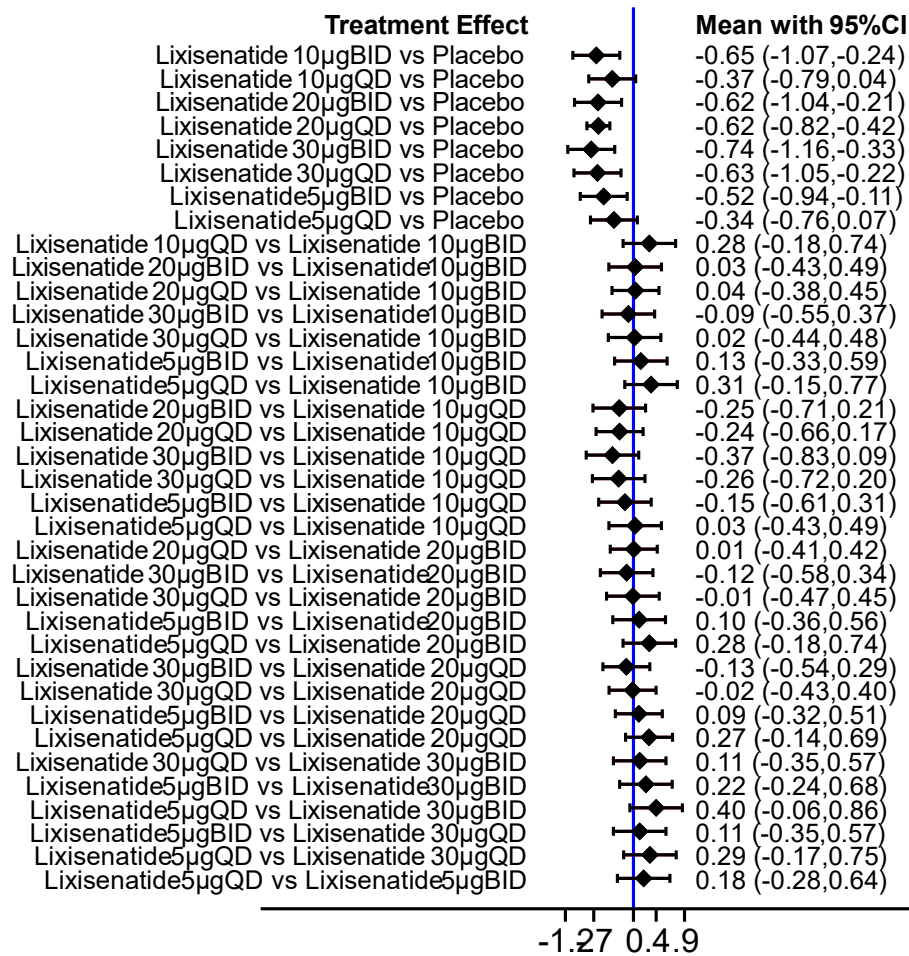
Figure S14.7: Effects of different doses of Lixisenatide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Lixisenatide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



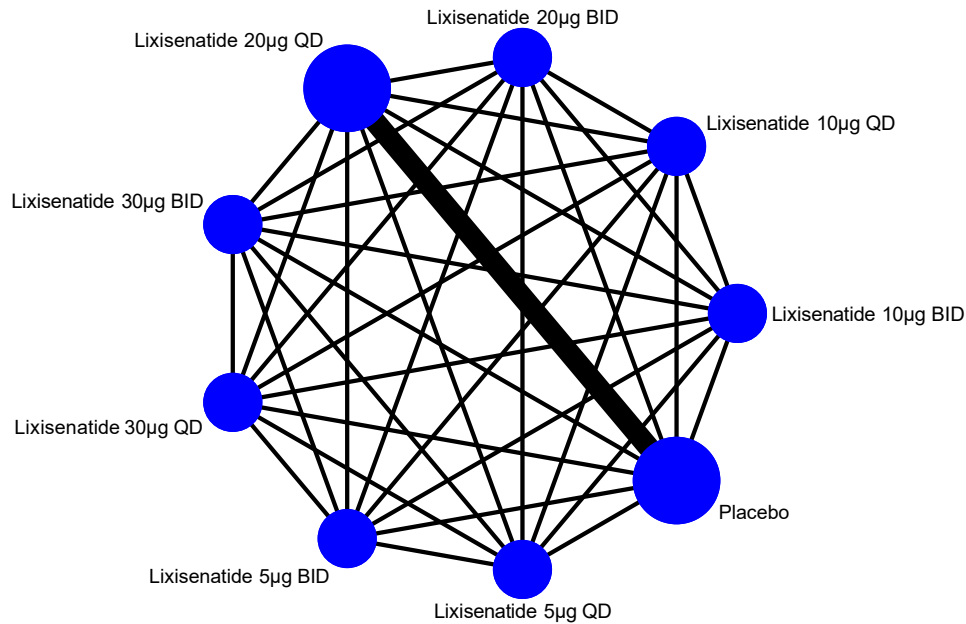
(A2) Forest plot of HbA1c



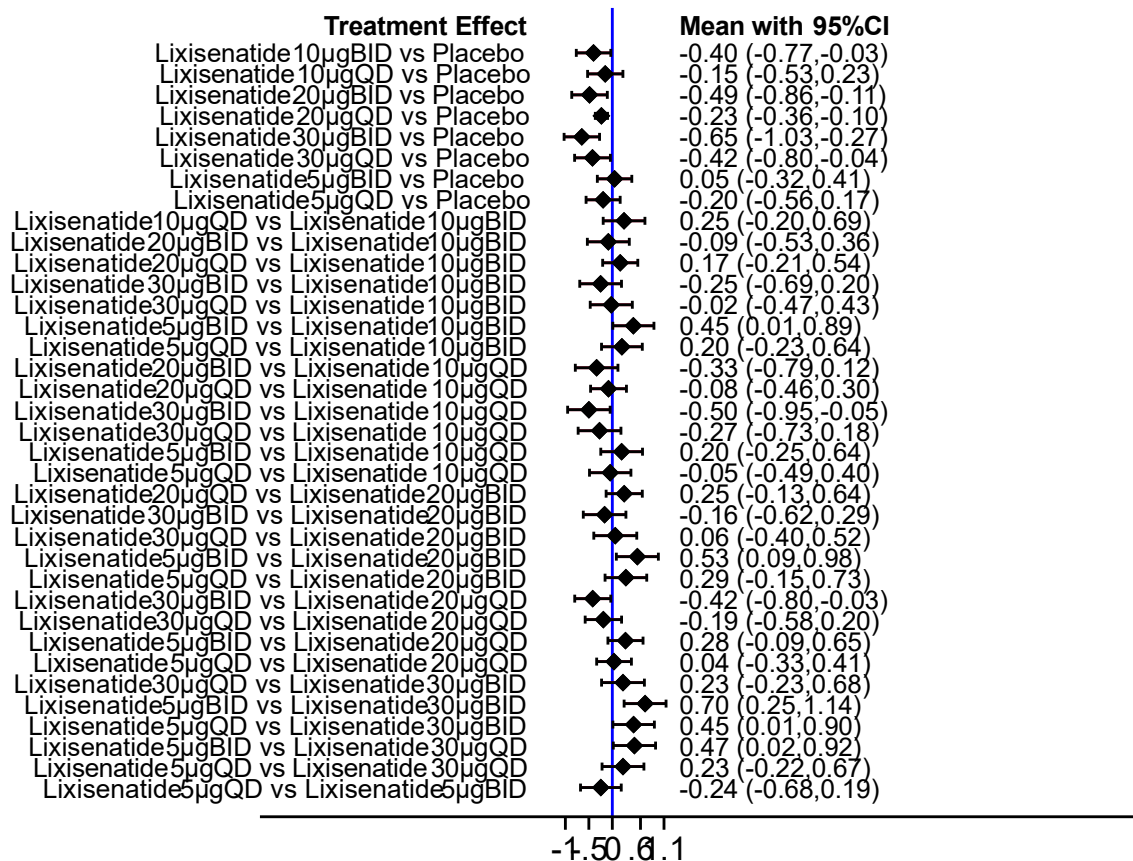
(A3) League table of HbA1c

Lixisenatide 30µg BID	0.09 (-0.37,0.55)	0.11 (-0.35,0.57)	0.13 (-0.29,0.54)	0.12 (-0.34,0.58)	0.22 (-0.24,0.68)	0.37 (-0.09,0.83)	0.40 (-0.06,0.86)	0.74 (0.33,1.16)
-0.09 (-0.55,0.37)	Lixisenatide 10µg BID	0.02 (-0.44,0.48)	0.04 (-0.38,0.45)	0.03 (-0.43,0.49)	0.13 (-0.33,0.59)	0.28 (-0.18,0.74)	0.31 (-0.15,0.77)	0.65 (0.24,1.07)
-0.11 (-0.57,0.35)	-0.02 (-0.48,0.44)	Lixisenatide 30µg QD	0.02 (-0.40,0.43)	0.01 (-0.45,0.47)	0.11 (-0.35,0.57)	0.26 (-0.20,0.72)	0.29 (-0.17,0.75)	0.63 (0.22,1.05)
-0.13 (-0.54,0.29)	-0.04 (-0.45,0.38)	-0.02 (-0.43,0.40)	Lixisenatide 20µg QD	-0.01 (-0.42,0.41)	0.09 (-0.32,0.51)	0.24 (-0.17,0.66)	0.27 (-0.14,0.69)	0.62 (0.42,0.82)
-0.12 (-0.58,0.34)	-0.03 (-0.49,0.43)	-0.01 (-0.47,0.45)	0.01 (-0.41,0.42)	Lixisenatide 20µg BID	0.10 (-0.36,0.56)	0.25 (-0.21,0.71)	0.28 (-0.18,0.74)	0.62 (0.21,1.04)
-0.22 (-0.68,0.24)	-0.13 (-0.59,0.33)	-0.11 (-0.57,0.35)	-0.09 (-0.51,0.32)	-0.10 (-0.56,0.36)	Lixisenatide 5µg BID	0.15 (-0.31,0.61)	0.18 (-0.28,0.64)	0.52 (0.11,0.94)
-0.37 (-0.83,0.09)	-0.28 (-0.74,0.18)	-0.26 (-0.72,0.20)	-0.24 (-0.66,0.17)	-0.25 (-0.71,0.21)	-0.15 (-0.61,0.31)	Lixisenatide 10µg QD	0.03 (-0.43,0.49)	0.37 (-0.04,0.79)
-0.40 (-0.86,0.06)	-0.31 (-0.77,0.15)	-0.29 (-0.75,0.17)	-0.27 (-0.69,0.14)	-0.28 (-0.74,0.18)	-0.18 (-0.64,0.28)	-0.03 (-0.49,0.43)	Lixisenatide 5µg QD	0.34 (-0.07,0.76)
-0.74 (-1.16,-0.33)	-0.65 (-1.07,-0.24)	-0.63 (-1.05,-0.22)	-0.62 (-0.82,-0.42)	-0.62 (-1.04,-0.21)	-0.52 (-0.94,-0.11)	-0.37 (-0.79,0.04)	-0.34 (-0.76,0.07)	Placebo

(B1) Network map of FPG



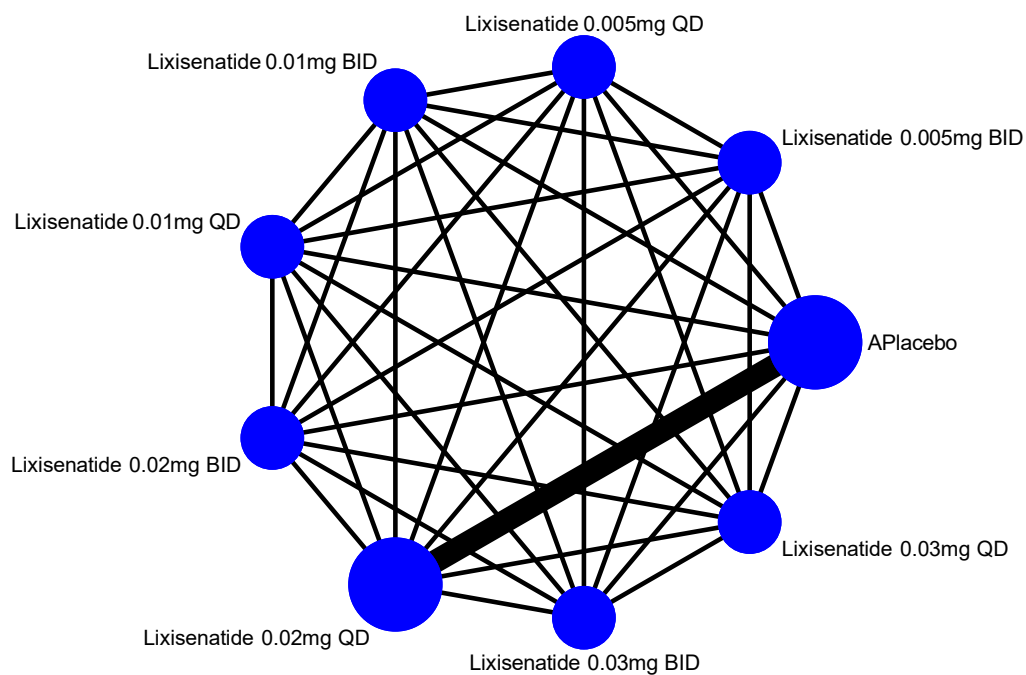
(B2) Forest plot of FPG



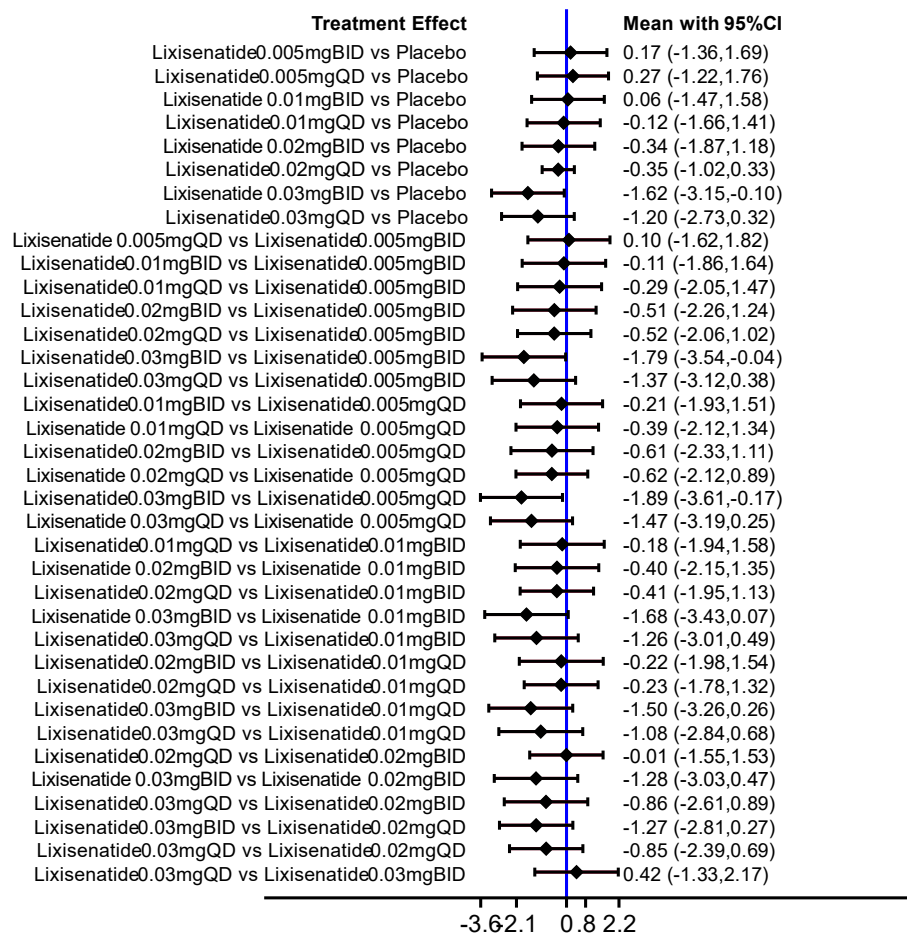
(B3) League table of FPG

Lixisenatide 30µg BID	0.16 (-0.29,0.62)	0.23 (-0.23,0.68)	0.25 (-0.19,0.69)	0.42 (0.03,0.80)	0.45 (0.01,0.90)	0.50 (0.05,0.95)	0.65 (0.27,1.03)	0.70 (0.25,1.14)
-0.16 (-0.62,0.29)	Lixisenatide 20µg BID	0.06 (-0.40,0.52)	0.09 (-0.36,0.53)	0.25 (-0.13,0.64)	0.29 (-0.15,0.73)	0.33 (-0.12,0.79)	0.49 (0.11,0.86)	0.53 (0.09,0.98)
-0.23 (-0.68,0.23)	-0.06 (-0.52,0.40)	Lixisenatide 30µg QD	0.02 (-0.43,0.47)	0.19 (-0.20,0.58)	0.23 (-0.22,0.67)	0.27 (-0.18,0.73)	0.42 (0.04,0.80)	0.47 (0.02,0.92)
-0.25 (-0.69,0.19)	-0.09 (-0.53,0.36)	-0.02 (-0.47,0.43)	Lixisenatide 10µg BID	0.17 (-0.21,0.54)	0.20 (-0.23,0.64)	0.25 (-0.20,0.69)	0.40 (0.03,0.77)	0.45 (0.01,0.89)
-0.42 (-0.80,-0.03)	-0.25 (-0.64,0.13)	-0.19 (-0.58,0.20)	-0.17 (-0.54,0.21)	Lixisenatide 20µg QD	0.04 (-0.33,0.41)	0.08 (-0.30,0.46)	0.23 (0.10,0.36)	0.28 (-0.09,0.65)
-0.45 (-0.90,-0.01)	-0.29 (-0.73,0.15)	-0.23 (-0.67,0.22)	-0.20 (-0.64,0.23)	-0.04 (-0.41,0.33)	Lixisenatide 5µg QD	0.05 (-0.40,0.49)	0.20 (-0.17,0.56)	0.24 (-0.19,0.68)
-0.50 (-0.95,-0.05)	-0.33 (-0.79,0.12)	-0.27 (-0.73,0.18)	-0.25 (-0.69,0.20)	-0.08 (-0.46,0.30)	-0.05 (-0.49,0.40)	Lixisenatide 10µg QD	0.15 (-0.23,0.53)	0.20 (-0.25,0.64)
-0.65 (-1.03,-0.27)	-0.49 (-0.86,-0.11)	-0.42 (-0.80,-0.04)	-0.40 (-0.77,-0.03)	-0.23 (-0.36,-0.10)	-0.20 (-0.56,0.17)	-0.15 (-0.53,0.23)	Placebo	0.05 (-0.32,0.41)
-0.70 (-1.14,-0.25)	-0.53 (-0.98,-0.09)	-0.47 (-0.92,-0.02)	-0.45 (-0.89,-0.01)	-0.28 (-0.65,0.09)	-0.24 (-0.68,0.19)	-0.20 (-0.64,0.25)	-0.05 (-0.41,0.32)	Lixisenatide 5µg BID

(C1) Network map of weight loss



(C2) Forest plot of weight loss



(C3) League table of weight loss

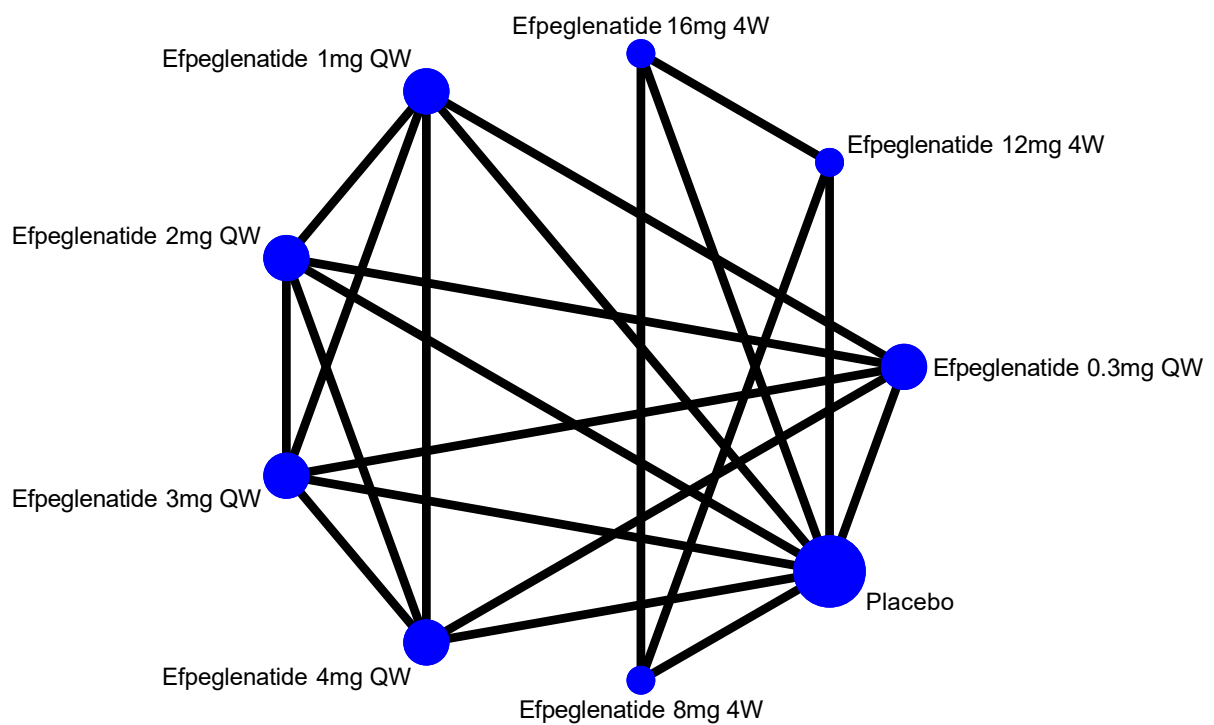
Lixisenatide 30µg BID	0.42 (-1.33,2.17)	1.27 (-0.27,2.81)	1.28 (-0.47,3.03)	1.50 (-0.26,3.26)	1.62 (0.10,3.15)	1.68 (-0.07,3.43)	1.79 (0.04,3.54)	1.89 (0.17,3.61)
-0.42 (-2.17,1.33)	Lixisenatide 30µg QD	0.85 (-0.69,2.39)	0.86 (-0.89,2.61)	1.08 (-0.68,2.84)	1.20 (-0.32,2.73)	1.26 (-0.49,3.01)	1.37 (-0.38,3.12)	1.47 (-0.25,3.19)
-1.27 (-2.81,0.27)	-0.85 (-2.39,0.69)	Lixisenatide 20µg QD	0.01 (-1.53,1.55)	0.23 (-1.32,1.78)	0.35 (-0.33,1.02)	0.41 (-1.13,1.95)	0.52 (-1.02,2.06)	0.62 (-0.89,2.12)
-1.28 (-3.03,0.47)	-0.86 (-2.61,0.89)	-0.01 (-1.55,1.53)	Lixisenatide 20µg BID	0.22 (-1.54,1.98)	0.34 (-1.18,1.87)	0.40 (-1.35,2.15)	0.51 (-1.24,2.26)	0.61 (-1.11,2.33)
-1.50 (-3.26,0.26)	-1.08 (-2.84,0.68)	-0.23 (-1.78,1.32)	-0.22 (-1.98,1.54)	Lixisenatide 10µg QD	0.12 (-1.41,1.66)	0.18 (-1.58,1.94)	0.29 (-1.47,2.05)	0.39 (-1.34,2.12)
-1.62 (-3.15,-0.10)	-1.20 (-2.73,0.32)	-0.35 (-1.02,0.33)	-0.34 (-1.87,1.18)	-0.12 (-1.66,1.41)	Placebo	0.06 (-1.47,1.58)	0.17 (-1.36,1.69)	0.27 (-1.22,1.76)
-1.68 (-3.43,0.07)	-1.26 (-3.01,0.49)	-0.41 (-1.95,1.13)	-0.40 (-2.15,1.35)	-0.18 (-1.94,1.58)	-0.06 (-1.58,1.47)	Lixisenatide 10µg BID	0.11 (-1.64,1.86)	0.21 (-1.51,1.93)
-1.79 (-3.54,-0.04)	-1.37 (-3.12,0.38)	-0.52 (-2.06,1.02)	-0.51 (-2.26,1.24)	-0.29 (-2.05,1.47)	-0.17 (-1.69,1.36)	-0.11 (-1.86,1.64)	Lixisenatide 5µg BID	0.10 (-1.62,1.82)
-1.89 (-3.61,-0.17)	-1.47 (-3.19,0.25)	-0.62 (-2.12,0.89)	-0.61 (-2.33,1.11)	-0.39 (-2.12,1.34)	-0.27 (-1.76,1.22)	-0.21 (-1.93,1.51)	-0.10 (-1.82,1.62)	Lixisenatide 5µg QD

Abbreviations: FPG, fasting plasma glucose.

