Online Supplementary Appendix

Table S1. Search Strategies

Data source	Search terms
PubMed	#1 Sodium glucose co-transporter 2
	#2 SGLT2 OR SGLT-2 OR SGLT 2
	#3 Tofogliflozin OR Empagliflozin OR Dapagliflozin OR Canagliflozin OR Sotagliflozin OR Luseogliflozin OR Ipragliflozin OR Remogliflozin OR Sergliflozin OR Ertugliflozin
	#4 OR#1 - #3
	#5 DPP-4 OR DDP4 OR DPP 4
	#6 Vildagliptin OR Saxagliptin OR Sitagliptin OR Linagliptin OR Alogliptin OR Dutogliptin OR Gemigliptin OR Camegliptin OR Teneligliptin
	#7 #5 OR #6
	#8 Meglitinide OR Mitiglinide OR Nateglinide OR Repaglinide
	#9 Sulphonylurea OR Acetohexamide OR Carbutamide OR Chlorpropamide OR Glibenclamide OR Glibornuride OR Gliclazide OR Glimepiride OR Glipizide OR Gliquidone OR Tolazamide OR Glyburide OR Glycopyramide
	#10 Alpha glucosidase inhibitor OR Acarbose OR Miglitol OR

	Voglibose
	#11 Glitazone OR Thiazolidinedione OR Pioglitazone OR Rivoglitazone OR Rosiglitazone
	#12 #4 OR #7 OR #8 OR #9 OR #10 #11
	#13 Diabetes mellitus or Diabetes
	#14 random*
	#15 "Randomized Controlled Trial"[Publication Type]
	#16 RCT or RCTs
	#17 OR/#14 - #16
	#18 #12 AND #13 AND #17
CENTRAL	TITLE-ABSTRACT- KEYWORDS (Sodium Glucose co-transporter 2 OR SGLT2 OR SGLT-2 OR SGLT 2 OR Tofogliflozin OR Empagliflozin OR Dapagliflozin OR Canagliflozin OR Sotagliflozin OR luseogliflozin OR Ipragliflozin OR Remogliflozin OR Sergliflozin OR Ertugliflozin OR DPP-4 OR DDP4 OR DPP 4 OR Vildagliptin OR Saxagliptin OR Sitagliptin OR Linagliptin OR Alogliptin OR Dutogliptin OR Gemigliptin OR Camegliptin OR Teneligliptin OR Meglitinide OR Mitiglinide OR Nateglinide OR Repaglinide OR Sulphonylurea OR Acetohexamide OR Carbutamide OR

	Chlorpropamide OR Glibenclamide OR Glibornuride OR Gliclazide OR Glimepiride OR Glipizide OR Gliquidone OR Tolazamide OR Glyburide OR Glycopyramide OR Alpha glucosidase inhibitor OR Acarbose OR Miglitol OR Voglibose OR Glitazone OR Thiazolidinedione OR Pioglitazone OR Rivoglitazone OR Rosiglitazone) AND (Diabetes mellitus or Diabetes)
Embase	TITLE-ABSTRACT-AUTHOR KEYWORDS (Sodium Glucose co-transporter 2 OR SGLT2 OR SGLT-2 OR SGLT 2 OR Tofogliflozin OR Empagliflozin OR Dapagliflozin OR Canagliflozin OR Sotagliflozin OR luseogliflozin OR Ipragliflozin OR Remogliflozin OR Sergliflozin OR Ertugliflozin OR DPP-4 OR DDP4 OR DPP 4 OR Vildagliptin OR Saxagliptin OR Sitagliptin OR Linagliptin OR Alogliptin OR Dutogliptin OR Gemigliptin OR Camegliptin OR Teneligliptin OR Meglitinide OR Mitiglinide OR Nateglinide OR Repaglinide OR Sulphonylurea OR Acetohexamide OR Carbutamide OR Chlorpropamide OR Glibenclamide OR Glibornuride OR Gliclazide OR Glimepiride OR Glipizide OR Gliquidone OR Tolazamide OR Glyburide OR Glycopyramide OR Alpha glucosidase inhibitor OR Acarbose OR Miglitol OR Voglibose OR Glitazone OR Thiazolidinedione OR Pioglitazone OR

Rivoglitazone OR Rosiglitazone) AND (Diabetes mellitus or Diabetes) AND (RCT* OR random*)

Table S2. Characteristics of included Studies

Author (year)	trial registration	Interventions	Sample size (n)	Mean Age (years)	Mean Sex (man%)	Mean HbA1c[u] (%)	Mean body weight (kg)	Mean BMI[t] (kg/m2)	Mean duration of diabetes (years)	Follow-up (weeks)
Bolinder (2014) [1]	NCT00855166	Dapa[a]: 10mg	89	60.6	55.1	7.2	92.1	32.1	6.0	102
		PLA[s]	91	60.8	56.0	7.2	90.9	31.7	5.5	102
		Dapa: 2.5mg	137	55	51	8.0	84.9		6	102
Baily (2013) [2]	NCT00528879	Dapa:5mg	137	54.3	50	8.2	84.7	NA[v]	6.4	102
		Dapa: 10mg	135	52.7	57	8.0	86.3		6.1	102
		PLA	137	53.7	55	8.1	87.7		5.8	102

Lava-Gonzalez (2013) [3]	NCT01106677	Cana[c]:100mg	368	55.3	47.0	7.9	88.8	32.4	6.7	52
		Cana:300mg	367	55.5	47.3	7.9	85.4	31.4	7.1	52
		Sita[f]: 100mg	366	55.5	45.0	7.9	87.7	32.0	6.8	52
Rosenstock (2015) [4]	NCT01606007	Dapa: 5mg	179	54	50	8.9	NA	31.5	7.4	24
		Saxa[g]: 10mg	176	55	47	9.0	NA	31.8	8.2	24
Del Prato (2015) [5]	NCT00660907	Dapa: 10mg	400	58.1	55.3	7.7	88.4	31.7	6.1	208
		Glip: 20mg	401	58.6	54.9	7.7	87.6	31.2	6.6	208
Merker (2015) [6]	NCT01159600	Empa[b]: 10mg	217	55.5	57.6	7.9	81.6	29.1	6.3	76
		Empa: 25mg	213	55.6	56.3	7.9	82.2	29.7		76

	/NCT0									
	128999	PLA	207	56.0	56.0	7.9	79.7	28.7		76
	0									
		Vild: 50mg	177	54.3	57.3	8.4	NA	32.1	6.8	24
BOSI	NCT00	Vild:100mg	185	53.9	61.5	8.4	NA	32.9	5.8	24
(2007) [7]	099892	PLA	182	54.9	53.1	8.3	NA	33.2	5.2	24
		Tene[j]:5mg	87	58.8	52.9	8.0	92.8	32.2	4.7	24
Bryson	NCT00	Tene:10mg	93	58.5	54.8	7.8	91.2	32.2	4.8	24
(2016) [8]	971243	Tene:20mg	91	58.3	61.5	8.0	94.7	33.0	5.3	24
		Tene:40mg	88	58.2	59.1	7.9	93.3	32.2	5.1	24

		PLA	88	58.9	53.4	7.9	92.1	32.0	4.8	24
Charbonnel (2006) [9]	NCT00865151	Sita:100mg	464	54.4	55.8	8.0	86.7	30.9	6.0	24
		PLA	237	54.7	59.5	8.0	89.6	31.5	6.6	24
Ahren (2004) [10]	NA	Vild: 50mg	42	58.4	61.9	7.6	NA	29.6	5.8	52
		PLA	29	54.3	75.9	7.8	NA	29.9	4.6	52
Handelsman (2017) [11]	NCT01682759	Oma: 25mg	376	58	54.0	7.5	87.5	31.2	7.6	54
		Glim^{m}: 6mg	375	58	56.3	7.4	88.7	31.7	7.7	54
Gadde	NCT01	Sita:100mg	122	54.3	54.1	8.4	88.1	31.6	7.9	28

(2017) [12]	652729	PLA	61	53.4	60.7	8.5	89.0	31.5	8.7	28
Du (2017) [13]	NCT02243176	Saxa: 5mg	238	54.7	61.8	8.2	73.3	26.4	5.1	24
		Acar[p]: 50mg	243	56.5	56.8	8.2	72.6	26.3	5.3	24
Yang (2016) [14]	NCT01095666	Dapa: 5mg	147	53.1	45.6	8.1	70.8	26.4	4.2	24
		Dapa: 10mg	152	54.6	57.9	8.2	71.4	26.2	5.3	24
		PLA	145	53.5	59.3	8.1	70.9	25.7	5.3	24
Lu (2016) [15]	NCT01505426	Ipra[d]: 50mg	87	53.9	50.6	7.7	70.36	26.6	6.4	24
		PLA	83	53.4	39.8	7.8	70.45	27.0	5.7	24
Tai (2016)	NCT02	Alog[i]: 25mg	44	53.8	61.4	8.2	NA	31.1	6.6	26

[16]	798172	Met: 1000mg	37	53.4	59.5	8.2	NA	30.6	6.6	26
DeFronzo (2015) [17]	NCT01422876	Empa: 10mg	137	56.1	56.9	8.0	86.1	30.9	NA	52
		Empa: 25mg	140	55.5	46.4	8.0	87.7	31.8	NA	52
		Lina[h]: 5mg	128	56.2	50.0	8.0	85.0	30.6	NA	52
Ji (2016) [18]	NCT01541956	Vild[e]: 50mg	2501	56.5	54.4	7.2	69.3	25.1	4.3	24
		Met:1000mg	484	56.2	49.6	7.2	68.7	25.1	4.1	24
Wang (2016) [19]	NCT01215097	Lina: 5mg	205	55.1	49.8	8.0	68.1	25.5	NA	24
		PLA	101	56.5	50	8.0	68.5	25.8	NA	24
Wang	NA	Saxa: 5mg	41	64.3	43.9	8.3	65.2	NA	12.3	26

(2015) [20]		Acar: 50mg	40	65.1	47.5	7.7	63.9		14.2	26
Scherntha ner (2015) [21]	NCT01 006603	Saxa:5mg	360	72.5	60.3	7.6	NA	29.9	7.6	52
		Glim:<6mg	360	72.7	63.3	7.6	NA	29.3	7.6	52
Ridderstra le (2014) [22]	NCT01 167881	Empa: 25mg	765	56.2	56	7.9	82.5	30.0	NA	104
		Glim:1-4mg	780	55.7	54	7.9	83.0	30.3	NA	104
Del Prato (2014) [23]	NCT00 856284	Alog:12.5mg	880	55.2	47.6	7.6	NA	31.3	5.7	104
		Alog: 25mg	885	55.5	51.1	7.6	NA	31.3	5.4	104
		Glip^{n}:5-20mg	874	55.4	50.5	7.6	NA	31.1	5.5	104

Derosa (2014) [24]	NA	Vild: 100mg	81	57.2	49.4	7.9	77.8	27.9	6.9	26
		Glim:6mg	86	59.8	49.8	7.7	77	27.6	6.8	26
Kashiwagi (2015) [25]	NCT01135433	Ipra: 50mg	112	56.2	58.9	8.3	68.52	26.0	7.4	24
		PLA	56	57.7	68.9	8.4	67.51	25.5	7.9	24
Cefalu (2013) [26]	NCT00968812	Cana:100mg	483	56.4	52	7.8	86.9	31.0	6.5	52
		Cana:300mg	485	55.8	50	7.8	86.6	31.2	6.7	52
		GLIM	482	56.3	55	7.8	86.5	30.9	6.6	52
Berndt-Zipfel (2013)	NA	Vild:100mg	22	57	68.2	7.4	99.3	34.6	8.4	24
		Glim:0.5-4m	22	60	59.1	7.3	93.7	33.3	6.1	24

[27]		g								
Yang (2012) [28]	NCT00813995	Sita:100mg	197	54.1	47	8.5	67.9	25.3	6.4	24
		PLA	198	55.1	55	8.5	68.9	25.3	7.3	24
Gallwitz (2012) [29]	NCT00622284	Lina: 5mg	777	59.8	60	7.7	86.1	86.1	NA	104
		Glim: 1mg	775	59.8	61	7.7	86.8	86.8		104
Derosa (2012) [30]	NA	Sita: 100mg	91	55.9	46.2	8.1	78.4	28.1	5.8	52
		PLA	87	54.8	50.2	8.0	78.6	28.9	5.4	52
Derosa- a	NA	Vild:100mg	84	54.2	50.0	8.1	76.9	27.9	6.1	52

