Appendix 1: Literature Search Strategy

Type 2 DM — Main Search

2016 Mar 5

OVID Multifile
Database: Embase Classic+Embase <1947 to 2016 March 04>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy	
1	exp Diabetes Mellitus, Type 2/ (266330)
2	Diabetes Mellitus/ (557998)
3	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or slow or stable or type 2 or type II or lipoatrophic) adj3 diabet*).tw,kw. (275289)
4	(MODY or NIDDM or T2DM).tw,kw. (45223)
5	or/1-4 (845937)
6	exp Diabetes Mellitus, Type 2/dt (66593)
7	Drug Combinations/ (114030)
8	Drug Therapy, Combination/ (196166)
9	6 and (7 or 8) (3517)
10	Hypoglycemic Agents/ (81238)
11	(antidiabetic? or anti-diabetic? or antihyperglyc?emic? or anti-hyperglyc?emic? or hypoglyc?emic? or antidiabetes or anti-diabetes).tw,kw. (89934)
12	Dipeptidyl-Peptidase IV Inhibitors/ (5438)
13	((DPP4 or DPP 4 or DPP IV) adj1 inhibitor?).tw,kw. (5838)
14	(dipeptidyl-peptidase IV adj2 inhibitor?).tw,kw. (1193)
15	(dipeptidyl-peptidase 4 adj2 inhibitor?).tw,kw. (2749)
16	gliptin?.tw,kw. (406)
17	(alogliptin or nesina or SYR 322 or SYR322 or HSDB 8203 or incresina or vipidia).tw,kw. (800)
18	JHC049LO86.rn. (139)
19	Linagliptin/ (1411)
20	(linagliptin or BI 1356 or ONDERO or tradjenta or trajenta or trayenta or trazenta).tw,kw. (1182)
21	3X29ZEJ4R2.rn. (192)
22	(saxagliptin or BMS 477118 or BMS477118 or HSDB 8199 or Onglyza or OPC 262).tw,kw. (1331)
23	9GB927LAJW.rn. (202)
24	exp Sitagliptin Phosphate/ (6074)

Search Strategy	
25	(sitagliptin or EC 690-730-1 or Glactiv or HSDB 7516 or januvia or “mk 0431” or mk0431 or mk 431 or ono 5435 or ristaben or sitagliptine or tesabel or tesavel or xelevia).tw,kw. (4518)
26	TS63EW8X6F.rn. (808)
27	Sodium-Glucose Transporter 2/ai (514)
28	(sodium-glucose transporter 2 inhibitor? or sodium-glucose cotransporter 2 inhibitor?).tw,kw. (420)
29	(sodium-glucose transporter 2 inhibitor? or sodium-glucose co-transporter 2 inhibitor?).tw,kw. (392)
30	((SGLT-2 or SGLT2) adj inhibitor?).tw,kw. (1855)
31	(sodium dependent glucose transporter 2 inhibitor? or sodium dependent glucose cotransporter 2 inhibitor?).tw,kw. (23)
32	(sodium dependent glucose transporter 2 inhibitor? or sodium dependent glucose co-transporter 2 inhibitor?).tw,kw. (14)
33	gliflozin?.tw,kw. (44)
34	Canagliflozin/ (916)
35	(canagliflozin or Invokana or JNJ 24831754* or JNJ 28431754 or TA 7284 or Prominad).tw,kw. (859)
36	0SAC974Z85.rn. (141)
37	(dapagliflozin or BMS 512148 or BMS512148 or edistride or forxiga or farxiga).tw,kw. (1079)
38	1ULL0QJ8UC.rn. (0)
39	(empagliflozin or BI 10773 or BI10773 or Jardiance).tw,kw. (645)
40	HDC1R2M35U.rn. (108)
41	Sulfonylurea Compounds/ (12899)
42	(sulfonylurea? or sulfonurea? or sulfonyl urea? or sulfonylcarbamide? or sulphonurea? or sulphonylurea?).tw,kw. (21551)
43	Chlorpropamide/ (7986)
44	(adiaben or apo-chlorpropamide or apochlorpropamide or abemide or “arodoc c” or asucrol or ascurol or biabenal or bioglumin or BRN 2218363 or catanil or CCRIS 155 or chlomide or chlormide or chlorodiabina or chloropropamide or chlorpromide or clorpropamide or copamide or chloronase or chlorpromide or clorpropamide or chloropropamide or chlorpropamid or chlorpropamide or chlorpropamidum or clorpropamid or clorpropamida).tw,kw. (3523)
45	(dabinese or deavynfar or diabaril or diabechlor or diabeedol or diabemide or diabenal or diabenese or diabeneza or diabet-pages or diabetoral or diabexan or diabiclor or diabines or diabinese or diabitex or diabitol or diamel ex or dibecon or dynalase or EINECS 202-314-5 or eubetin or glicoben or glisema or glucamide or glycemin or glymese or HSDB 2051 or hypomide or insilange or insogen or insulase).tw,kw. (732)
46	(melormin or meldian or melitase or mellinese or millinese or NCI-C01752 or NSC 44634 or NSC 626720 or neo-toltinon or oradian or P 607 or pamidin or prodiaben or pubetin or stabinol or tesmel or “p chlorobenzolsulphonylglycolic acid nitrile” or para chlorobenzenesulfonylglycolic acid nitrile or

Search Strategy	
	parachlorobenzene sulfonylglycolic acid nitrile or U-3818 or U-9818).tw,kw. (172)
47	WTM2C3IL2X.rn. (1810)
48	Gliclazide/ (5655)
49	(gliclazide or diaglyk or diaikron or diabrezide or diamicron or BRN 1657836 or EINECS 244-260-5 or gen-gliclazide or gliklazid or gliclazida or gliclazidum or glimicron or glyade or glyclazide or glycazide or nordialex or predian or S 1702 or S 852 or SE 1702).tw,kw. (3352)
50	G4PX8C4HKV.rn. (767)
51	(glimepiride or amaryl or amarel or BRN 5365754 or CCRIS 7083 or endial or euglim or glemax or glimepirid or glimepirida or glimepiridum or glimerid or glorion or HOE 490 or HOE490 or solosa or “s 80 8490”).tw,kw. (3176)
52	6KY687524K.rn. (658)
53	Glyburide/ (27473)
54	(adiab or amecladin or apo-glibenclamide or azuglucon or bastiverit or benclamin or betanase or betanese 5 or BRN 2230085 or calabren or clamide or clibenclamide or cytagon or dangbinol or daonil or debtan or diabasan or diabeta or dibelet or duraglucon or EINECS 233-570-6 or euclamin or euglucan or euglucon or euglykon).tw,kw. (1292)
55	(GBN 5 or gen-glybe or gewaglucon or gilemal or glamide or glencamide or gliban or glibeclamid or glibemid or gliben or glibenbeta or glibenclamid or glibenclamida or glibenclamide or glibenclamidum or glibenhexal or glibenil or glibens or glibesyn or glibet or glibetic or glibil or gliboral or glicem or glidiabet or gliformin or glikeyer or glimel or glimide or glimidstada or glisulin or glitisol or glubate or gluben).tw,kw. (17385)
56	(glucobene or glucohexal or glucolon or glucomid or gluconic or glucoremed or glucoven or glukoreduct or glulo or glyamid or glyben or glybencamidum or glybencenamide or glybenclamid or glybenclamide or glybendamine or glybenzyclamide or glybenzcyclamide or glyburide or glycolande or glycomin or glynase or HB 419 or HB 420 or hemi-daonil or hexaglucon or humedia or insol or lederglib or libanil or lisaglucon or locose or lodulce).tw,kw. (6708)
57	(maninil or manoglucon or med-glionil or melix or micronase or miglucan or nadib or neogluconin or norglicem 5 or normoglucon or orabetic or pira or praeciglucon or prodiabet or renabetic or RP-1127 or semi-daonil or semi-euglucon or semi-gliben-puren n or sugril or suraben or tiabet or U 26452 or U-26 452 or UR 606 or yuglucon or xeltic).tw,kw. (680)
58	SX6K58TVWC.rn. (5768)
59	Tolbutamide/ (18758)
60	(abemin or aglicem or aglicid or aglycid or apo-tolbutamide or arcosal or arkozal or artosin or artosina or artozin or beglucin or BRN 1984428 or butamid or butamide or butamidum or CCRIS 592 or “D 860” or diabecid or diaben or diabenyl or diabeton or diabesan or diasulfon or diabetamid or diabetol or diabuton or diatol or dirastan or diasulin or diaval or dolipol or drabet).tw,kw. (630)
61	(EINECS 200-594-3 or fresan or glicemin or glicotron or glycotron or guabeta or glyconon or HLS 831 or HSDB 3393 or hypoglycone or ipoglicone or ipoglucos or mermol or metil glucosulfina or