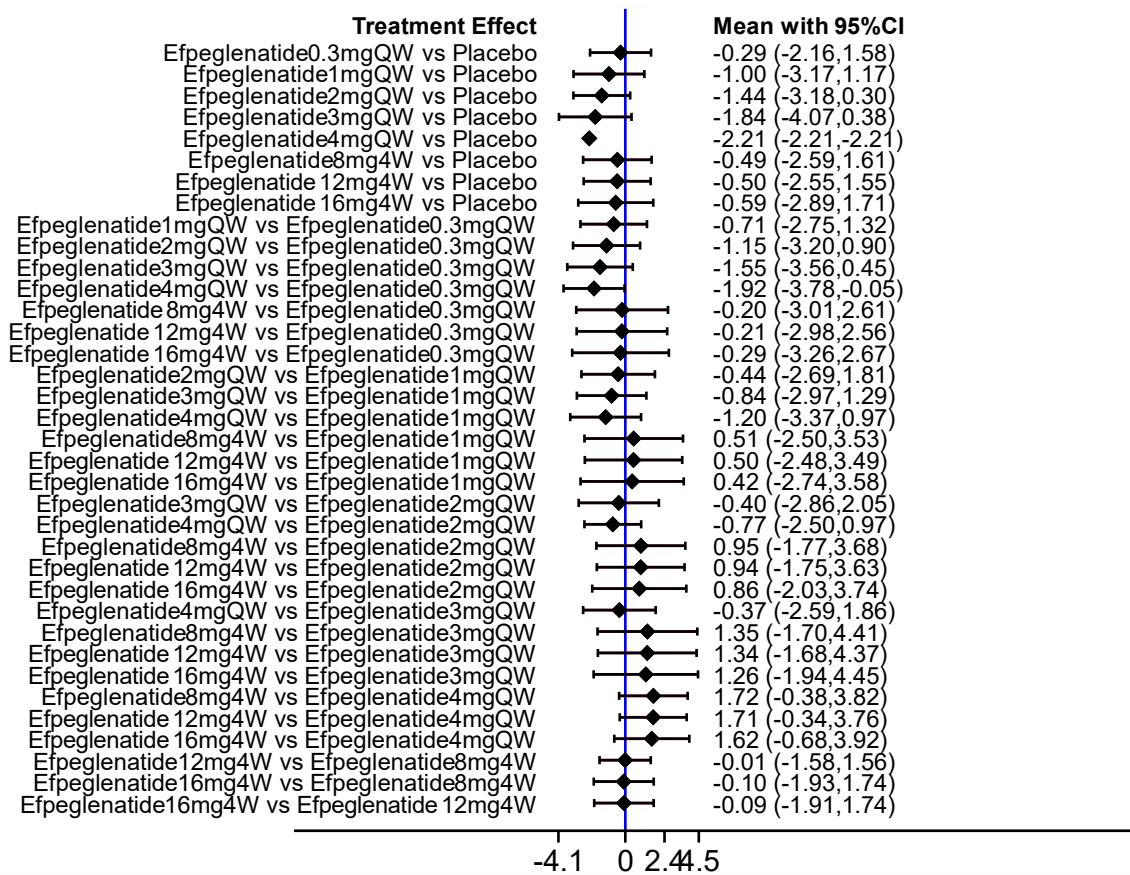
Figure S14.8: Effects of different doses of Efpeglenatide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Efpeglenatide on various indicators of diabetes (A)HbA1c, (B) FPG, (C) weight loss. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



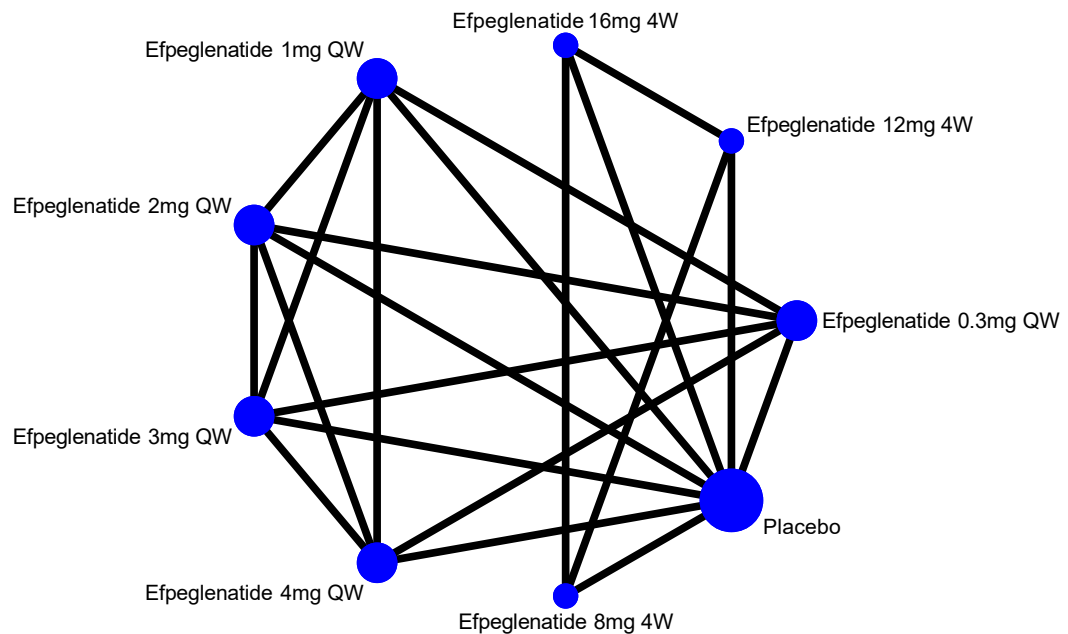
(A2) Forest plot of HbA1c



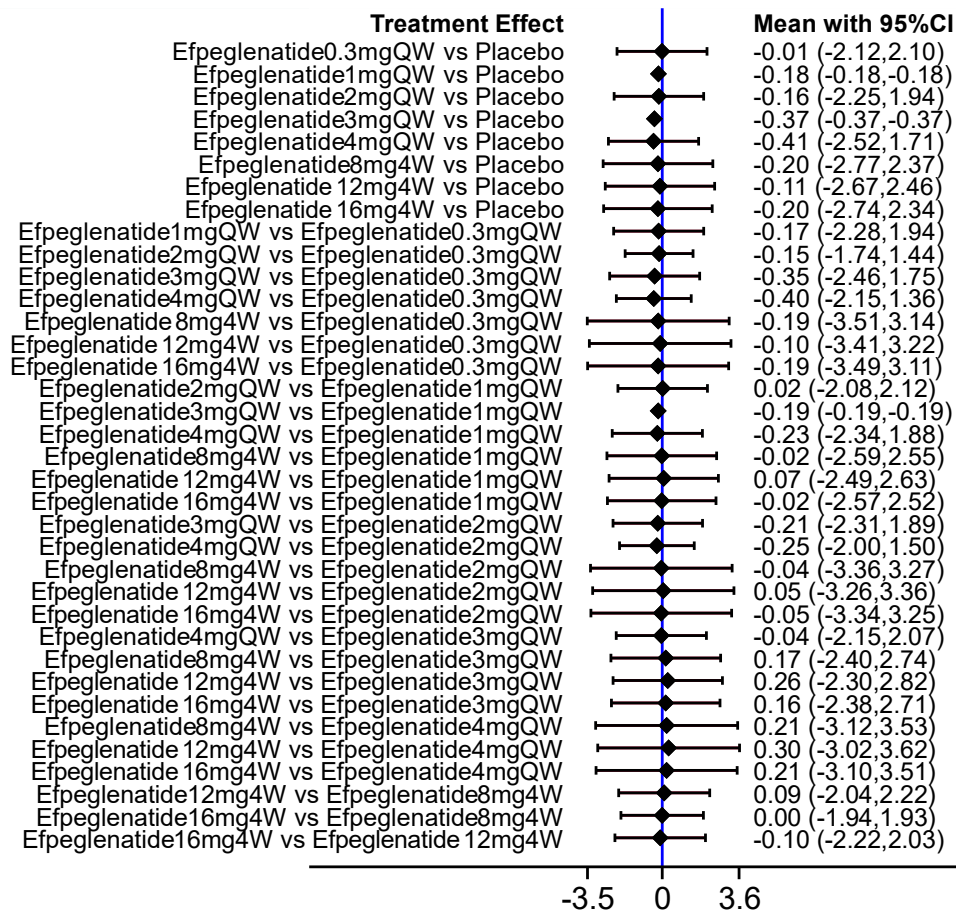
(A3) League table of HbA1c

Efpeglenatide 4mg QW	0.37 (- 1.86,2.59)	0.77 (- 0.97,2.50)	1.20 (- 0.97,3.37)	1.62 (- 0.68,3.92)	1.72 (- 0.38,3.82)	1.71 (- 0.34,3.76)	1.92 (0.05,3.78)	2.21 (2.21,2.21)
-0.37 (- 2.59,1.86)	Efpeglenatide 3mg QW	0.40 (- 2.05,2.86)	0.84 (- 1.29,2.97)	1.26 (- 1.94,4.45)	1.35 (- 1.70,4.41)	1.34 (- 1.68,4.37)	1.55 (- 0.45,3.56)	1.84 (- 0.38,4.07)
-0.77 (- 2.50,0.97)	-0.40 (- 2.86,2.05)	Efpeglenatide 2mg QW	0.44 (- 1.81,2.69)	0.86 (- 2.03,3.74)	0.95 (- 1.77,3.68)	0.94 (- 1.75,3.63)	1.15 (- 0.90,3.20)	1.44 (- 0.30,3.18)
-1.20 (- 3.37,0.97)	-0.84 (- 2.97,1.29)	-0.44 (- 2.69,1.81)	Efpeglenatide 1mg QW	0.42 (- 2.74,3.58)	0.51 (- 2.50,3.53)	0.50 (- 2.48,3.49)	0.71 (- 1.32,2.75)	1.00 (- 1.17,3.17)
-1.62 (- 3.92,0.68)	-1.26 (- 4.45,1.94)	-0.86 (- 3.74,2.03)	-0.42 (- 3.58,2.74)	Efpeglenatide 16mg 4W	0.10 (- 1.74,1.93)	0.09 (- 1.74,1.91)	0.29 (- 2.67,3.26)	0.59 (- 1.71,2.89)
-1.72 (- 3.82,0.38)	-1.35 (- 4.41,1.70)	-0.95 (- 3.68,1.77)	-0.51 (- 3.53,2.50)	-0.10 (- 1.93,1.74)	Efpeglenatide 8mg 4W	-0.01 (- 1.58,1.56)	0.20 (- 2.61,3.01)	0.49 (- 1.61,2.59)
-1.71 (- 3.76,0.34)	-1.34 (- 4.37,1.68)	-0.94 (- 3.63,1.75)	-0.50 (- 3.49,2.48)	-0.09 (- 1.91,1.74)	0.01 (- 1.56,1.58)	Efpeglenatide 12mg 4W	0.21 (- 2.56,2.98)	0.50 (- 1.55,2.55)
-1.92 (-3.78,- 0.05)	-1.55 (- 3.56,0.45)	-1.15 (- 3.20,0.90)	-0.71 (- 2.75,1.32)	-0.29 (- 3.26,2.67)	-0.20 (- 3.01,2.61)	-0.21 (- 2.98,2.56)	Efpeglenatide 0.3mg QW	0.29 (- 1.58,2.16)
-2.21 (-2.21,- 2.21)	-1.84 (- 4.07,0.38)	-1.44 (- 3.18,0.30)	-1.00 (- 3.17,1.17)	-0.59 (- 2.89,1.71)	-0.49 (- 2.59,1.61)	-0.50 (- 2.55,1.55)	-0.29 (- 2.16,1.58)	Placebo

(B1) Network map of FPG



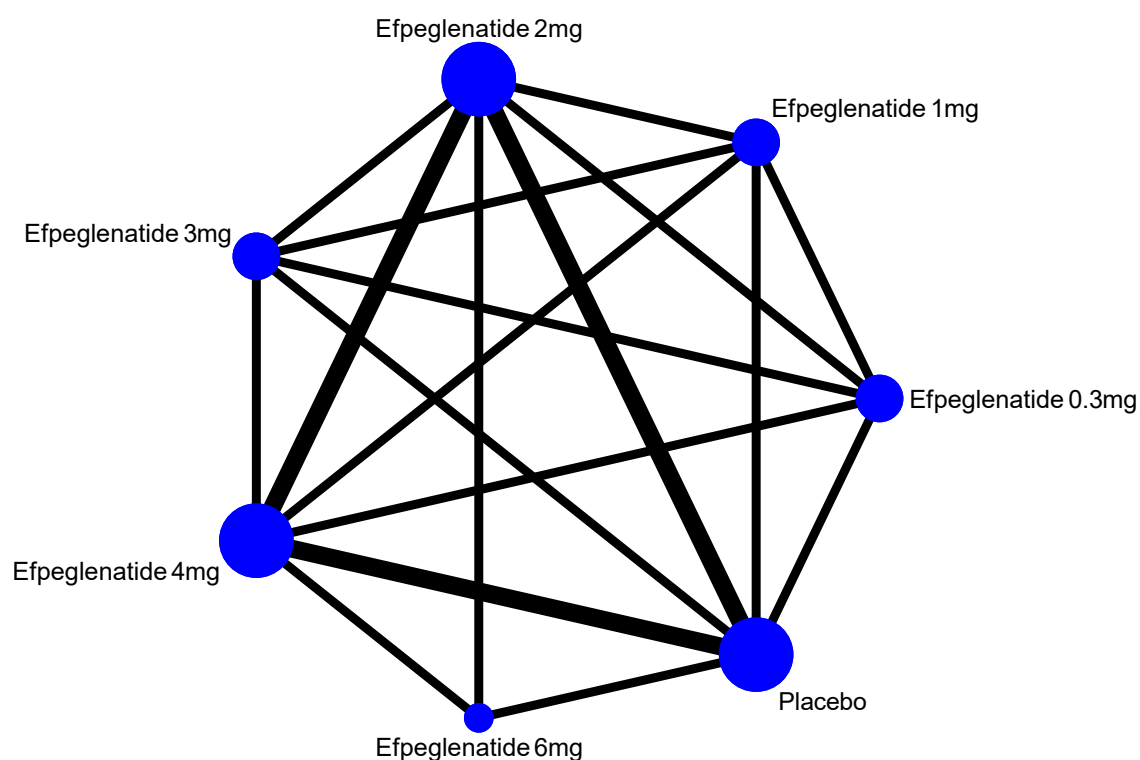
(B2) Forest plot of FPG



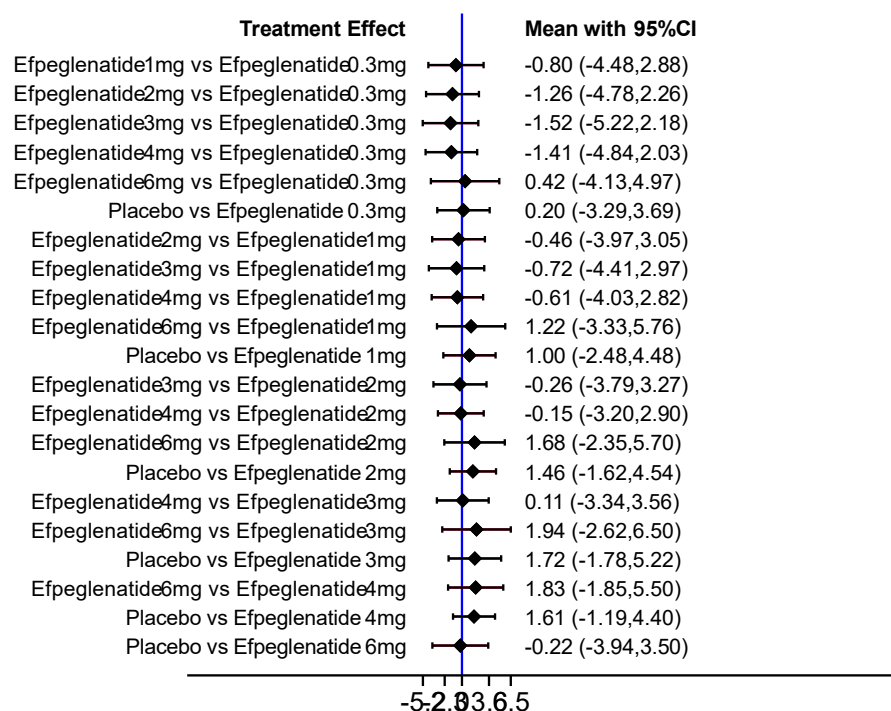
(B3) League table of FPG

Efpeglenatide 3mg QW	-0.04 (-2.15,2.07)	0.19 (0.19,0.19)	0.17 (-2.40,2.74)	0.16 (-2.38,2.71)	0.21 (-1.89,2.31)	0.26 (-2.30,2.82)	0.35 (-1.75,2.46)	0.37 (0.37,0.37)
0.04 (-2.07,2.15)	Efpeglenatide 4mg QW	0.23 (-1.88,2.34)	0.21 (-3.12,3.53)	0.21 (-3.10,3.51)	0.25 (-1.50,2.00)	0.30 (-3.02,3.62)	0.40 (-1.36,2.15)	0.41 (-1.71,2.52)
-0.19 (-0.19,-0.19)	-0.23 (-2.34,1.88)	Efpeglenatide 1mg QW	-0.02 (-2.59,2.55)	-0.02 (-2.57,2.52)	0.02 (-2.08,2.12)	0.07 (-2.49,2.63)	0.17 (-1.94,2.28)	0.18 (0.18,0.18)
-0.17 (-2.74,2.40)	-0.21 (-3.53,3.12)	0.02 (-2.55,2.59)	Efpeglenatide 8mg 4W	-0.00 (-1.94,1.93)	0.04 (-3.27,3.36)	0.09 (-2.04,2.22)	0.19 (-3.14,3.51)	0.20 (-2.37,2.77)
-0.16 (-2.71,2.38)	-0.21 (-3.51,3.10)	0.02 (-2.52,2.57)	0.00 (-1.93,1.94)	Efpeglenatide 16mg 4W	0.05 (-3.25,3.34)	0.10 (-2.03,2.22)	0.19 (-3.11,3.49)	0.20 (-2.34,2.74)
-0.21 (-2.31,1.89)	-0.25 (-2.00,1.50)	-0.02 (-2.12,2.08)	-0.04 (-3.36,3.27)	-0.05 (-3.34,3.25)	Efpeglenatide 2mg QW	0.05 (-3.26,3.36)	0.15 (-1.44,1.74)	0.16 (-1.94,2.25)
-0.26 (-2.82,2.30)	-0.30 (-3.62,3.02)	-0.07 (-2.63,2.49)	-0.09 (-2.22,2.04)	-0.10 (-2.22,2.03)	-0.05 (-3.36,3.26)	Efpeglenatide 12mg 4W	0.10 (-3.22,3.41)	0.11 (-2.46,2.67)
-0.35 (-2.46,1.75)	-0.40 (-2.15,1.36)	-0.17 (-2.28,1.94)	-0.19 (-3.51,3.14)	-0.19 (-3.49,3.11)	-0.15 (-1.74,1.44)	-0.10 (-3.41,3.22)	Efpeglenatide 0.3mg QW	0.01 (-2.10,2.12)
-0.37 (-0.37,-0.37)	-0.41 (-2.52,1.71)	-0.18 (-0.18,-0.18)	-0.20 (-2.77,2.37)	-0.20 (-2.74,2.34)	-0.16 (-2.25,1.94)	-0.11 (-2.67,2.46)	-0.01 (-2.12,2.10)	Placebo

(C1) Network map of weight loss



(C2) Forest plot of weight loss



(C3) League table of weight loss

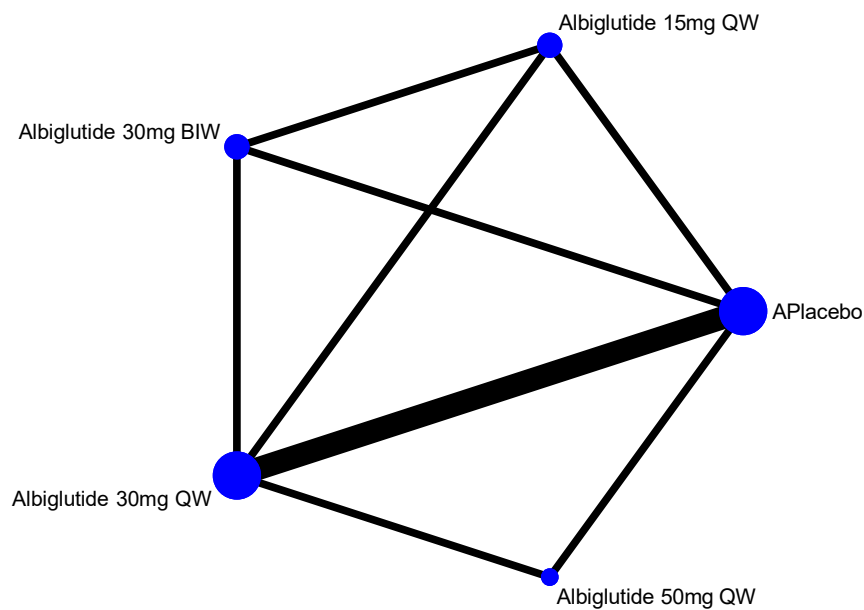
Efpeglenatide 4mg	-0.11 (-3.56,3.34)	0.15 (-2.90,3.20)	0.61 (-2.82,4.03)	1.41 (-2.03,4.84)	1.83 (-1.85,5.50)	1.61 (-1.19,4.40)
0.11 (-3.34,3.56)	Efpeglenatide 3mg	0.26 (-3.27,3.79)	0.72 (-2.97,4.41)	1.52 (-2.18,5.22)	1.94 (-2.62,6.50)	1.72 (-1.78,5.22)
-0.15 (-3.20,2.90)	-0.26 (-3.79,3.27)	Efpeglenatide 2mg	0.46 (-3.05,3.97)	1.26 (-2.26,4.78)	1.68 (-2.35,5.70)	1.46 (-1.62,4.54)
-0.61 (-4.03,2.82)	-0.72 (-4.41,2.97)	-0.46 (-3.97,3.05)	Efpeglenatide 1mg	0.80 (-2.88,4.48)	1.22 (-3.33,5.76)	1.00 (-2.48,4.48)
-1.41 (-4.84,2.03)	-1.52 (-5.22,2.18)	-1.26 (-4.78,2.26)	-0.80 (-4.48,2.88)	Efpeglenatide 0.3mg	0.42 (-4.13,4.97)	0.20 (-3.29,3.69)
-1.83 (-5.50,1.85)	-1.94 (-6.50,2.62)	-1.68 (-5.70,2.35)	-1.22 (-5.76,3.33)	-0.42 (-4.97,4.13)	Efpeglenatide 6mg	-0.22 (-3.94,3.50)
-1.61 (-4.40,1.19)	-1.72 (-5.22,1.78)	-1.46 (-4.54,1.62)	-1.00 (-4.48,2.48)	-0.20 (-3.69,3.29)	0.22 (-3.50,3.94)	Placebo

Abbreviations: FPG, fasting plasma glucose; QW, once weekly; 4W, once monthly.

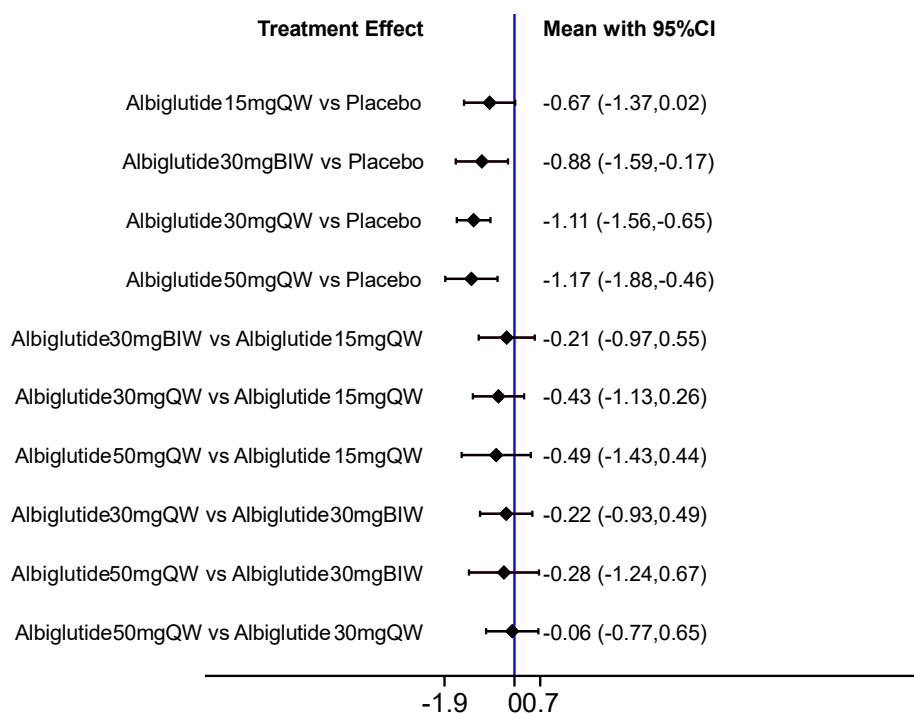
Figure S14.9: Effects of different doses of Albiglutide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Albiglutide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D)HDL, (E) LDL, (F) TC, (G) TG. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



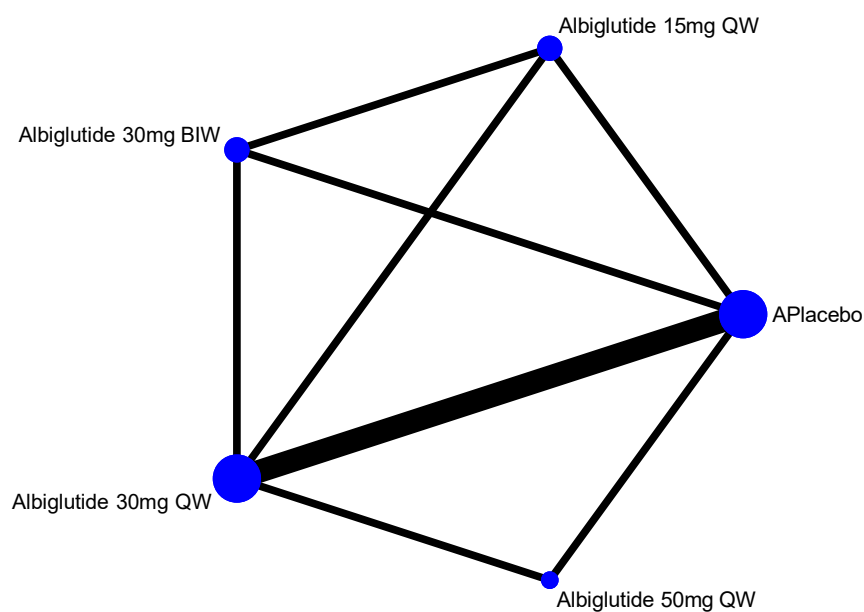
(A2) Forest plot of HbA1c



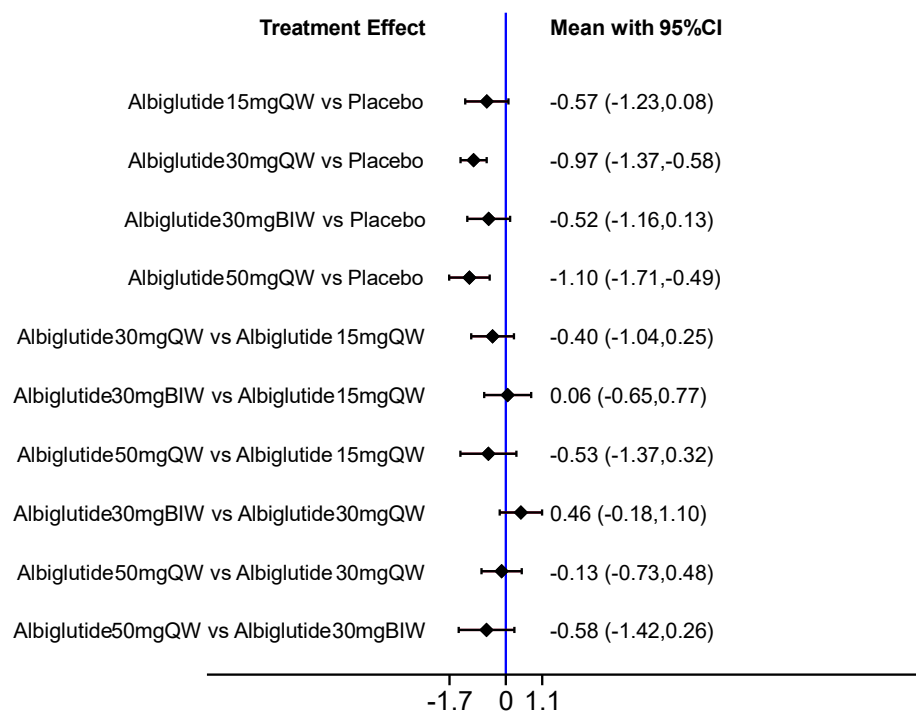
(A3) League table of HbA1c

Albiglutide 50mg QW	0.06 (-0.65, 0.77)	0.28 (-0.67, 1.24)	0.49 (-0.44, 1.43)	1.17 (0.46, 1.88)
-0.06 (-0.77, 0.65)	Albiglutide 30mg QW	0.22 (-0.49, 0.93)	0.43 (-0.26, 1.13)	1.11 (0.65, 1.56)
-0.28 (-1.24, 0.67)	-0.22 (-0.93, 0.49)	Albiglutide 30mg BIW	0.21 (-0.55, 0.97)	0.88 (0.17, 1.59)
-0.49 (-1.43, 0.44)	-0.43 (-1.13, 0.26)	-0.21 (-0.97, 0.55)	Albiglutide 15mg QW	0.67 (-0.02, 1.37)
-1.17 (-1.88, -0.46)	-1.11 (-1.56, -0.65)	-0.88 (-1.59, -0.17)	-0.67 (-1.37, 0.02)	Placebo