(2012) [31]		PLA	83	52.4	51.8	8.2	78.5	27.8	6.3	52
Yang (2011) [32]	NCT00661362	Saxa: 5mg	283	53.8	48.1	7.9	68.9	26.3	5.1	24
		PLA	287	54.4	48.4	7.9	69	26.1	5.1	24
Bergenstal (2012) [33]	NCT00754988	Sita:100mg	185	55.5	59	7.9	92.5	32.4	6.0	24
		PLA	93	56.1	52	8.0	91.1	32.5	5.5	24
Pan (2012) [34]	NA	Vild:100mg	146	54.2	50.0	8.1	71.58	26.0	4.9	24
		Vild:50mg	148	53,7	55.4	8.1	68.36	25.0	5.0	24
		PLA	144	54.5	54.2	8.0	69.83	25.5	5.2	24

Jeon (2011) [35]	NA	Vild:100mg	54	53.5	68.6	8.0	NA	22.7	5.9	32
		Glim: 4mg	52	55.4	60.8	8.1	NA	22.3	5.9	32
Seck (2010) [36]	NCT00094770	Sita:100mg	248	57.6	57.3	7.3	88.5	30.9	5.8	104
		Glip:5-20mg	256	57.0	62.9	7.3	90.3	31.3	5.7	104
Goke (2010) [37]	NA	Saxa: 5mg	428	57.5	49.5	7.7	88.7	31.5	5.5	52
		Glip:5-20mg	430	57.6	54.0	7.7	88.6	31.3	5.4	52
Matthews (2010) [38]	EudraT200400455921	Vild:2-6mg	1562	57.5	53.1	7.3	89.5	31.9	5.7	104
		Glim:100mg	1556	57.5	53.9	7.3	88.9	31.7	5.7	104

Filozof (2010) [39]	NA	Vild:100mg	513	59.2	52.2	8.5	85.7	31.2	6.4	52
		Glic:80-320 mg	494	59.7	51.8	8.5	84.2	30.8	6.8	52
Filozof-a (2010) [40]	NCT00396357	Vild:100mg	456	56.9	49.6	7.4	84.6	31.1	4.6	24
		Met	458	57.0	55	7.3	84.4	31.2	4.7	24
Arechavaleta (2011) [41]	NCT00701090	Sita:100mg	516	56.3	55.0	7.5	80.6	29.7	6.8	30
		Glim:1-6mg	519	56.2	53.8	7.5	82.0	30.2	6.7	30
Taskinen (2011) [42]	NCT00601250	Lina:5mg	523	56.5	53	8.1	82.2	29.9	NA	24
		PLA	177	56.6	57	8.0	83.3	30.1	NA	24

Goodman (2009) [43]	NA	Vild:100mg	248	54.9	52.8	8.5	NA	31.4	NA	24
		PLA	122	54.5	67.2	8.7	NA	31.7	NA	24
Bergenstal (2010) [44]	NCT00637273	Sita:100mg	166	52	52	8.5	87	32	5	26
		Piog[q]:45mg	165	53	48	8.5	88	32	6	26
Nauck (2009) [45]	NCT00286442	Alog:12.5mg	213	55	47.4	7.9	NA	32	6	26
		Alog:25mg	210	54	57.3	7.9	NA	32	6	26
		PLA	104	56	48	8.0	NA	32	6	26
DeFronzo (2009)	NCT00121667	Saxa:2.5mg	192	54.7	43.2	8.1	85.97	31.7	6.7	24
		Saxa:5mg	191	54.7	53.9	8.1	87.26	31.2	6.4	24

[46]		Saxa:10mg	181	54.2	52.5	8.0	87.83	31.1	6.3	24
		PLA	179	54.8	53.6	8.1	87.14	31.6	6.7	24
Bolli		Vild:50mg	295	56.3	61.7	8.4	91.8	32.2	6.4	52
(2009)	NA									
[47]		Piog:30mg	281	57.0	64.1	8.4	91.2	32.1	6.4	52
Raz		Sita:100mg	96	53.6	49.0	9.3	81.5	30.1	8.4	30
(2008)	NCT00									
[48]	337610	PLA	94	56.1	58.5	9.1	81.2	30.4	7.3	30
Xiao		Glip: 5-10mg	40	53.6	58.3	8.7		26.6		24
(2015)	NA	Piog:					NA		NA	
[49]		15-45mg	40	54.2	59.8	8.7		26.5		24

Ohira (2014) [50]	NA	Glim: 1mg	30	62.2	50	8.6	NA	24.49	NA	26
		Piog: 15mg	30	63.7	63.3	8.5		23.61		26
Genovese (2013) [51]	NCT00772174	Piog	110	57	59.1	6.92	88.8	32.4	5.8	26
		PLA	103	57.8	60.2	7.02	89	32.6	5.7	26
Pfutzner (2011) [52]	NCT00770653	Glim: 4mg	150	59	64.1	7.4	94.1	32.5	5.9	24
		Piog: 30mg	155	59	64.1	7.1	96.2	32.6	6.2	24
Petrica (2011) [53]	NA	Glim: 4mg	39	58.8	NA	7.49	NA	33.71	10.17	52
		Piog: 30mg	39	56.8	NA	7.7	NA	32.1	10	52

Petrica (2009) [54]	NA	Glim: 4mg	22	63.2	41.2	7.58	NA	33.55	10.4	26
		Rosi^{r}: 4mg	22	63	41.2	7.72	NA	33.58	10.53	26
Khanolkar (2008) [55]	NA	Glic: 80mg	25	56	60	7.08	NA	33.66	NA	26
		Rosi: 4mg	25	59	56	7.33	NA	34.55	NA	26
Kelly (2007) [56]	NCT00123643	Glyb: 20mg	16	63.1	62.5	7.3	95	NA	NA	26
		Rosi: 8mg	20	57.9	45	7.8	96.9	NA	NA	26
Umpierrez (2006) [57]	NA	Glim: 2-8mg	101	51.6	55.2	8.41	NA	34.54	4.9	28
		Piog: 30-45mg	109	55.7	52.3	8.31	NA	33.81	5.9	28

Ristic (2006) [58]	NA	Glic:80-240 mg	129	61.6	50.4	7.6	NA	29.5	6.7	24
		Nate[o]: 180-540mg	133	62	54.2	7.67	NA	28.5	7.16	24
Garber (2006) [59]	NA	Glib[k]: 5-10mg	160	56	56	8.5	93	32	5	24
		Rosi: 4-8mg	158	56	65	8.4	94	32	6	24
Bakris (2006) [60]	NA	Glyb: 5mg	185	58.8	69	8.3	90.3	31.8	7.6	32
		Rosi: 4mg	204	60	63	8.5	89.2	31.6	8	32
Negro	NA	Rosi: 8mg	19	60.3	52.6	8.4	84.1	28.3	7.1	52

(2005) [61]		PLA	19	59	63.2	8.1	83.6	29.3	6.6	52
Matthews (2005) [62]	NA	Glic[i]: 80-320 mg	313	57	49.2	8.53	92.7	32.6	5.5	52
		Piog: 15-45mg	317	56	50.8	8.71	91.8	32.6	5.8	52
Derosa (2005) [63]	NA	Glic: 2mg	47	52	48.9	7.9	75.6	26.8	4	52
		Rosi: 4mg	48	54	52.1	8	74.2	26.6	5	52
Phillips (2003)	NA	Acar: 100-200mg	40	58.37	65	8.05	89.77	30.75	5.32	24

[64]		PLA	43	62.3	76.7	7.82	87.88	30.09	6.06	24
Halimi (2000) [65]	NA	Acar: 100mg	59	56	28	8.6	NA	30.1	9.5	26
		PLA	70	55	44	8.5	NA	29.7	9	26
Ferrannini (2013) [66]	NCT00881530	Empa: 10mg	166	60	50	7.88	89.6	30.2	NA	78
		Empa: 25mg	166	60	53	7.91	89.5	30.3	NA	78
		Sita: 100mg	56	60	51.8	8.03	88.6	30	NA	78
Blonde (2016) [67]	NCT01106651	Cana: 100mg	241	64.3	51.5	7.8	88.4	31.4	12.3	26
		Cana: 300mg	236	63.4	54.7	7.7	88.8	31.5	11.3	26
		PLA	237	63.2	60.3	7.8	91.1	31.8	11.4	52

Dei Cas (2017) [68]	NCT01822548	Vild: 100mg	40	61	65	7.7	NA	29.1	NA	52
		Glim: 2.5-5mg	24	63	71	7.7	NA	28.9	NA	52

Note: [a]Dapa: Dapagliflozin; [b]Empa: Empagliflozin; [c]Cana: Canagliflozin; [d]Ipra: Ipragliflozin; [e]Vild: Vildagliptin; [f]Sita: Sitagliptin; [g]Saxa: Saxagliptin; [h]Lina: Linagliptin; [i]Alog: Alogliptin; [j]Tene: Teneligliptin; [k]Glib: Glyburide; [l]Glic: Gliclazide; [m]Glim: Glimepiride; [n]Glip: Glipizide; [o]Nate: Nateglinide; [p]Acar: Acarbose; [q]Piog: Pioglitazone; [r]Rosi: Rosiglitazone; [s]PLA: Placebo. [t]BMI: body mass index; [u]HbA1c: glycated hemoglobin; [v]NA: not applicable.

Table S3. Assessment of risk of bias in individual studies

Study	Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting
Bolinder (2014) [1]	Low	Unclear	Low	Unclear	High	Low
Baily (2013) [2]	Low	Low	Low	Unclear	Low	Low
Lava-Gonzalez (2013) [3]	Low	Unclear	Low	Unclear	Low	Low
Rosenstock (2015) [4]	Unclear	Unclear	Low	Unclear	Low	Low
Del Prato (2015) [5]	Low	Low	Low	Unclear	Low	Low
Merker (2015) [6]	Low	Low	Low	Unclear	Low	Low
BOSI (2007) [7]	Unclear	Unclear	Low	Unclear	High	Low
Bryson (2016)	Low	Low	Low	Unclear	High	Low

[8]						
Charbonnel (2006) [9]	Unclear	Unclear	Low	Unclear	High	Low
Ahren (2004) [10]	Unclear	Unclear	Low	Unclear	High	Low
Handelsman (2017) [11]	Low	Unclear	Low	Unclear	High	Low
Gadde (2017) [12]	Low	Low	Low	Unclear	Low	Low
Du (2017) [13]	Low	Unclear	Low	Unclear	High	Low
Yang (2016) [14]	Low	Unclear	Low	Unclear	High	Low
Lu (2016) [15]	Low	Low	Low	Unclear	Low	Low
Tai (2016) [16]	Low	Unclear	Low	Unclear	High	Low
DeFronzo (2015) [17]	Low	Low	Low	Unclear	High	Low
Ji (2016) [18]	Low	Unclear	Low	Unclear	High	Low
Wang (2016)	Low	Low	Low	Low	Low	Low

[19]						
Wang (2015) [20]	Unclear	Unclear	Unclear	Unclear	Low	High
Schernthaner (2015) [21]	Low	Low	Low	Unclear	High	Low
Ridderstrale (2014) [22]	Low	Low	Low	Unclear	High	Low
Del Prato (2014) [23]	Unclear	Unclear	Low	Low	High	Low
Derosa (2014) [24]	Unclear	Unclear	Low	Unclear	High	High
Kashiwagi (2015) [25]	Unclear	Unclear	Low	Unclear	Low	Low
Cefalu (2013) [26]	Low	Low	Low	Unclear	Low	Low
Berndt-Zipfel (2013) [27]	Unclear	Unclear	High	Unclear	Unclear	High
Yang (2012) [28]	Low	Unclear	Low	Unclear	Low	Low

Gallwitz (2012) [29]	Low	Low	Low	Unclear	High	Low
Derosa (2012) [30]	Low	Unclear	Low	Unclear	Low	High
Derosa- a (2012) [31]	Unclear	Unclear	Low	Unclear	Low	High
Yang (2011) [32]	Low	Unclear	Low	Unclear	High	Low
Bergenstal (2012) [33]	Unclear	Low	Low	Unclear	High	Low
Pan (2012) [34]	Unclear	Unclear	Low	Unclear	Low	High
Jeon (2011) [35]	Unclear	Unclear	High	Unclear	Low	High
Seck (2010) [36]	Unclear	Unclear	Low	Unclear	High	Low
Goke (2010) [37]	Low	Low	Low	Unclear	High	Low
Matthews	Unclear	Unclear	Low	Unclear	High	Low