Search Strategy	
	mobenol or NCI-C01763 or NSC 23813 or neo antiglycemikos or neo diabetal or neo norboral or neobellin or neoinsoral).tw,kw. (29)
62	(orabet or oralin or oresan or orezan or orinade or orinase or orinaz or orsinon or osdiabet or oterben or pramidex or proinsul or rastinon or SK-tolbutamide or tarasina or tobutamine or tol ortab or tolbet or tolbugen or tolbusal or tolbutamid or tolbutamida or tolbutamide or tolbutamidum or tolbutone or tolbutamte or tolbutol or tolbutylharnstoff or tolbutylurea or tolglybutamide or tolsiran or tolubetin or toluran or tolurast or tosula or toluina or tolumid or toluvan or tolylsulfonylbutylurea or “U 2043” or willbutamide).tw,kw. (11849)
63	982XCM1FOI.rn. (5177)
64	Thiazolidinediones/ (20146)
65	(thiazolidinedione* or TZD or TZDs).tw,kw. (12397)
66	(pioglitazone* or actos or AD 4833 or piomed or U 72107A or U72 107A or cereluc or glidipion or glita or glitase or glustin or paglitaz or pioglit or sepioglin or zactos).tw,kw. (11333)
67	X4OV71U42S.rn. (2980)
68	(rosiglitazone* or avandia or BRL 49653-C or BRL 49653 or nyracta or rezult or rossini or venvia).tw,kw. (12978)
69	05V02F2KDG.rn. (3774)
70	exp Glucagon-Like Peptide 1/aa (980)
71	((glucagon-like peptide-1 or GLP-1 or GLP1 or GLP-1R or GLP1R) adj2 analog*).tw,kw. (2996)
72	Glucagon-Like Peptide-1 Receptor/ (3946)
73	((glucagon-like peptide-1 or GLP-1 or GLP1 or GLP-1R or GLP1R) adj2 (receptor? or protein?)).tw,kw. (7207)
74	Receptors, Glucagon/ag (716)
75	((glucagon-like peptide-1 or GLP-1 or GLP1 or GLP-1R or GLP1R) adj2 agonist*).tw,kw. (5289)
76	incretin mimetic*.tw,kw. (754)
77	(dulaglutide or LY-2189265 or LY2189265 or trulicity).tw,kw. (315)
78	WTT295HSY5.rn. (34)
79	(AC 2993 or AC 2993A or AC-2993 or AC002993 or AC2993 or AC2993A or baietta or byetta or bydureon or DA 3091 or exenatide or exendin 4 or HSDB 7789 or LY 2148568 or LY2148568 or PT302 or Ex4 peptide or ITCA 650).tw,kw. (7065)
80	9P1872D4OL.rn. (1654)
81	Liraglutide/ (4905)
82	(liraglutida or liraglutide or liraglutidum or HSDB 8205 or NN-2211 or NN2211 or NNC 90-1170 or saxenda or victoza).tw,kw. (3920)
83	839I73S42A.rn. (697)
84	Insulin, Long-Acting/ (4078)
85	((long-acting or LA or semilente or semi-lente or slow* acting or intermediate-acting) adj (insulin* or

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	analog*)).tw,kw. (3627)
86	Insulin Detemir/ (3156)
87	(detemir or determir or levemir or NN-304 or NN304).tw,kw. (2636)
88	4FT78T86XV.rn. (432)
89	Insulin Glargine/ (8182)
90	(abasaglar or abasria or basaglar or glargine or HOE-901 or HOE901 or lantus or ly 2963016 or ly2963016 or optisulin or toujeo).tw,kw. (6280)
91	2ZM8CX04RZ.rn. (1259)
92	exp Insulin, Short-Acting/ (1999)
93	((fast-acting or quick-acting or short-acting or rapid* acting) adj (insulin? or analog*)).tw,kw. (3052)
94	(insulin aspart* or (B28 adj1 insulin?) or (B28 adj1 insulin?) or (B28asp* adj1 insulin?) or NovoLog* or NovoMix* or Novo Mix* or NovoRapid*).tw,kw. (3086)
95	D933668QVX.rn. (528)
96	(lispro or lyspro or humalog or liprolog).tw,kw. (3712)
97	(apidra or glulisine).tw,kw. (1017)
98	7XIY785AZD.rn. (132)
99	exp Insulin, Isophane/ (7864)
100	(actraphan? or berlinsulin or “humulin i” or “humulin n” or insulatard or (insulin? adj3 monotard) or isophane or (insulin? adj2 NPH) or (insulin? adj2 protamine) or isofane or isophan or isophane or isophone or mixtard or novolin or nph iletin or nph umuline or orgasuline or protaphan or protaphane or protophane or prozinc or (zinc adj2 insulin?) or (zinc adj1 protamine)).tw,kw. (6799)
101	2ZM8CX04RZ.rn. (1259)
102	exp Insulin/ (461486)
103	(insulin? adj1 regular).tw,kw. (2886)
104	(insulin? adj1 human).tw,kw. (12859)
105	(nph insulin? or humulin or novolin).tw,kw. (4347)
106	((insulin? adj1 (pork or porcine or pig or pigs)) or hypurin).tw,kw. (2880)
107	(alogliptin adj3 metformin).tw,kw. (27)
108	(metformin adj2 nesina).tw,kw. (0)
109	(kazano or nesimet or nesina or nesinamet or vipdomet).tw,kw. (80)
110	(linagliptin adj2 metformin).tw,kw. (72)
111	(jentadueto or trajenta duo or trajentamet or trayebta duo or trayenta duo).tw,kw. (28)
112	(saxagliptin adj3 metformin).tw,kw. (135)
113	(komboglyze or kombiglyze or comboglyze or duoglyze).tw,kw. (35)
114	“Sitagliptin Phosphate, Metformin Hydrochloride Drug Combination”/ (5)
115	(sitagliptin adj3 metformin).tw,kw. (459)

Search Strategy	
116	(janumet or efficib or gliptamet or Januet or ristfor or velmetia or mk 0431a).tw,kw. (169)
117	(metformin adj3 dapagliflozin).tw,kw. (70)
118	(ebymect or xigduo).tw,kw. (20)
119	(empagliflozin adj3 metformin).tw,kw. (22)
120	(jardiamet or jardiancemet or synjardy).tw,kw. (3)
121	(metformin adj3 rosiglitazone).tw,kw. (817)
122	(avandamet or interac).tw,kw. (308)
123	Glycoside Hydrolase Inhibitors/ (2932)
124	((alpha-amylase or alpha-glucosidase or glucosidase or glycoside) adj2 inhibitor?).tw,kw. (6829)
125	Acarbose/ (7337)
126	(acarbose or ag 5421 or ag5421 or alpha ghi or bay g 5421 or bay g5421 or glibose or glicobase or glucobay or gluconase or glucor or glumida or prandase or precise or rebose).tw,kw. (307456)
127	T58MSI464G.rn. (1139)
128	(hb 699 or hb699 or meglitinide?).tw,kw. (642)
129	(actulin or ag ee 388 or ag ee388 or ag ee 623 or ag ee623 or enyglid or gluconorm or novonorm or prandin or rapilan or repaglinide or sestrine).tw,kw. (1882)
130	(a 4166 or a4166 or ay 4166 or ay4166 or djn 608 or djn608 or fasticor or glinate or nateglinide or sdz djn 608 or sdz djn608 or senaglinide or starlix or starsis or trazec or “ym 026”).tw,kw. (1413)
131	(bay 1099 or bay m 1099 or bay m1099 or bay1099 or diastabol or glyset or miglitol or plumarol).tw,kw. (855)
132	0V5436JAQW.rn. (194)
133	(ao 128 or ao128 or basen or “en 116 077” or en 116077 or “en116 077” or en116077 or glustat or voglibose).tw,kw. (713)
134	or/9-133 (943368)
135	5 and 134 (232691)
136	(controlled clinical trial or randomized controlled trial).pt. (493183)
137	clinical trials as topic.sh. (175057)
138	(randomi#ed or randomly or RCT$1 or placebo*).tw. (1662366)
139	((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw. (328932)
140	trial.ti. (349371)
141	or/136-140 (2094448)
142	135 and 141 (27582)
143	exp Animals/ not (exp Animals/ and Humans/) (13903716)
144	142 not 143 (18521)
145	Adolescent/ not (exp Adult/ and Adolescent/) (1002401)
146	exp Child/ not (exp Adult/ and exp Child/) (2892676)