(B1) Network map of FPG



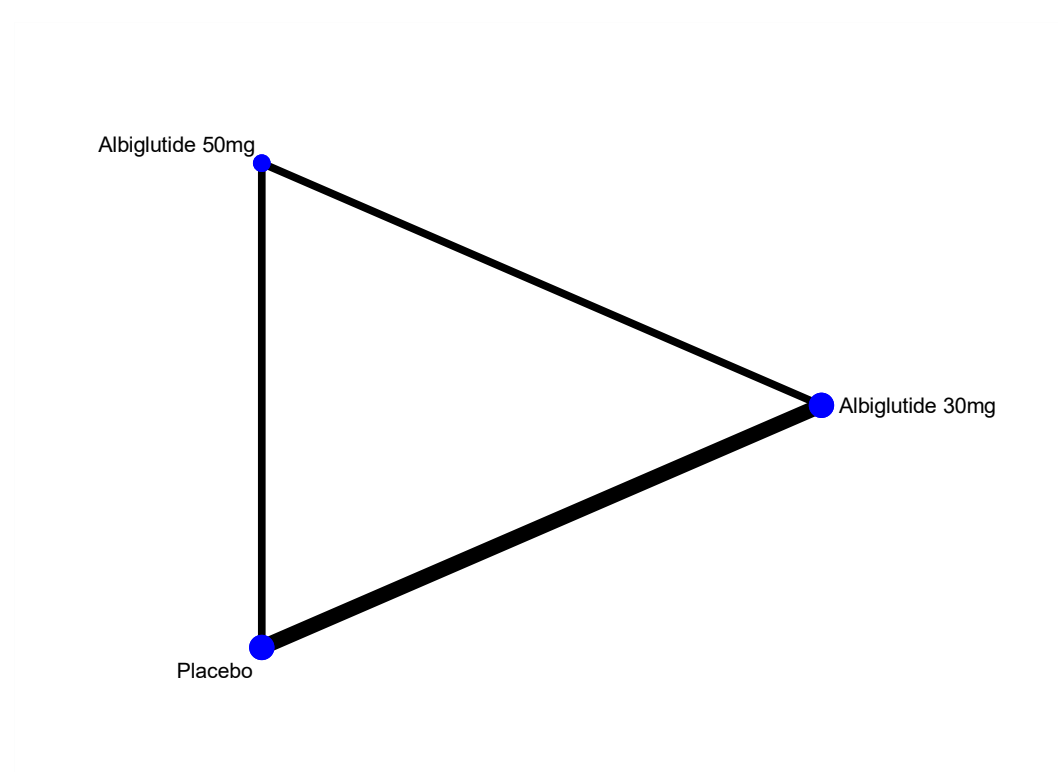
(B2) Forest plot of FPG



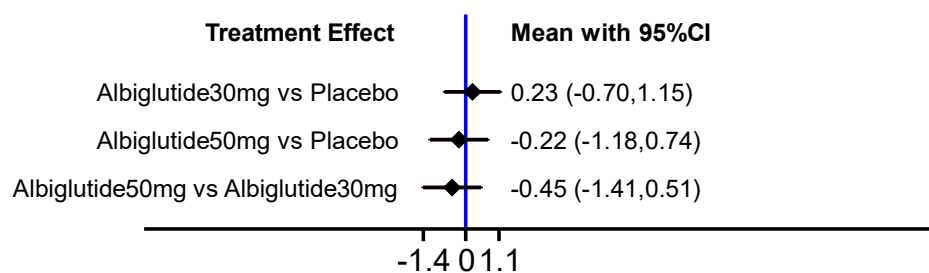
(B3) League table of FPG

Albiglutide 50mg QW	0.13 (-0.48,0.73)	0.53 (-0.32,1.37)	0.58 (-0.26,1.42)	1.10 (0.49,1.71)
-0.13 (-0.73,0.48)	Albiglutide 30mg QW	0.40 (-0.25,1.04)	0.46 (-0.18,1.10)	0.97 (0.58,1.37)
-0.53 (-1.37,0.32)	-0.40 (-1.04,0.25)	Albiglutide 15mg QW	0.06 (-0.65,0.77)	0.57 (-0.08,1.23)
-0.58 (-1.42,0.26)	-0.46 (-1.10,0.18)	-0.06 (-0.77,0.65)	Albiglutide 30mg QIW	0.52 (-0.13,1.16)
-1.10 (-1.71,-0.49)	-0.97 (-1.37,-0.58)	-0.57 (-1.23,0.08)	-0.52 (-1.16,0.13)	Placebo

(C1) Network map of weight loss



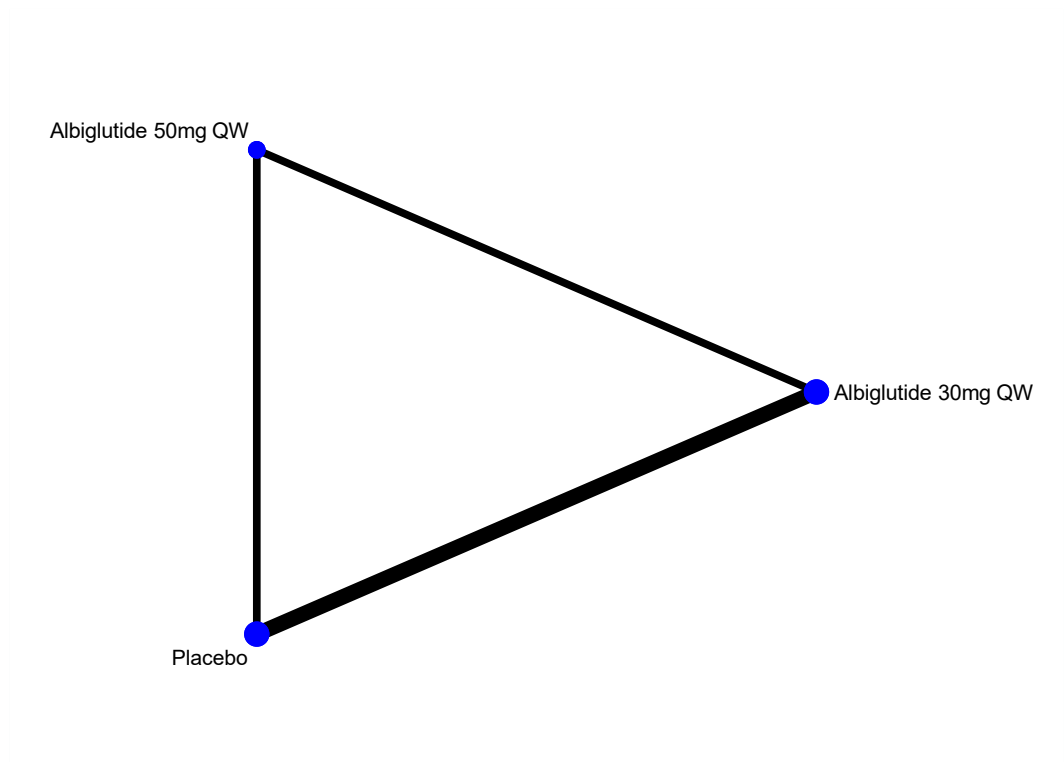
(C2) Forest plot of weight loss



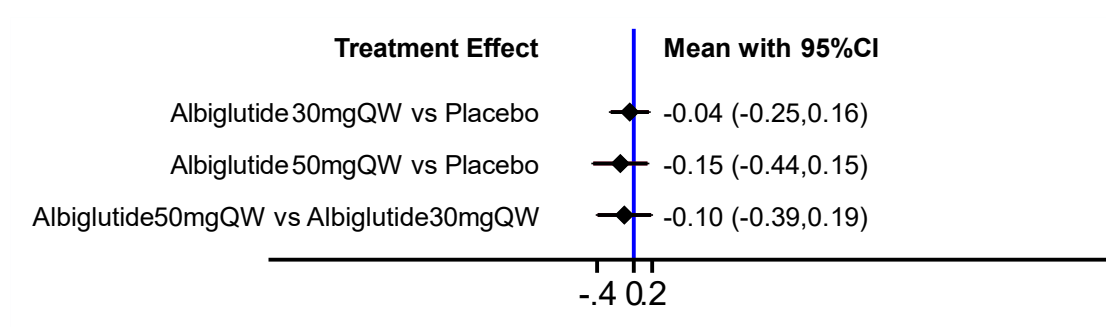
(C3) League table of weight loss

Albiglutide 50mg	0.22 (-0.74,1.18)	0.45 (-0.51,1.41)
-0.22 (-1.18,0.74)	Placebo	0.23 (-0.70,1.15)
-0.45 (-1.41,0.51)	-0.23 (-1.15,0.70)	Albiglutide 30mg

(D1) Network map of HDL



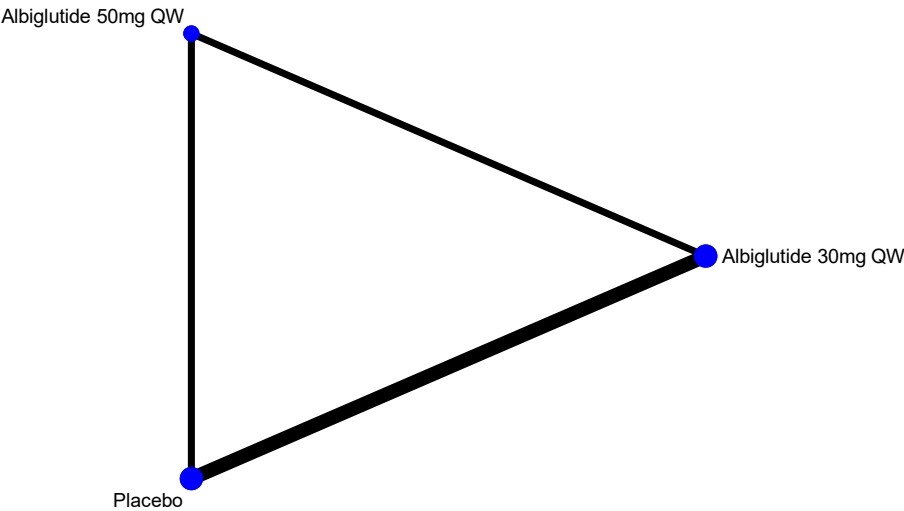
(D2) Forest plot of HDL



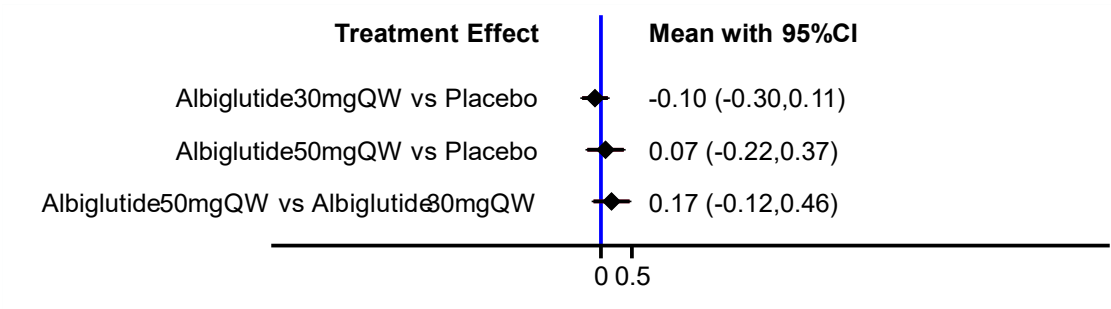
(D3) League table of HDL

Placebo	-0.04 (-0.25,0.16)	-0.15 (-0.44,0.15)
0.04 (-0.16,0.25)	Albiglutide 30mg QW	-0.10 (-0.39,0.19)
0.15 (-0.15,0.44)	0.10 (-0.19,0.39)	Albiglutide 50mg QW

(E1) Network map of LDL



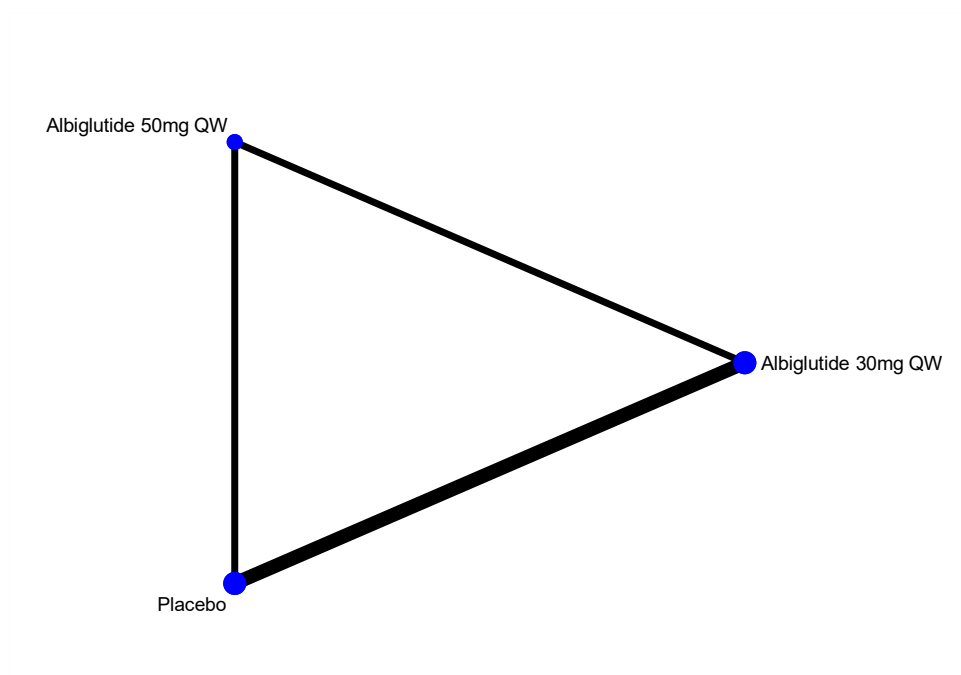
(E2) Forest plot of LDL



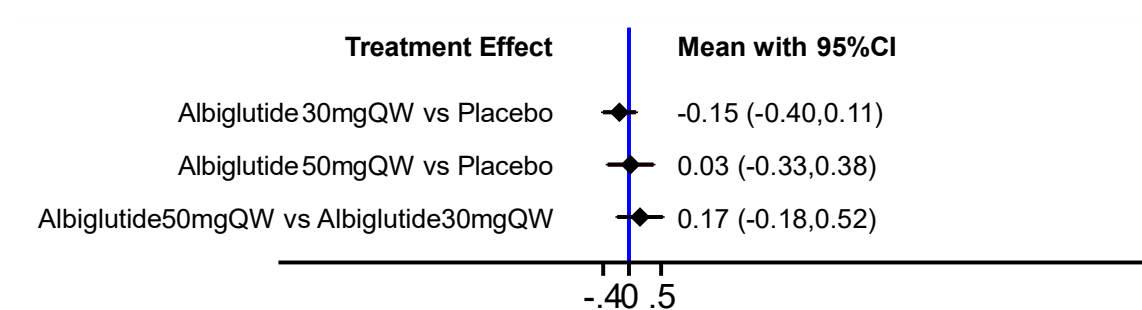
(E3) League table of LDL

Albiglutide 30mg QW	0.10 (-0.11,0.30)	0.17 (-0.12,0.46)
-0.10 (-0.30,0.11)	Placebo	0.07 (-0.22,0.37)
-0.17 (-0.46,0.12)	-0.07 (-0.37,0.22)	Albiglutide 50mg QW

(F1) Network map of TC



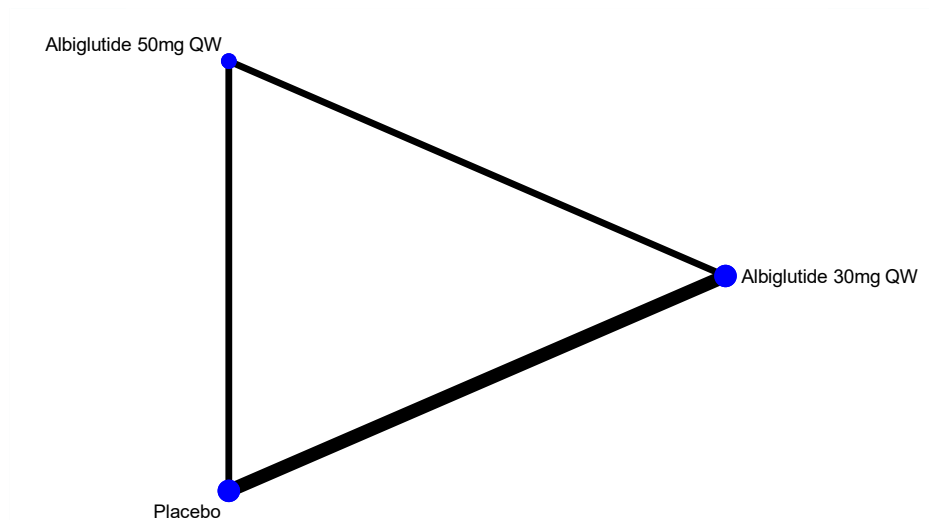
(F2) Forest plot of TC



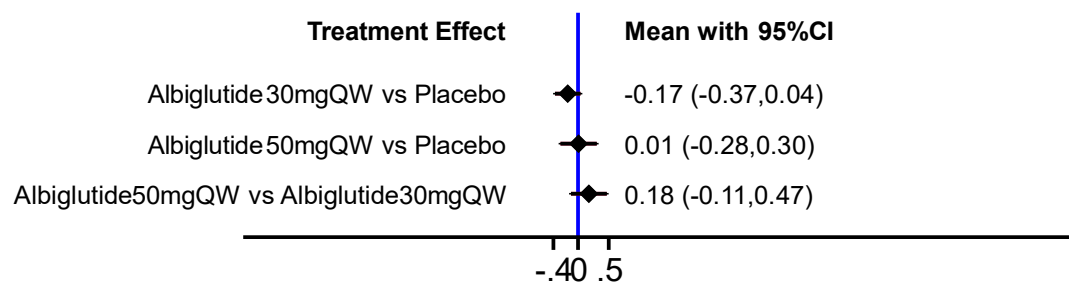
(F3) League table of TC

Albiglutide 30mg QW	0.15 (-0.11,0.40)	0.17 (-0.18,0.52)
-0.15 (-0.40,0.11)	Placebo	0.03 (-0.33,0.38)
-0.17 (-0.52,0.18)	-0.03 (-0.38,0.33)	Albiglutide 50mg QW

(G1) Network map of TG



(G2) Forest plot of TG



(G3) League table of TG

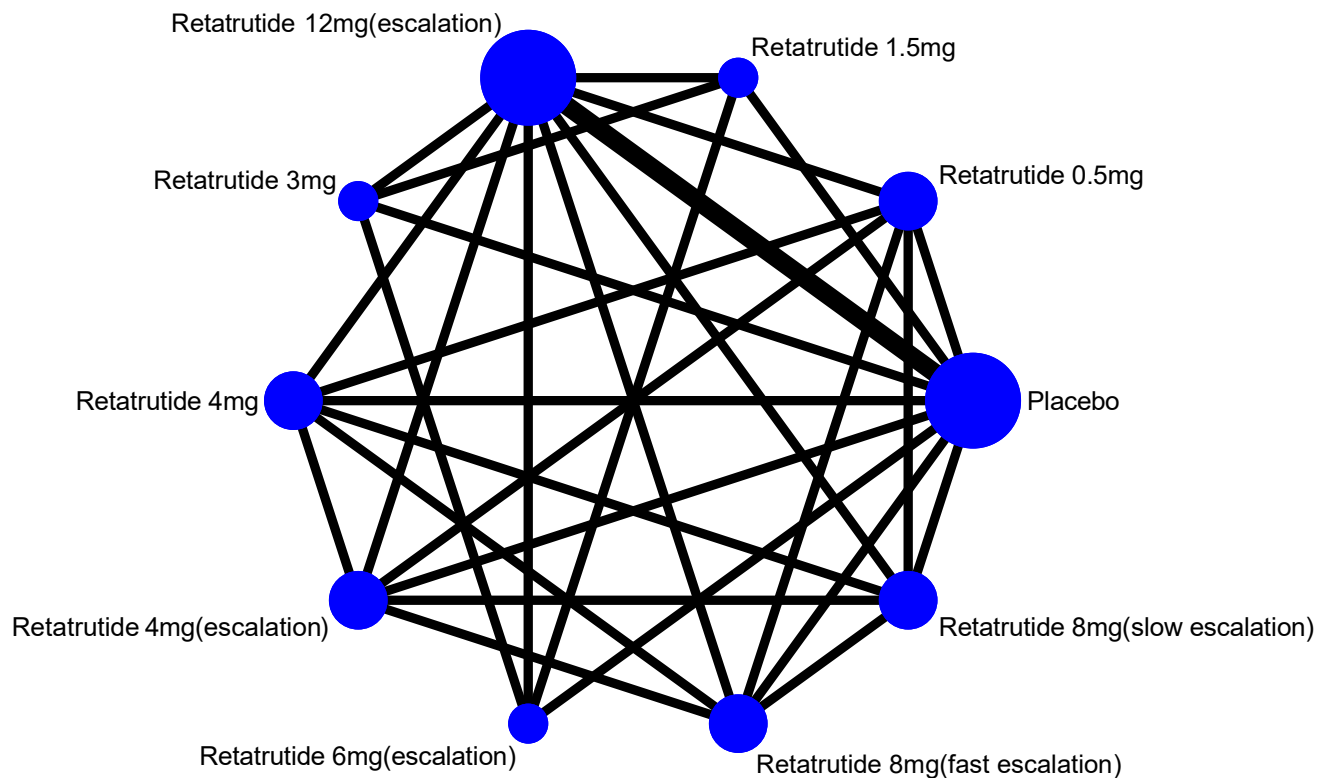
Albiglutide 30mg	0.18 (-0.11,0.47)	0.17 (-0.04,0.37)
-0.18 (-0.47,0.11)	Albiglutide 50mg	-0.01 (-0.30,0.28)
-0.17 (-0.37,0.04)	0.01 (-0.28,0.30)	Placebo

(G3) League table of TG

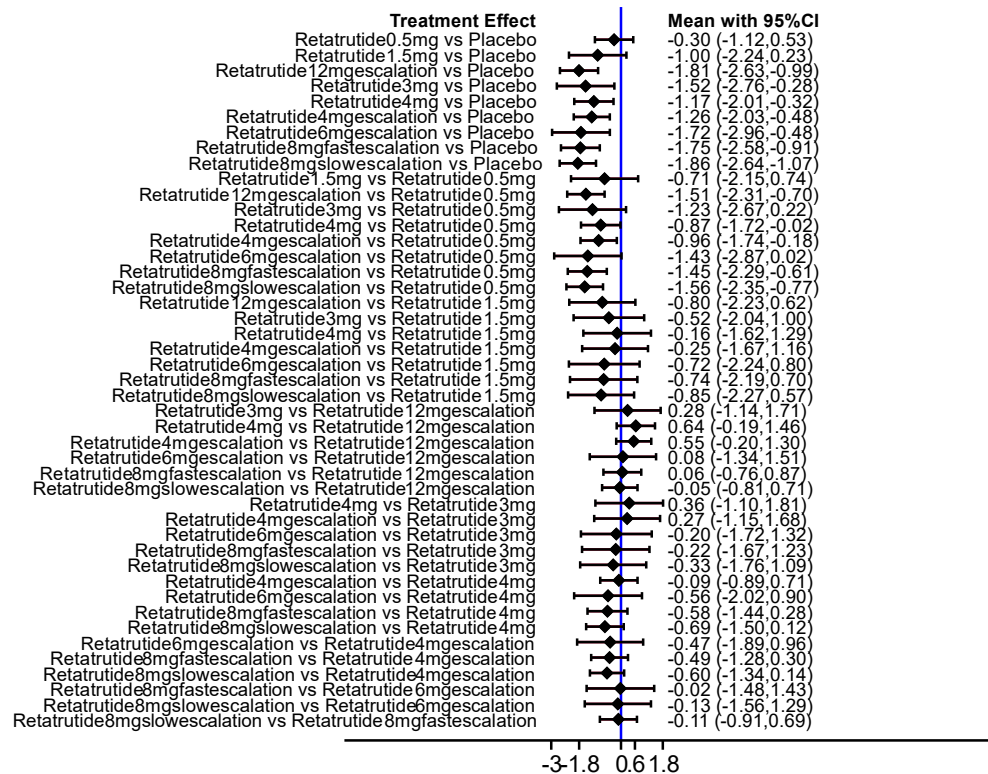
Figure S14.10: Effects of different doses of Retatrutide on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Retatrutide on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) waist circumference. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



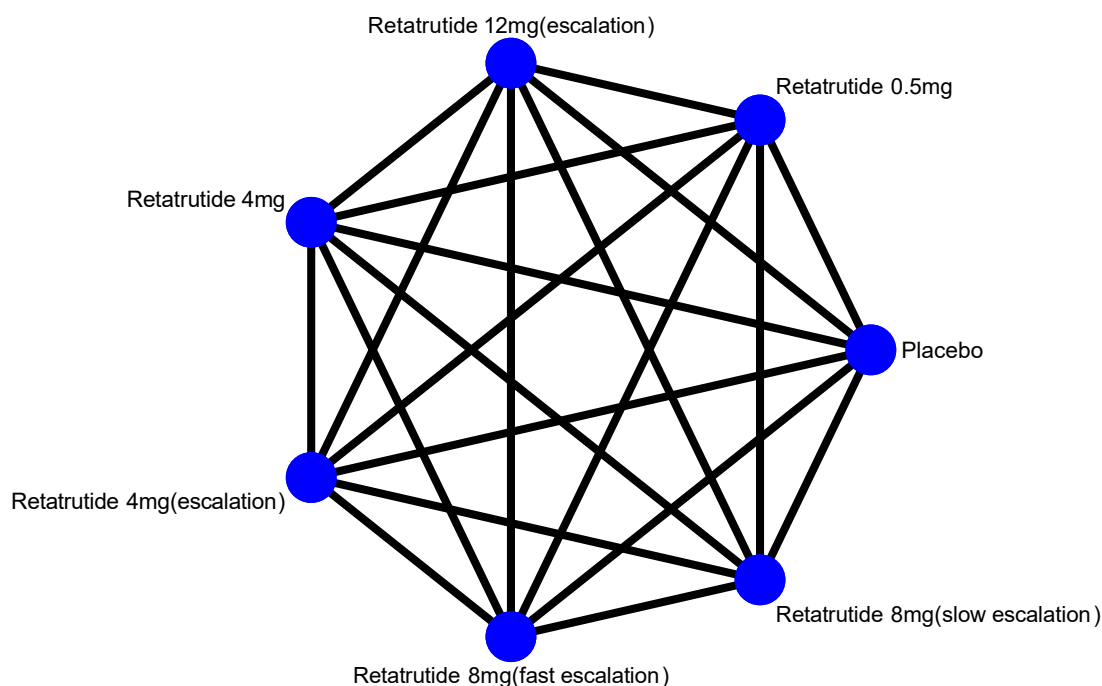
(A2) Forest plot of HbA1c



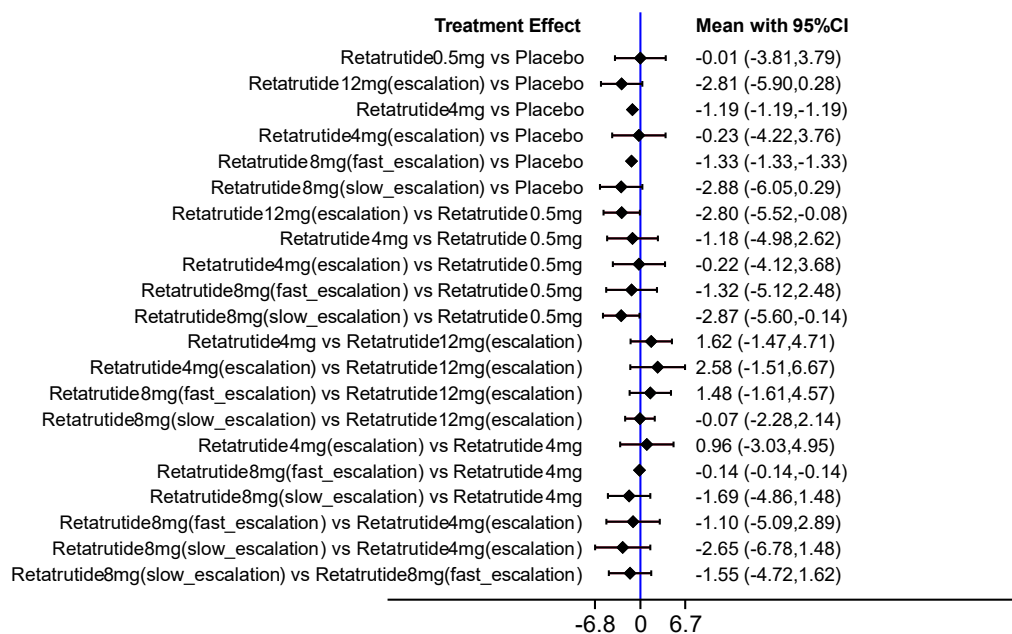
(A3) League table of HbA1c

Retatrutide 8mg(slowescalation)	0.05 (-0.71, 0.81)	0.11 (-0.69, 0.91)	0.13 (-1.29, 1.56)	0.33 (-1.09, 1.76)	0.60 (-0.14, 1.34)	0.69 (-0.12, 1.50)	0.85 (-0.57, 2.27)	1.56 (0.77, 2.35)	1.86 (1.07, 2.64)
-0.05 (-0.81, 0.71)	Retatrutide 12mg(escalation)	0.06 (-0.76, 0.87)	0.08 (-1.34, 1.51)	0.28 (-1.14, 1.71)	0.55 (-0.20, 1.30)	0.64 (-0.19, 1.46)	0.80 (-0.62, 2.23)	1.51 (0.70, 2.31)	1.81 (0.99, 2.63)
-0.11 (-0.91, 0.69)	-0.06 (-0.87, 0.76)	Retatrutide 8mg(fastescalation)	0.02 (-1.43, 1.48)	0.22 (-1.23, 1.67)	0.49 (-0.30, 1.28)	0.58 (-0.28, 1.44)	0.74 (-0.70, 2.19)	1.45 (0.61, 2.29)	1.75 (0.91, 2.58)
-0.13 (-1.56, 1.29)	-0.08 (-1.51, 1.34)	-0.02 (-1.48, 1.43)	Retatrutide 6mg(escalation)	0.20 (-1.32, 1.72)	0.47 (-0.96, 1.89)	0.56 (-0.90, 2.02)	0.72 (-0.80, 2.24)	1.43 (0.02, 2.87)	1.72 (0.48, 2.96)
-0.33 (-1.76, 1.09)	-0.28 (-1.71, 1.14)	-0.22 (-1.67, 1.23)	-0.20 (-1.72, 1.32)	Retatrutide 3mg	0.27 (-1.15, 1.68)	0.36 (-1.10, 1.81)	0.52 (-1.00, 2.04)	1.23 (0.22, 2.67)	1.52 (0.28, 2.76)
-0.60 (-1.34, 0.14)	-0.55 (-1.30, 0.20)	-0.49 (-1.28, 0.30)	-0.47 (-1.89, 0.96)	-0.27 (-1.68, 1.15)	Retatrutide 4mg(escalation)	0.09 (-0.71, 0.89)	0.25 (-1.16, 1.67)	0.96 (0.18, 1.74)	1.26 (0.48, 2.03)
-0.69 (-1.50, 0.12)	-0.64 (-1.46, 0.19)	-0.58 (-1.44, 0.28)	-0.56 (-2.02, 0.90)	-0.36 (-1.81, 1.10)	-0.09 (-0.89, 0.71)	Retatrutide 4mg	0.16 (-1.29, 1.62)	0.87 (0.02, 1.72)	1.17 (0.32, 2.01)
-0.85 (-2.27, 0.57)	-0.80 (-2.23, 0.62)	-0.74 (-2.19, 0.70)	-0.72 (-2.24, 0.80)	-0.52 (-2.04, 1.00)	-0.25 (-1.67, 1.16)	-0.16 (-1.62, 1.29)	Retatrutide 1.5mg	0.71 (-0.74, 2.15)	1.00 (-0.23, 2.24)
-1.56 (-2.35, -0.77)	-1.51 (-2.31, -0.70)	-1.45 (-2.29, -0.61)	-1.43 (-2.87, 0.02)	-1.23 (-2.67, 0.22)	-0.96 (-1.74, -0.18)	-0.87 (-1.72, -0.02)	-0.71 (-2.15, 0.74)	Retatrutide 0.5mg	0.30 (-0.53, 1.12)
-1.86 (-2.64, -1.07)	-1.81 (-2.63, -0.99)	-1.75 (-2.58, -0.91)	-1.72 (-2.96, -0.48)	-1.52 (-2.76, -0.28)	-1.26 (-2.03, -0.48)	-1.17 (-2.01, -0.32)	-1.00 (-2.24, 0.23)	-0.30 (-1.12, 0.53)	Placebo