(2010) [38]						
Filozof (2010) [39]	Unclear	Unclear	Low	Low	High	Low
Filozof-a (2010) [40]	Unclear	Unclear	Low	Low	Low	High
Arechavaleta (2011) [41]	Low	Unclear	Low	Unclear	High	Low
Taskinen (2011) [42]	Unclear	Unclear	Low	Unclear	Low	High
Goodman (2009) [43]	Unclear	Unclear	Low	Unclear	Low	Low
Bergenstal (2010) [44]	Low	Low	Low	Unclear	High	Low
Nauck (2009) [45]	Low	Low	Low	Unclear	High	Low
DeFronzo (2009) [46]	Low	Low	Low	Unclear	High	Low
Bolli (2009) [47]	Unclear	Low	Low	Unclear	Unclear	Low

Raz (2008) [48]	Low	Unclear	Low	Unclear	Low	Low
Xiao (2015) [49]	Low	Unclear	High	Unclear	Low	High
Ohira (2014) [50]	Unclear	Low	High	Unclear	Low	High
Genovese (2013) [51]	Unclear	Unclear	Low	Unclear	Low	High
Pfutzner (2011) [52]	Unclear	Unclear	Low	Unclear	High	High
Petrica (2011) [53]	Unclear	Unclear	High	Unclear	Low	High
Petrica (2009) [54]	Unclear	Unclear	High	High	Low	High
Khanolkar (2008) [55]	Unclear	Unclear	High	Unclear	Low	High
Kelly (2007) [56]	Unclear	Unclear	Low	Unclear	Low	Low
Umpierrez	Unclear	Unclear	High	Unclear	High	Low

(2006) [57]						
Ristic (2006) [58]	Low	Low	Low	Unclear	High	High
Garber (2006) [59]	Unclear	Unclear	Low	Unclear	High	High
Bakris (2006) [60]	Unclear	Unclear	Low	Unclear	High	High
Negro (2005) [61]	Unclear	Unclear	High	Unclear	Unclear	High
Matthews (2005) [62]	Unclear	Unclear	Low	Unclear	High	Low
Derosa (2005) [63]	Unclear	Unclear	Low	Unclear	Low	High
Phillips (2003) [64]	Unclear	Unclear	Low	Unclear	Low	Low
Halimi (2000) [65]	Unclear	Unclear	Low	Unclear	High	High
Ferrannini (2013) [66]	Unclear	Unclear	Low	Unclear	Low	Low

Blonde (2016) [67]	Unclear	Unclear	Low	Unclear	Low	Low
Dei Cas (2017) [68]	Unclear	Unclear	Low	Unclear	Low	Low

Table S4. Assessment of loop inconsistency in networks

Loop	Inconsistency factor	95% confidence interval	P-value	Loop heterogeneity tau^2
HbA1c[a]				
PLA[k]-DPP4[g]-AGI[h]	0.43	0.06-0.81	0.024	0.021
PLA-SGLT2[f]-SU[j]-TZD[i]	0.23	0.00-0.81	0.497	0.041
SGLT2-DPP4-SU	0.10	0.00-0.30	0.30	0.009
PLA-SGLT2-DPP4	0.08	0.00-0.36	0.572	0.028
DPP4-SU-TZD	0.06	0.00-0.37	0.710	0.016
PLA-DPP4-TZD	0.02	0.00-0.53	0.932	0.033
2h-PPG[b]				
PLA-SGLT2-DPP4	1.10	0.00-3.65	0.396	0.468
PLA-DPP4-TZD	0.44	0.00-3.32	0.737	0.468
FPG[c]				
PLA-DPP4-AGI	0.49	0.00-1.10	0.122	0.056
DPP4-SU-TZD	0.40	0.00-1.10	0.260	0.099
PLA-SGLT2-DPP4	0.34	0.00-0.74	0.098	0.053
SGLT2-DPP4-SU	0.09	0.00-0.68	0.769	0.084
Body weight				
PLA-SGLT2-DPP4	0.82	0.00-1.65	0.052	0.132
PLA-SGLT2-SU-TZD	0.45	0.00-3.33	0.758	0.152
DPP4-SU-TZD	0.56	0.00-1.62	0.290	0.101

PLA-DPP4-TZD	0.21	0.00-3.00	0.882	0.140
SGLT2-DPP4-SU	0.12	0.00-0.70	0.679	0.027
PLA-DPP4-AGI	0.09	0.00-1.91	0.921	0.130
All-cause mortality				
PLA-SGLT2-DPP4	0.94	0.00-3.57	0.486	0.000
SGLT2-DPP4-SU	0.02	0.00-2.16	0.982	0.000
MACE[d]				
DPP4-SU-TZD	1.13	0.00-4.78	0.544	0.000
PLA-SGLT2-DPP4	0.38	0.00-2.23	0.693	0.000
SGLT2-DPP4-SU	0.00	0.00-1.62	0.999	0.000
Serious adverse event				
PLA-SGLT2-SU-TZD	1.10	0.00-3.56	0.377	0.063
DPP4-SU-TZD	0.62	0.00-1.39	0.118	0.003
SGLT2-DPP4-SU	0.48	0.00-1.04	0.094	0.028
PLA-DPP4-TZD	0.28	0.00-2.66	0.818	0.000
PLA-SGLT2-DPP4	0.25	0.00-0.87	0.467	0.000
Hypoglycemia				
DPP4-SU-TZD	1.76	0.00-4.15	0.150	0.149
SGLT2-DPP4-SU	0.41	0.00-1.37	0.403	0.146
PLA-SGLT2-DPP4	0.04	0.00-0.88	0.929	0.000
UTI[e]				
SGLT2-DPP4-SU	0.43	0.00-1.11	0.220	0.068

PLA-SGLT2-DPP4	0.08	0.00-0.69	0.781	0.000
Diarrhea				
SGLT2-DPP4-SU	1.16	0.00-2.89	0.191	0.000
PLA-SGLT2-DPP4	0.60	0.00-2.81	0.592	0.501
DPP4-SU-TZD	0.12	0.00-0.97	0.775	0.000

Note: [a]HbA1c, glycated hemoglobin; [b]2h-PPG, 2-h postprandial glucose; [c]FPG, fasting plasma glucose; [d]MACE, major adverse cardiovascular event; [e]UTI, urinary tract infection. [f]SGLT2, sodium-glucose co-transporter-2 inhibitor; [g]DPP4, dipeptidyl peptidase-4 inhibitor; [h]AGI, alpha-glucosidase inhibitor; [i]TZD, thiazolidinedione; [j]SU, sulfonylurea; [k]PLA, placebo.

Table S5. Assessment of global inconsistency in networks using the 'design-by-treatment' interaction model

Network outcome	Chi square	P value for test of global inconsistency
HbA1c[a]	7.31	0.1987
2h-PPG[b]	1.12	0.5720
FPG[c]	8.00	0.0914
Body weight	7.36	0.1949
All-cause mortality	0.74	0.6909
MACE[d]	0.6	0.8974
Hypoglycemia	3.82	0.2814
Serious adverse event	5.65	0.2267
UTI[e]	1.57	0.4558
Diarrhea	3.29	0.3496

Note: [a]HbA1c, glycated hemoglobin; [b]2h-PPG, 2-h postprandial glucose; [c]FPG, fasting plasma glucose; [d]MACE, major adverse cardiovascular event; [e]UTI, urinary tract infection.

Table S6. Pairwise random-effects meta-analyses for efficacy and safety outcomes

	Drug A	Drug B	No. of trials	No. of participants	OR / WMD (95% CI)	Heterogeneity I^2 (%)
HbA1c[a]						
	SGLT-2 inhibitor	PLA	7	2841	-0.66 (-0.85-0.48)	83
	DPP-4 inhibitor	PLA	17	6556	-0.64 (-0.73-0.55)	72
	AGI	PLA	2	210	-1.02 (-1.09-0.94)	0
	TZD	PLA	2	251	-0.86 (-1.69-0.03)	94
	DPP-4 inhibitor	Met	3	3980	-0.17 (-0.21-0.14)	0
	SU	Glitinide	1	247	-0.16 (-0.38,0.06)	/
	DPP-4 inhibitor	AGI	2	562	-0.10 (-0.19,0.00)	0
	SGLT-2 inhibitor	SU	3	3771	-0.12 (-0.21-0.02)	50
	SU	TZD	11	1908	0.03 (-0.13,0.20)	69

	DPP-4 inhibitor	SU	12	10374	0.06 (-0.01,0.13)	71
	DPP-4 inhibitor	TZD	2	892	0.14 (-0.16,0.44)	71
	SGLT-2 inhibitor	DPP-4 inhibitor	4	2126	-0.09 (-0.23,0.04)	58
2h-PPG[b]						
	SGLT-2 inhibitor	PLA	1	358	-2.55 (-3.09-2.01)	/
	DPP-4 inhibitor	PLA	7	2384	-1.76 (-2.35-1.18)	86
	AGI	PLA	1	129	-2.50 (-3.77-1.23)	/
	SGLT-2 inhibitor	DPP-4 inhibitor	1	291	-1.89 (-2.43-1.35)	/
	DPP-4 inhibitor	Met	1	81	-0.21 (-0.61,0.19)	/
	DPP-4 inhibitor	SU	3	703	-0.06 (-0.57,0.45)	42
	DPP-4 inhibitor	AGI	1	478	0.30 (-0.19,0.79)	/
	SU	TZD	1	95	0.33	

					(-0.12,0.78)	
FPG[c]						
	SGLT-2 inhibitor	PLA	7	2841	-1.32 (-1.57-1.06)	67
	DPP-4 inhibitor	PLA	16	6099	-0.97 (-1.13-0.82)	64
	AGI	PLA	2	210	-1.62 (-2.74-0.50)	81
	SGLT-2 inhibitor	DPP-4 inhibitor	4	2324	-0.68 (-0.91-0.46)	38
	DPP-4 inhibitor	Met	2	995	-0.68 (-1.65,0.29)	38
	SGLT-2 inhibitor	SU	2	2346	-0.65 (-0.81-0.49)	0
	SU	Glitinide	1	247	-0.19 (-0.68,0.30)	/
	DPP-4 inhibitor	AGI	2	562	-0.15 (-0.36,0.06)	24
	SU	TZD	6	1428	0.03 (-0.33,0.40)	58
	DPP-4 inhibitor	SU	13	12116	0.18 (-0.03,0.38)	82

DPP-4 inhibitor	TZD	2	889	0.60 (0.25,0.96)	0

Body weight

SGLT-2 inhibitor	PLA	7	2848	-1.97 (-2.37-1.56)	63
DPP-4 inhibitor	PLA	10	3035	-0.29 (-0.61,0.03)	62
AGI	PLA	1	81	-0.89 (-2.05,0.27)	/
TZD	PLA	2	251	2.40 (0.01,4.79)	0
SGLT-2 inhibitor	SU	3	3783	-4.47 (-4.75-4.20)	0
SGLT-2 inhibitor	DPP-4 inhibitor	3	1962	-2.41 (-2.78-2.04)	0
DPP-4 inhibitor	SU	11	11338	-1.94 (-2.15-1.73)	43
SU	TZD	5	1020	-0.26 (-1.23,0.70)	64
DPP-4 inhibitor	Met	1	3192	0.51 (0.28,0.74)	/
DPP-4	AGI	1	481	0.69	/

inhibitor				(0.19,1.19)	
DPP-4 inhibitor	TZD	2	898	-2.95 (-4.08-1.81)	75
All-cause mortality					
SGLT-2 inhibitor	PLA	5	1977	0.87 (0.13,5.97)	0
DPP-4 inhibitor	PLA	10	4050	0.29 (0.05,1.87)	0
SGLT-2 inhibitor	SU	3	3809	0.67 (0.28,1.63)	0
SGLT-2 inhibitor	DPP-4 inhibitor	3	1861	0.77 (0.09,6.30)	0
DPP-4 inhibitor	SU	9	12805	0.80 (0.45,1.43)	0
SU	TZD	2	887	2.44 (0.21,27.86)	0
SU	Glitinide	1	256	1.03 (0.02,52.38)	/
DPP-4 inhibitor	AGI	1	461	1.00 (0.02,50.39)	/
DPP-4 inhibitor	Met	2	3167	0.42 (0.03,6.76)	0

MACE[d]