Search Strategy	
147	exp Infant/ not (exp Adult/ and exp Infant/) (1546227)
148	or/145-147 (3676743)
149	144 not 148 (18221)
150	(comment or editorial or interview or news or newspaper article).pt. (1628874)
151	(letter not (letter and randomized controlled trial)).pt. (1826480)
152	149 not (150 or 151) (17868)
153	152 use prmz (9578)
154	diabetes mellitus/ (557998)
155	non insulin dependent diabetes mellitus/ (266146)
156	lipoatrophic diabetes mellitus/ (434)
157	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or slow or stable or type 2 or type II or lipoatrophic) adj3 diabet*).tw,kw. (275289)
158	(MODY or NIDDM or T2DM).tw,kw. (45223)
159	or/154-158 (845997)
160	non insulin dependent diabetes mellitus/dt (66555)
161	drug combination/ (55587)
162	160 and 161 (550)
163	antidiabetic agent/ (88027)
164	oral antidiabetic agent/ (15334)
165	(antidiabetic? or anti-diabetic? or antihyperglyc?emic? or anti-hyperglyc?emic? or hypoglyc?emic? or antidiabetes or anti-diabetes).tw,kw. (89934)
166	dipeptidyl peptidase IV inhibitor/ (7382)
167	((DPP4 or DPP 4 or DPP IV) adj1 inhibitor?).tw,kw. (5838)
168	(dipeptidyl-peptidase IV adj2 inhibitor?).tw,kw. (1193)
169	(dipeptidyl-peptidase 4 adj2 inhibitor?).tw,kw. (2749)
170	gliptin?.tw,kw. (406)
171	alogliptin/ (980)
172	(alogliptin or nesina or SYR 322 or SYR322 or HSDB 8203 or incresina or vipidia).tw,kw. (800)
173	850649-62-6.rn. (464)
174	850649-61-5.rn. (838)
175	linagliptin/ (1411)
176	(linagliptin or BI 1356 or ONDERO or tradjenta or trajenta or trayenta or trazenta).tw,kw. (1182)
177	668270-12-0.rn. (938)
178	saxagliptin/ (1825)
179	(saxagliptin or BMS 477118 or BMS477118 or HSDB 8199 or Onglyza or OPC 262).tw,kw. (1331)
180	361442-04-8.rn. (1522)

Search Strategy	
181	945667-22-1.rn. (1455)
182	sitagliptin/ (6073)
183	(sitagliptin or EC 690-730-1 or Glactiv or HSDB 7516 or januvia or “mk 0431” or mk0431 or mk 431 or ono 5435 or ristaben or sitagliptine or tesabel or tesavel or xelevia).tw,kw. (4518)
184	486460-32-6.rn. (4204)
185	sodium glucose cotransporter 2 inhibitor/ (702)
186	(sodium-glucose transporter 2 inhibitor? or sodium-glucose cotransporter 2 inhibitor?).tw,kw. (420)
187	(sodium-glucose transporter 2 inhibitor? or sodium-glucose co-transporter 2 inhibitor?).tw,kw. (392)
188	((SGLT-2 or SGLT2) adj inhibitor?).tw,kw. (1855)
189	(sodium dependent glucose transporter 2 inhibitor? or sodium dependent glucose cotransporter 2 inhibitor?).tw,kw. (23)
190	(sodium dependent glucose transporter 2 inhibitor? or sodium dependent glucose co-transporter 2 inhibitor?).tw,kw. (14)
191	gliflozin?.tw,kw. (44)
192	canagliflozin/ (916)
193	(canagliflozin or invokana or JNJ 24831754* or JNJ 28431754 or TA 7284 or prominad).tw,kw. (859)
194	842133-18-0.rn. (540)
195	dapagliflozin/ (1020)
196	(dapagliflozin or BMS 512148 or BMS512148 or edistride or forxiga or farxiga).tw,kw. (1079)
197	461432-26-8.rn. (705)
198	empagliflozin/ (556)
199	(empagliflozin or BI 10773 or BI10773 or jardiance).tw,kw. (645)
200	864070-44-0.rn. (386)
201	sulfonylurea derivative/ (8351)
202	(sulfonylurea? or sulfonurea? or sulfonyl urea? or sulfonylcarbamide? or sulphonurea? or sulphonylurea?).tw,kw. (21551)
203	chlorpropamide/ (7986)
204	(adiaben or apo-chlorpropamide or apochlorpropamide or abemide or “arodoc c” or asucrol or ascurol or biabenal or bioglumin or BRN 2218363 or catanil or CCRIS 155 or chlomide or chlormide or chlorodiabina or chloropropamide or chlorpromide or clorpropamide or copamide or chloronase or chlorpromide or clorpropamide or chloropropamide or chlorpropamid or chlorpropamide or chlorpropamidum or clorpropamid or clorpropamida).tw,kw. (3523)
205	(dabinese or deavynfar or diabaril or diabechlor or diabeedol or diabemide or diabenal or diabenese or diabeneza or diabet-pages or diabetoral or diabexan or diabiclor or diabines or diabinese or diabitex or diabitol or diamel ex or dibecon or dynalase or EINECS 202-314-5 or eubetin or glicoben or glisema or glucamide or glycemin or glymese or HSDB 2051 or hypomide or insilange or insogen or insulase).tw,kw. (732)

Search Strategy	
206	(melormin or meldian or melitase or mellinese or millinese or NCI-C01752 or NSC 44634 or NSC 626720 or neo-toltinon or oradian or P 607 or pamidin or prodiaben or pubetin or stabinol or tesmel or "p chlorobenzolsulphonylglycolic acid nitrile" or para chlorobenzenesulfonylglycolic acid nitrile or parachlorobenzene sulfonylglycolic acid nitrile or U-3818 or U-9818).tw,kw. (172)
207	94-20-2.rn. (5862)
208	gliclazide/ (5655)
209	(gliclazide or diaglyk or diaikron or diabrezide or diamicron or BRN 1657836 or EINECS 244-260-5 or gen-gliclazide or gliklazid or gliclazida or gliclazidum or glimicron or glyade or glyclazide or glycazide or nordialex or predian or S 1702 or S 852 or SE 1702).tw,kw. (3352)
210	21187-98-4.rn. (4621)
211	glimepiride/ (5332)
212	(glimepiride or amaryl or amarel or BRN 5365754 or CCRIS 7083 or endial or euglim or glemax or glimepirid or glimepirida or glimepiridum or glimerid or glorion or HOE 490 or HOE490 or solosa or "s 80 8490").tw,kw. (3176)
213	93479-97-1.rn. (4884)
214	glibenclamide/ (27473)
215	(adiab or amecladin or apo-glibenclamide or azuglucon or bastiverit or benclamin or betanase or betanese 5 or BRN 2230085 or calabren or clamide or clibenclamide or cytagon or dangbinol or daonil or debtan or diabasan or diabeta or dibelet or duraglucon or EINECS 233-570-6 or euclamin or euglucan or euglucon or euglykon).tw,kw. (1292)
216	(GBN 5 or gen-glybe or gewaglucon or gilemal or glamide or glencamide or gliban or glibeclamid or glibemid or gliben or glibenbeta or glibenclamid or glibenclamida or glibenclamide or glibenclamidum or glibenhexal or glibenil or glibens or glibesyn or glibet or glibetic or glibil or gliboral or glicem or glidiabet or gliformin or glikeyer or glimel or glimide or glimidstada or glisulin or glitisol or glubate or gluben).tw,kw. (17385)
217	(glucobene or glucohexal or glucolon or glucomid or gluconic or glucoremed or glucoven or glukoreduct or glulo or glyamid or glyben or glybencamidum or glybencenamide or glybenclamid or glybenclamide or glybendamine or glybenzyclamide or glybenzcyclamide or glyburide or glycolande or glycomin or glynase or HB 419 or HB 420 or hemi-daonil or hexaglucon or humedia or insol or lederglib or libanil or lisaglucon or locose or lodulce).tw,kw. (6708)
218	(maninil or manoglucon or med-glionil or melix or micronase or miglucan or nadib or neogluconin or norglicem 5 or normoglucon or orabetic or pira or praeciglucon or prodiabet or renabetic or RP-1127 or semi-daonil or semi-euglucon or semi-gliben-puren n or sugril or suraben or tiabet or U 26452 or U-26 452 or UR 606 or yuglucon or xeltic).tw,kw. (680)
219	10238-21-8.rn. (20454)
220	tolbutamide/ (18758)
221	(abemin or aglicem or aglicid or aglycid or apo-tolbutamide or arcosal or arkozal or artosin or artosina or artozin or beglucin or BRN 1984428 or butamid or butamide or butamidum or CCRIS