(B1) Network map of FPG



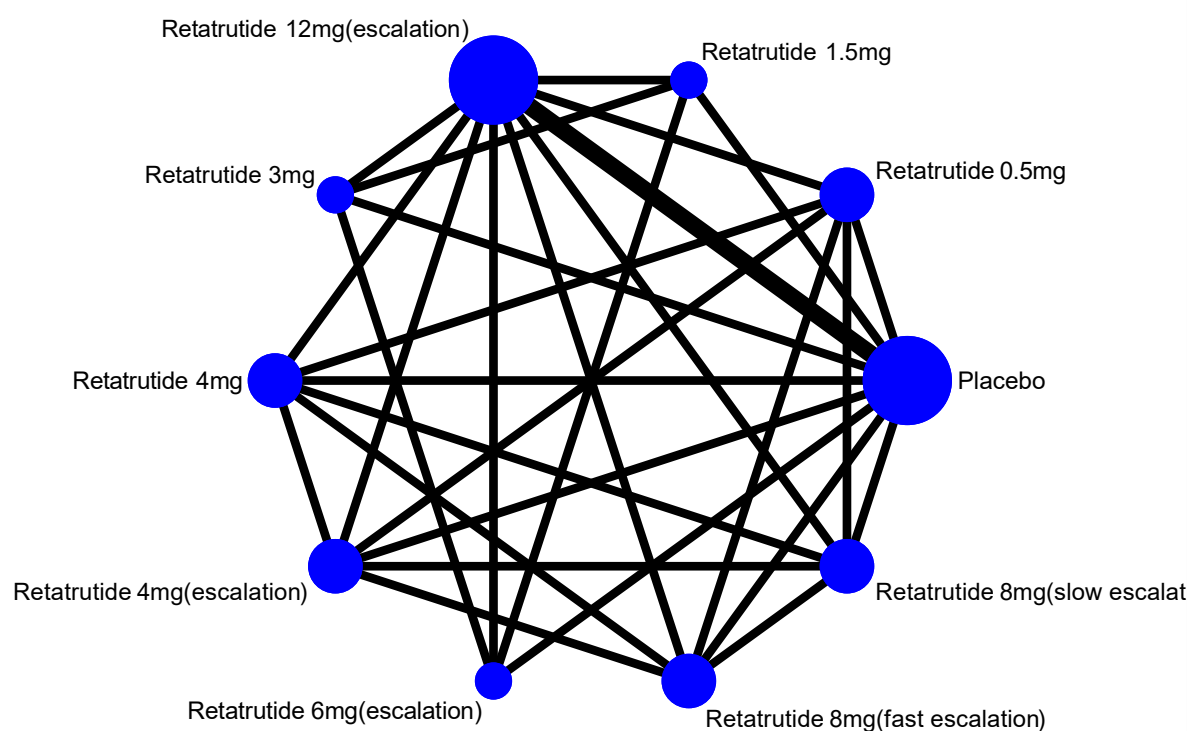
(B2) Forest plot of FPG



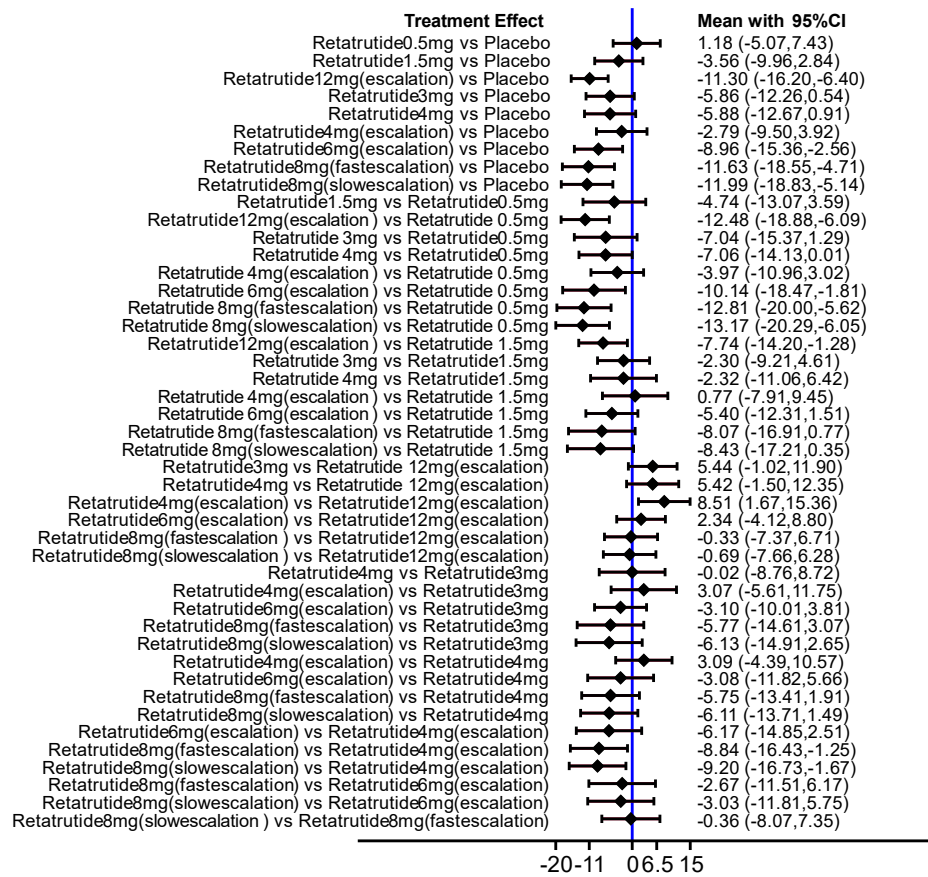
(B3) League table of FPG

Retatrutide 8mg (slow escalation)	0.07 (-2.14,2.28)	1.55 (-1.62,4.72)	1.69 (-1.48,4.86)	2.65 (-1.48,6.78)	2.87 (0.14,5.60)	2.88 (-0.29,6.05)
-0.07 (-2.28,2.14)	Retatrutide 12mg (escalation)	1.48 (-1.61,4.57)	1.62 (-1.47,4.71)	2.58 (-1.51,6.67)	2.80 (0.08,5.52)	2.81 (-0.28,5.90)
-1.55 (-4.72,1.62)	-1.48 (-4.57,1.61)	Retatrutide 8mg (fast escalation)	0.14 (0.14,0.14)	1.10 (-2.89,5.09)	1.32 (-2.48,5.12)	1.33 (1.33,1.33)
-1.69 (-4.86,1.48)	-1.62 (-4.71,1.47)	-0.14 (-0.14,-0.14)	Retatrutide 4mg	0.96 (-3.03,4.95)	1.18 (-2.62,4.98)	1.19 (1.19,1.19)
-2.65 (-6.78,1.48)	-2.58 (-6.67,1.51)	-1.10 (-5.09,2.89)	-0.96 (-4.95,3.03)	Retatrutide 4mg (escalation)	0.22 (-3.68,4.12)	0.23 (-3.76,4.22)
-2.87 (-5.60,-0.14)	-2.80 (-5.52,-0.08)	-1.32 (-5.12,2.48)	-1.18 (-4.98,2.62)	-0.22 (-4.12,3.68)	Retatrutide 0.5mg	0.01 (-3.79,3.81)
-2.88 (-6.05,0.29)	-2.81 (-5.90,0.28)	-1.33 (-1.33,-1.33)	-1.19 (-1.19,-1.19)	-0.23 (-4.22,3.76)	-0.01 (-3.81,3.79)	Placebo

(C1) Network map of weight loss



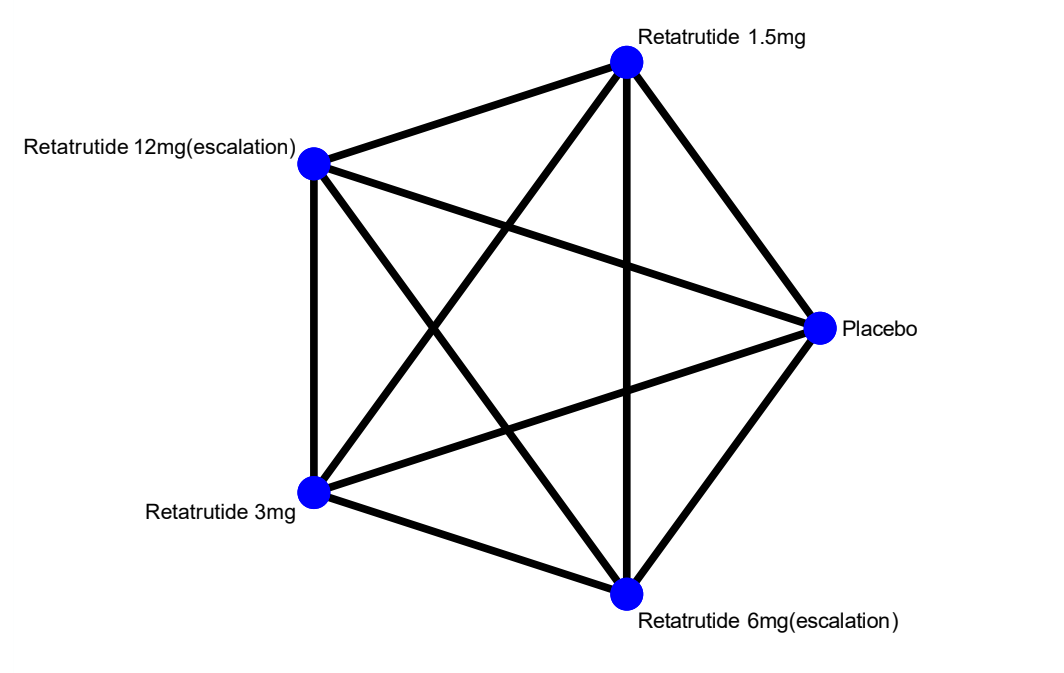
(C2) Forest plot of weight loss



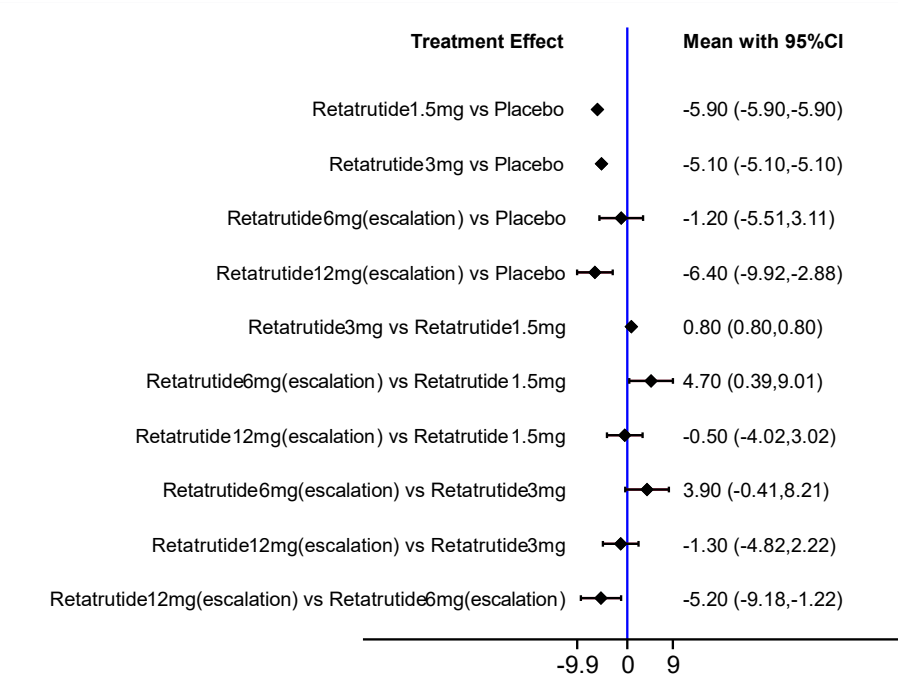
(C3) League table of weight loss

Retatrutide 8mg(slow escalation)	0.69 (-6.28,7.66)	0.36 (-7.35,8.07)	3.03 (-5.75,11.81)	6.13 (-2.65,14.91)	6.11 (-1.49,13.71)	8.43 (-0.35,17.21)	9.20 (1.67,16.73)	11.99 (5.14,18.83)	13.17 (6.05,20.29)
-0.69 (-7.66,6.28)	Retatrutide 12mg(escalation)	-0.33 (-7.37,6.71)	2.34 (-4.12,8.80)	5.44 (-1.02,11.90)	5.42 (-1.50,12.35)	7.74 (1.28,14.20)	8.51 (1.67,15.36)	11.30 (6.40,16.20)	12.48 (6.09,18.88)
-0.36 (-8.07,7.35)	0.33 (-6.71,7.37)	Retatrutide 8mg(fast escalation)	2.67 (-6.17,11.51)	5.77 (-3.07,14.61)	5.75 (-1.91,13.41)	8.07 (-0.77,16.91)	8.84 (1.25,16.43)	11.63 (4.71,18.55)	12.81 (5.62,20.00)
-3.03 (-11.81,5.75)	-2.34 (-8.80,4.12)	-2.67 (-11.51,6.17)	Retatrutide 6mg(escalation)	3.10 (-3.81,10.01)	3.08 (-5.66,11.82)	5.40 (-1.51,12.31)	6.17 (-2.51,14.85)	8.96 (2.56,15.36)	10.14 (1.81,18.47)
-6.13 (-14.91,2.65)	-5.44 (-11.90,1.02)	-5.77 (-14.61,3.07)	-3.10 (-10.01,3.81)	Retatrutide 3mg	-0.02 (-8.76,8.72)	2.30 (-4.61,9.21)	3.07 (-5.61,11.75)	5.86 (-0.54,12.26)	7.04 (-1.29,15.37)
-6.11 (-13.71,1.49)	-5.42 (-12.35,1.50)	-5.75 (-13.41,1.91)	-3.08 (-11.82,5.66)	0.02 (-8.72,8.76)	Retatrutide 4mg	2.32 (-6.42,11.06)	3.09 (-4.39,10.57)	5.88 (-0.91,12.67)	7.06 (-0.01,14.13)
-8.43 (-17.21,0.35)	-7.74 (-14.20,-1.28)	-8.07 (-16.91,0.77)	-5.40 (-12.31,1.51)	-2.30 (-9.21,4.61)	-2.32 (-11.06,6.42)	Retatrutide 1.5mg	0.77 (-7.91,9.45)	3.56 (-2.84,9.96)	4.74 (-3.59,13.07)
-9.20 (-16.73,-1.67)	-8.51 (-15.36,-1.67)	-8.84 (-16.43,-1.25)	-6.17 (-14.85,2.51)	-3.07 (-11.75,5.61)	-3.09 (-10.57,4.39)	-0.77 (-9.45,7.91)	Retatrutide 4mg(escalation)	2.79 (-3.92,9.50)	3.97 (-3.02,10.96)
-11.99 (-18.83,-5.14)	-11.30 (-16.20,-6.40)	-11.63 (-18.55,-4.71)	-8.96 (-15.36,-2.56)	-5.86 (-12.26,0.54)	-5.88 (-12.67,0.91)	-3.56 (-9.96,2.84)	-2.79 (-9.50,3.92)	Placebo	1.18 (-5.07,7.43)
-13.17 (-20.29,-6.05)	-12.48 (-18.88,-6.09)	-12.81 (-20.00,-5.62)	-10.14 (-18.47,-1.81)	-7.04 (-15.37,1.29)	-7.06 (-14.13,0.01)	-4.74 (-13.07,3.59)	-3.97 (-10.96,3.02)	-1.18 (-7.43,5.07)	Retatrutide 0.5mg

(D1) Network map of waist circumference



(D2) Forest plot of waist circumference



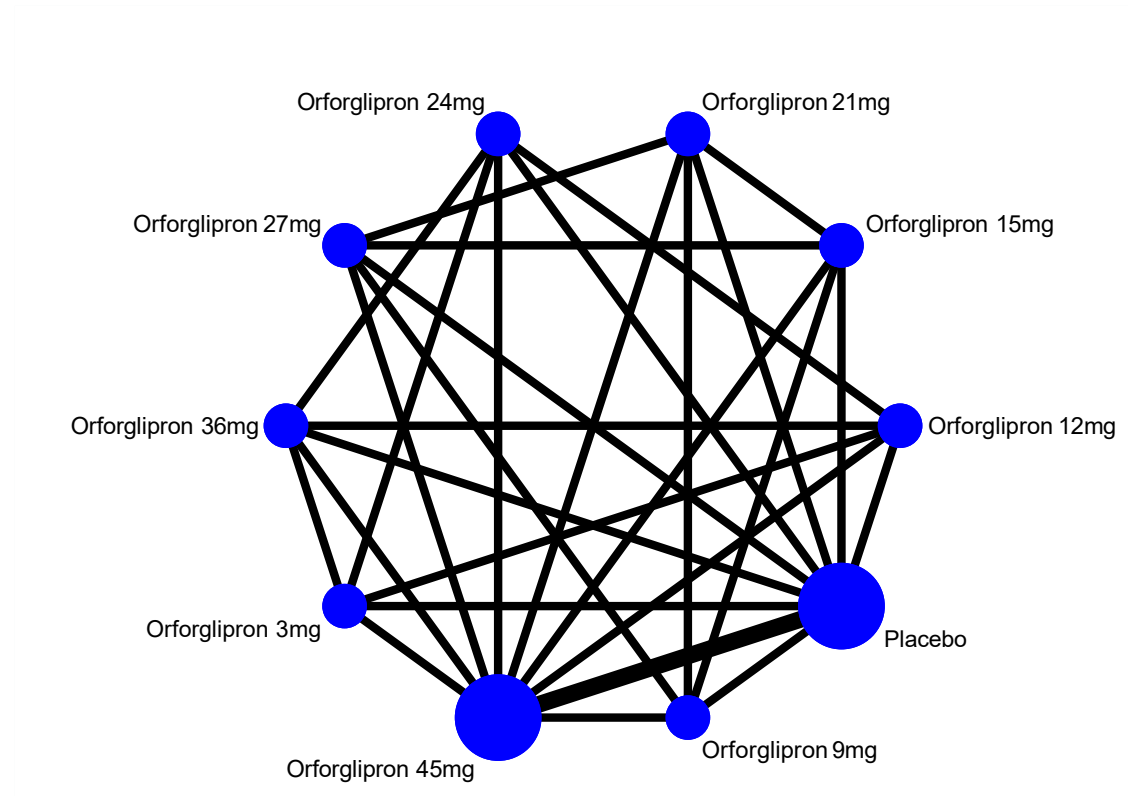
(D3) League table of waist circumference

Retatrutide 1.5mg	-0.50 (- 4.02,3.02)	0.80 (0.80,0.80)	4.70 (0.39,9.01)	5.90 (5.90,5.90)
0.50 (- 3.02,4.02)	Retatrutide 12mg(escalation)	1.30 (- 2.22,4.82)	5.20 (1.22,9.18)	6.40 (2.88,9.92)
-0.80 (-0.80,- 0.80)	-1.30 (- 4.82,2.22)	Retatrutide 3mg	3.90 (- 0.41,8.21)	5.10 (5.10,5.10)
-4.70 (-9.01,- 0.39)	-5.20 (-9.18,- 1.22)	-3.90 (- 8.21,0.41)	Retatrutide 6mg(escalation)	1.20 (- 3.11,5.51)
-5.90 (-5.90,- 5.90)	-6.40 (-9.92,- 2.88)	-5.10 (-5.10,- 5.10)	-1.20 (- 5.51,3.11)	Placebo

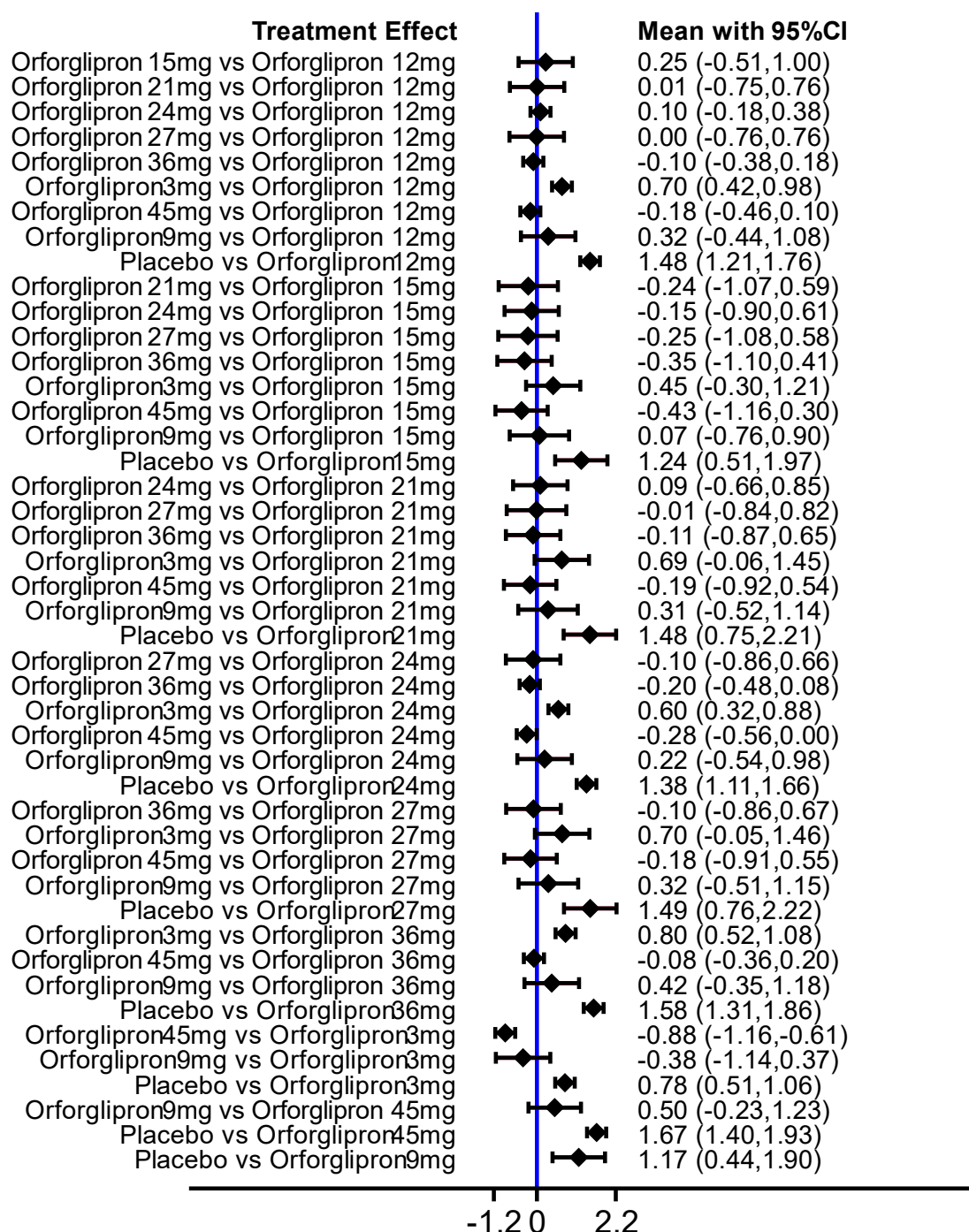
Figure S14.11: Effects of different doses of Orforglipron on various indicators of T2D.

Network meta-analysis maps of the studies examining the efficacy of different doses of Orforglipron on various indicators of diabetes (A) HbA1c, (B) FPG, (C) weight loss, (D) BMI, (E) waist circumference. The size of the nodes relates to the number of participants in that intervention type, and the thickness of lines between the interventions relates to the number of studies for that comparison.