SGLT-2 inhibitor	PLA	6	2699	0.49 (0.20,1.16)	0
DPP-4 inhibitor	PLA	9	4468	0.64 (0.25,1.67)	0
DPP-4 inhibitor	TZD	2	908	0.42 (0.06,3.00)	0
SU	TZD	1	290	0.34 (0.03,3.29)	/
DPP-4 inhibitor	SU	8	8771	0.69 (0.45,1.06)	0
SGLT-2 inhibitor	SU	3	3809	0.73 (0.32,1.67)	0
SGLT-2 inhibitor	DPP-4 inhibitor	4	2253	0.99 (0.20,4.82)	0

Serious adverse event

SGLT-2 inhibitor	PLA	7	2861	0.77 (0.57,1.05)	0
DPP-4 inhibitor	PLA	14	6181	0.97 (0.69,1.36)	0
TZD	PLA	1	213	2.86 (0.29,27.94)	/

DPP-4 inhibitor	TZD	2	906	0.45 (0.25,0.81)	0
DPP-4 inhibitor	Met	3	4081	0.68 (0.10,4.80)	49
DPP-4 inhibitor	SU	11	12971	0.97 (0.85,1.11)	16
DPP-4 inhibitor	AGI	1	461	2.52 (0.48,13.13)	/
SGLT-2 inhibitor	DPP-4 inhibitor	4	2249	0.63 (0.41,0.95)	0
SGLT-2 inhibitor	SU	3	3809	0.95 (0.59,1.52)	81
SU	TZD	4	1282	0.81 (0.41,1.61)	49
Hypoglycemia					
SGLT-2 inhibitor	PLA	7	2861	0.79 (0.56,1.12)	0
DPP-4 inhibitor	PLA	14	6181	0.58 (0.33,1.01)	0
DPP-4 inhibitor	SU	10	11968	0.11 (0.08,0.15)	75
DPP-4	Met	3	4081	0.68	0

inhibitor				(0.33,1.49)	
DPP-4 inhibitor	AGI	1	461	0.74 (0.16,3.36)	/
DPP-4 inhibitor	TZD	1	331	5.09 (0.59,44.08)	/
SU	TZD	4	1489	7.75 (5.10,11.76)	60.4
SGLT-2 inhibitor	SU	3	3809	0.09 (0.06,0.15)	76
SGLT-2 inhibitor	DPP-4 inhibitor	4	2249	1.45 (0.85,2.48)	0
SU	Glitinide	1	256	1.04 (0.58,1.88)	/
UTI[e]					
SGLT-2 inhibitor	PLA	6	2693	1.16 (0.83,1.63)	0
DPP-4 inhibitor	PLA	9	4127	1.13 (0.81,1.59)	0
SGLT-2 inhibitor	SU	3	3809	1.24 (0.90,1.70)	44
SGLT-2 inhibitor	DPP-4 inhibitor	4	2249	0.93 (0.66,1.31)	0

DPP-4 inhibitor	SU	6	7725	0.86 (0.54,1.36)	73
DPP-4 inhibitor	AGI	1	463	1.51 (0.53,4.32)	/
DPP-4 inhibitor	TZD	1	331	1.52 (0.53,4.37)	/
Diarrhea					
SGLT-2 inhibitor	PLA	5	2523	0.95 (0.64,1.43)	0
DPP-4 inhibitor	PLA	11	4965	0.72 (0.38,1.33)	67
AGI[h]	PLA[l]	1	83	1.09 (0.32,3.70)	/
DPP-4 inhibitor	Met[j]	1	914	0.52 (0.30,0.90)	/
DPP-4 inhibitor	SU	9	11875	0.97 (0.83,1.13)	0
DPP-4 inhibitor	TZD	2	906	1.13 (0.65,1.95)	0
SU	TZD[i]	2	616	1.29 (0.68,2.43)	0
SGLT-2	SU[k]	2	2359	0.79	0

inhibitor				(0.58,1.09)	
SGLT-2	DPP-4	2	795	2.85	37
inhibitor[f]	inhibitor[g]			(0.32,25.64)	

Note: [a]HbA1c, glycated hemoglobin; [b]2h-PPG, 2-h postprandial glucose; [c]FPG, fasting plasma glucose; [d]MACE, major adverse cardiovascular event; [e]UTI, urinary tract infection; [f]SGLT-2 inhibitor, sodium-glucose co-transporter-2 inhibitor; [g]DPP-4 inhibitor, dipeptidyl peptidase-4 inhibitor; [h]AGI, α-glucosidase inhibitor; [i]TZD, thiazolidinedione; [j]Met, high dose metformin; [k]SU, sulfonylurea; [l]PLA, placebo.

Table S7. Contributions of direct evidence in the entire network

	Drug A	Drug B	No. of trials	Contribution to the network, %
HbA1c[a]				
	SGLT-2 inhibitor	PLA	7	4.4
	DPP-4 inhibitor	PLA	17	9.4
	AGI	PLA	2	8.9
	TZD	PLA	2	0.5
	DPP-4 inhibitor	Met	3	11.1
	SU	Glitinide	1	11.1
	DPP-4 inhibitor	AGI	2	9.1
	SGLT-2 inhibitor	SU	3	10.0
	SU	TZD	11	8.9
	DPP-4 inhibitor	SU	12	18.0
	DPP-4 inhibitor	TZD	2	3.1
	SGLT-2 inhibitor	DPP-4 inhibitor	4	5.6
2h-PPG[b]				
	SGLT-2 inhibitor	PLA	1	9.5

DPP-4 inhibitor	PLA	7	10.8
AGI	PLA	1	3.5
SGLT-2 inhibitor	DPP-4 inhibitor	1	12.4
DPP-4 inhibitor	Met	1	13.8
DPP-4 inhibitor	SU	3	23.0
DPP-4 inhibitor	AGI	1	13.4
SU	TZD	1	13.8
FPG[c]			
SGLT-2 inhibitor	PLA	7	6.8
DPP-4 inhibitor	PLA	16	11.5
AGI	PLA	2	0.6
SGLT-2 inhibitor	DPP-4 inhibitor	4	8.1
DPP-4 inhibitor	Met	2	11.3
SGLT-2 inhibitor	SU	2	13.1
SU	Glitinide	1	11.3
DPP-4 inhibitor	AGI	2	11.1
SU	TZD	6	6.9
DPP-4 inhibitor	SU	13	11.8

DPP-4 inhibitor	TZD	2	7.5
Body weight			
SGLT-2 inhibitor	PLA	7	8.2
DPP-4 inhibitor	PLA	10	11.3
AGI	PLA	1	2.9
TZD	PLA	2	1.4
SGLT-2 inhibitor	SU	3	11.6
SGLT-2 inhibitor	DPP-4 inhibitor	3	7.3
DPP-4 inhibitor	SU	11	17.0
SU	TZD	5	7.8
DPP-4 inhibitor	Met	1	14.3
DPP-4 inhibitor	AGI	1	12.6
DPP-4 inhibitor	TZD	2	5.8
All-cause mortality			
SGLT-2 inhibitor	PLA	5	6.7
DPP-4 inhibitor	PLA	10	9.8
SGLT-2 inhibitor	SU	3	11.8

SGLT-2 inhibitor	DPP-4 inhibitor	3	3.2
DPP-4 inhibitor	SU	9	22.4
SU	TZD	2	11.5
SU	Glitinide	1	11.5
DPP-4 inhibitor	AGI	1	11.5
DPP-4 inhibitor	Met	2	11.5
MACE[d]			
SGLT-2 inhibitor	PLA	6	15.5
DPP-4 inhibitor	PLA	9	15.9
DPP-4 inhibitor	TZD	2	15.9
SU	TZD	1	6.8
DPP-4 inhibitor	SU	8	22.3
SGLT-2 inhibitor	SU	3	16.9
SGLT-2 inhibitor	DPP-4 inhibitor	4	6.7
Serious adverse event			
SGLT-2 inhibitor	PLA	7	10.2
DPP-4 inhibitor	PLA	14	12.1

TZD	PLA	1	0.7
DPP-4 inhibitor	TZD	2	7.2
DPP-4 inhibitor	Met	3	14.4
DPP-4 inhibitor	SU	11	19.4
DPP-4 inhibitor	AGI	1	14.4
SGLT-2 inhibitor	DPP-4 inhibitor	4	7.8
SGLT-2 inhibitor	SU	3	6.4
SU	TZD	4	7.4
Hypoglycemia			
SGLT-2 inhibitor	PLA	7	10.0
DPP-4 inhibitor	PLA	14	7.6
DPP-4 inhibitor	SU	10	18.9
DPP-4 inhibitor	Met	3	11.2
DPP-4 inhibitor	AGI	1	11.2
DPP-4 inhibitor	TZD	1	0.8
SU	TZD	4	11.0
SGLT-2 inhibitor	SU	3	10.7

	SGLT-2 inhibitor	DPP-4 inhibitor	4	7.3
	SU	Glitinide	1	11.2
UTI[e]				
	SGLT-2 inhibitor	PLA	6	12.9
	DPP-4 inhibitor	PLA	9	13.7
	SGLT-2 inhibitor	SU	3	13.5
	SGLT-2 inhibitor	DPP-4 inhibitor	4	13.2
	DPP-4 inhibitor	SU	6	12.0
	DPP-4 inhibitor	AGI	1	17.4
	DPP-4 inhibitor	TZD	1	17.4
Diarrhea				
	SGLT-2 inhibitor	PLA	5	15.2
	DPP-4 inhibitor	PLA	11	8.5
	AGI[h]	PLA[l]	1	12.5
	DPP-4 inhibitor	Met[j]	1	12.5
	DPP-4 inhibitor	SU	9	19.1
	DPP-4 inhibitor	TZD	2	7.6

SU	TZD[i]	2	5.8
SGLT-2 inhibitor	SU[k]	2	18.3
SGLT-2 inhibitor[f]	DPP-4 inhibitor[g]	2	0.5

Note: [a]HbA1c, glycated hemoglobin; [b]2h-PPG, 2-h postprandial glucose; [c]FPG, fasting plasma glucose; [d]MACE, major adverse cardiovascular event; [e]UTI, urinary tract infection; [f]SGLT-2 inhibitor, sodium-glucose co-transporter-2 inhibitor; [g]DPP-4 inhibitor, dipeptidyl peptidase-4 inhibitor; [h]AGI, α-glucosidase inhibitor; [i]TZD, thiazolidinedione; [j]Met, high dose metformin; [k]SU, sulfonylurea; [l]PLA, placebo.

Table S8. Sensitivity analyses for the primary outcomes

HbA1c, %							
PLA[a]	**-0.72 (-0.84, 0.60)**	**-0.62 (-0.70-0.53)**	**-0.65 (-0.77-0.54)**	**-0.65 (-0.81-0.50)**	**-0.99 (-1.26-0.72)**	**-0.48 (-0.81-0.15)**	**-0.49 (-0.89-0.10)**
0.72 (0.60,0.84)	**SGLT2[b]**	0.10 (-0.02,0.22)	0.07 (-0.06,0.20)	0.07 (-0.11,0.24)	-0.27 (-0.56,0.03)	0.24 (-0.10,0.59)	0.23 (-0.17,0.63)
0.62 (0.53,0.70)	-0.10 (-0.22,0.02)	**DPP4[c]**	-0.04 (-0.13,0.05)	-0.04 (-0.18,0.11)	**-0.37 (-0.65-0.09)**	0.14 (-0.18,0.46)	0.12 (-0.26,0.51)
0.65 (0.54,0.77)	-0.07 (-0.20,0.06)	0.04 (-0.05,0.13)	**SU[g]**	-0.00 (-0.14,0.14)	**-0.34 (-0.63-0.04)**	0.18 (-0.16,0.51)	0.16 (-0.22,0.54)
0.65 (0.50,0.81)	-0.07 (-0.24,0.11)	0.04 (-0.11,0.18)	0.00 (-0.14,0.14)	**TZD[e]**	**-0.34 (-0.65-0.02)**	0.18 (-0.18,0.53)	0.16 (-0.24,0.56)
0.99 (0.72,1.26)	0.27 (-0.03,0.56)	**0.37 (0.09,0.65)**	**0.34 (0.04,0.63)**	**0.34 (0.02,0.65)**	**AGI[d]**	**0.51 (0.08,0.94)**	**0.50 (0.02,0.97)**
0.48 (0.15,0.81)	-0.24 (-0.59,0.10)	-0.14 (-0.46,0.18)	-0.18 (-0.51,0.16)	-0.18 (-0.53,0.18)	**-0.51 (-0.94-0.08)**	**Met[f]**	-0.02 (-0.52,0.49)
0.49 (0.10,0.89)	-0.23 (-0.63,0.17)	-0.12 (-0.51,0.26)	-0.16 (-0.54,0.22)	-0.16 (-0.56,0.24)	**-0.50 (-0.97-0.02)**	0.02 (-0.49,0.52)	**Meglitinide**
Body weight, kg							
PLA	**-2.10 (-2.46-1.74)**	-0.07 (-0.39,0.25)	**2.05 (1.66,2.44)**	**2.64 (2.01,3.27)**	-0.89 (-2.30,0.52)		
2.10 (1.74,2.46)	**SGLT2**	**2.03 (1.64,2.42)**	**4.15 (3.75,4.56)**	**4.74 (4.09,5.40)**	1.21 (-0.24,2.66)		
0.07 (-0.25,0.39)	**-2.03 (-2.42-1.64)**	**DPP4**	**2.12 (1.82,2.41)**	**2.71 (2.15,3.27)**	-0.82 (-2.26,0.62)		