Search Strategy	
	592 or "D 860" or diabecid or diaben or diabenyl or diabeton or diabesan or diasulfon or diabetamid or diabetol or diabuton or diatol or dirastan or diasulin or diaval or dolipol or drabet).tw,kw. (630)
222	(EINECS 200-594-3 or fresan or glicemin or glicotron or glycotron or guabeta or glyconon or HLS 831 or HSDB 3393 or hypoglycone or ipoglicone or ipoglucos or mermol or metil glucosulfina or mobenol or NCI-C01763 or NSC 23813 or neo antiglycemikos or neo diabetal or neo norboral or neobellin or neoinsoral).tw,kw. (29)
223	(orabet or oralin or oresan or orezan or orinade or orinase or orinaz or orsinon or osdiabet or oterben or pramidex or proinsul or rastinon or SK-tolbutamide or tarasina or tobutamine or tol ortab or tolbet or tolbugen or tolbusal or tolbutamid or tolbutamida or tolbutamide or tolbutamidum or tolbutone or tolbutamte or tolbutol or tolbutylharnstoff or tolbutylurea or tolglybutamide or tolsiran or tolubetin or toluran or tolurast or tosula or toluina or tolumid or toluvan or tolylsulfonylbutylurea or "U 2043" or willbutamide).tw,kw. (11849)
224	64-77-7.rn. (12174)
225	2,4 thiazolidinedione derivative/ (10823)
226	(thiazolidinedione* or TZD or TZDs).tw,kw. (12397)
227	pioglitazone/ (14830)
228	(pioglitazone* or actos or AD 4833 or piomed or U 72107A or U72 107A or cereluc or glidipion or glita or glitase or glustin or paglitaz or pioglit or sepioglin or zactos).tw,kw. (11333)
229	112529-15-4.rn. (0)
230	rosiglitazone/ (15989)
231	(rosiglitazone* or avandia or BRL 49653-C or BRL 49653 or nyracta or rezult or rossini or venvia).tw,kw. (12978)
232	155141-29-0.rn. (14702)
233	glucagon like peptide 1 receptor agonist/ (2110)
234	((glucagon-like peptide-1 or GLP-1 or GLP1 or GLP-1R or GLP1R) adj2 analog*).tw,kw. (2996)
235	((glucagon-like peptide-1 or GLP-1 or GLP1 or GLP-1R or GLP1R) adj2 (receptor? or protein?)).tw,kw. (7207)
236	((glucagon-like peptide-1 or GLP-1 or GLP1 or GLP-1R or GLP1R) adj2 agonist*).tw,kw. (5289)
237	incretin mimetic*.tw,kw. (754)
238	dulaglutide/ (307)
239	(dulaglutide or LY-2189265 or LY2189265 or trulicity).tw,kw. (315)
240	923950-08-7.rn. (211)
241	exendin 4/ (7217)
242	(AC 2993 or AC 2993A or AC-2993 or AC002993 or AC2993 or AC2993A or baietta or byetta or bydureon or DA 3091 or exenatide or exendin 4 or HSDB 7789 or LY 2148568 or LY2148568 or PT302 or Ex4 peptide or ITCA 650).tw,kw. (7065)
243	141758-74-9.rn. (5627)

Search Strategy	
244	liraglutide/ (4905)
245	(liraglutida or liraglutide or liraglutidum or HSDB 8205 or NN-2211 or NN2211 or NNC 90-1170 or saxenda or victoza).tw,kw. (3920)
246	204656-20-2.rn. (3097)
247	long acting insulin/ (4078)
248	((long-acting or LA or semilente or semi-lente or slow* acting or intermediate-acting) adj (insulin* or analog*)).tw,kw. (3627)
249	insulin detemir/ (3156)
250	(detemir or determir or levemir or NN-304 or NN304).tw,kw. (2636)
251	169148-63-4.rn. (2341)
252	insulin glargine/ (8182)
253	(abasaglar or abasria or basaglar or glargine or HOE-901 or HOE901 or lantus or ly 2963016 or ly2963016 or optisulin or toujeo).tw,kw. (6280)
254	160337-95-1.rn. (5715)
255	short acting insulin/ (820)
256	((fast-acting or quick-acting or short-acting or rapid* acting) adj (insulin? or analog*)).tw,kw. (3052)
257	insulin aspart/ (4398)
258	(insulin aspart* or (B28 adj1 insulin?) or (B28 adj1 insulin?) or (B28asp* adj1 insulin?) or NovoLog* or NovoMix* or Novo Mix* or NovoRapid*).tw,kw. (3086)
259	116094-23-6.rn. (3429)
260	insulin lispro/ (5176)
261	(lispro or lyspro or humalog or liprolog or ly 275585 or ly275585).tw,kw. (3714)
262	133107-64-9.rn. (4016)
263	isophane insulin/ (7863)
264	(actraphan? or berlinsulin or “humulin i” or “humulin n” or insulatard or (insulin? adj3 monotard) or isophane or (insulin? adj2 NPH) or (insulin? adj2 protamine) or isofane or isophan or isophane or isophone or mixtard or novolin or nph iletin or nph umuline or orgasuline or protaphan or protaphane or protophane or prozinc or (zinc adj2 insulin?) or (zinc adj1 protamine)).tw,kw. (6799)
265	9004-17-5.rn. (6246)
266	(insulin? adj1 regular).tw,kw. (2886)
267	human insulin/ (4542)
268	(insulin? adj1 human).tw,kw. (12859)
269	(h tronin or humulin or nazlin).tw,kw. (1813)
270	pig insulin/ (1396)
271	((insulin? adj1 (pork or porcine or pig or pigs)) or hypurin).tw,kw. (2880)
272	alogliptin plus metformin/ (25)

Search Strategy	
273	(alogliptin adj3 metformin).tw,kw. (27)
274	(metformin adj2 nesina).tw,kw. (0)
275	(kazano or nesimet or nesina or nesinamet or vipdomet).tw,kw. (80)
276	linagliptin plus metformin/ (41)
277	(linagliptin adj2 metformin).tw,kw. (72)
278	(jentadueto or trajenta duo or trajentamet or trayebta duo or trayenta duo).tw,kw. (28)
279	metformin plus saxagliptin/ (71)
280	(saxagliptin adj3 metformin).tw,kw. (135)
281	(komboglyze or kombiglyze or comboglyze or duoglyze).tw,kw. (35)
282	metformin plus sitagliptin/ (271)
283	(sitagliptin adj3 metformin).tw,kw. (459)
284	(janumet or efficib or gliptamet or Januet or ristfor or velmetia or mk 0431a).tw,kw. (169)
285	dapagliflozin plus metformin/ (19)
286	(metformin adj3 dapagliflozin).tw,kw. (70)
287	(ebymect or Xigduo).tw,kw. (20)
288	empagliflozin plus metformin/ (3)
289	(empagliflozin adj3 metformin).tw,kw. (22)
290	(jardiamet or jardiancemet or synjardy).tw,kw. (3)
291	metformin plus rosiglitazone/ (427)
292	(metformin adj3 rosiglitazone).tw,kw. (817)
293	(avandamet or interac).tw,kw. (308)
294	622402-70-4.rn. (0)
295	glycosidase inhibitor/ (1164)
296	((alpha-amylase or alpha-glucosidase or glucosidase or glycoside) adj2 inhibitor?).tw,kw. (6829)
297	acarbose/ (7337)
298	(acarbose or ag 5421 or ag5421 or alpha ghi or bay g 5421 or bay g5421 or glibose or glicobase or glucobay or gluconase or glucor or glumida or prandase or precise or rebose).tw,kw. (307456)
299	56180-94-0.rn. (5929)
300	meglitinide/ (1388)
301	(hb 699 or hb699 or meglitinide?).tw,kw. (642)
302	repaglinide/ (3158)
303	(actulin or ag ee 388 or ag ee388 or ag ee 623 or ag ee623 or enyglid or gluconorm or novonorm or prandin or rapilan or repaglinide or sestrine).tw,kw. (1882)
304	135062-02-1.rn. (3031)
305	nateglinide/ (2352)
306	(a 4166 or a4166 or ay 4166 or ay4166 or djn 608 or djn608 or fasticor or glinate or nateglinide or