(A1) Network map of HbA1c



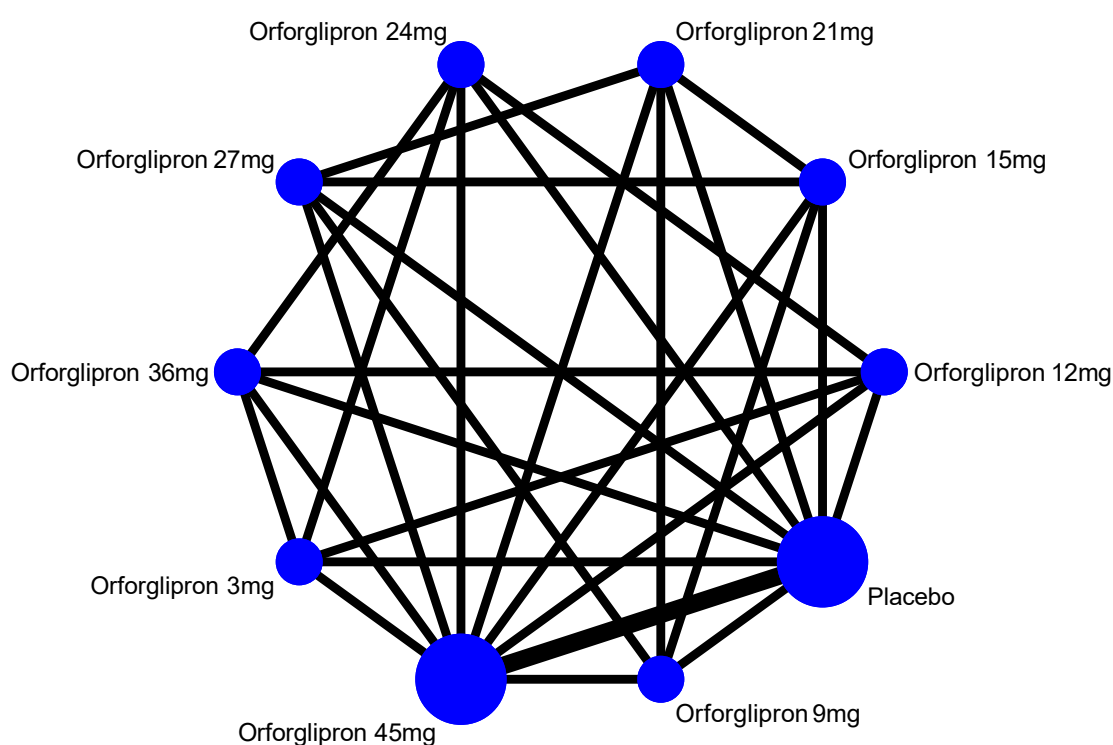
(A2) Forest plot of HbA1c



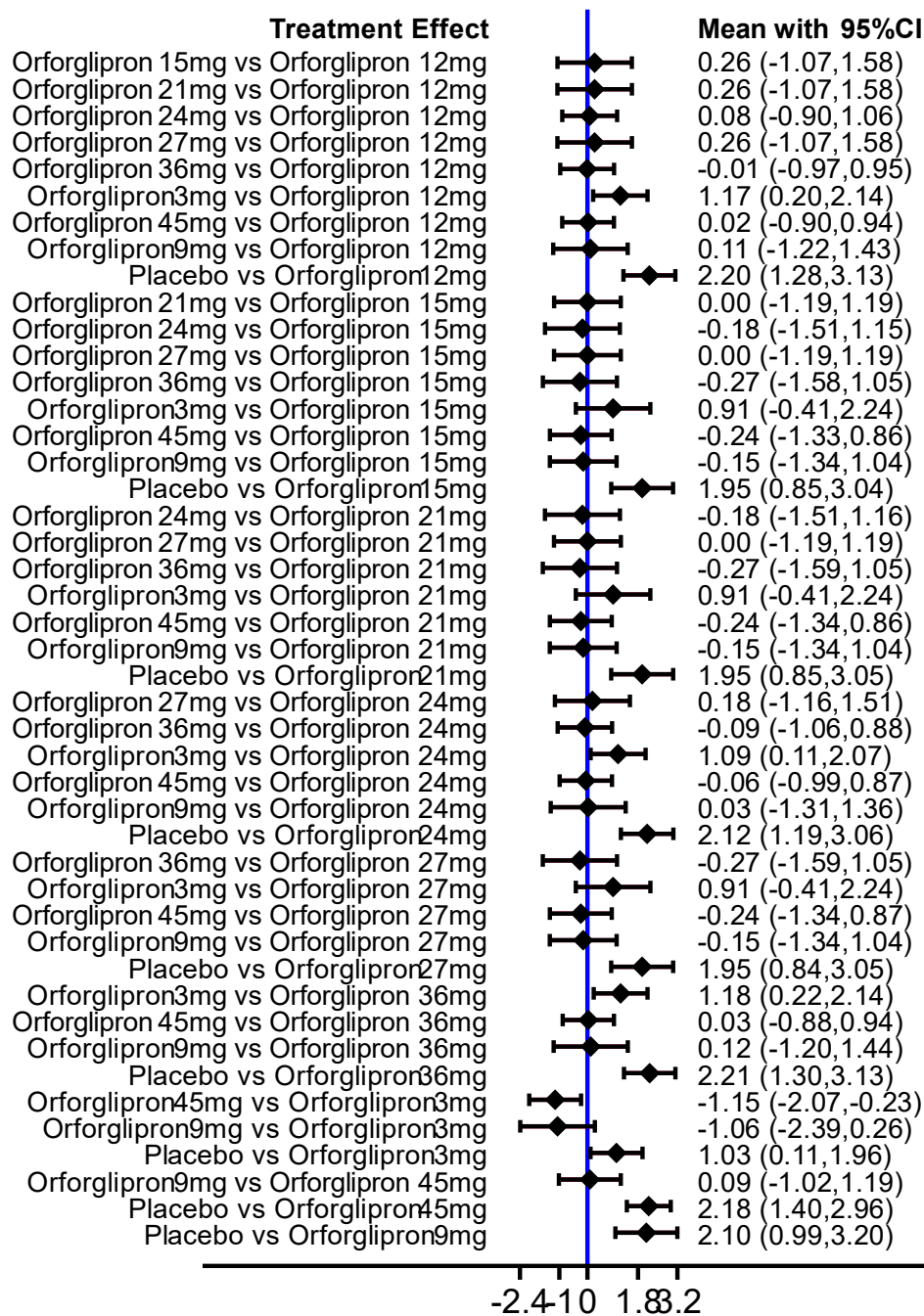
(A3) League table of HbA1c

Orforglipron 45mg	0.08 (-0.20,0.36)	0.18 (-0.55,0.91)	0.18 (-0.10,0.46)	0.19 (-0.54,0.92)	0.28 (0.00,0.56)	0.43 (-0.30,1.16)	0.50 (-0.23,1.23)	0.88 (0.61,1.16)	1.67 (1.40,1.93)
-0.08 (-0.36,0.20)	Orforglipron 36mg	0.10 (-0.67,0.86)	0.10 (-0.18,0.38)	0.11 (-0.65,0.87)	0.20 (-0.08,0.48)	0.35 (-0.41,1.10)	0.42 (-0.35,1.18)	0.80 (0.52,1.08)	1.58 (1.31,1.86)
-0.18 (-0.91,0.55)	-0.10 (-0.86,0.67)	Orforglipron 27mg	0.00 (-0.76,0.76)	0.01 (-0.82,0.84)	0.10 (-0.66,0.86)	0.25 (-0.58,1.08)	0.32 (-0.51,1.15)	0.70 (-0.05,1.46)	1.49 (0.76,2.22)
-0.18 (-0.46,0.10)	-0.10 (-0.38,0.18)	-0.00 (-0.76,0.76)	Orforglipron 12mg	0.01 (-0.75,0.76)	0.10 (-0.18,0.38)	0.25 (-0.51,1.00)	0.32 (-0.44,1.08)	0.70 (0.42,0.98)	1.48 (1.21,1.76)
-0.19 (-0.92,0.54)	-0.11 (-0.87,0.65)	-0.01 (-0.84,0.82)	-0.01 (-0.76,0.75)	Orforglipron 21mg	0.09 (-0.66,0.85)	0.24 (-0.59,1.07)	0.31 (-0.52,1.14)	0.69 (-0.06,1.45)	1.48 (0.75,2.21)
-0.28 (-0.56,-0.00)	-0.20 (-0.48,0.08)	-0.10 (-0.86,0.66)	-0.10 (-0.38,0.18)	-0.09 (-0.85,0.66)	Orforglipron 24mg	0.15 (-0.61,0.90)	0.22 (-0.54,0.98)	0.60 (0.32,0.88)	1.38 (1.11,1.66)
-0.43 (-1.16,0.30)	-0.35 (-1.10,0.41)	-0.25 (-1.08,0.58)	-0.25 (-1.00,0.51)	-0.24 (-1.07,0.59)	-0.15 (-0.90,0.61)	Orforglipron 15mg	0.07 (-0.76,0.90)	0.45 (-0.30,1.21)	1.24 (0.51,1.97)
-0.50 (-1.23,0.23)	-0.42 (-1.18,0.35)	-0.32 (-1.15,0.51)	-0.32 (-1.08,0.44)	-0.31 (-1.14,0.52)	-0.22 (-0.98,0.54)	-0.07 (-0.90,0.76)	Orforglipron 9mg	0.38 (-0.37,1.14)	1.17 (0.44,1.90)
-0.88 (-1.16,-0.61)	-0.80 (-1.08,-0.52)	-0.70 (-1.46,0.05)	-0.70 (-0.98,-0.42)	-0.69 (-1.45,0.06)	-0.60 (-0.88,-0.32)	-0.45 (-1.21,0.30)	-0.38 (-1.14,0.37)	Orforglipron 3mg	0.78 (0.51,1.06)
-1.67 (-1.93,-1.40)	-1.58 (-1.86,-1.31)	-1.49 (-2.22,-0.76)	-1.48 (-1.76,-1.21)	-1.48 (-2.21,-0.75)	-1.38 (-1.66,-1.11)	-1.24 (-1.97,-0.51)	-1.17 (-1.90,-0.44)	-0.78 (-1.06,-0.51)	Placebo

(B1) Network map of FPG



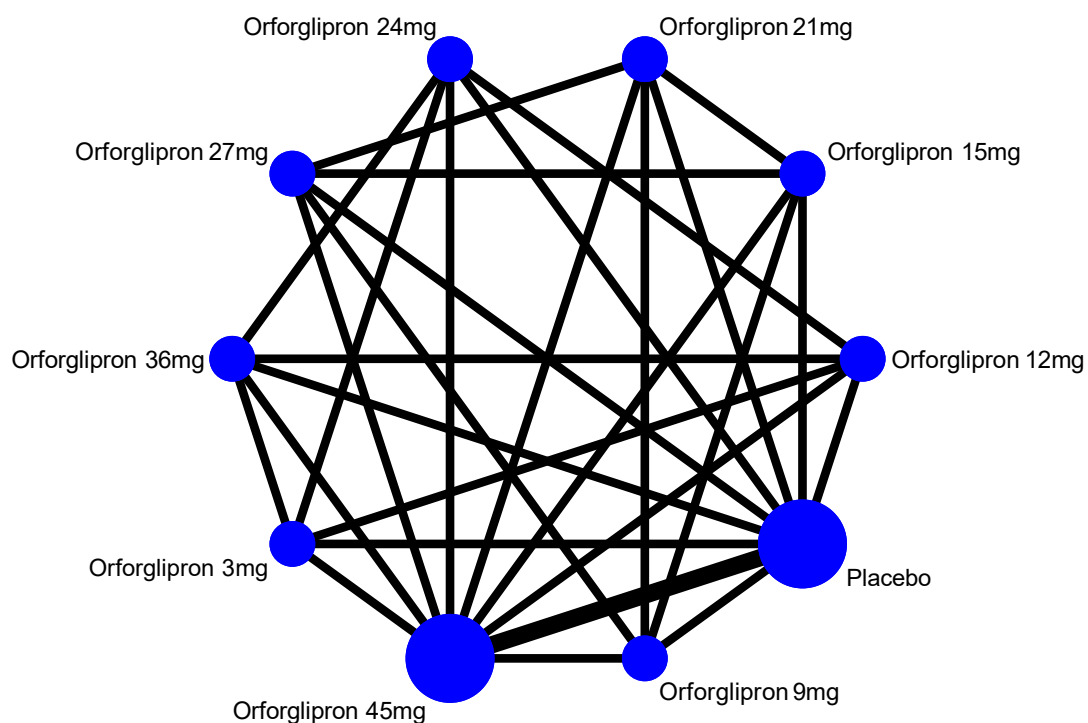
(B2) Forest plot of FPG



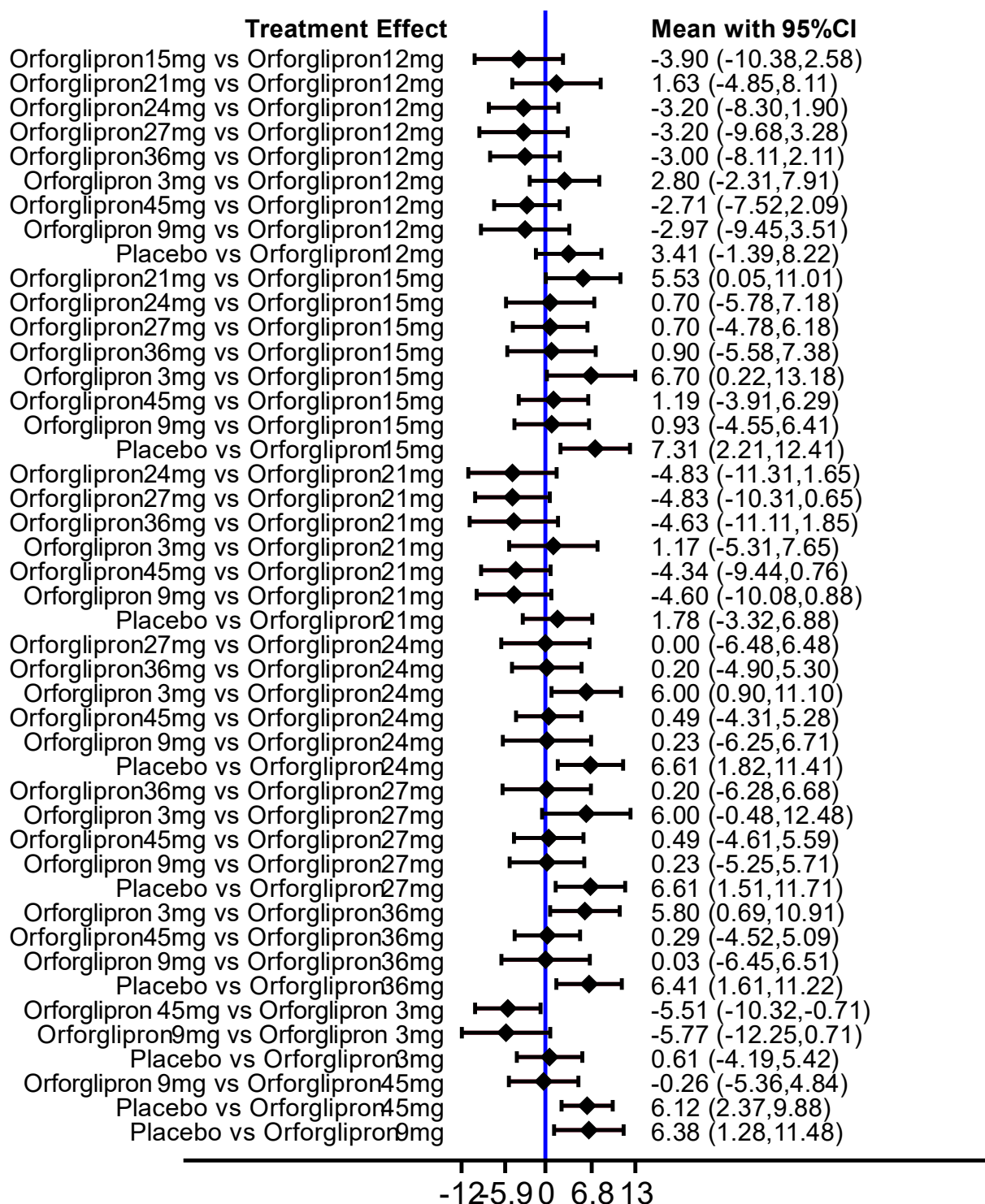
(B3) League table of FPG

Orforglipron n 36mg	0.01 (- 0.95,0.97)	0.03 (- 0.88,0.94)	0.09 (- 0.88,1.06)	0.12 (- 1.20,1.44)	0.27 (- 1.05,1.59)	0.27 (- 1.05,1.58)	0.27 (- 1.05,1.59)	1.18 (0.22,2.14)	2.21 (1.30,3.13)
-0.01 (- 0.97,0.95)	Orforglipron n 12mg	0.02 (- 0.90,0.94)	0.08 (- 0.90,1.06)	0.11 (- 1.22,1.43)	0.26 (- 1.07,1.58)	0.26 (- 1.07,1.58)	0.26 (- 1.07,1.58)	1.17 (0.20,2.14)	2.20 (1.28,3.13)
-0.03 (- 0.94,0.88)	-0.02 (- 0.94,0.90)	Orforglipron n 45mg	0.06 (- 0.87,0.99)	0.09 (- 1.02,1.19)	0.24 (- 0.86,1.34)	0.24 (- 0.86,1.33)	0.24 (- 0.87,1.34)	1.15 (0.23,2.07)	2.18 (1.40,2.96)
-0.09 (- 1.06,0.88)	-0.08 (- 1.06,0.90)	-0.06 (- 0.99,0.87)	Orforglipron n 24mg	0.03 (- 1.31,1.36)	0.18 (- 1.16,1.51)	0.18 (- 1.15,1.51)	0.18 (- 1.16,1.51)	1.09 (0.11,2.07)	2.12 (1.19,3.06)
-0.12 (- 1.44,1.20)	-0.11 (- 1.43,1.22)	-0.09 (- 1.19,1.02)	-0.03 (- 1.36,1.31)	Orforglipron n 9mg	0.15 (- 1.04,1.34)	0.15 (- 1.04,1.34)	0.15 (- 1.04,1.34)	1.06 (- 0.26,2.39)	2.10 (0.99,3.20)
-0.27 (- 1.59,1.05)	-0.26 (- 1.58,1.07)	-0.24 (- 1.34,0.86)	-0.18 (- 1.51,1.16)	-0.15 (- 1.34,1.04)	Orforglipron n 21mg	0.00 (- 1.19,1.19)	-0.00 (- 1.19,1.19)	0.91 (- 0.41,2.24)	1.95 (0.85,3.05)
-0.27 (- 1.58,1.05)	-0.26 (- 1.58,1.07)	-0.24 (- 1.33,0.86)	-0.18 (- 1.51,1.15)	-0.15 (- 1.34,1.04)	-0.00 (- 1.19,1.19)	Orforglipron n 15mg	-0.00 (- 1.19,1.19)	0.91 (- 0.41,2.24)	1.95 (0.85,3.04)
-0.27 (- 1.59,1.05)	-0.26 (- 1.58,1.07)	-0.24 (- 1.34,0.87)	-0.18 (- 1.51,1.16)	-0.15 (- 1.34,1.04)	0.00 (- 1.19,1.19)	0.00 (- 1.19,1.19)	Orforglipron n 27mg	0.91 (- 0.41,2.24)	1.95 (0.84,3.05)
-1.18 (- 2.14,-0.22)	-1.17 (- 2.14,-0.20)	-1.15 (- 2.07,-0.23)	-1.09 (- 2.07,-0.11)	-1.06 (- 2.39,0.26)	-0.91 (- 2.24,0.41)	-0.91 (- 2.24,0.41)	-0.91 (- 2.24,0.41)	Orforglipron n 3mg	1.03 (0.11,1.96)
-2.21 (- 3.13,-1.30)	-2.20 (- 3.13,-1.28)	-2.18 (- 2.96,-1.40)	-2.12 (- 3.06,-1.19)	-2.10 (- 3.20,-0.99)	-1.95 (- 3.05,-0.85)	-1.95 (- 3.04,-0.85)	-1.95 (- 3.05,-0.84)	-1.03 (- 1.96,-0.11)	Placebo

(C1) Network map of weight loss



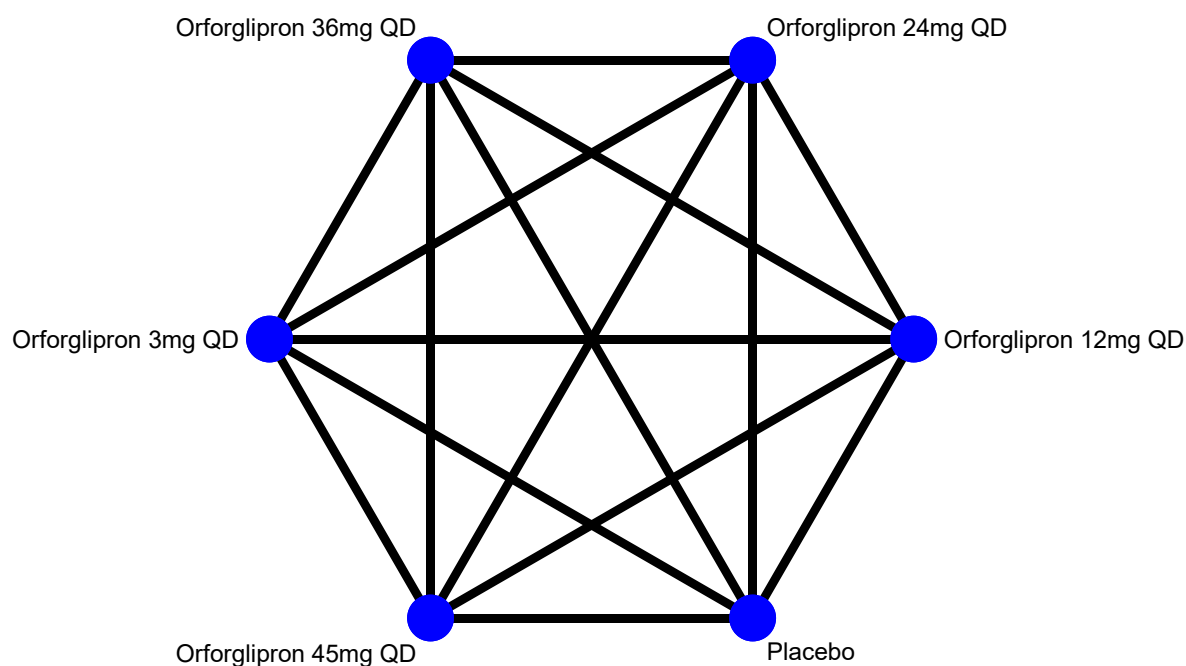
(C2) Forest plot of weight loss



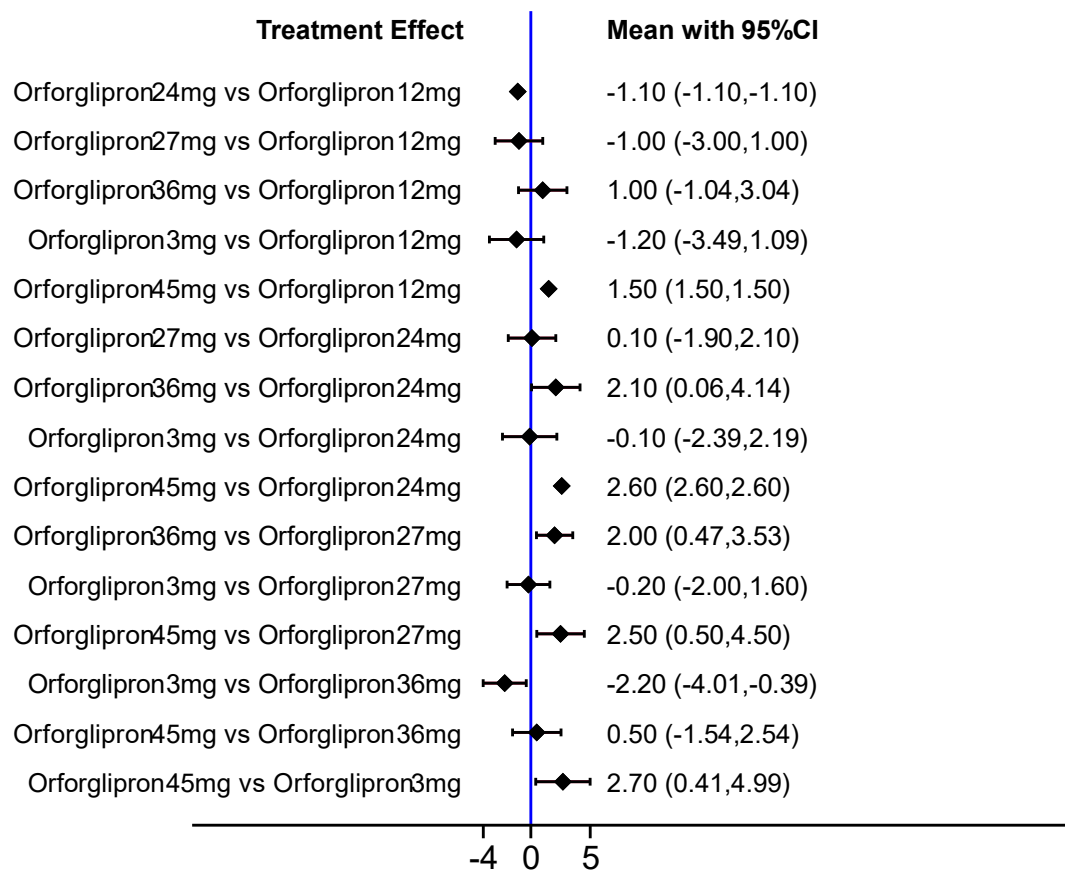
(C3) League table of weight loss

Orforglipron 15mg	0.70 (-5.78,7.18)	0.70 (-4.78,6.18)	0.90 (-5.58,7.38)	0.93 (-4.55,6.41)	1.19 (-3.91,6.29)	3.90 (-2.58,10.38)	5.53 (0.05,11.01)	6.70 (0.22,13.18)	7.31 (2.21,12.41)
-0.70 (-7.18,5.78)	Orforglipron 24mg	0.00 (-6.48,6.48)	0.20 (-4.90,5.30)	0.23 (-6.25,6.71)	0.49 (-4.31,5.28)	3.20 (-1.90,8.30)	4.83 (-1.65,11.31)	6.00 (0.90,11.10)	6.61 (1.82,11.41)
-0.70 (-6.18,4.78)	-0.00 (-6.48,6.48)	Orforglipron 27mg	0.20 (-6.28,6.68)	0.23 (-5.25,5.71)	0.49 (-4.61,5.59)	3.20 (-3.28,9.68)	4.83 (-0.65,10.31)	6.00 (-0.48,12.48)	6.61 (1.51,11.71)
-0.90 (-7.38,5.58)	-0.20 (-5.30,4.90)	-0.20 (-6.68,6.28)	Orforglipron 36mg	0.03 (-6.45,6.51)	0.29 (-4.52,5.09)	3.00 (-2.11,8.11)	4.63 (-1.85,11.11)	5.80 (0.69,10.91)	6.41 (1.61,11.22)
-0.93 (-6.41,4.55)	-0.23 (-6.71,6.25)	-0.23 (-5.71,5.25)	-0.03 (-6.51,6.45)	Orforglipron 9mg	0.26 (-4.84,5.36)	2.97 (-3.51,9.45)	4.60 (-0.88,10.08)	5.77 (-0.71,12.25)	6.38 (1.28,11.48)
-1.19 (-6.29,3.91)	-0.49 (-5.28,4.31)	-0.49 (-5.59,4.61)	-0.29 (-5.09,4.52)	-0.26 (-5.36,4.84)	Orforglipron 45mg	2.71 (-2.09,7.52)	4.34 (-0.76,9.44)	5.51 (0.71,10.32)	6.12 (2.37,9.88)
-3.90 (-10.38,2.58)	-3.20 (-8.30,1.90)	-3.20 (-9.68,3.28)	-3.00 (-8.11,2.11)	-2.97 (-9.45,3.51)	-2.71 (-7.52,2.09)	Orforglipron 12mg	1.63 (-4.85,8.11)	2.80 (-2.31,7.91)	3.41 (-1.39,8.22)
-5.53 (-11.01,-0.05)	-4.83 (-11.31,1.65)	-4.83 (-10.31,0.65)	-4.63 (-11.11,1.85)	-4.60 (-10.08,0.88)	-4.34 (-9.44,0.76)	-1.63 (-8.11,4.85)	Orforglipron 21mg	1.17 (-5.31,7.65)	1.78 (-3.32,6.88)
-6.70 (-13.18,-0.22)	-6.00 (-11.10,-0.90)	-6.00 (-12.48,0.48)	-5.80 (-10.91,-0.69)	-5.77 (-12.25,0.71)	-5.51 (-10.32,-0.71)	-2.80 (-7.91,2.31)	-1.17 (-7.65,5.31)	Orforglipron 3mg	0.61 (-4.19,5.42)
-7.31 (-12.41,-2.21)	-6.61 (-11.41,-1.82)	-6.61 (-11.71,-1.51)	-6.41 (-11.22,-1.61)	-6.38 (-11.48,-1.28)	-6.12 (-9.88,-2.37)	-3.41 (-8.22,1.39)	-1.78 (-6.88,3.32)	-0.61 (-5.42,4.19)	Placebo