-2.05 (-2.44-1.66)	**-4.15 (-4.56-3.75)**	**-2.12 (-2.41-1.82)**	**SU**	**0.59 (0.03,1.15)**	**-2.94 (-4.40-1.48)**
-2.64 (-3.27-2.01)	**-4.74 (-5.40-4.09)**	**-2.71 (-3.27-2.15)**	**-0.59 (-1.15-0.03)**	**TZD**	**-3.53 (-5.07-1.99)**
			—		
0.89 (-0.52,2.30)	-1.21 (-2.66,0.24)	0.82 (-0.62,2.26)	**2.94 (1.48,4.40)**	**3.53 (1.99,5.07)**	**AGI**
MACE					
PLA	0.57 (0.27,1.22)	0.55 (0.25,1.20)	0.80 (0.36,1.80)	1.81 (0.29,11.16)	
1.74 (0.82,3.71)	**SGLT2**	0.95 (0.46,1.97)	1.39 (0.70,2.77)	3.14 (0.52,18.83)	
1.83 (0.84,4.01)	1.05 (0.51,2.18)	**DPP4**	1.46 (0.98,2.19)	3.30 (0.63,17.29)	
1.25 (0.56,2.82)	0.72 (0.36,1.43)	0.68 (0.46,1.02)	**SU**	2.26 (0.42,12.06)	
0.55 (0.09,3.43)	0.32 (0.05,1.91)	0.30 (0.06,1.58)	0.44 (0.08,2.37)	**TZD**	
All-cause mortality					
PLA	0.65 (0.22,1.89)	0.62 (0.23,1.67)	0.82 (0.29,2.37)	0.29 (0.02,4.00)	0.77 (0.04,15.12)
1.54 (0.53,4.47)	**SGLT2**	0.95 (0.40,2.25)	1.26 (0.58,2.75)	0.44 (0.04,5.56)	1.19 (0.07,21.29)
1.62 (0.60,4.40)	1.06 (0.44,2.51)	**DPP4**	1.33 (0.77,2.31)	0.47 (0.04,5.53)	1.26 (0.07,21.32)

1.22 (0.42,3.50)	0.79 (0.36,1.72)	0.75 (0.43,1.29)	**SU**	0.35 (0.03,3.90)	0.94 (0.06,15.14)
3.45 (0.25,47.73)	2.25 (0.18,28.13)	2.13 (0.18,25.06)	2.84 (0.26,31.46)	**TZD**	2.68 (0.07,105.41)
1.29 (0.07,25.19)	0.84 (0.05,15.02)	0.80 (0.05,13.49)	1.06 (0.07,17.07)	0.37 (0.01,14.71)	**AGI**

Note: Bold and underline fonts indicate statistically significant differences. [a]PLA, placebo; [b]SGLT2, sodium-glucose co-transporter-2 inhibitor; [c]DPP4, dipeptidyl peptidase-4 inhibitor; [d]AGI, alpha-glucosidase inhibitor; [e]TZD, thiazolidinedione; [f]Met, high dose metformin; [g]SU, sulfonylurea.

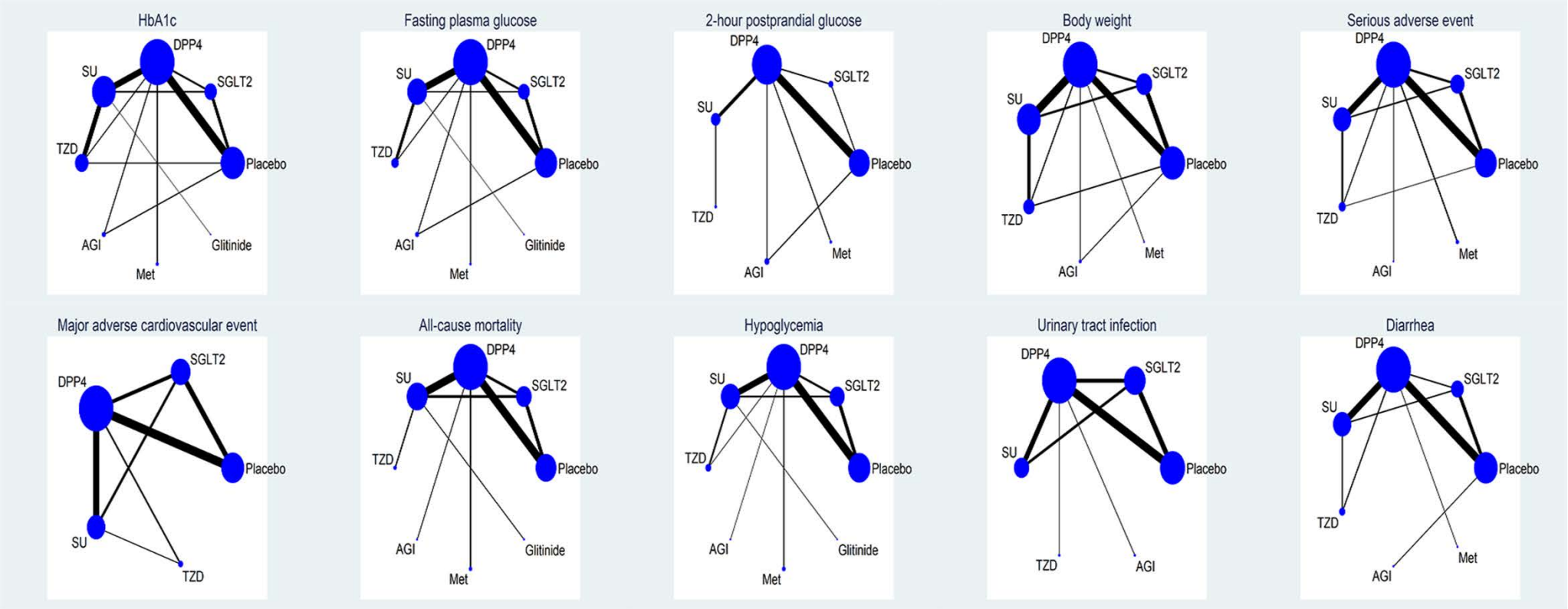

Figure S1. Network maps of efficacy and safety outcomes of oral antidiabetic drugs.

Note: SGLT2, sodium-glucose co-transporter-2 inhibitor; DPP4, dipeptidyl peptidase-4 inhibitor; AGI, alpha-glucosidase inhibitor; TZD, thiazolidinedione; Met, high dose metformin; SU, sulfonylurea； Glitinide, meglitinide.