Search Strategy	
	sdz djn 608 or sdz djn608 or senaglinide or starlix or starsis or trazec or "ym 026").tw,kw. (1413)
307	105816-04-4.rn. (2291)
308	miglitol/ (1309)
309	(bay 1099 or bay m 1099 or bay m1099 or bay1099 or diastabol or glyset or miglitol or plumarol).tw,kw. (855)
310	72432-03-2.rn. (1271)
311	voglibose/ (928)
312	(ao 128 or ao128 or basen or "en 116 077" or en 116077 or "en116 077" or en116077 or glustat or voglibose).tw,kw. (713)
313	83480-29-9.rn. (1011)
314	or/162-313 (587197)
315	159 and 314 (138063)
316	randomized controlled trial/ or controlled clinical trial/ (1029931)
317	exp "clinical trial (topic)"/ (183028)
318	(randomi#ed or randomly or RCT$1 or placebo*).tw. (1662366)
319	((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw. (328932)
320	trial.ti. (349371)
321	or/316-320 (2287790)
322	315 and 321 (24744)
323	exp animal experimentation/ or exp models animal/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (42125725)
324	exp human/ or exp human experimentation/ or exp human experiment/ (32720153)
325	323 not 324 (9407230)
326	322 not 325 (23943)
327	exp Juvenile/ not (exp Adult/ and exp Juvenile/) (2103525)
328	326 not 327 (23758)
329	editorial.pt. (896572)
330	letter.pt. not (letter.pt. and randomized controlled trial/) (1822001)
331	328 not (329 or 330) (23398)
332	331 use emczd (16259)
333	153 or 332 (25837)
334	limit 333 to yr = "2014-2016" (5544)
335	remove duplicates from 334 (4459)
336	limit 333 to yr = "2012-2013" (4826)
337	remove duplicates from 336 (3926)
338	limit 333 to yr = "2009-2011" (5440)

Search Strategy
339 remove duplicates from 338 (4300)
340 limit 333 to yr = "2002-2008" (5814)
341 remove duplicates from 340 (4233)
342 limit 333 to yr = "1800-2001" (4211)
343 remove duplicates from 342 (3246)
344 335 or 337 or 339 or 341 or 343 (20164) [TOTAL UNIQUE RECORDS]
345 344 use prmz (9490) [MEDLINE UNIQUE RECORDS]
346 344 use emczd (10674) [EMBASE UNIQUE RECORDS]

Cochrane Library

ID	Search	Hits
#1	[mh "Diabetes Mellitus, Type 2"]	10494
#2	[mh ^"Diabetes Mellitus"]	2731
#3	((adult or "ketosis-resistant" or matur* or late or ("non-insulin" next depend*) or (noninsulin next depend*) or slow or stable or "type 2" or "type II" or lipoatrophic) near/3 diabet*):ti,ab,kw	19979
#4	(MODY or NIDDM or T2DM):ti,ab,kw	2925
#5	(or #1-#4)	22212
#6	[mh "Diabetes Mellitus, Type 2"/DT]	4793
#7	[mh "Drug Combinations"]	11668
#8	[mh ^"Drug Therapy, Combination"]	27341
#9	#6 and (#7 or #8)	1080
#10	[mh "Hypoglycemic Agents"]	6208
#11	(antidiabetic* or (anti next diabetic*) or antihyperglycemic* or antihyperglycaemic* or (anti next hyperglycemic*) or (anti next hyperglycaemic*) or hypoglycemic* or hypoglycaemic* or antidiabetes or (anti next diabetes)):ti,ab,kw	8917
#12	[mh "Dipeptidyl-Peptidase IV Inhibitors"]	387
#13	((DPP4 or "DPP 4" or "DPP IV") near/1 inhibitor*):ti,ab,kw	379
#14	("dipeptidyl-peptidase IV" near/2 inhibitor*):ti,ab,kw	592
#15	("dipeptidyl-peptidase 4" near/2 inhibitor*):ti,ab,kw	281
#16	(gliptin or gliptins):ti,ab,kw	9
#17	(alogliptin or nesina or "SYR 322" or SYR322 or "HSDB 8203" or incresina or vipidia):ti,ab,kw	87
#18	[mh Linagliptin]	52
#19	(linagliptin or "BI 1356" or ONDERO or tradjenta or trajenta or trayenta or trazenta):ti,ab,kw	154
#20	(saxagliptin or "BMS 477118" or BMS477118 or "HSDB 8199" or Onglyza or "OPC 262"):ti,ab,kw	163
#21	[mh "Sitagliptin Phosphate"]	206
#22	(sitagliptin or "EC 690-730-1" or Glactiv or "HSDB 7516" or januvia or "mk 0431" or mk0431 or "mk 431" or "ono 5435" or ristaben or sitagliptine or tesabel or tesavel or xelevia):ti,ab,kw	533
#23	[mh "Sodium-Glucose Transporter 2"/AI]	85
#24	(("sodium-glucose transporter 2" or "sodium-glucose cotransporter 2") next inhibitor*):ti,ab,kw	95
#25	(("sodium-glucose transporter 2" or "sodium-glucose co-transporter 2") next inhibitor*):ti,ab,kw	66
#26	(("SGLT-2" or SGLT2) next inhibitor*):ti,ab,kw	171