(D1) Network map of BMI



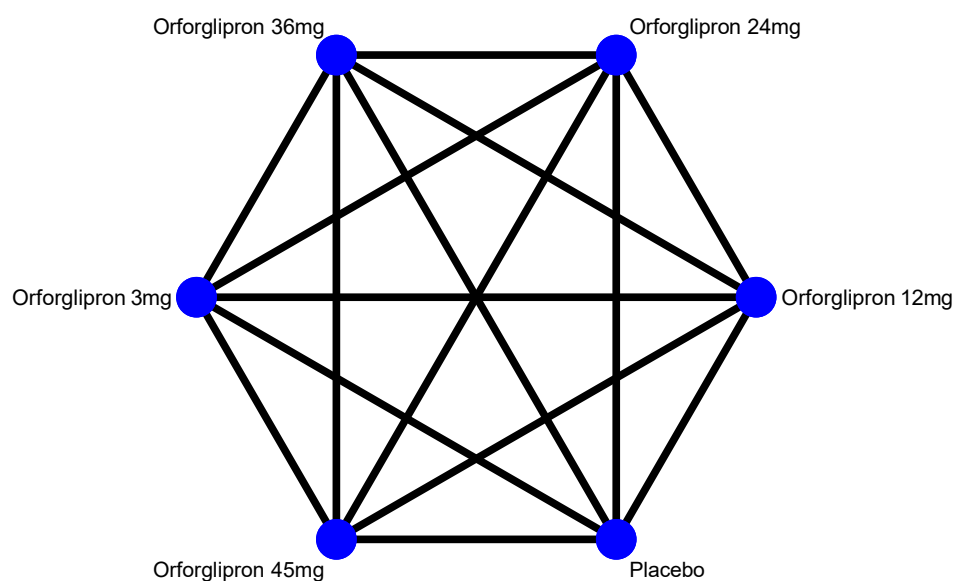
(D2) Forest plot of BMI



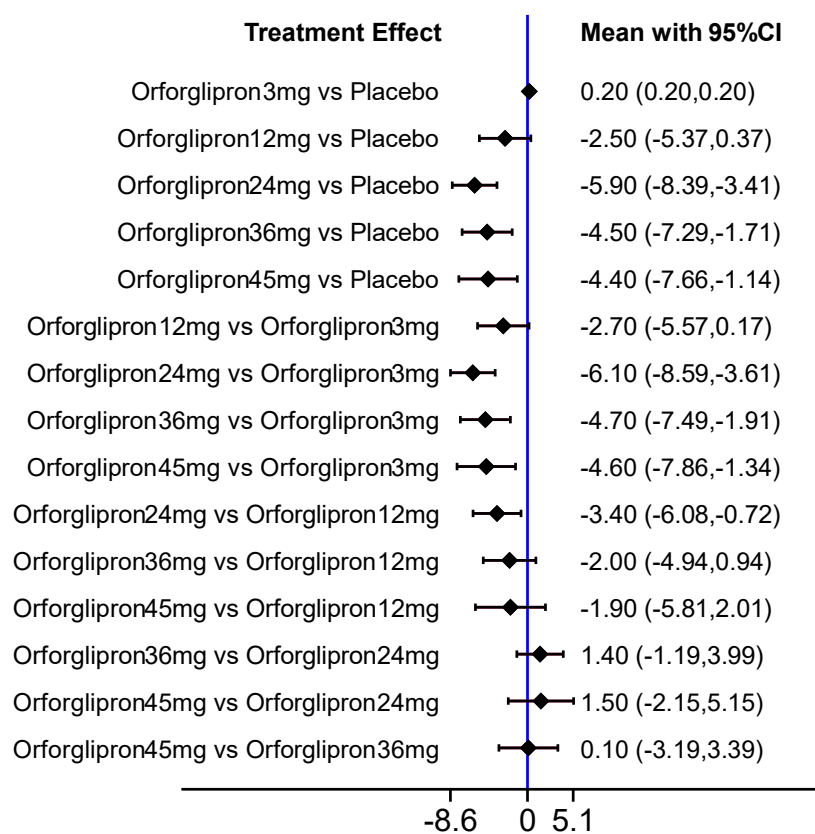
(D3) League table of BMI

Orforglipron 24mg	-0.10 (-2.39,2.19)	0.10 (-1.90,2.10)	1.10 (1.10,1.10)	2.10 (0.06,4.14)	2.60 (2.60,2.60)
0.10 (-2.19,2.39)	Orforglipron 45mg	0.20 (-1.60,2.00)	1.20 (-1.09,3.49)	2.20 (0.39,4.01)	2.70 (0.41,4.99)
-0.10 (-2.10,1.90)	-0.20 (-2.00,1.60)	Orforglipron 36mg	1.00 (-1.00,3.00)	2.00 (0.47,3.53)	2.50 (0.50,4.50)
-1.10 (-1.10,-1.10)	-1.20 (-3.49,1.09)	-1.00 (-3.00,1.00)	Orforglipron 12mg	1.00 (-1.04,3.04)	1.50 (1.50,1.50)
-2.10 (-4.14,-0.06)	-2.20 (-4.01,-0.39)	-2.00 (-3.53,-0.47)	-1.00 (-3.04,1.04)	Orforglipron 3mg	0.50 (-1.54,2.54)
-2.60 (-2.60,-2.60)	-2.70 (-4.99,-0.41)	-2.50 (-4.50,-0.50)	-1.50 (-1.50,-1.50)	-0.50 (-2.54,1.54)	Placebo

(E1) Network map of waist circumference



(E2) Forest plot of waist circumference



(E3) League table of waist circumference

Orforglipro n 24mg	1.40 (- 2.25,5.05)	1.50 (- 2.06,5.06)	3.40 (0.42,6.38)	5.90 (2.86,8.94)	6.10 (3.13,9.07)
-1.40 (- 5.05,2.25)	Orforglipro n 36mg	0.10 (- 3.62,3.82)	2.00 (- 1.04,5.04)	4.50 (1.09,7.91)	4.70 (0.84,8.56)
-1.50 (- 5.06,2.06)	-0.10 (- 3.82,3.62)	Orforglipro n 45mg	1.90 (- 0.98,4.78)	4.40 (1.05,7.75)	4.60 (0.83,8.37)
-3.40 (- 6.38,-0.42)	-2.00 (- 5.04,1.04)	-1.90 (- 4.78,0.98)	Orforglipro n 12mg	2.50 (- 1.00,6.00)	2.70 (- 0.49,5.89)
-5.90 (- 8.94,-2.86)	-4.50 (- 7.91,-1.09)	-4.40 (- 7.75,-1.05)	-2.50 (- 6.00,1.00)	Placebo	0.20 (- 3.13,3.53)
-6.10 (- 9.07,-3.13)	-4.70 (- 8.56,-0.84)	-4.60 (- 8.37,-0.83)	-2.70 (- 5.89,0.49)	-0.20 (- 3.53,3.13)	Orforglipro n 3mg

Appendix 15: Comparison of the effects of GLP-1RAs with different follow-up durations

Table S15: Comparison of the effects of GLP-1RAs with different follow-up durations

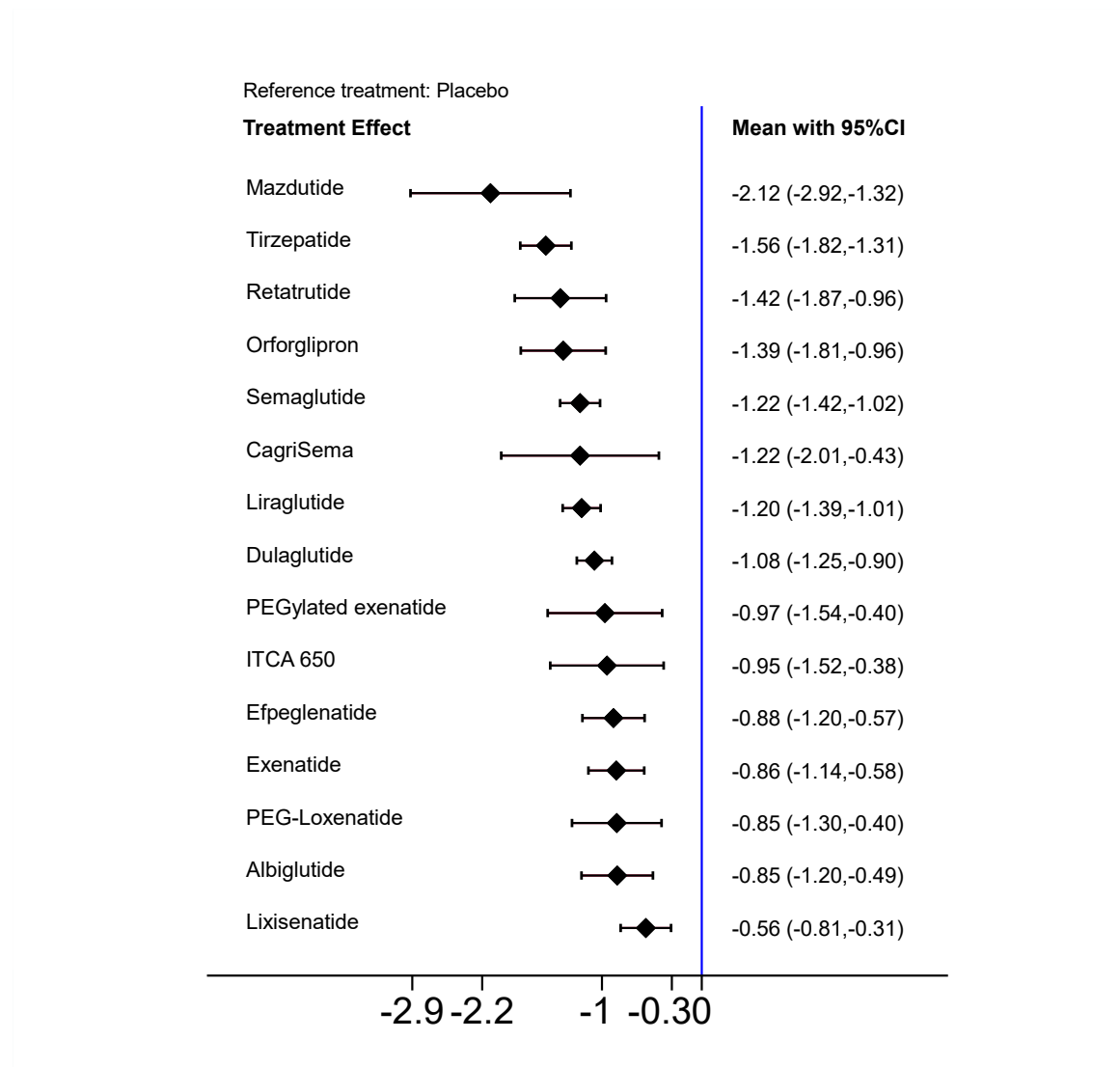
GLP-1 RA	Follow-up duration	HbA1c (%)	FPG (mmol/L)	Weight (kg)
Mazdutide	short-term	-2.12 (-2.92, -1.32)	-1.38(-2.43, 0.33)	-2.30 (-4.28, -0.32)
	medium-term	NA	NA	-2.34 (-4.93, 0.26)
	long-term	NA	NA	NA
Tirzepatide	short-term	-1.56 (-1.82, -1.31)	-1.30 (-2.08, -0.52)	-4.05 (-4.88, -3.22)
	medium-term	-1.80 (-2.08, -1.52)	-2.58 (-3.08, -2.09)	-7.73 (-9.00, -6.45)
	long-term	-2.26 (-2.75, -1.77)	-4.44 (-5.44, -3.44)	-9.57 (-12.25, -6.90)
Retatrutide	short-term	-1.42(-1.87, -0.96)	NA	-5.70 (-7.29, -4.11)
	medium-term	-1.14 (-1.67, -0.62)	-1.79 (-2.98, -0.60)	-7.95 (-9.95, -5.95)
	long-term	NA	NA	NA
Orforglipron	short-term	1.39 (-1.81, -0.96)	-2.07(-2.62, -1.51)	-4.88 (-6.35, -3.41)
	medium-term	-1.54 (-2.01, -1.07)	-2.16 (-3.03, -1.30)	-4.95 (-6.90, -3.01)
	long-term	NA	NA	NA
CagriSema	short-term	-1.22 (-2.01, -0.43)	NA	-0.36 (-8.44, -4.27)
	medium-term	-1.73 (-2.50, -0.96)	-2.83 (-4.23, -1.44)	-14.18 (-17.08, -11.28)
	long-term	NA	NA	NA
Semaglutide	short-term	-1.22 (-1.42, -1.02)	-1.92 (-2.35, -1.49)	-1.86 (-2.47, -1.25)
	medium-term	-1.33 (-1.54, -1.12)	-2.03 (-2.46, -1.61)	-3.28 (-4.20, -2.37)
	long-term	-1.24 (-1.60, -0.88)	-1.65 (-2.87, -0.44)	-2.75 (-4.60, -0.89)
Dulaglutide	short-term	-1.08 (-1.25, -0.90)	-1.70 (-2.00, -1.40)	-0.93 (-1.53, -0.34)
	medium-term	-0.94 (-1.14, -0.74)	-1.22 (-1.73, -0.72)	-0.93 (-1.80, -0.06)
	long-term	-1.25 (-1.67, -0.83)	-2.09 (-2.89, -1.29)	-0.86 (-3.03, 1.32)
Liraglutide	short-term	-1.20(1.39, -1.01)	-1.43 (-1.80, -1.06)	-1.17 (-1.78, -0.57)
	medium-term	-0.92 (-1.13, -0.71)	-1.29 (-1.78, -0.80)	-1.57 (-2.39, -0.75)
	long-term	-1.21 (-1.57, -0.85)	-1.65 (-2.40, -0.91)	-1.15 (-2.80, 0.49)
Exenatide	short-term	-0.86(-1.14, -0.58)	-0.76 (-1.50, -0.03)	-0.58 (-1.58, 0.41)
	medium-term	-0.81 (-1.06, -0.57)	-0.63 (-1.48, 0.23)	-1.04 (-2.20, 0.12)
	long-term	-0.62 (-1.14, -0.11)	NA	-0.49 (-3.23, 2.26)
Lixisenatide	short-term	-0.56(-0.81, -0.31)	-0.72 (-1.14, -0.29)	-0.68 (-1.61, 0.24)
	medium-term	-0.62 (-0.89, -0.35)	-0.62 (-1.14, -0.09)	-0.32 (-1.43, 0.79)
	long-term	NA	NA	NA
Efpeglenatide	short-term	-0.88(-1.20, -0.57)	-1.49 (-2.63, -0.35)	-0.52 (-2.10, 1.05)
	medium-term	-0.71 (-1.08, -0.33)	-0.60 (-2.32, 1.11)	-0.71 (-3.00, 1.58)
	long-term	-1.02 (-1.66, -0.38)	-0.88 (-2.24, 0.48)	-1.58 (-5.47, 2.31)
ITCA 650	short-term	-0.95 (-1.52, -0.38)	NA	-0.50 (-2.53, 1.53)
	medium-term	-0.91 (-1.45, -0.37)	NA	-1.36 (-4.13, 1.41)

	long-term	NA	NA	NA
PEG-Loxenatide	short-term	-0.85 (-1.30, -0.40)	-1.91 (-3.25, 0.57)	NA
	medium-term	-0.90 (-1.29, -0.52)	-1.17 (-1.87, -0.47)	0.27 (-1.45, 2.00)
	long-term	NA	NA	NA
PEGylated exenatide	short-term	-0.97 (-1.54, -0.40)	-1.68 (-2.52, -0.84)	-0.34 (-1.95, 1.27)
	medium-term	NA	NA	-0.34 (-2.83, 2.15)
	long-term	NA	NA	NA
Albiglutide	short-term	-0.85 (-1.20, -0.49)	-1.37(-1.94, -0.79)	-0.30 (-3.66, 3.06)
	medium-term	-0.93 (-1.34, -0.52)	-1.34 (-2.15, -0.52)	NA
	long-term	-0.92 (-1.40, -0.44)	-1.78 (-2.81, -0.74)	-0.04 (-2.73, 2.65)

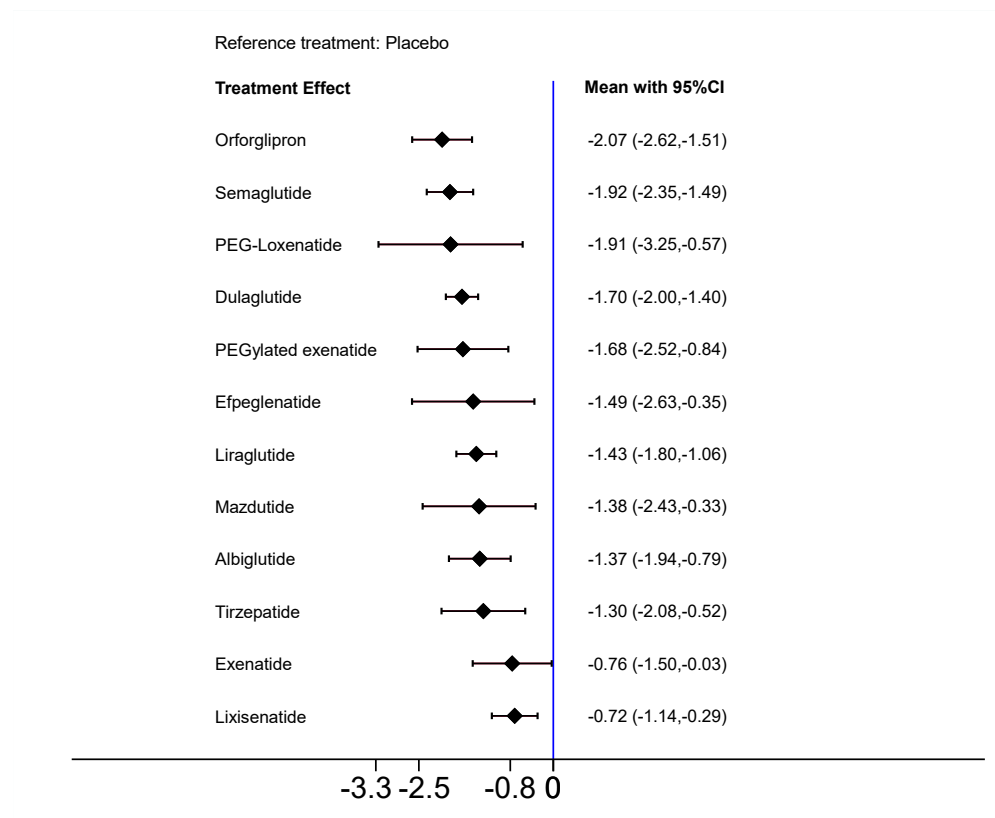
Data are presented as mean differences (95% confidence intervals). Short-term follow-up duration: 3-6 months; medium-term follow-up duration: 6-12 months; Long-term follow-up duration: >12 months.

Figure S15.1: The effects of GLP-1RAs in short-term intervention (3-6 months).

(A) Forest plot of HbA1c



(B) Forest plot of FPG



(C) weight loss

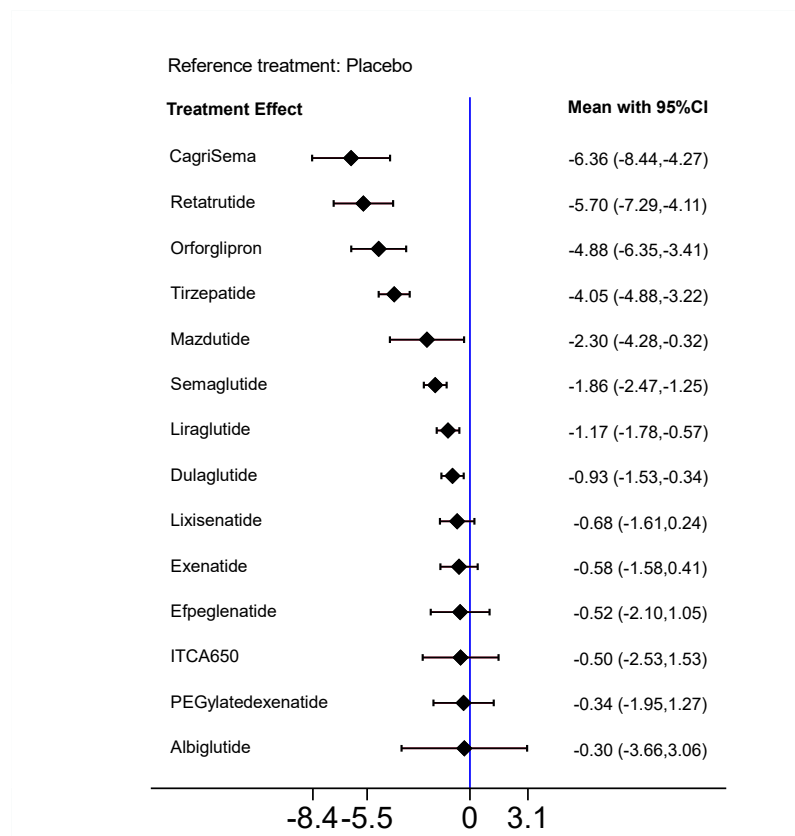
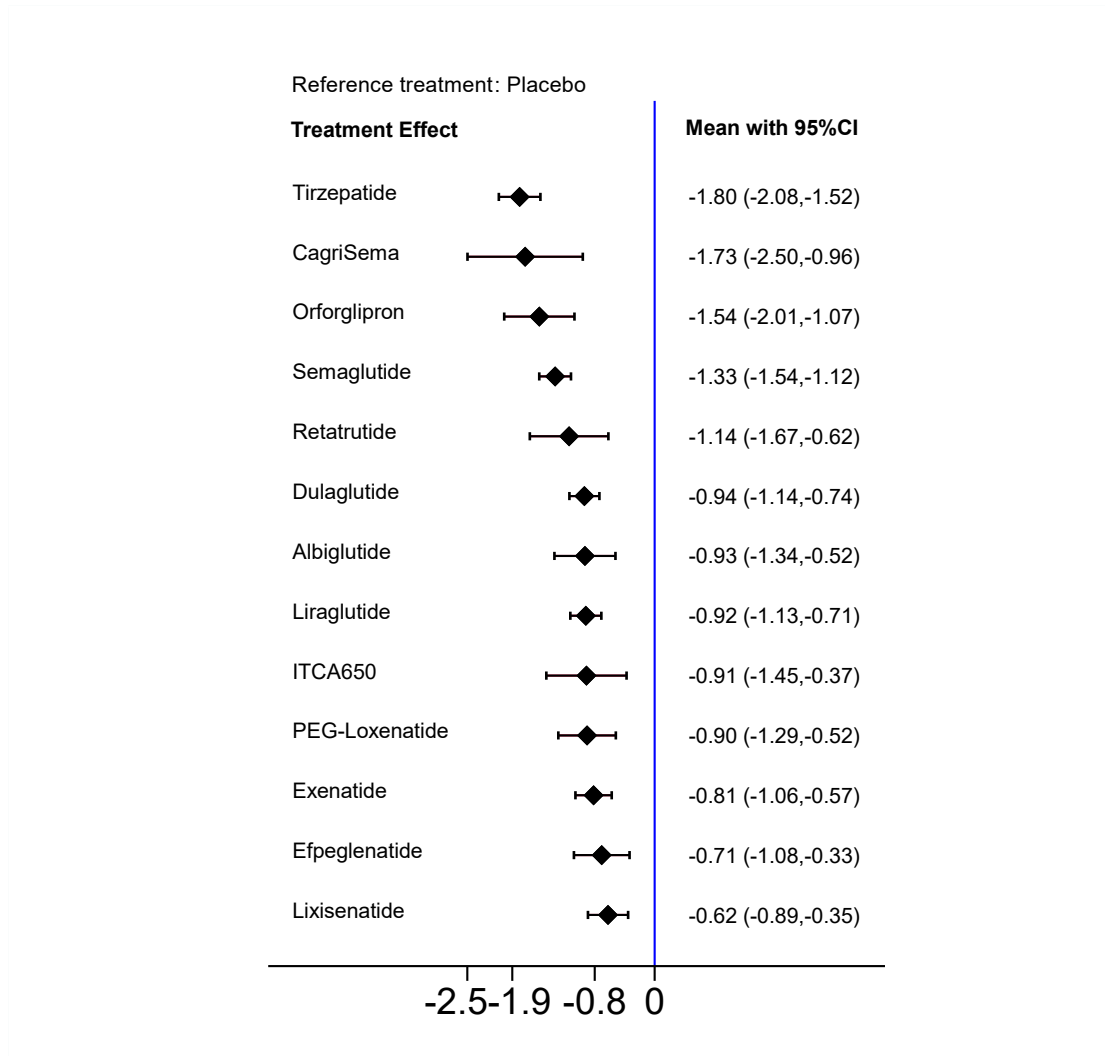
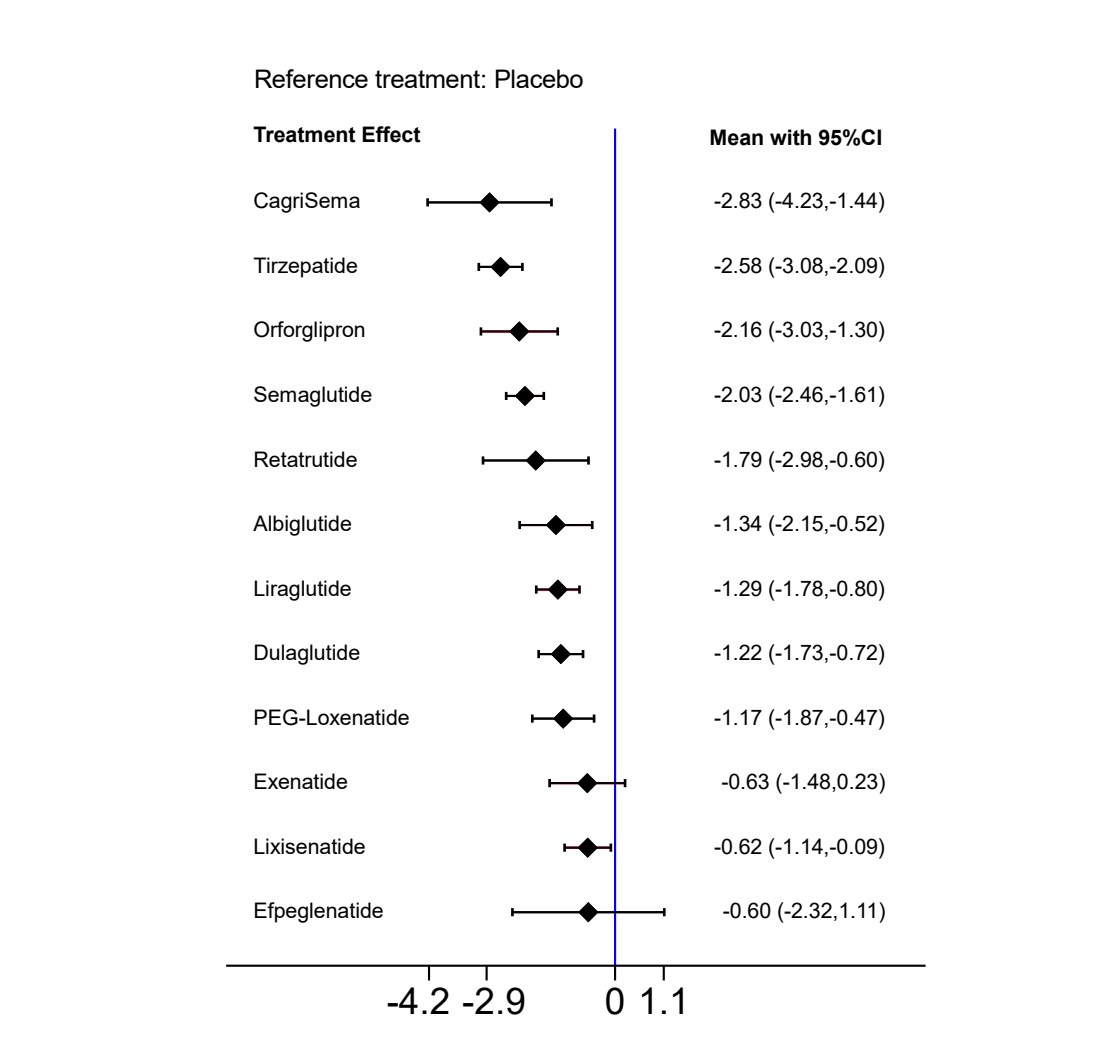


Figure S15.2: The effects of GLP-1RAs in medium-term intervention (6 months-12 months).