Figure S2. Network estimates of treatment effects for oral antidiabetic drugs

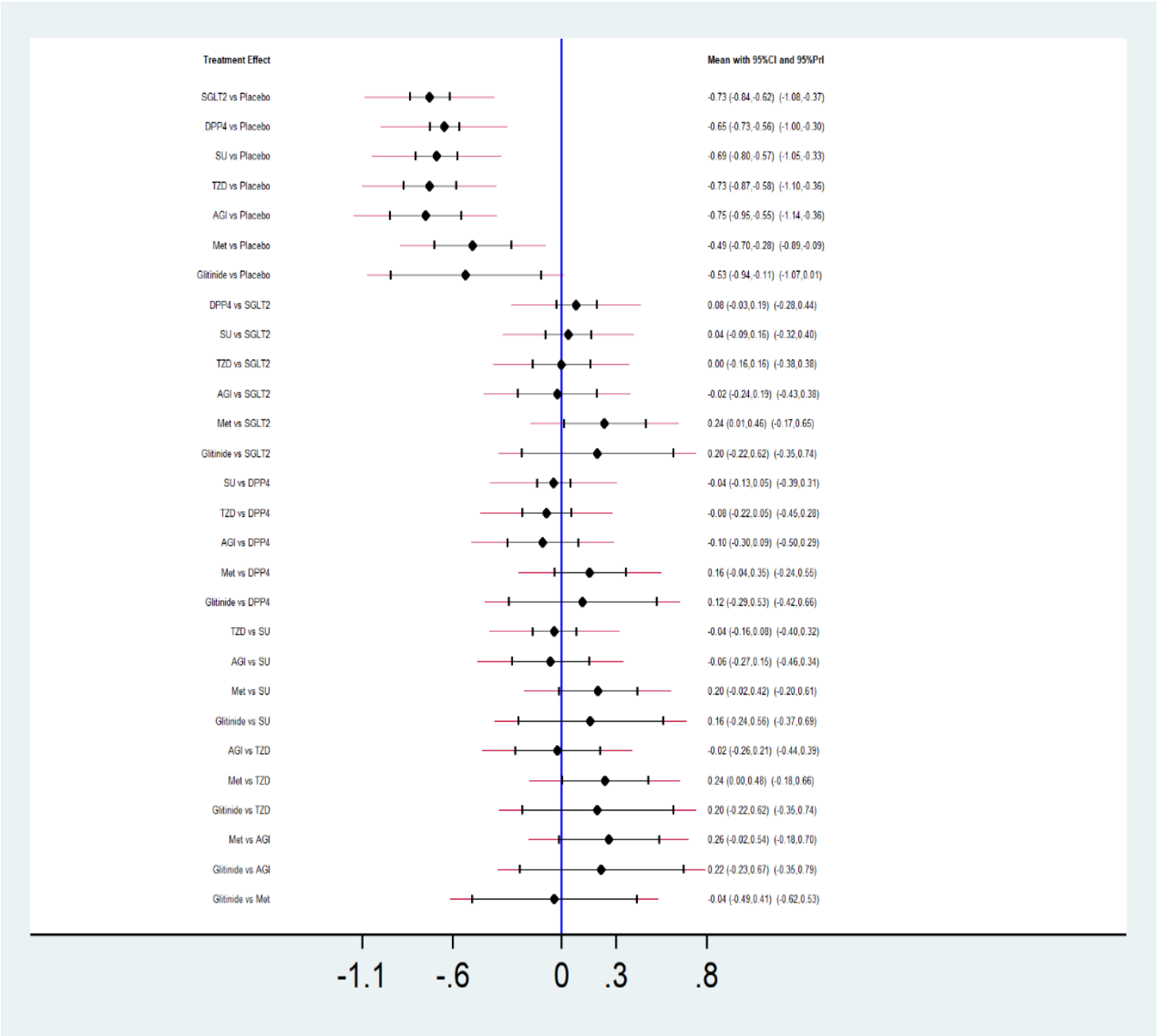

Figure S2.a HbA1c

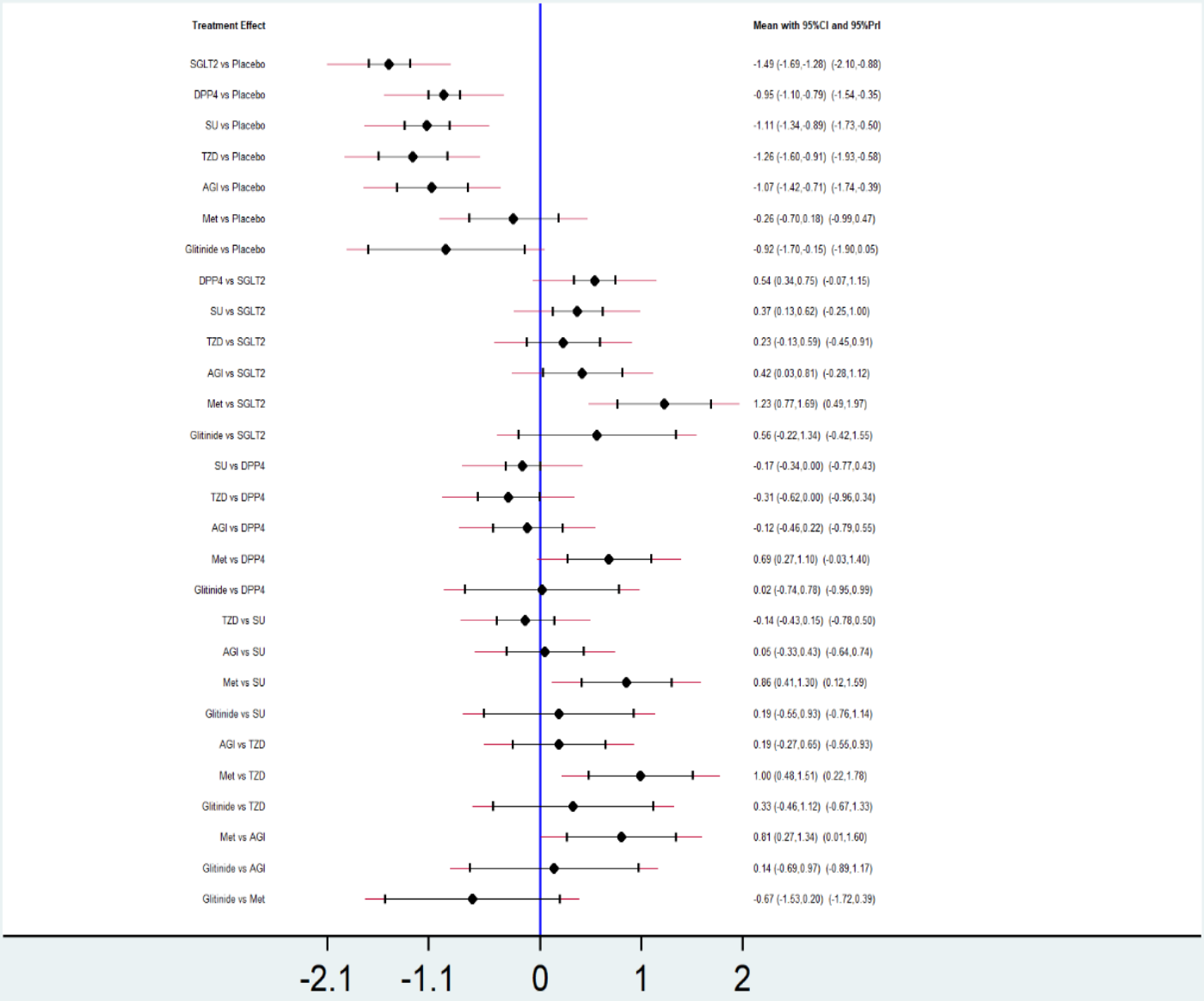

Figure S2.b FPG

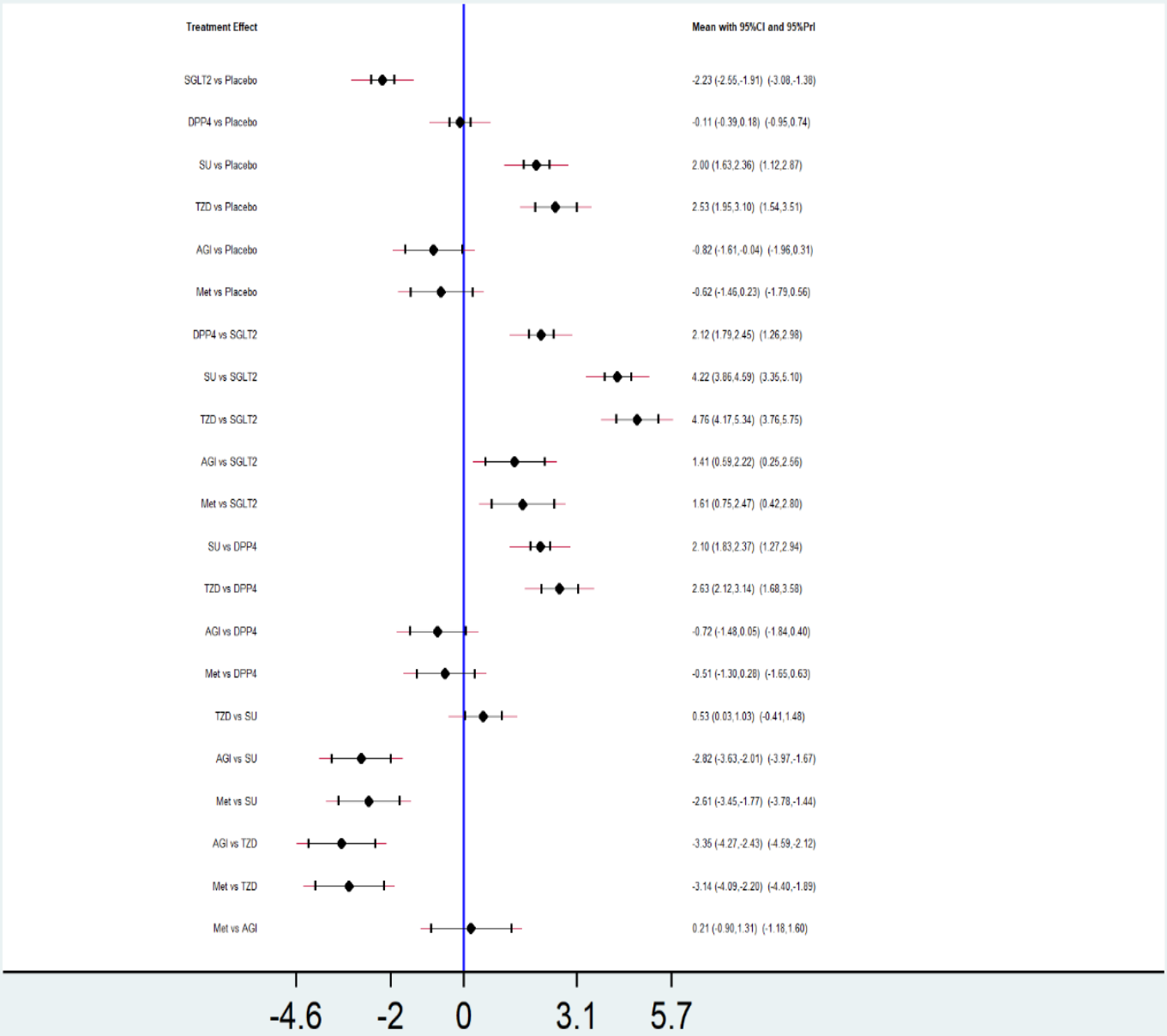

Figure S2.c Body weight

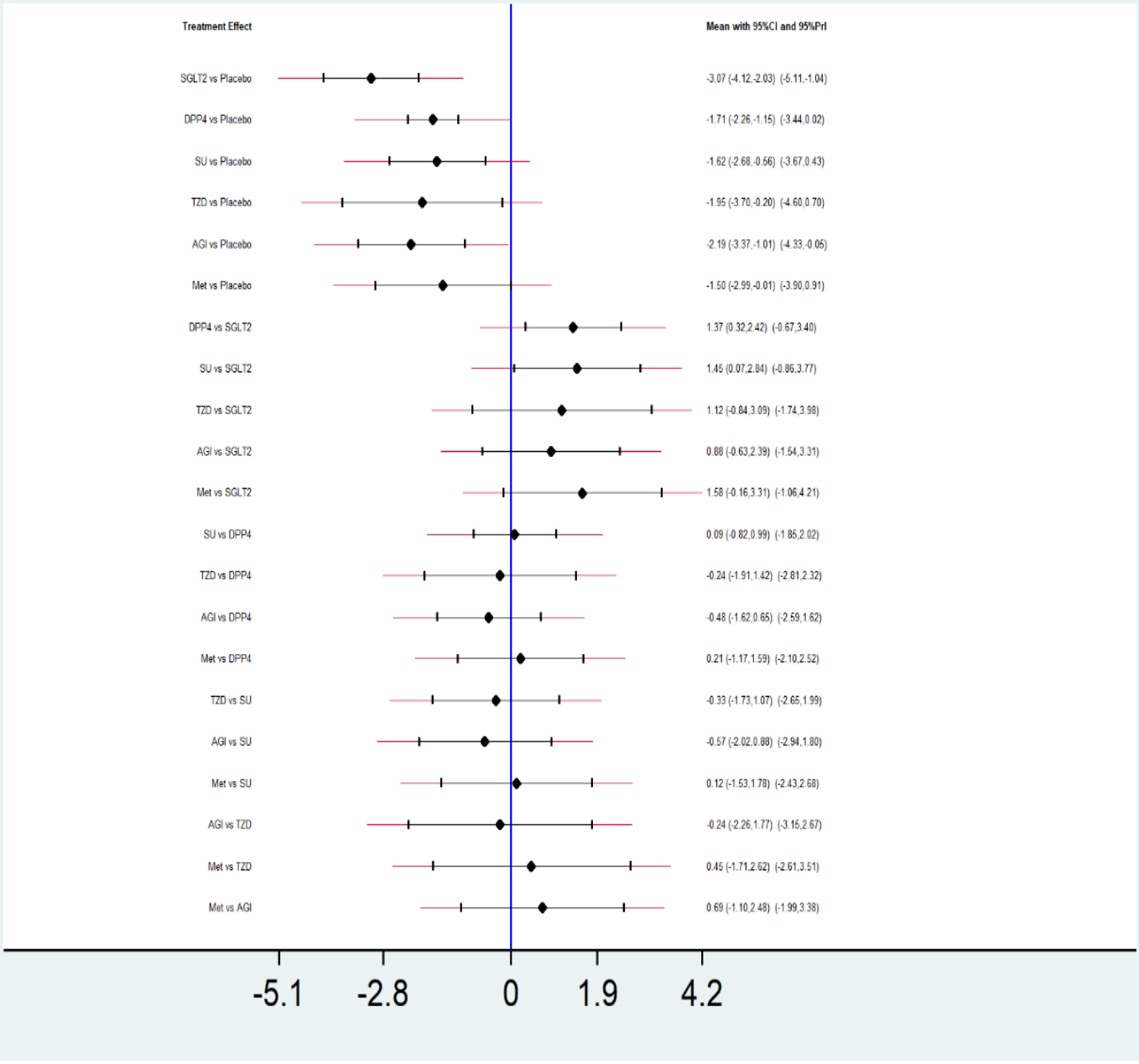

Figure S2.d 2h-PPG

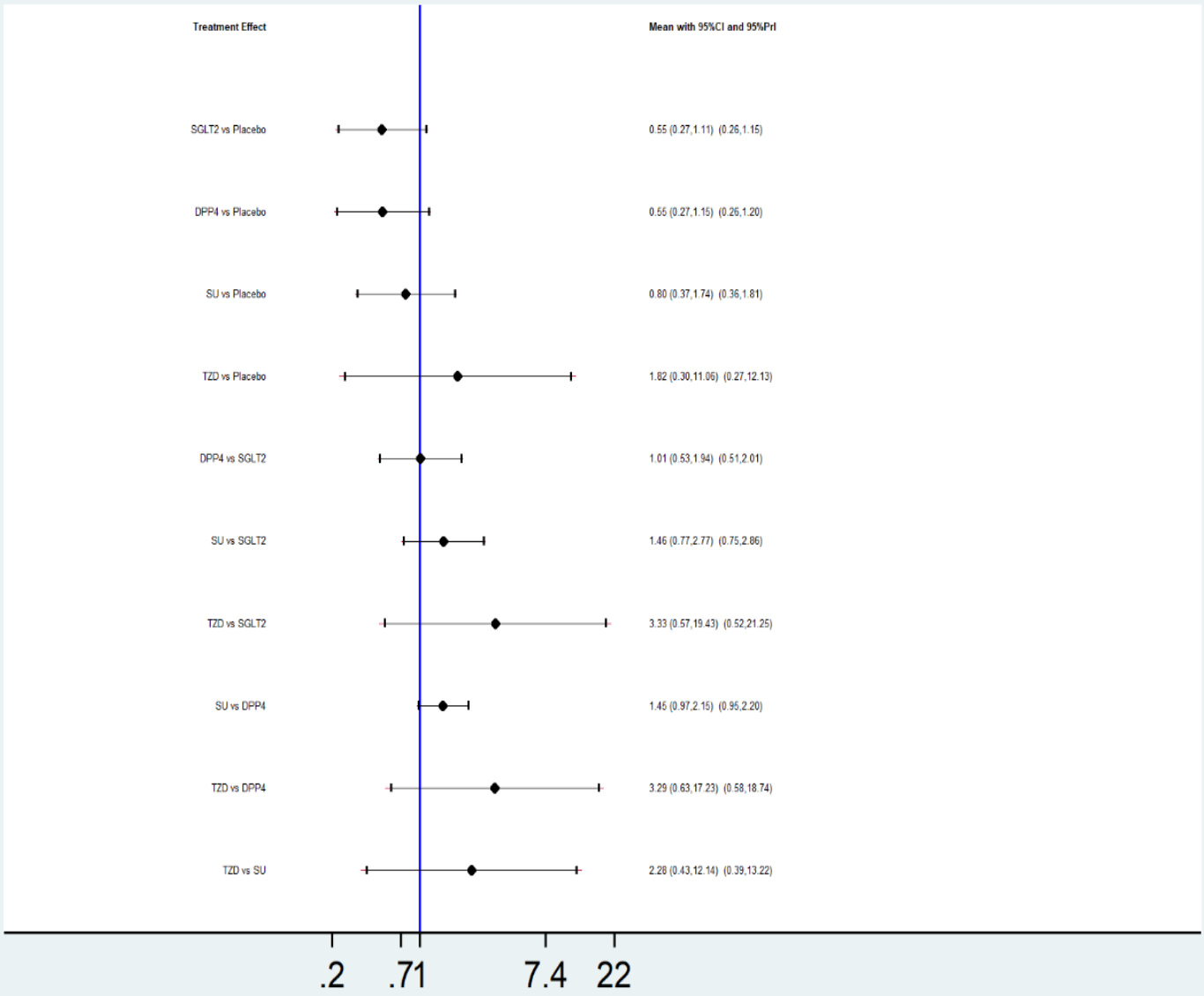