ID	Search	Hits
#27	((“sodium dependent glucose transporter 2” or “sodium dependent glucose cotransporter 2”) next inhibitor*):ti,ab,kw	2
#28	((“sodium dependent glucose transporter 2” or “sodium dependent glucose co-transporter 2”) next inhibitor*):ti,ab,kw	1
#29	(gliflozin or gliflozins):ti,ab,kw	1
#30	[mh Canagliflozin]	44
#31	(canagliflozin or Invokana or (JNJ next 24831754*) or “JNJ 28431754” or “TA 7284” or Prominad):ti,ab,kw	115
#32	(dapagliflozin or “BMS 512148” or BMS512148 or edistride or forxiga or farxiga):ti,ab,kw	173
#33	(empagliflozin or “BI 10773” or BI10773 or Jardiance):ti,ab,kw	138
#34	[mh ^”Sulfonylurea Compounds”]	649
#35	(sulfonylurea* or sulfonurea* or (sulfonyl next urea*) or sulfonylcarbamide* or sulphonurea* or sulphonylurea*):ti,ab,kw	1858
#36	[mh Chlorpropamide]	74
#37	(adiaben or “apo-chlorpropamide” or apochlorpropamide or abemide or “arodoc c” or asucrol or ascurol or biabenal or bioglumin or “BRN 2218363” or catanil or “CCRIS 155” or chlomide or chlormide or chlorodiabina or chloropropamide or chlorpromide or clorpropamide or copamide or chloronase or chlorpromide or clorpropamide or chloropropamide or chlorpropamid or chlorpropamide or chlorpropamidum or clorpropamid or clorpropamida):ti,ab,kw	126
#38	(dabinese or deavynfar or diabaril or diabechlor or diabeedol or diabemide or diabenal or diabenese or diabeneza or “diabet-pages” or diabetoral or diabexan or diabiclor or diabines or diabinese or diabitex or diabitol or “diamel ex” or dibecon or dynalase or “EINECS 202-314-5” or eubetin or glicoben or glisema or glucamide or glycemin or glymese or “HSDB 2051” or hypomide or insilange or insogen or insulase):ti,ab,kw	3
#39	(melormin or meldian or melitase or mellinese or millinese or “NCI-C01752” or “NSC 44634” or “NSC 626720” or “neo-toltinon” or oradian or “P 607” or pamidin or prodiaben or pubetin or stabinol or tesmel or “p chlorobenzolsulphonylglycolic acid nitrile” or “para chlorobenzenesulfonylglycolic acid nitrile” or “parachlorobenzene sulfonylglycolic acid nitrile” or “U-3818” or “U-9818”):ti,ab,kw	7
#40	[mh Gliclazide]	154
#41	(gliclazide or diaglyk or diaikron or diabrezide or diamicron or “BRN 1657836” or “EINECS 244-260-5” or “gen-gliclazide” or gliklazid or gliclazida or gliclazidum or glimicron or glyade or glyclazide or glycazide or nordialex or predian or “S 1702” or “S 852” or “SE 1702”):ti,ab,kw	368
#42	(glimepiride or amaryl or amarel or “BRN 5365754” or “CCRIS 7083” or endial or euglim or glemax or glimepirid or glimepirida or glimepiridum or glimerid or glorion or “HOE 490” or HOE490 or solosa or “s 80 8490”):ti,ab,kw	537
#43	[mh Glyburide]	506
#44	(adiab or amecladin or “apo-glibenclamide” or azuglucon or bastiverit or benclamin or betanase or “betanese 5” or “BRN 2230085” or calabren or clamide or clibenclamide or cytagon or dangbinol or daonil or debtan or diabasan or diabeta or dibelet or duraglucon or “EINECS 233-570-6” or euclamin or euglucan or euglucon or euglykon):ti,ab,kw	33
#45	(“GBN 5” or “gen-glybe” or gewaglucon or gilemal or glamide or glencamide or gliban or glibeclamid or glibemid or gliben or glibenbeta or glibenclamid or glibenclamida or glibenclamide or glibenclamidum or glibenhexal or glibenil or glibens or glibesyn or glibet or glibetic or glibil or gliboral or glicem or glidiabet or gliformin or glikeyer or glimel or glimide or glimidstada or glisulin or glitisol or glubate or gluben):ti,ab,kw	763
#46	(glucobene or glucohexal or glucolon or glucomid or gluconic or glucoremed or glucoven or glukoreduct or glulo or glyamid or glyben or glybencamidum or glybencenamide or glybenclamid or glybenclamide or glybendamine or glybenzyclamide or glybenzcyclamide or glyburide or glycolande or glycomin or glynase or “HB 419” or “HB 420” or “hemi-daonil” or hexaglucon or humedia or insol or lederglib or libanil or lisaglucon or locose or lodulce):ti,ab,kw	632
#47	(maninil or manoglucon or “med-glionil” or melix or micronase or miglucan or nadib or neogluconin or “norglicem 5” or normoglucon or orabetic or pira or praeciglucon or prodiabet or renabetic or “RP-1127” or	14

ID	Search	Hits
	"semi-daonil" or "semi-euglucon" or "semi-gliben-puren n" or sugril or suraben or tiabet or "U 26452" or "U-26 452" or "UR 606" or yuglucon or xeltic):ti,ab,kw	
#48	[mh Tolbutamide]	135
#49	(abemin or aglicem or aglicid or aglycid or "apo-tolbutamide" or arcosal or arkozal or artosin or artosina or artozin or beglucin or "BRN 1984428" or butamid or butamide or butamidum or "CCRIS 592" or "D 860" or diabecid or diaben or diabenyl or diabeton or diabesan or diasulfon or diabetamid or diabetol or diabuton or diatol or dirastan or diasulin or diaval or dolipol or drabet):ti,ab,kw	0
#50	("EINECS 200-594-3" or fresan or glicemin or glicotron or glycotron or guabeta or glyconon or "HLS 831" or "HSDB 3393" or hypoglycone or ipoglicone or ipoglucos or mermol or "metil glucosulfina" or mobenol or "NCI-C01763" or "NSC 23813" or "neo antiglycemikos" or "neo diabetal" or "neo norboral" or neobellin or neoinsoral):ti,ab,kw	0
#51	(orabet or oralin or oresan or orezan or orinade or orinase or orinaz or orsinon or osdiabet or oterben or pramidex or proinsul or rastinon or "SK-tolbutamide" or tarasina or tobutamine or tol ortab or tolbet or tolbugen or tolbusal or tolbutamid or tolbutamida or tolbutamide or tolbutamidum or tolbutone or tolbutamte or tolbutol or tolbutylharnstoff or tolbutylurea or tolglybutamide or tolsiran or tolubetin or toluran or tolurast or tosula or toluina or tolumid or toluvan or tolylsulfonylbutylurea or "U 2043" or willbutamide):ti,ab,kw	230
#52	[mh Thiazolidinediones]	1248
#53	(thiazolidinedione* or TZD or TZDs):ti,ab,kw	1554
#54	(pioglitazone* or actos or "AD 4833" or piomed or "U 72107A" or "U72 107A" or cereluc or glidipion or glita or glitase or glustin or paglitaz or pioglit or sepioglin or zactos):ti,ab,kw	1224
#55	(rosiglitazone* or avandia or "BRL 49653-C" or "BRL 49653" or nyracta or rezult or rossini or venvia):ti,ab,kw	817
#56	[mh "Glucagon-Like Peptide 1"/AA]	147
#57	(("glucagon-like peptide-1" or "GLP-1" or GLP1 or "GLP-1R" or GLP1R) near/2 analog*):ti,ab,kw	170
#58	[mh "Glucagon-Like Peptide-1 Receptor"]	48
#59	(("glucagon-like peptide-1" or "GLP-1" or GLP1 or "GLP-1R" or GLP1R) near/2 (receptor* or protein*)):ti,ab,kw	344
#60	[mh "Receptors, Glucagon"/AG]	47
#61	(("glucagon-like peptide-1" or "GLP-1" or GLP1 or "GLP-1R" or GLP1R) near/2 agonist*):ti,ab,kw	309
#62	(incretin next mimetic*):ti,ab,kw	23
#63	(dulaglutide or "LY-2189265" or LY2189265 or trulicity):ti,ab,kw	62
#64	("AC 2993" or "AC 2993A" or "AC-2993" or AC002993 or AC2993 or AC2993A or baietta or byetta or bydureon or "DA 3091" or exenatide or "exendin 4" or "HSDB 7789" or "LY 2148568" or "LY2148568" or PT302 or "Ex4 peptide" or "ITCA 650"):ti,ab,kw	421
#65	[mh Liraglutide]	106
#66	(liraglutida or liraglutide or liraglutidum or "HSDB 8205" or "NN-2211" or NN2211 or "NNC 90-1170" or saxenda or victoza):ti,ab,kw	378
#67	[mh "Insulin, Long-Acting"]	776
#68	(("long-acting" or LA or semilente or semi-lente or (slow* next acting) or "intermediate-acting") next (insulin* or analog*)):ti,ab,kw	290
#69	[mh "Insulin Detemir"]	103
#70	(detemir or determir or levemir or "NN-304" or NN304):ti,ab,kw	297
#71	[mh "Insulin Glargine"]	368
#72	(abasaglar or abasria or basaglar or glargine or "HOE-901" or HOE901 or lantus or "ly 2963016" or ly2963016 or optisulin or toujeo):ti,ab,kw	935
#73	[mh "Insulin, Short-Acting"]	488
#74	(("fast-acting" or "quick-acting" or "short-acting" or (rapid* next acting)) next (insulin* or analog*)):ti,ab,kw	374
#75	((insulin next aspart*) or (B28 near/1 insulin*) or (B28 near/1 insulin*) or (B28asp* near/1 insulin*) or	534