(A) Forest plot of HbA1c



(B) Forest plot of FPG



(C) weight loss

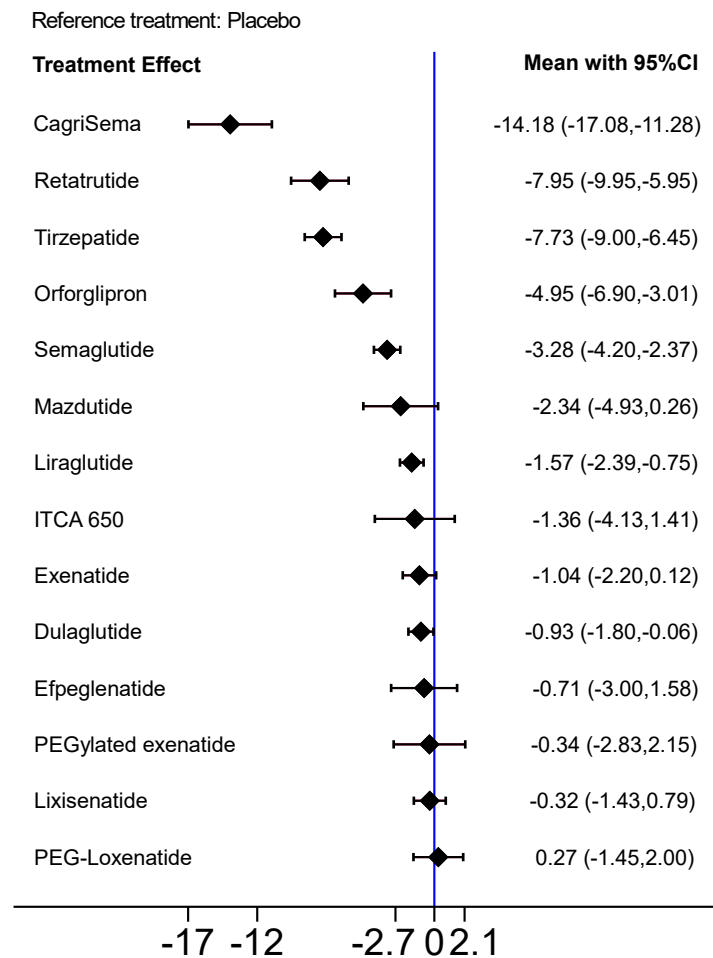
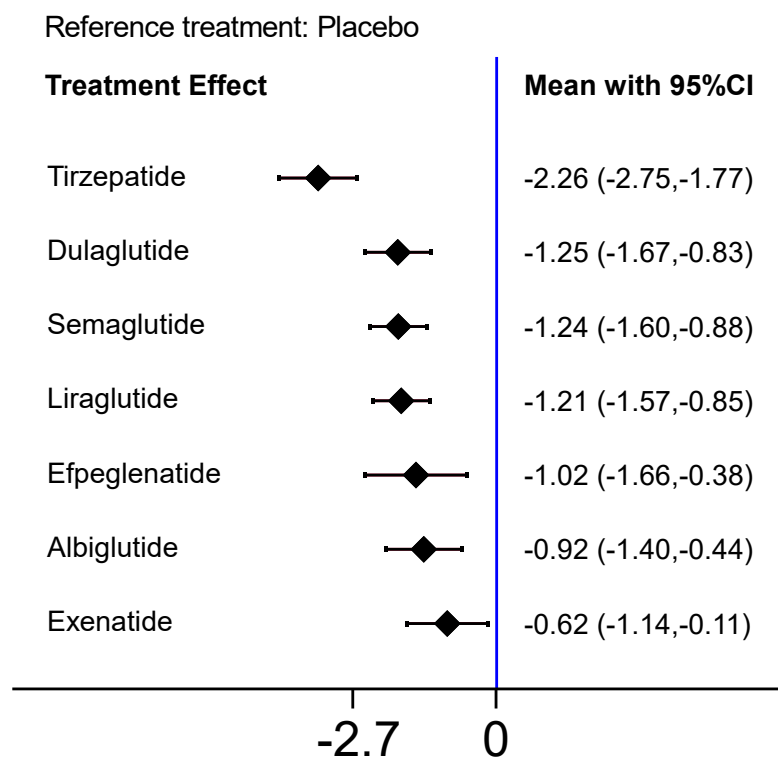
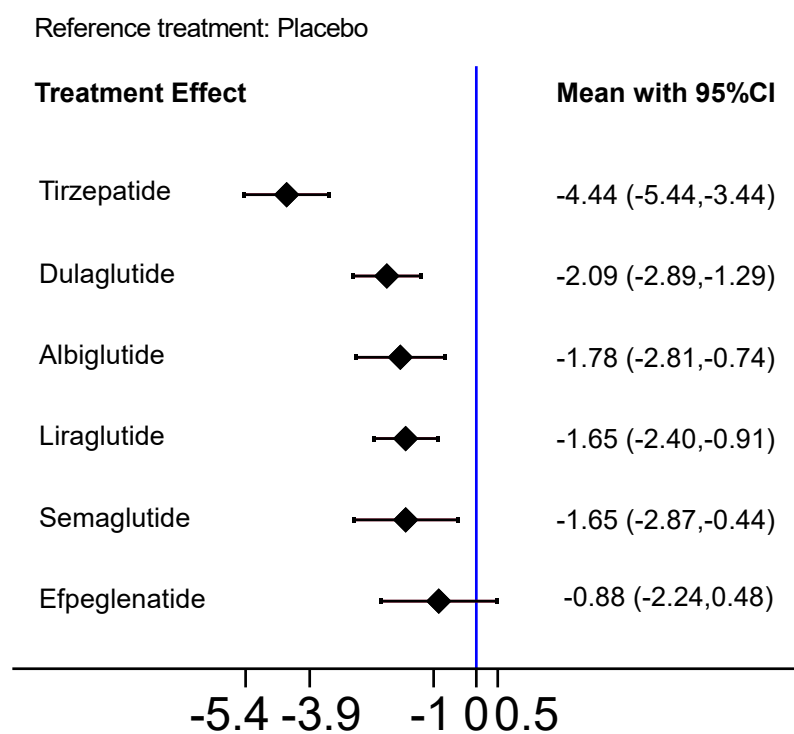


Figure S15.3: The effects of GLP-1RAs in long-term intervention (>12 months).

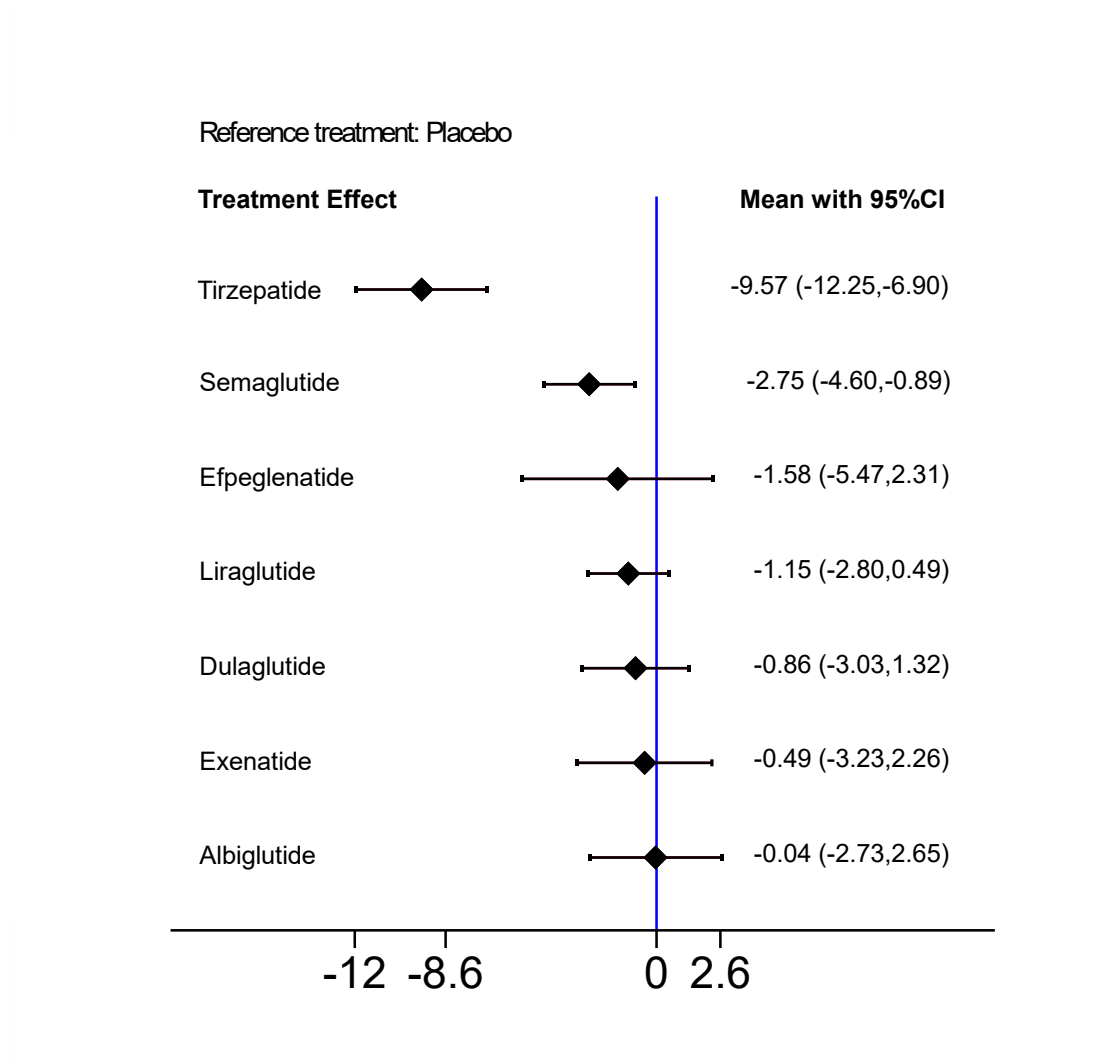
(A) Forest plot of HbA1c



(B) Forest plot of FPG



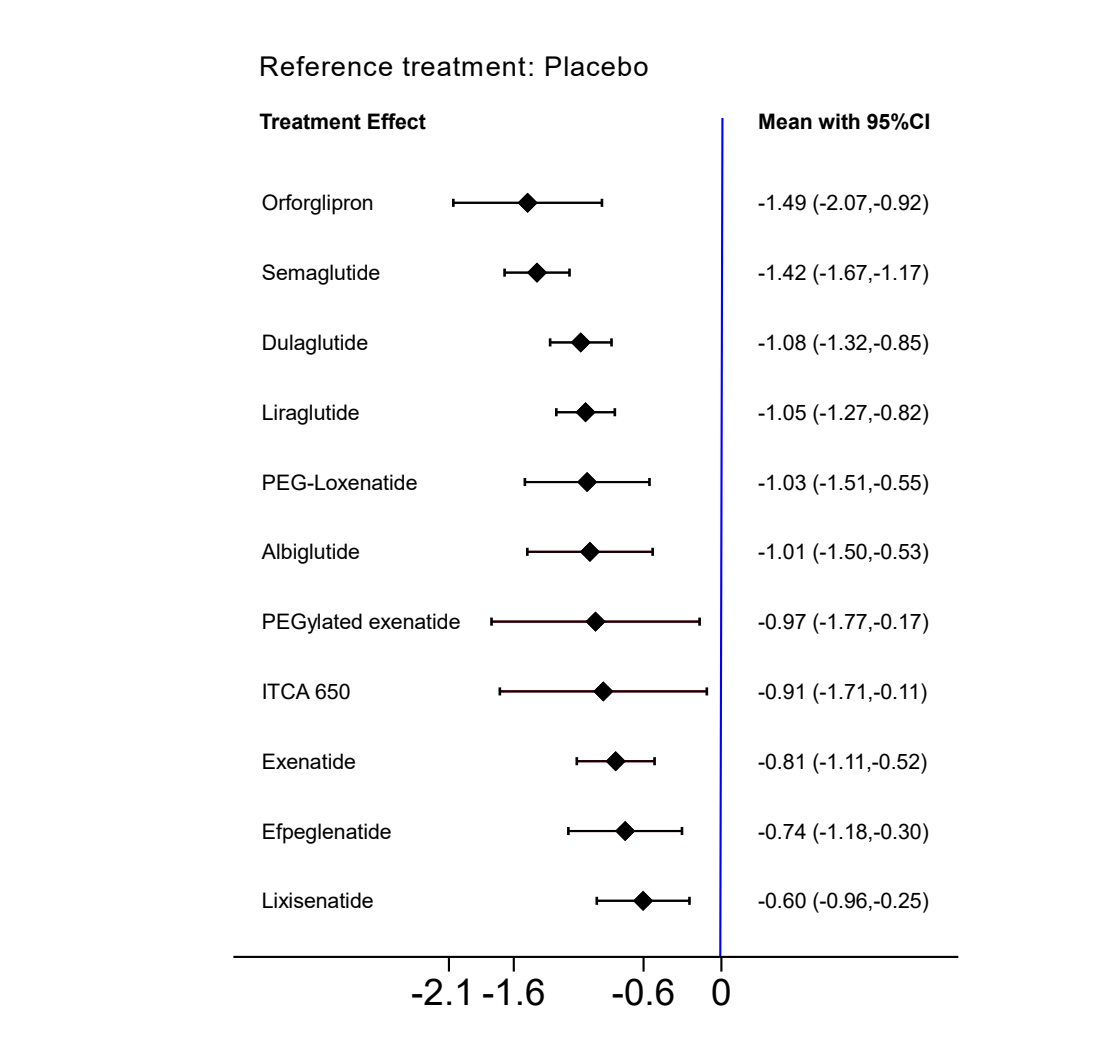
(C) weight loss



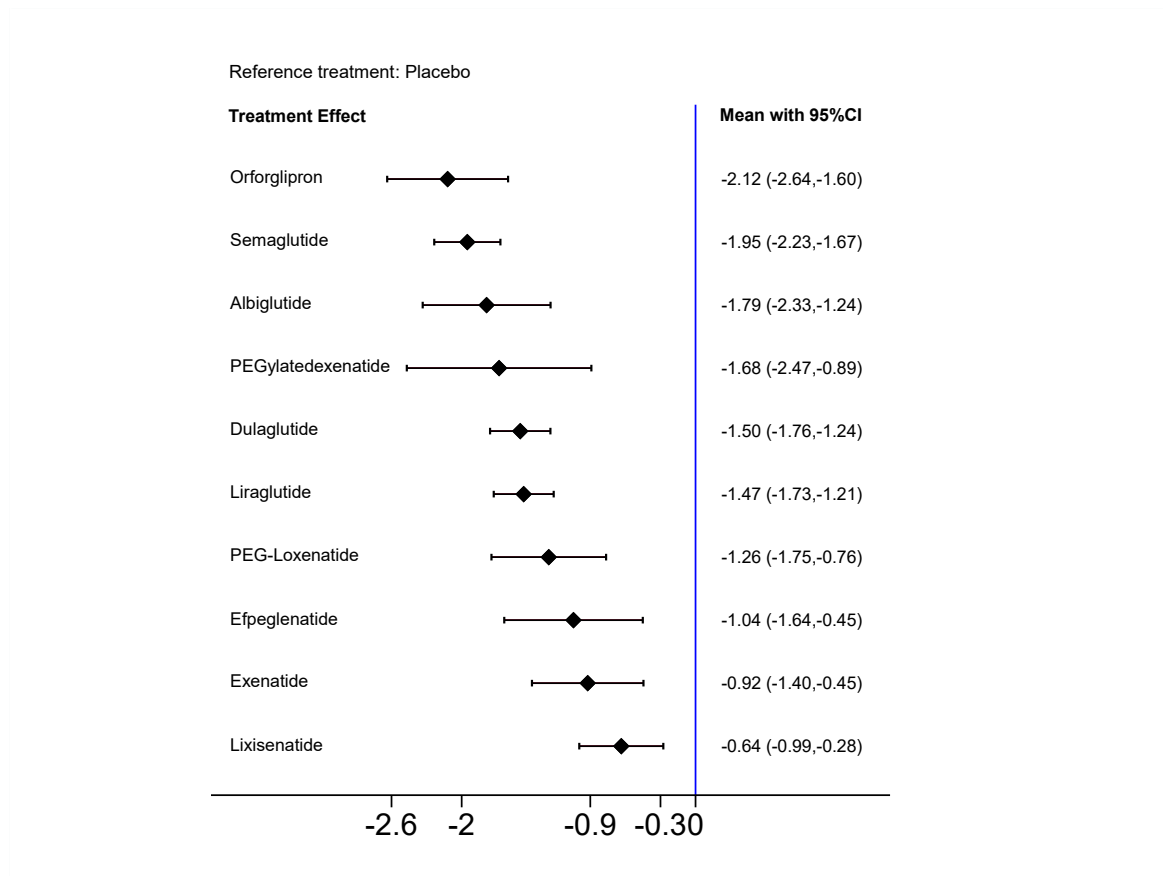
Appendix 16: Subgroup analysis of single agonist and dual/triple agonists

Figure S16.1: Effect of single agonist on T2D indicators.