Figure S2.e Major adverse cardiovascular events

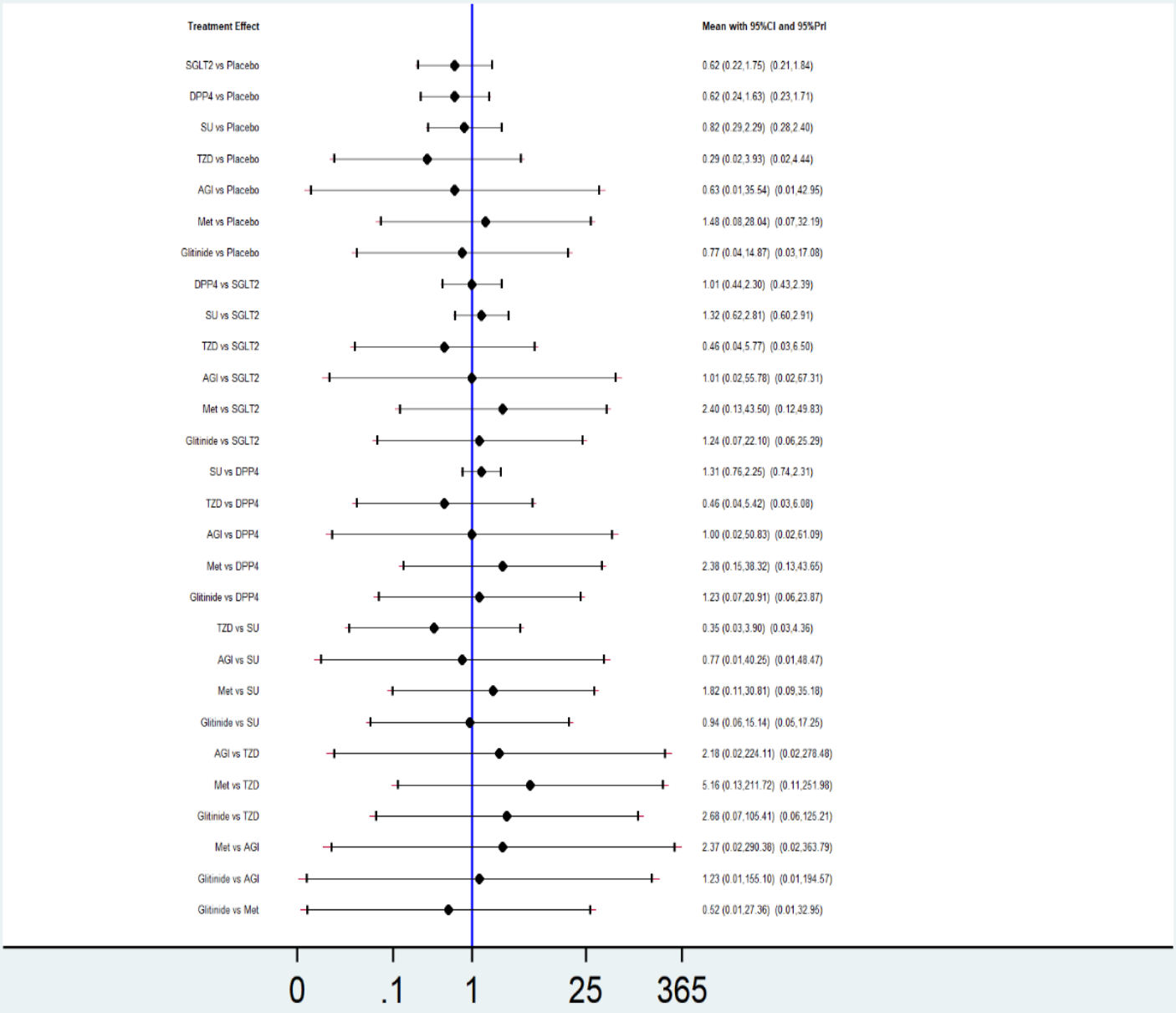

Figure S2.f All-cause mortality

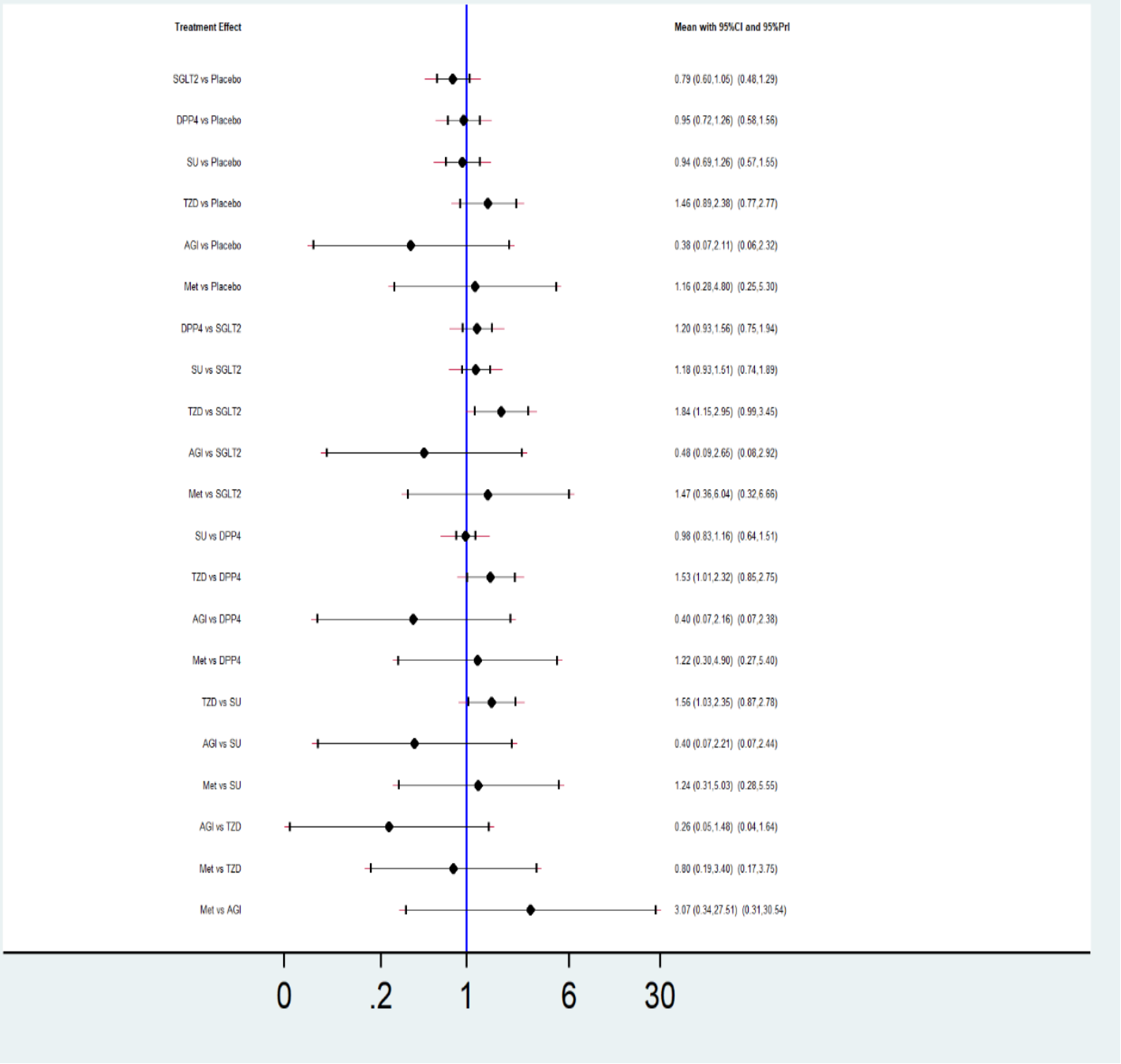

Figure S2.g Serious adverse event

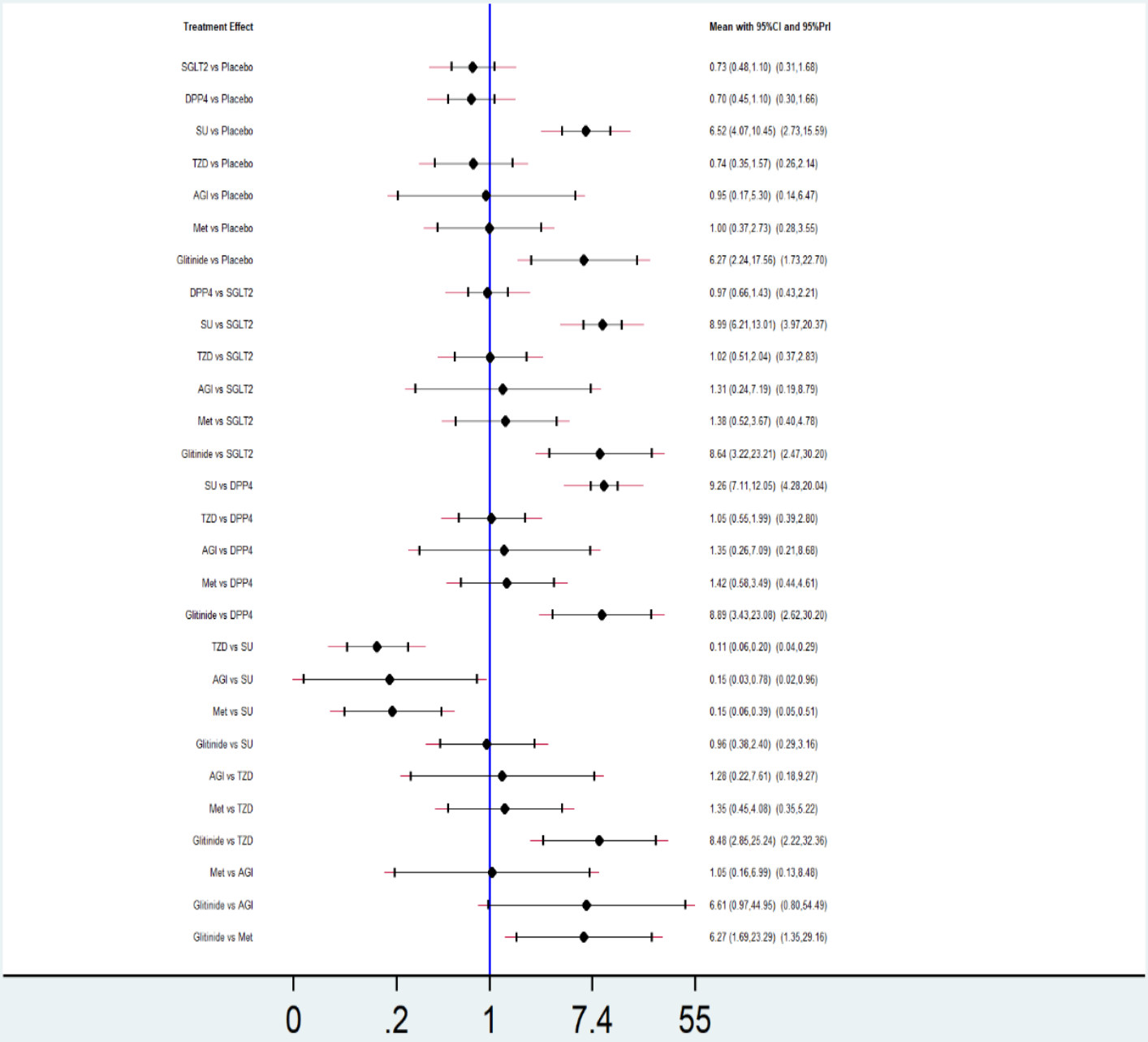

Figure S2.h Hypoglycemia

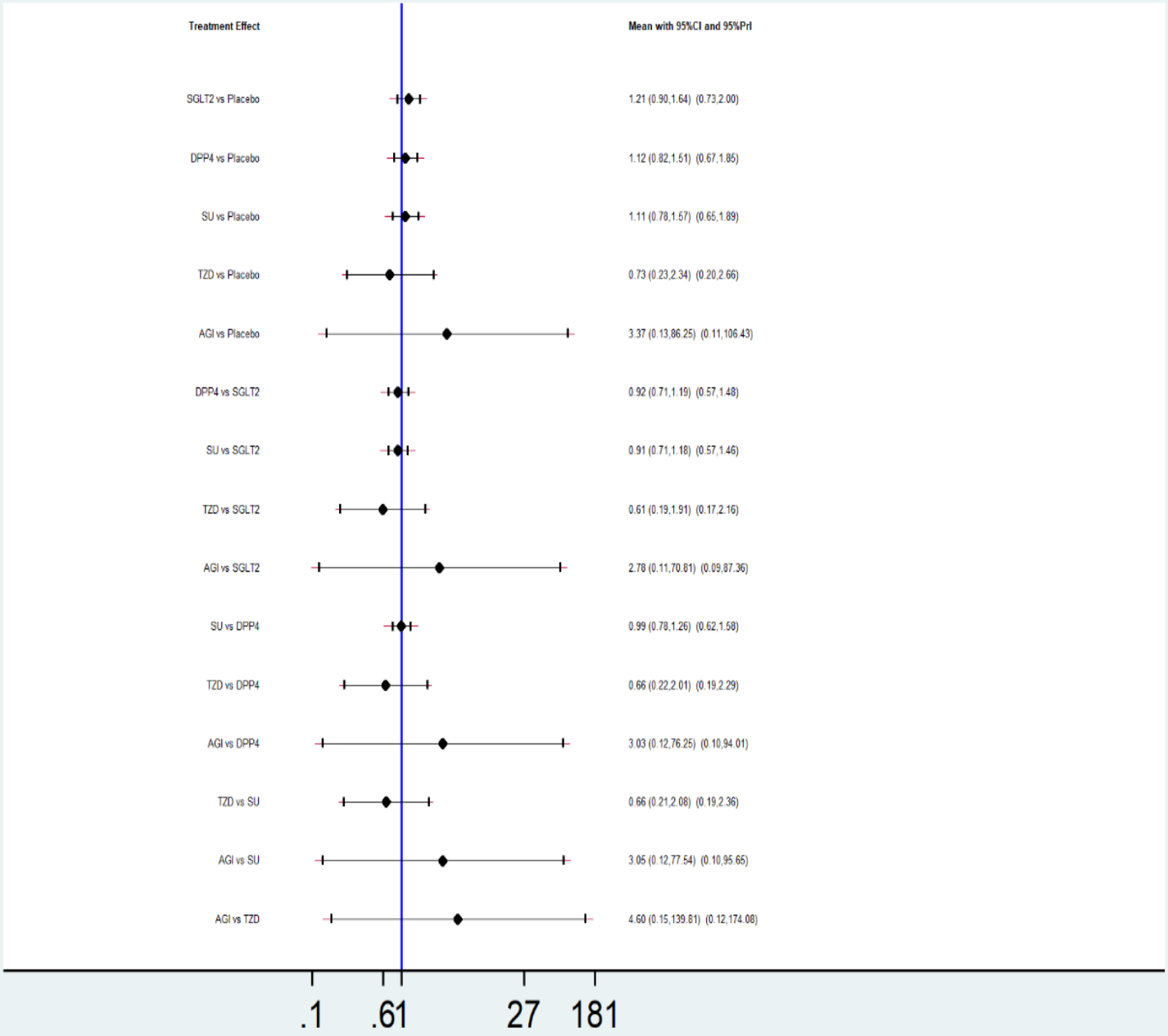

Figure S2.i Urinary tract infection

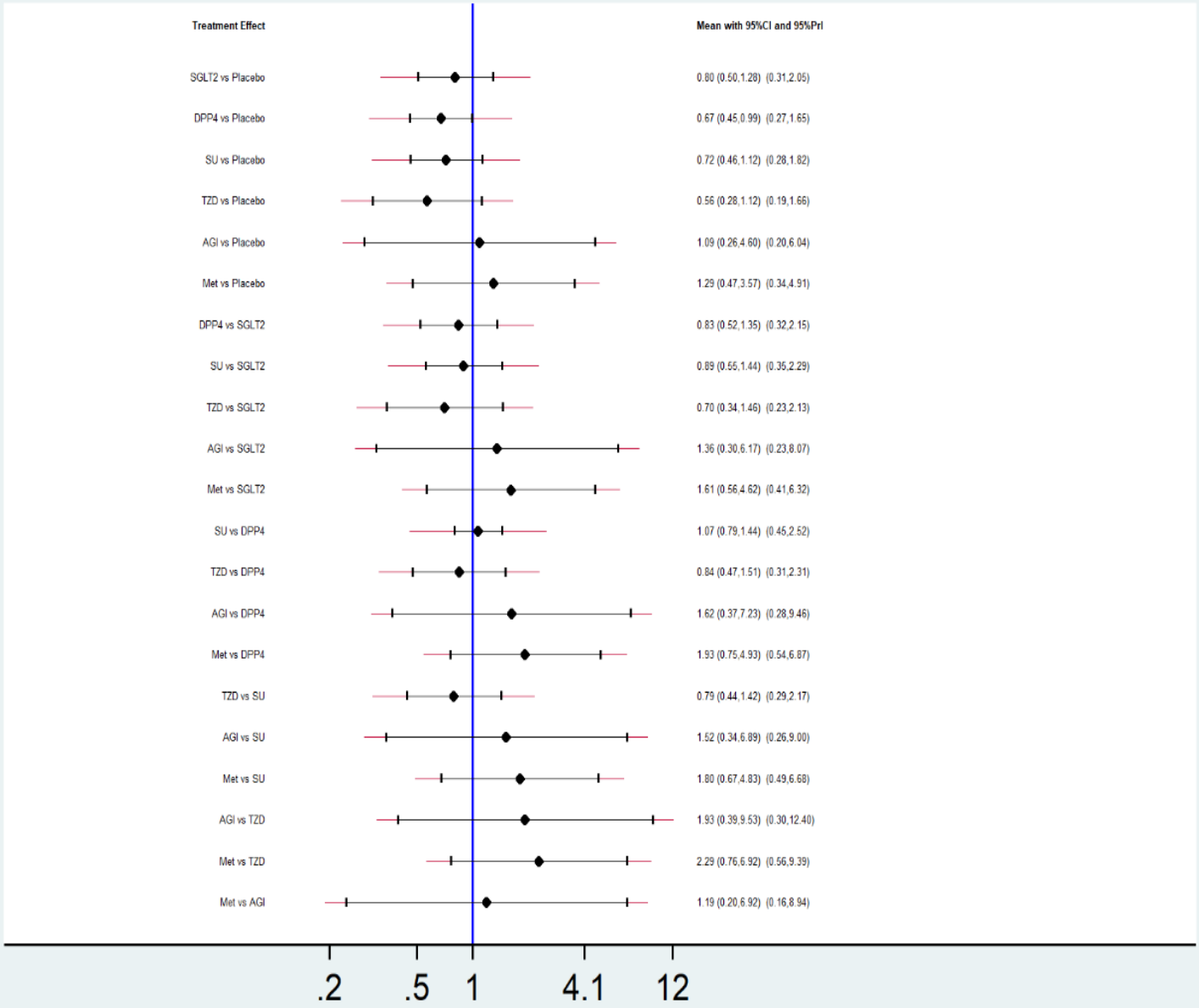