ID	Search	Hits
	NovoLog* or NovoMix* or (Novo next Mix*) or NovoRapid*):ti,ab,kw	
#76	(lispro or lyspro or humalog or liprolog):ti,ab,kw	528
#77	(apidra or glulisine):ti,ab,kw	125
#78	[mh "Insulin, Isophane"]	304
#79	(actraphan* or berlinsulin or "humulin i" or "humulin n" or insulatard or (insulin* near/3 monotard) or isophane or (insulin* near/2 NPH) or (insulin* near/2 protamine) or isofane or isophan or isophane or isophone or mixtard or novolin or "nph iletin" or "nph umuline" or orgasuline or protaphan or protaphane or protophane or prozinc or (zinc near/2 insulin*) or (zinc near/1 protamine)):ti,ab,kw	829
#80	[mh Insulin]	9438
#81	(insulin* near/1 regular):ti,ab,kw	403
#82	(insulin* near/1 human):ti,ab,kw	2565
#83	((nph next insulin*) or humulin or novolin):ti,ab,kw	428
#84	((insulin* near/1 (pork or porcine or pig or pigs)) or hypurin):ti,ab,kw	167
#85	(alogliptin near/3 metformin):ti,ab,kw	8
#86	(metformin near/2 nesina):ti,ab,kw	0
#87	(kazano or nesimet or nesina or nesinamet or vipdomet):ti,ab,kw	1
#88	(linagliptin near/2 metformin):ti,ab,kw	42
#89	(jentadueto or "trajenta duo" trajentamet or "trayebta duo" or "trayenta duo"):ti,ab,kw	2
#90	(saxagliptin near/3 metformin):ti,ab,kw	52
#91	(komboglyze or kombiglyze or comboglyze or duoglyze):ti,ab,kw	2
#92	[mh "Sitagliptin Phosphate, Metformin Hydrochloride Drug Combination"]	1
#93	(sitagliptin near/3 metformin):ti,ab,kw	119
#94	(janumet or efficib or gliptamet or Januet or ristfor or velmetia or "mk 0431a"):ti,ab,kw	2
#95	(metformin near/3 dapagliflozin):ti,ab,kw	43
#96	(ebymect or xigduo):ti,ab,kw	0
#97	(empagliflozin near/3 metformin):ti,ab,kw	25
#98	(jardiamet or jardiancemet or synjardy):ti,ab,kw	0
#99	(metformin near/3 rosiglitazone):ti,ab,kw	185
#100	(avandamet or interac):ti,ab,kw	8
#101	[mh "Glycoside Hydrolase Inhibitors"]	137
#102	(("alpha-amylase" or "alpha-glucosidase" or glucosidase or glycoside) near/2 inhibitor*)	438
#103	[mh Acarbose]	238
#104	(acarbose or "ag 5421" or ag5421 or "alpha ghi" or "bay g 5421" or "bay g5421" or glibose or glicobase or glucobay or gluconase or glucor or glumida or prandase or precise or rebose):ti,ab,kw	2642
#105	("hb 699" or hb699 or meglitinide*):ti,ab,kw	38
#106	(actulin or "ag ee 388" or "ag ee388" or "ag ee 623" or "ag ee623" or enyglid or gluconorm or novonorm or prandin or rapilan or repaglinide or sestrine):ti,ab,kw	207
#107	("a 4166" or a4166 or "ay 4166" or ay4166 or "djn 608" or djn608 or fasticor or glinate or nateglinide or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026"):ti,ab,kw	172
#108	("bay 1099" or "bay m 1099" or "bay m1099" or bay1099 or diastabol or glyset or miglitol or plumarol):ti,ab,kw	127
#109	("ao 128" or ao128 or basen or "en 116 077" or "en 116077" or "en116 077" or en116077 or glustat or voglibose):ti,ab,kw	120
#110	(or #9-#109)	22251

ID	Search	Hits
#111	#5 and #110	10283

CENTRAL – 9573

PubMed (*newest records only*)

Search	Query	Items Found
#90	Search #88 AND #89	53
#89	Search publisher[sb] OR 2016/03/01:2016/03/17[edat]	487139
#88	Search #85 NOT (#86 OR #87)	11953
#87	Search letter[pt] NOT (letter[pt] AND randomized controlled trial[pt])	903578
#86	Search comment[pt] OR editorial[pt] OR interview[pt] OR news[pt] OR newspaper article[pt]	1128869
#85	Search #80 NOT #84	12435
#84	Search #81 OR #82 OR #83	1621786
#83	Search Infant[mesh] not (Adult[mesh] and Infant[mesh])	735164
#82	Search Child[mesh] not (Adult[mesh] and Child[mesh])	1037160
#81	Search Adolescent[mesh] not (Adult[mesh] and Adolescent[mesh])	508484
#80	Search #78 NOT #79	12561
#79	Search Animals[mesh] NOT (Animals[mesh] AND humans[mesh])	4187523
#78	Search (#76 AND #77)	12808
#77	Search (#4 AND #69)	75398
#76	Search #71 or #72 or #73 OR #74 OR #75	1115734
#75	Search trial [ti]	149291
#74	Search single blind*[tw] OR single mask*[tw] OR single dumm*[tw] OR double blind*[tw] OR double mask*[tw] OR double dumm*[tw] OR triple blind*[tw] OR triple mask*[tw] OR triple dumm*[tw] OR treble blind*[tw] OR treble mask*[tw] OR treble dumm*[tw]	193913
#73	Search randomised[tw] OR randomized[tw] OR randomly[tw] or RCT[tw] OR RCTs[tw] OR placebo*[tw]	870866
#72	Search “clinical trials as topic”[mesh]	287364
#71	Search controlled clinical trial[pt] OR randomized controlled trial[pt]	492381
#69	Search #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	2755452
#68	Search “ao 128”[tw] OR ao128[tw] OR basen[tw] OR “en 116 077”[tw] OR “en 116077”[tw] OR “en116 077”[tw] OR en116077[tw] OR glustat[tw] OR voglibose[tw]	274
#67	Search “hb 699”[tw] OR hb699[tw] OR meglitinide*[tw] OR actulin[tw] OR “ag ee 388”[tw] OR “ag ee388”[tw] OR “ag ee 623”[tw] OR “ag ee623”[tw] OR enyglid[tw] OR gluconorm[tw] OR novonorm[tw] OR prandin[tw] OR rapilan[tw] OR repaglinide[tw] OR sestrine[tw] OR “a 4166”[tw] OR a4166[tw] OR “ay 4166”[tw] OR ay4166[tw] OR “djn 608”[tw] OR djn608[tw] OR fasticor[tw] OR glinate[tw] OR nateglinide[tw] OR sdz djn 608[tw] OR sdz djn608[tw] OR senaglinide[tw] OR starlix[tw] OR starsis[tw] OR trazec[tw] OR “ym 026”[tw] OR “bay 1099”[tw] OR “bay m 1099”[tw] OR “bay m1099”[tw] OR bay1099[tw] OR diastabol[tw] OR glyset[tw] OR miglitol[tw] OR plumarol[tw] OR 0V5436JAQW[EC/RN Number]	1507
#66	Search acarbose[tw] OR “ag 5421”[tw] OR ag5421[tw] OR “alpha ghi”[tw] OR “bay g 5421”[tw] OR “bay g5421”[tw] OR glibose[tw] OR glicobase[tw] OR glucobay[tw] OR gluconase[tw] OR glucor[tw] OR glumida[tw] OR prandase[tw] OR precise[tw] OR rebose[tw] OR T58MSI464G[EC/RN Number]	135060