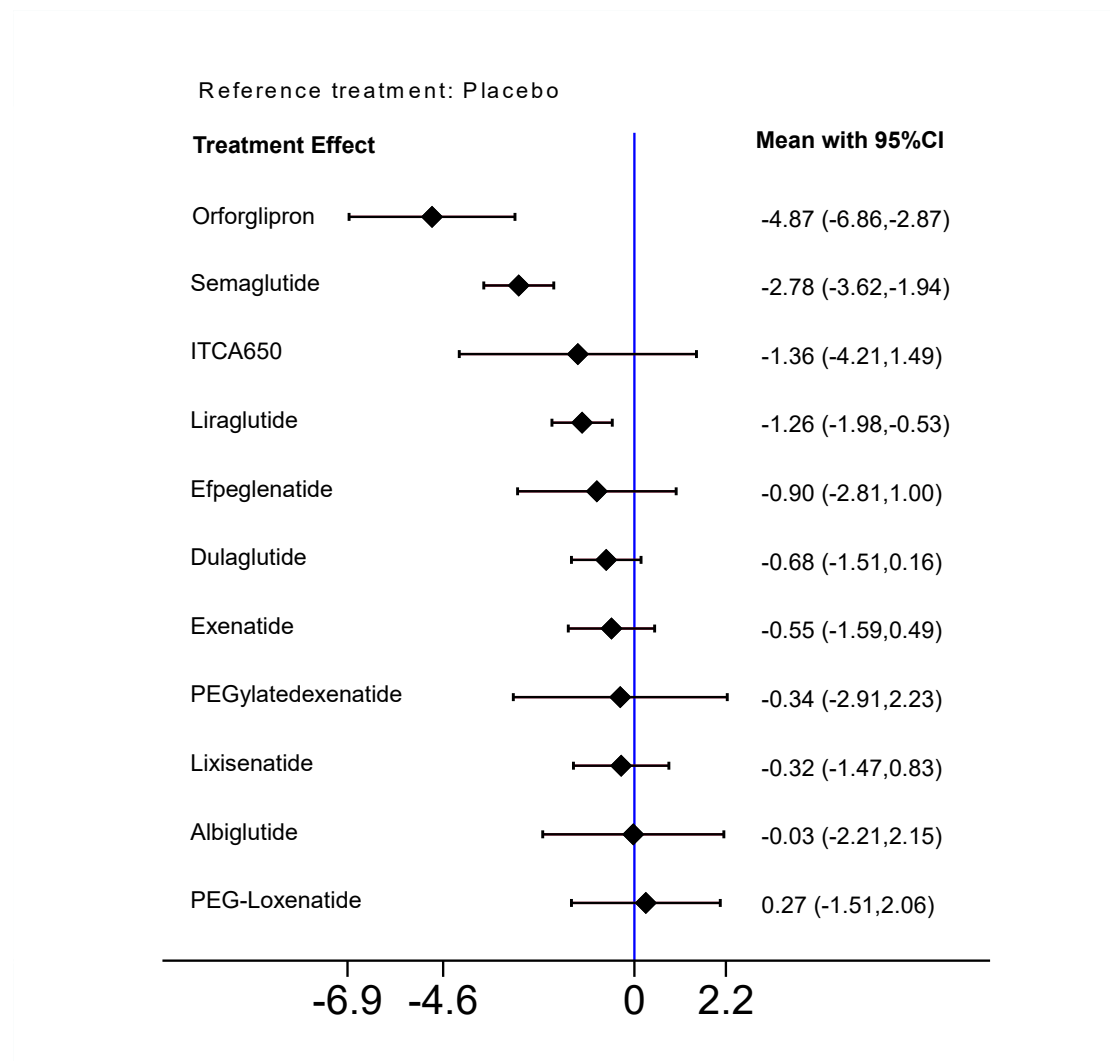
(A) Forest plot of HbA1c



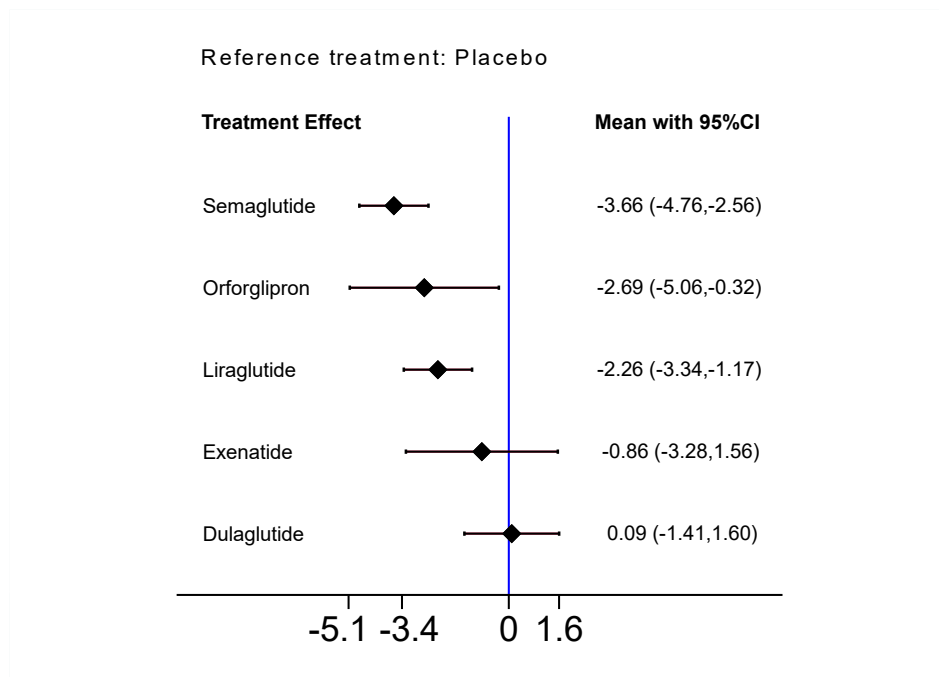
(B) Forest plot of FPG



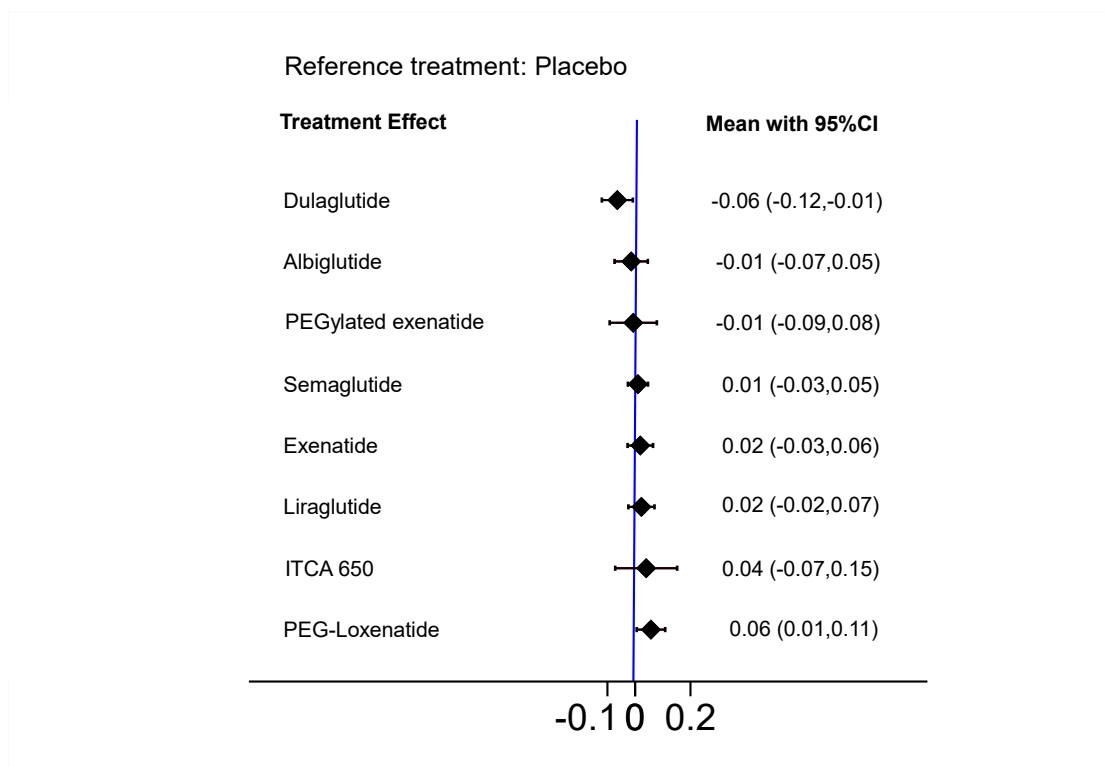
(C) Forest plot weight loss



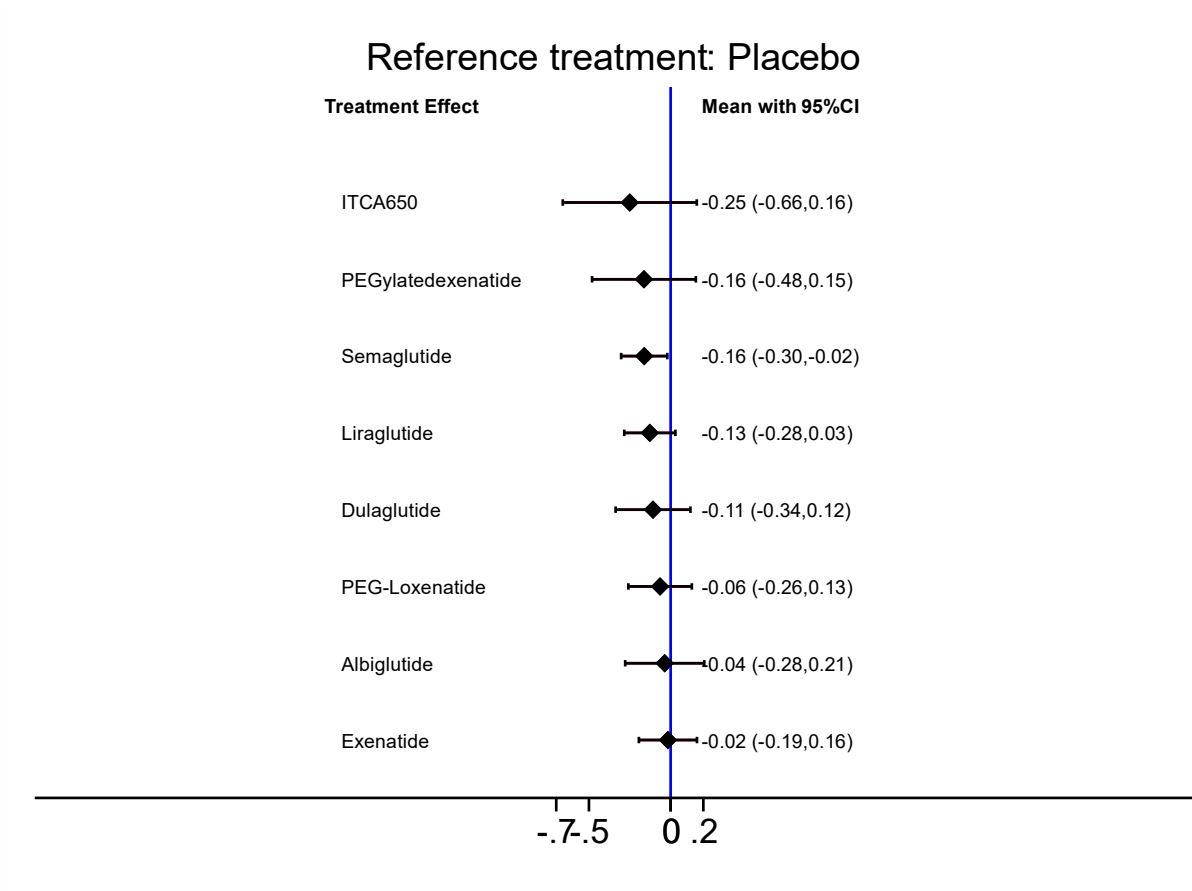
(D) Forest plot of waist circumference



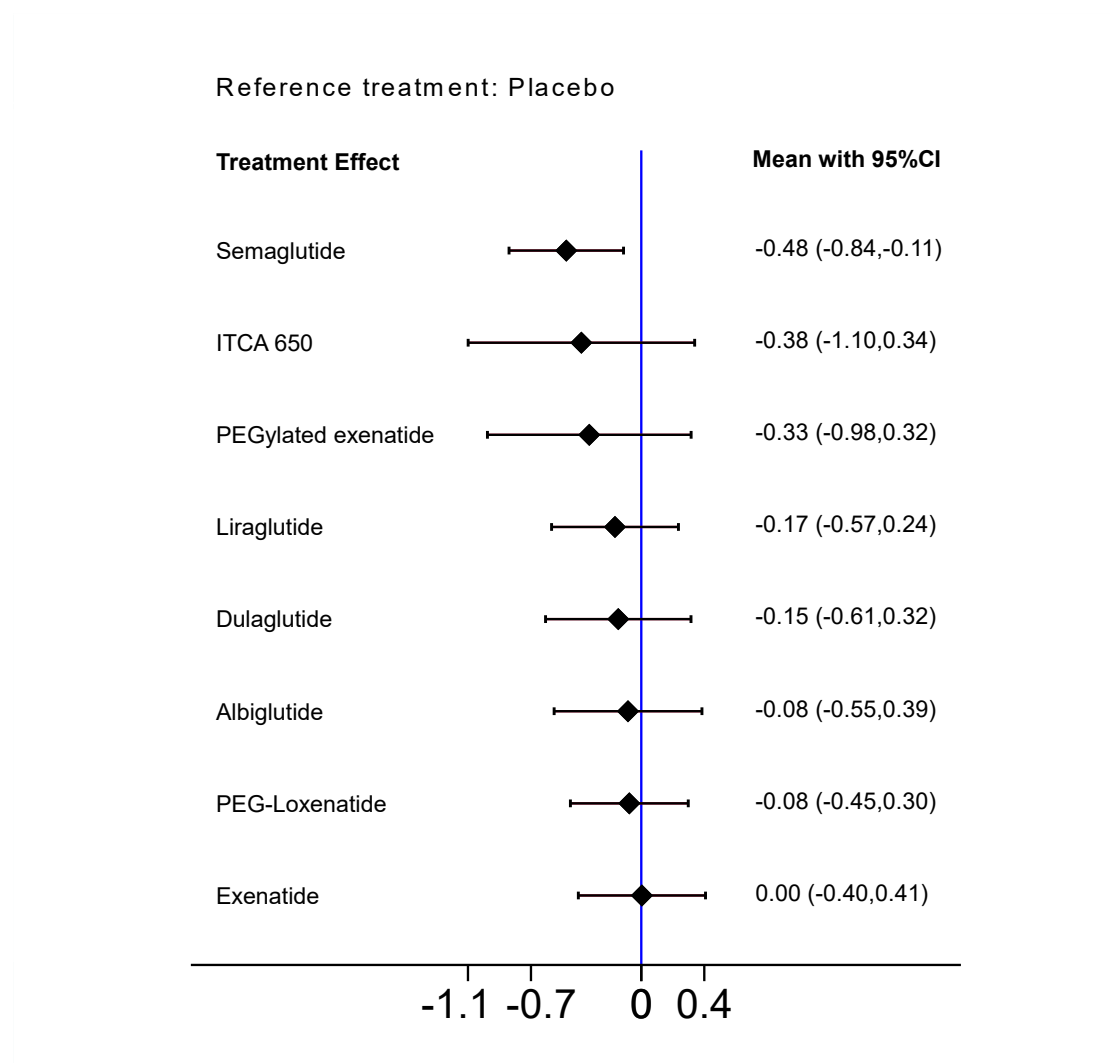
(E) Forest plot of HDL



(F) Forest plot of LDL



(G) Forest plot of TC



(H) Forest plot of TG

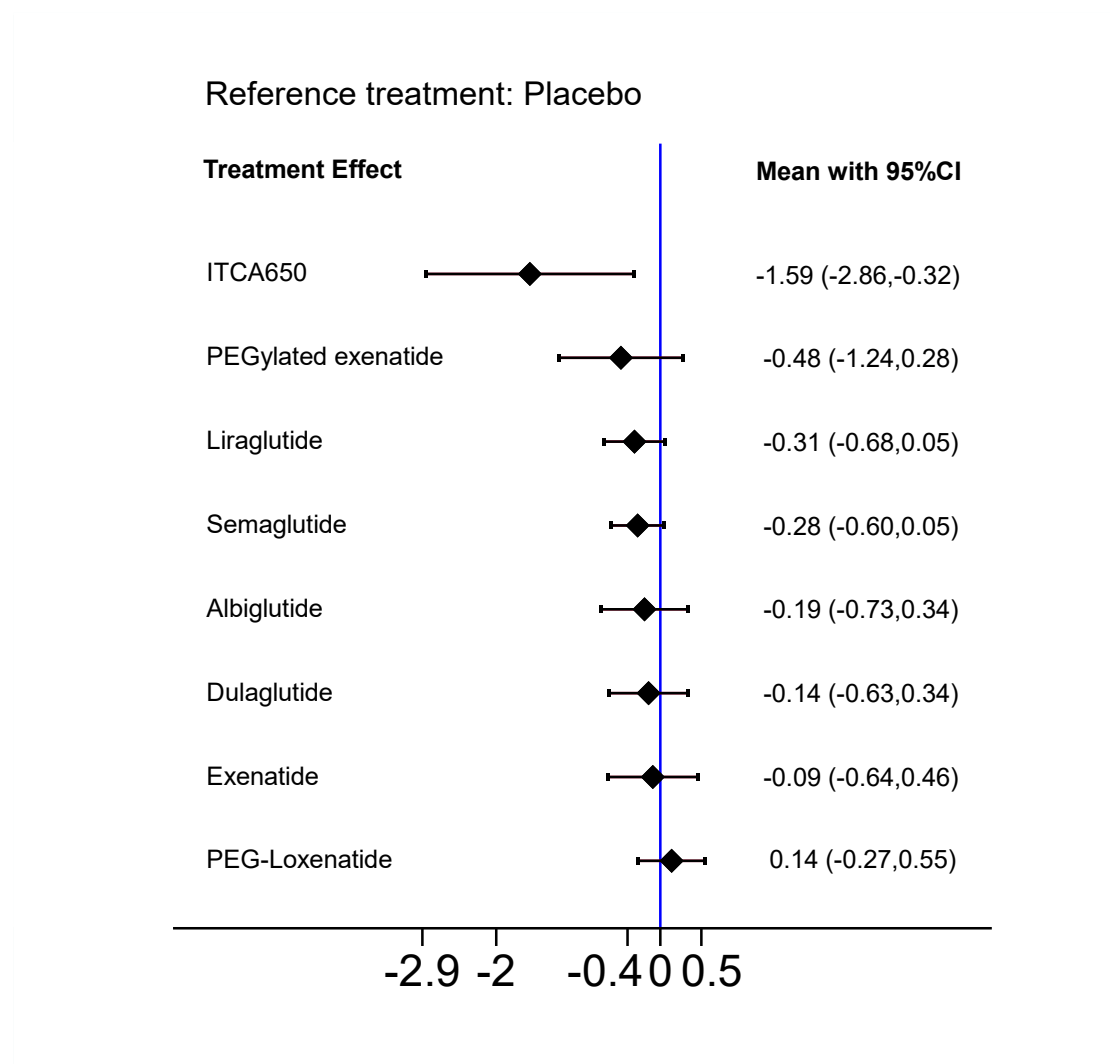
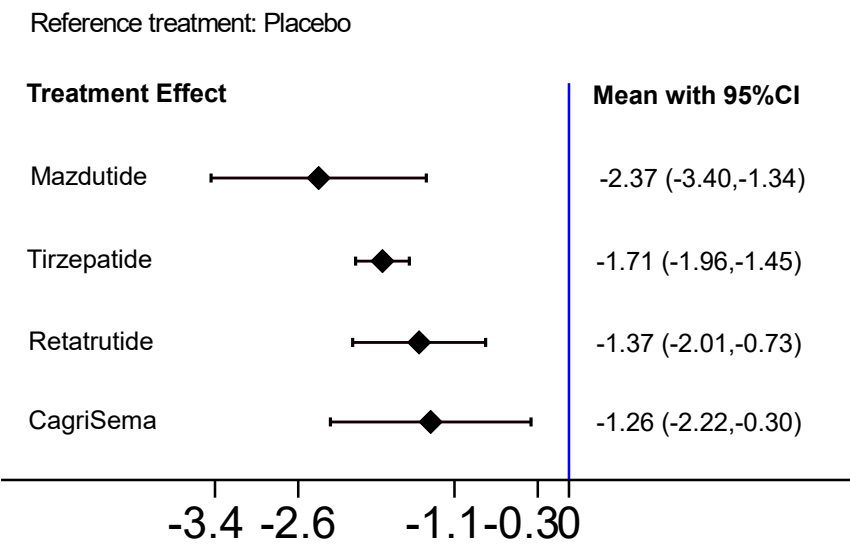
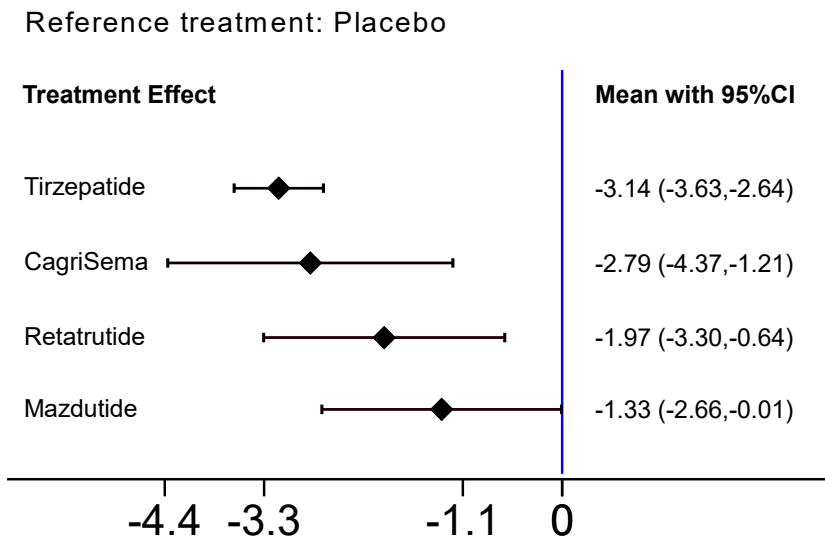


Figure S16.2: Effect of dual/triple agonists on T2D indicators.

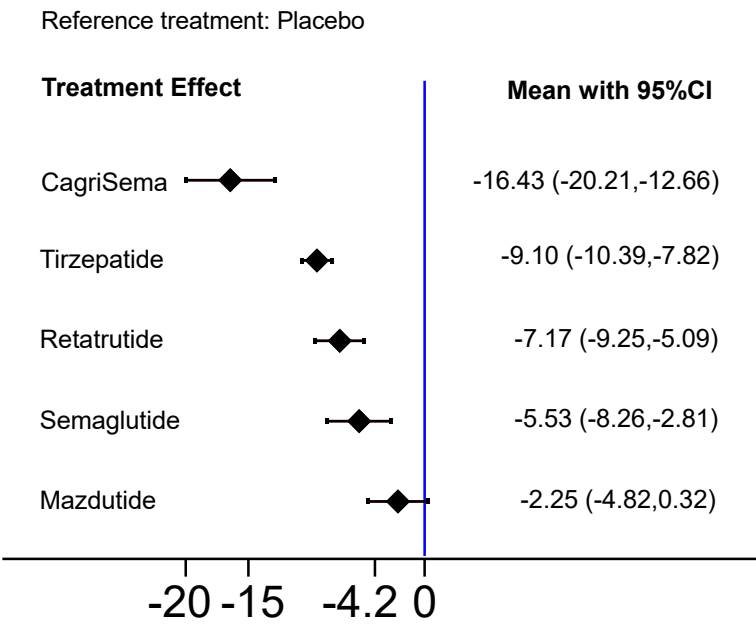
(A) Forest plot of HbA1c



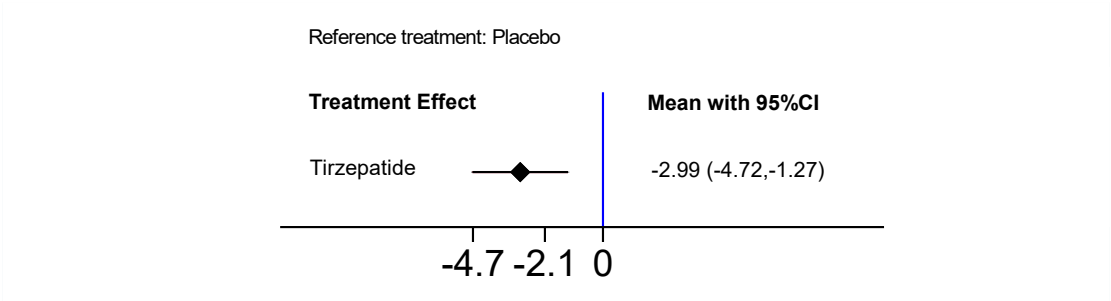
(B) Forest plot of FPG



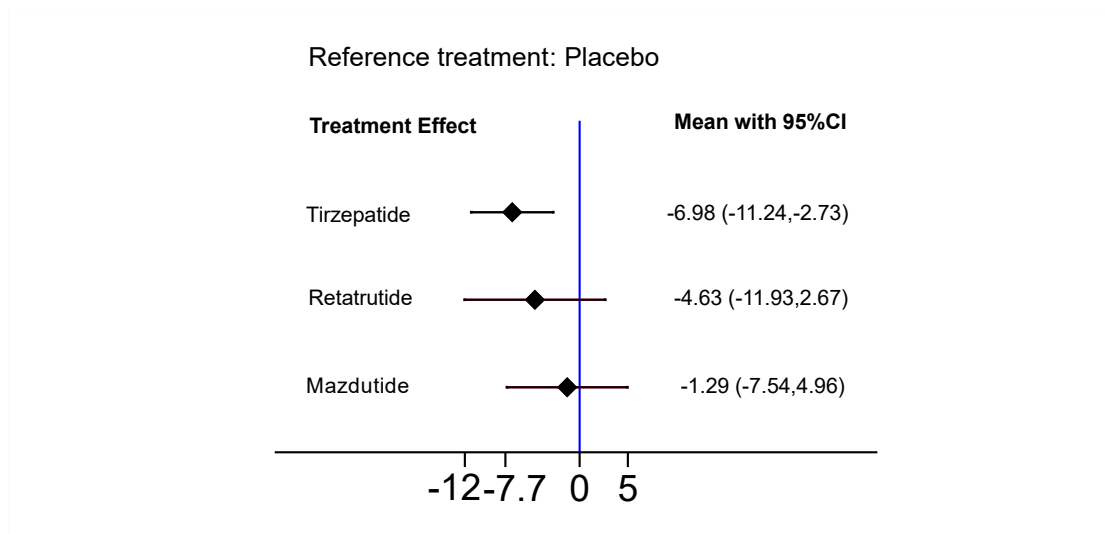
(C) weight loss



(D) Forest plot of BMI



(E) Forest plot of waist circumference



Appendix 17: Estimates of network meta-analyses for adverse events vs. placebo

Comparison of different doses of various GLP-1RAs.

GLP-1 agents and dosage	Discontinuation of GLP-1 agonist/analog due to AE		No. of patients with diarrhea		No. of patients with nausea		No. of patients with vomiting	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
Albiglutide 15mg QW	0.90	(-1.14, 2.93)	0.12	(0.01, 2.13)	2.31	(0.31, 17.24)	2.66	(0.23, 30.33)
Albiglutide 30mg QW	0.31	(-0.53, 1.15)	0.99	(0.59, 1.66)	1.21	(0.69, 2.13)	1.35	(0.13, 13.65)
Albiglutide 50mg QW	1.75	(0.55, 2.94)	1.33	(0.62, 2.83)	1.12	(0.46, 2.74)	0.58	(-1.91, 3.07)
Albiglutide 30mg QIW	0.88	(-1.16, 2.91)	1.41	(0.44, 4.52)	2.27	(0.30, 16.90)	2.60	(0.23, 29.73)
Semaglutide 0.5mg QW sc	1.16	(0.46, 1.87)	2.36	(1.13, 4.93)	3.15	(1.42, 6.98)	1.33	(0.64, 2.02)
Semaglutide 1mg QW sc	3.17	(1.42, 7.08)	2.25	(1.19, 4.26)	3.49	(1.79, 6.81)	4.28	(1.93, 9.46)
Semaglutide 3mg QD po	1.50	(0.46, 0.89)	2.94	(1.25, 6.88)	1.57	(0.65, 3.77)	1.43	(0.44, 4.60)
Semaglutide 7mg QD po	2.42	(0.80, 7.37)	1.57	(0.62, 3.97)	1.88	(0.77, 4.61)	1.83	(0.59, 5.70)
Semaglutide 14mg QD po	4.02	(1.43, 11.31)	2.55	(1.24, 5.23)	3.49	(1.62, 7.54)	3.83	(1.45, 10.09)
Semaglutide 25mg QD po	5.04	(1.67, 15.20)	2.68	(1.20, 6.01)	5.87	(2.13, 16.20)	7.01	(2.37, 20.70)
Semaglutide 50mg QD po	5.22	(1.73, 15.72)	3.00	(1.34, 6.70)	5.93	(2.15, 16.35)	7.57	(2.57, 22.34)
Exenatide 2mg QW	5.38	(1.31, 22.09)	2.17	(0.77, 6.15)	1.78	(0.61, 5.19)	1.68	(0.59, 4.79)
Exenatide 0.005mg BID	3.55	(0.91, 13.75)	1.58	(0.66, 3.79)	1.03	(0.22, 1.85)	3.04	(1.14, 8.05)
Exenatide 0.01mg BID	9.83	(2.76, 34.94)	2.19	(0.93, 5.18)	4.31	(1.73, 10.73)	4.39	(1.71, 11.29)
Exenatide 0.8mg QW	2.20	(0.06, 78.17)			0.23	(0.01, 6.29)	0.37	(0.02, 8.72)
Exenatide 5mg QMS	5.38	(0.08, 366.94)	0.43	(0.05, 3.30)	2.31	(0.31, 17.40)	1.08	(0.12, 9.73)
Exenatide 8mg QMS	5.21	(0.08, 355.13)	0.88	(0.15, 5.34)	3.37	(0.47, 24.05)	2.24	(0.31, 16.04)
Exenatide 11mg QMS	16.69	(0.47, 589.89)	1.19	(0.21, 6.85)	3.51	(0.49, 25.14)	3.02	(0.44, 20.67)
PB-119 75µg QW	3.00	(0.12, 77.60)			9.45	(0.43, 208.14)	3.00	(0.12, 78.05)

PB-119 150µg QW	3.00 (0.12, 77.60)		24.53 (1.21, 499.25)	19.14 (1.03, 354.47)
PB-119 200µg QW	3.00 (0.12, 77.60)		63.23 (3.20, 1251.19)	36.62 (2.04, 657.44)
ITCA 650 40µg QD	3.29 (1.14, 9.49)	1.56 (0.51, 3.41)	4.11 (1.31, 12.84)	11.77 (3.17, 43.73)
ITCA 650 60µg QD	2.29 (0.76, 6.86)	1.31 (0.61, 3.98)	4.24 (1.36, 13.23)	16.05 (4.37, 59.04)
Liraglutide 1.8mg QD	2.70 (1.31, 5.57)	1.62 (1.05, 2.51)	3.88 (2.06, 7.30)	2.21 (1.19, 4.09)
Liraglutide 1.2mg QD	2.47 (0.87, 7.03)	0.98 (0.44, 2.15)	2.74 (1.08, 6.99)	1.73 (0.70, 4.29)
Liraglutide 3mg QD	2.95 (1.42, 6.13)	2.50 (1.63, 3.81)	3.62 (1.90, 6.90)	3.45 (1.92, 6.20)
Liraglutide 0.9mg QD	0.96 (0.18, 5.21)	2.29 (0.35, 14.88)	1.68 (0.19, 14.72)	
Liraglutide 0.1mg QD	0.32 (0.01, 7.32)			
Liraglutide 0.3mg QD	0.31 (0.01, 7.16)			
Liraglutide 0.6mg QD	0.32 (0.01, 7.32)			
Tirzepatide 1mg QW	0.43 (0.09, 2.04)	1.16 (0.39, 3.41)	0.31 (0.07, 1.40)	0.83 (0.10, 6.82)
Tirzepatide 5mg QW	1.30 (0.75, 2.25)	2.48 (1.28, 4.81)	1.86 (1.09, 3.18)	2.47 (0.51, 11.96)
Tirzepatide 10mg QW	1.65 (0.97, 2.81)	2.37 (1.35, 4.15)	3.07 (1.95, 4.82)	3.84 (0.84, 17.56)
Tirzepatide 15mg QW	2.26 (1.35, 3.77)	2.81 (1.63, 4.85)	3.70 (2.37, 5.77)	5.85 (1.29, 26.46)
Dulaglutide 0.1 mg QW	0.21 (0.01, 4.29)	1.14 (0.18, 7.38)	1.15 (-0.15, 2.45)	0.95 (0.14, 6.36)
Dulaglutide 0.25 mg QW	0.63 (0.08, 5.27)	0.89 (0.08, 9.27)	0.33 (0.02, 6.81)	
Dulaglutide 0.5 mg QW	0.64 (0.14, 2.96)	1.48 (0.36, 6.12)	3.99 (1.05, 15.15)	0.32 (0.02, 6.08)
Dulaglutide 0.75 mg QW	0.75 (0.36, 1.58)	1.53 (0.76, 3.08)	2.45 (1.54, 3.88)	2.07 (0.94, 4.58)
Dulaglutide 1 mg QW	0.21 (0.01, 4.42)	0.57 (0.06, 5.84)	3.24 (0.89, 11.84)	0.32 (0.02, 6.08)
Dulaglutide 1.5 mg QW	1.08 (0.55, 2.13)	2.21 (1.23, 3.98)	1.47 (0.99, 1.94)	3.54 (1.72, 7.28)
Dulaglutide 3mg QW	1.64 (0.64, 4.21)	4.04 (1.61, 10.17)	4.78 (2.43, 9.38)	3.24 (1.22, 8.55)
Dulaglutide 4.5 mg QW	1.97 (0.76, 5.15)	3.63 (1.42, 9.27)	6.11 (3.15, 11.84)	4.70 (1.83, 12.08)
Mazdutide 3mg QW	1.47 (1.47, 1.47)	5.00 (5.00, 5.00)	3.67 (0.25, 54.70)	0.76 (0.03, 20.76)
Mazdutide 4.5mg QW	5.00 (0.70, 35.72)	8.27 (1.07, 64.20)	1.57 (0.10, 25.49)	2.60 (0.08, 89.10)
Mazdutide 6mg QW	1.47 (0.21, 10.22)	5.00 (0.42, 59.44)	1.57 (0.11, 23.44)	0.03 (0.01, 67.76)

Lixisenatide 5µg QD	1.15 (0.09, 11.38)	0.74 (0.18, 2.99)	1.35 (0.33, 5.62)	3.37 (0.40, 28.07)
Lixisenatide 10µg QD	2.07 (0.21, 20.34)	1.06 (0.29, 3.84)	2.25 (0.61, 8.34)	5.47 (0.77, 39.00)
Lixisenatide 20µg QD	2.72 (1.02, 7.24)	1.30 (0.82, 2.04)	5.23 (3.21, 8.53)	4.73 (2.17, 10.30)
Lixisenatide 30µg QD	5.61 (0.71, 44.35)	1.02 (0.28, 3.68)	9.38 (3.00, 29.32)	20.30 (3.62, 113.81)
Lixisenatide 5µg BID	0.39 (0.01, 11.38)	0.77 (0.19, 3.11)	1.41 (0.35, 5.85)	5.36 (0.75, 38.20)
Lixisenatide 10µg BID	1.92 (0.20, 18.83)	0.98 (0.27, 3.54)	2.88 (0.83, 9.99)	6.87 (1.05, 45.03)
Lixisenatide 20µg BID	7.65 (1.00, 48.82)	1.60 (0.50, 5.05)	4.93 (1.51, 16.11)	9.11 (1.46, 56.79)
Lixisenatide 30µg BID	4.65 (0.57, 37.71)	4.47 (1.66, 12.01)	8.64 (2.75, 27.10)	3.44 (0.41, 28.62)
PEX168 0.1mg QW	0.74 (0.20, 2.78)	2.89 (0.60, 13.94)	1.39 (0.23, 8.53)	2.17 (0.19, 24.55)
PEX168 0.2mg QW	1.82 (0.56, 5.87)	4.29 (1.05, 17.54)	9.55 (2.15, 42.42)	11.71 (1.49, 92.08)
Efpeglenatide 0.3mg QW	0.69 (0.03, 15.20)	4.53 (0.67, 30.67)	0.52 (0.15, 1.78)	0.88 (0.03, 27.40)
Efpeglenatide 1mg QW	0.69 (0.03, 15.20)	0.81 (0.06, 10.76)	0.38 (0.10, 1.46)	2.71 (0.20, 36.14)
Efpeglenatide 2mg QW	2.05 (0.71, 5.94)	2.29 (0.48, 10.87)	1.33 (0.63, 2.80)	9.23 (1.13, 75.29)
Efpeglenatide 3mg QW	5.37 (0.94, 30.61)	3.63 (0.51, 25.78)	1.24 (0.45, 3.41)	9.12 (0.97, 85.76)
Efpeglenatide 4mg QW	2.21 (0.77, 6.32)	3.82 (0.76, 19.25)	2.27 (1.15, 4.48)	20.47 (2.67, 156.83)
Efpeglenatide 6mg QW	3.99 (1.46, 10.92)	8.29 (1.48, 46.43)	3.69 (1.77, 7.70)	23.43 (2.81, 195.06)
Efpeglenatide 8mg QM	6.39 (0.74, 55.14)	2.41 (0.38, 15.21)	18.05 (2.27, 143.42)	4.36 (0.88, 21.67)
Efpeglenatide 12mg QM	7.62 (0.90, 60.40)	2.09 (0.33, 13.39)	42.00 (5.39, 327.41)	8.00 (1.70, 37.60)
Efpeglenatide 16mg QM	8.71 (1.05, 72.42)	3.01 (0.49, 18.64)	37.57 (4.82, 292.70)	11.33 (2.46, 52.21)
Orforglipron 3mg QD po	1.32 (0.05, 32.23)	2.27 (0.23, 22.11)	8.43 (0.74, 96.53)	4.10 (0.53, 31.50)
Orforglipron 9mg QD po	0.27 (0.00, 17.68)	0.35 (0.01, 12.87)	5.84 (0.30, 113.66)	28.81 (3.16, 262.71)
Orforglipron 12mg QD po	1.65 (0.07, 39.25)	1.58 (0.16, 15.61)	16.44 (1.47, 183.40)	17.91 (2.99, 107.14)
Orforglipron 15mg QD po	0.81 (0.02, 27.27)	1.05 (0.06, 17.35)	7.29 (0.39, 137.53)	23.58 (2.68, 207.47)
Orforglipron 21mg QD po	2.97 (0.12, 75.88)	0.74 (0.05, 11.95)	5.47 (0.31, 96.01)	4.72 (0.48, 45.88)
Orforglipron 24mg QD po	2.35 (0.10, 55.49)	1.45 (0.14, 14.69)	14.14 (1.25, 160.11)	25.11 (4.20, 150.25)
Orforglipron 27mg QD po	0.91 (0.03, 30.68)	2.22 (0.16, 30.95)	3.65 (0.18, 73.36)	28.81 (3.16, 262.71)

Orforglipron 36mg QD po	1.72 (0.07, 40.38)	1.43 (0.15, 14.09)	12.40 (1.11, 138.30)	23.35 (3.99, 136.50)
Orforglipron 45mg QD po	0.89 (0.05, 14.60)	2.37 (0.34, 16.56)	14.12 (1.56, 127.61)	26.66 (4.84, 146.96)
Retatrutide 0.5 mg QW sc	1.30 (0.20, 8.36)	0.61 (0.10, 3.55)	0.73 (0.14, 3.72)	1.09 (0.03, 19.72)
Retatrutide 1.5 mg QW sc	5.31 (0.52, 53.82)	2.66 (0.43, 16.28)	0.30 (0.01, 6.29)	2.95 (0.26, 33.43)
Retatrutide 3mg QW sc	0.69 (0.02, 20.07)	0.53 (0.05, 5.65)	0.81 (0.11, 6.18)	0.73 (0.03, 19.72)
Retatrutide 4 mg QW sc escalation	0.43 (0.02, 10.24)	2.46 (0.39, 15.61)	1.94 (0.31, 12.07)	2.43 (0.27, 21.83)
Retatrutide 4 mg QW sc	1.30 (0.14, 11.83)	8.61 (1.98, 37.50)	6.77 (1.59, 28.86)	0.74 (0.03, 17.38)
Retatrutide 6mg QW sc escalation	0.69 (0.02, 20.07)	1.18 (0.17, 8.11)	3.41 (0.69, 16.89)	0.73 (0.03, 19.72)
Retatrutide 8 mg QW sc slow escalation	3.04 (0.48, 19.23)	6.15 (1.37, 27.67)	7.49 (1.82, 30.77)	3.72 (0.53, 26.00)
Retatrutide 8 mg QW sc fast escalation	4.48 (0.75, 26.68)	10.63 (2.51, 45.08)	14.52 (3.65, 57.72)	8.01 (1.37, 46.91)
Retatrutide 12 mg QW sc escalation	3.36 (0.72, 15.74)	4.85 (1.42, 16.55)	5.16 (1.60, 16.64)	5.25 (1.07, 25.67)

Abbreviations: CI, confidence interval; AE, adverse events; OR, odds ratio; QD, once daily; QW, once weekly; BID, twice daily; BIW: twice weekly; QMS, once monthly suspension)