Figure S2.j Diarrhea

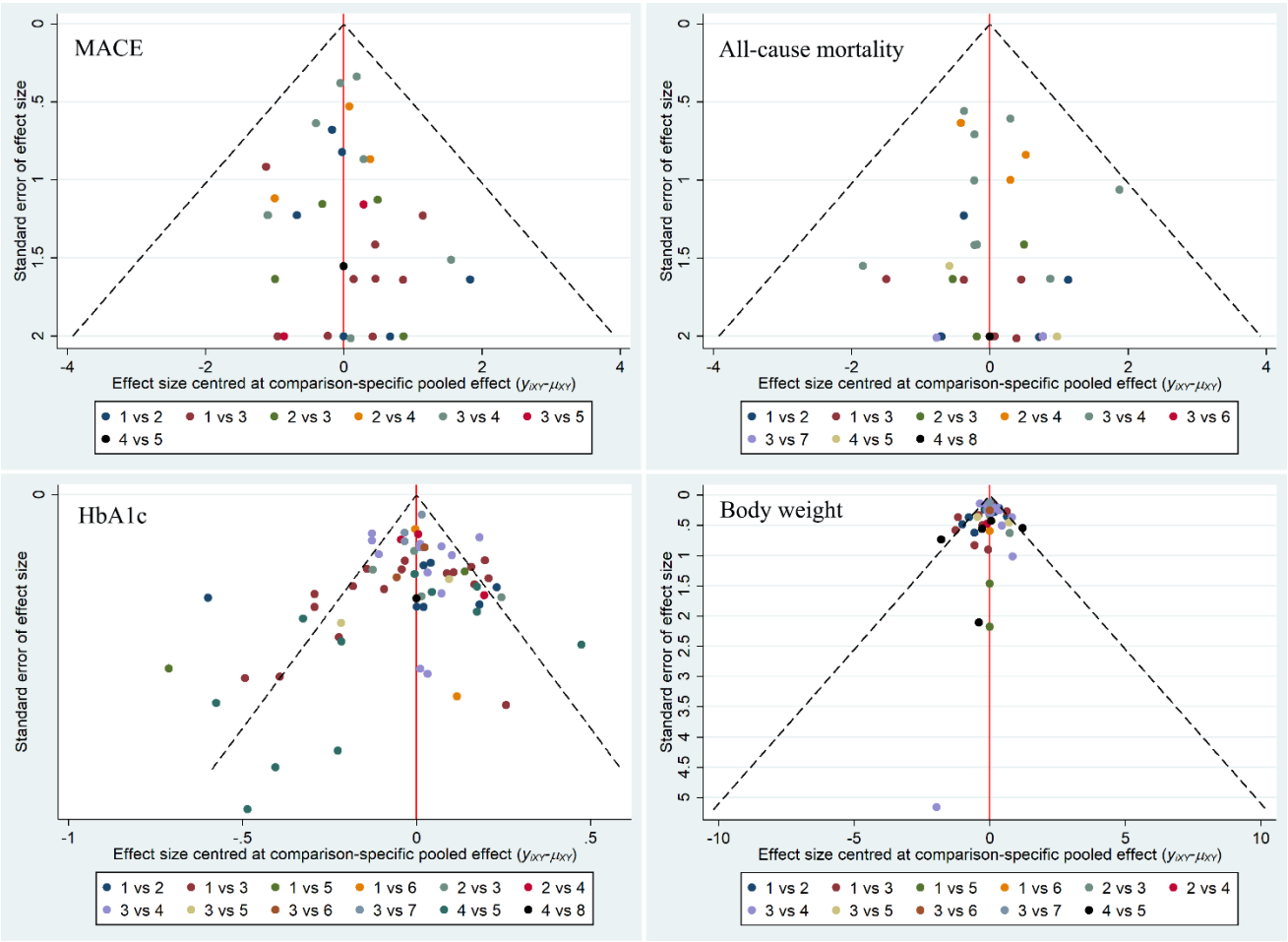

Figure S3. Comparison-adjusted funnel plot for the network meta-analysis on primary outcomes.

Note: 1=Placebo; 2=SGLT-2 inhibitor; 3=DPP-4 inhibitor; 4= Sulfonylurea; 5= Thiazolidinedione; 6=alpha-Glucosidase Inhibitor; 7=High dose metformin; 8= Meglitinide

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