Search	Query	Items Found
#65	Search Acarbose[mesh]	1140
#64	Search alpha-amylase inhibitor*[tw] OR alpha-glucosidase inhibitor*[tw] OR glucosidase inhibitor*[tw] OR glycoside inhibitor*[tw]	2631
#63	Search Glycoside Hydrolase Inhibitors[mesh]	1776
#62	Search (sitagliptin[tw] AND metformin[tw]) OR janumet[tw] OR efficib[tw] OR gliptamet[tw] OR Januet[tw] OR ristfor[tw] OR velmetia[tw] OR “mk 0431a”[tw] OR (metformin[tw] AND dapagliflozin[tw]) OR ebymect[tw] OR xigduo[tw] OR (empagliflozin[tw] AND metformin[tw]) OR jardiamet[tw] OR jardiancemet[tw] OR synjardy[tw] OR (metformin[tw] AND rosiglitazone[tw]) OR avandamet[tw] OR interac[tw]	1283
#61	Search “Sitagliptin Phosphate, Metformin Hydrochloride Drug Combination”[mesh]	5
#60	Search (alogliptin[tw] AND metformin[tw]) OR (nesina[tw] AND metformin[tw]) OR kazano[tw] OR nesimet[tw] OR nesina[tw] OR nesinamet[tw] OR vipdomet[tw] OR (linagliptin[tw] AND metformin[tw]) OR jentadueto[tw] OR trajenta duo[tw] OR trajentamet[tw] OR trayebta duo[tw] OR trayenta duo[tw] OR (saxagliptin[tw] AND metformin[tw]) OR komboglyze[tw] OR kombiglyze[tw] OR comboglyze[tw] OR duoglyze[tw]	1313
#59	Search pork insulin*[tw] OR porcine insulin*[tw] OR pig insulin*[tw] OR pigs insulin*[tw] OR hypurin[tw]	7723
#58	Search regular insulin*[tw] OR human insulin*[tw] OR nph insulin*[tw] OR humulin[tw] OR novolin[tw]	7626
#57	Search Insulin [mesh]	165022
#56	Search actraphan*[tw] OR berlinsulin[tw] OR “humulin i”[tw] OR “humulin n”[tw] OR insulatard[tw] OR (insulin*[tw] AND monotard[tw]) OR isophane[tw] OR (insulin*[tw] AND NPH[tw]) OR (insulin*[tw] AND protamine[tw]) OR isofane[tw] OR isophan[tw] OR isophane[tw] OR isophone[tw] OR mixtard[tw] OR novolin[tw] OR “nph iletin”[tw] OR nph umuline[tw] OR orgasuline[tw] OR protaphan[tw] OR protaphane[tw] OR protophane[tw] OR prozinc[tw] OR zinc insulin*[tw] OR zinc protamine[tw] OR protamine zinc[tw] OR 2ZM8CX04RZ[EC/RN Number]	3436
#55	Search Insulin, Isophane[mesh]	917
#54	Search lispro[tw] OR lyspro[tw] OR humalog[tw] OR liprolog[tw] OR apidra[tw] OR glulisine[tw] OR 7XIY785AZD[EC/RN Number]	1309
#53	Search fast-acting insulin*[tw] OR quick-acting insulin*[tw] OR short-acting insulin*[tw] OR rapid acting insulin*[tw] OR rapidly acting insulin*[tw] OR fast-acting analog*[tw] OR quick-acting analog*[tw] OR short-acting analog*[tw] OR rapid acting analog*[tw] OR rapidly acting analog*[tw] OR insulin aspart*[tw] OR B28 insulin*[tw] OR B28 insulin*[tw] OR B28asp insulin*[tw] OR NovoLog*[tw] OR NovoMix*[tw] OR Novo Mix*[tw] OR NovoRapid*[tw] OR D933668QVX[EC/RN Number]	3630
#52	Search Insulin, Short-Acting[mesh]	1250
#51	Search abasaglar[tw] OR abasria[tw] OR basaglar[tw] OR glargine[tw] OR “HOE-901”[tw] OR HOE901[tw] OR lantus[tw] OR ly 2963016[tw] OR ly2963016[tw] OR optisulin[tw] OR toujeo[tw] OR 2ZM8CX04RZ[EC/RN Number]	2026
#50	Search Insulin Glargine[mesh]	1261
#49	Search detemir[tw] OR determir[tw] OR levemir[tw] OR “NN-304”[tw] OR NN304[tw] OR 4FT78T86XV[EC/RN Number]	820
#48	Search Insulin Detemir[mesh]	433
#47	Search long-acting insulin*[tw] OR LA insulin*[tw] OR semilente insulin*[tw] OR semi-lente insulin*[tw] OR slow acting insulin*[tw] OR slower acting insulin*[tw] OR intermediate-acting insulin*[tw] OR long-acting analog*[tw] OR LA analog*[tw] OR semilente analog*[tw] OR semi-lente analog*[tw] OR slow acting analog*[tw] OR slower acting analog*[tw] OR intermediate-acting analogn*[tw]	10580
#46	Search Insulin, Long-Acting[mh:noexp]	2528
#45	Search liraglutida[tw] OR liraglutide[tw] OR liraglutidum[tw] OR “HSDB 8205”[tw] OR “NN-2211”[tw] OR NN2211[tw] OR “NNC 90-1170”[tw] OR saxenda[tw] OR victoza[tw] OR 839I73S42A[EC/RN Number]	1286
#44	Search Liraglutide[mesh]	705

Search	Query	Items Found
#43	Search "AC 2993"[tw] OR "AC 2993A"[tw] OR "AC-2993"[tw] OR AC002993[tw] OR AC2993[tw] OR AC2993A[tw] OR baietta[tw] OR byetta[tw] OR bydureon[tw] OR "DA 3091"[tw] OR exenatide[tw] OR "exendin 4"[tw] OR "HSDB 7789"[tw] OR LY 2148568[tw] OR LY2148568[tw] OR PT302[tw] OR "Ex4 peptide"[tw] OR "ITCA 650"[tw] OR 9P1872D4OL[EC/RN Number]	2536
#42	Search glucagon-like peptide-1 agonist*[tw] OR GLP-1 agonist*[tw] OR GLP1 agonist*[tw] OR GLP-1R agonist*[tw] OR GLP1R agonist*[tw] OR incretin mimetic*[tw] OR dulaglutide[tw] OR LY-2189265[tw] OR LY2189265[tw] OR trulicity[tw] OR WTT295HSY5[EC/RN Number]	1012
#41	Search "receptors, glucagon/agonists"[MeSH Terms]	710
#40	Search glucagon-like peptide-1 receptor*[tw] OR GLP-1 receptor*[tw] OR GLP1 receptor*[tw] OR GLP-1R receptor*[tw] OR GLP1R receptor*[tw] OR glucagon-like peptide-1 protein*[tw] OR GLP- protein*[tw] OR GLP1 protein*[tw] OR GLP-1R protein*[tw] OR GLP1R protein*[tw]	5630
#39	Search Glucagon-Like Peptide-1 Receptor[mesh]	1542
#38	Search glucagon-like peptide-1 analog*[tw] OR GLP-1 analog*[tw] OR GLP1 analog*[tw] OR GLP-1R analog*[tw] OR GLP1R analog*[tw]	1261
#37	Search "glucagon like peptide 1/analogs and derivatives"[MeSH]	977
#36	Search rosiglitazone*[tw] OR avandia[tw] OR "BRL 49653-C"[tw] OR "BRL 49653"[tw] OR nyracta[tw] OR rezult[tw] OR rossini[tw] OR venvia[tw] OR 05V02F2KDG[EC/RN Number]	5549
#35	Search thiazolidinedione*[tw] OR TZD[tw] OR TZDs[tw] OR pioglitazone*[tw] OR actos[tw] OR "AD 4833"[tw] OR piomed[tw] OR "U 72107A"[tw] OR "U72 107A"[tw] OR cereluc[tw] OR glidipion[tw] OR glita[tw] OR glitase[tw] OR glustin[tw] OR paglitaz[tw] OR pioglit[tw] OR sepioglin[tw] OR zactos[tw] OR X4OV71U42S[EC/RN Number]	12847
#34	Search Thiazolidinediones[mesh]	9929
#33	Search abemin[tw] OR aglicem[tw] OR aglicid[tw] OR aglycid[tw] OR apo-tolbutamide[tw] OR arcosal[tw] OR arkozal[tw] OR artosin[tw] OR artosina[tw] OR artozin[tw] OR beglucin[tw] OR "BRN 1984428"[tw] OR butamid[tw] OR butamide[tw] OR butamidum[tw] OR "CCRIS 592"[tw] OR "D 860"[tw] OR diabecid[tw] OR diaben[tw] OR diabenyl[tw] OR diabeton[tw] OR diabesan[tw] OR diasulfon[tw] OR diabetamid[tw] OR diabetol[tw] OR diabuton[tw] OR diatol[tw] OR dirastan[tw] OR diasulin[tw] OR diaval[tw] OR dolipol[tw] OR drabbet[tw] OR EINECS 200-594-3[tw] OR fresan[tw] OR glicemin[tw] OR glicotron[tw] OR glycotron[tw] OR guabeta[tw] OR glyconon[tw] OR "HLS 831"[tw] OR "HSDB 3393"[tw] OR hypoglycone[tw] OR ipoglicone[tw] OR ipoglucos[tw] OR mermol[tw] OR metil glucosulfina[tw] OR mobenol[tw] OR NCI-C01763[tw] OR NSC 23813[tw] OR neo antiglycemikos[tw] OR neo diabetal[tw] OR neo norboral[tw] OR neobellin[tw] OR neoinsoral[tw] OR orabet[tw] OR oralin[tw] OR oresan[tw] OR orezan[tw] OR orinade[tw] OR orinase[tw] OR orinaz[tw] OR orsinon[tw] OR osdiabet[tw] OR oterben[tw] OR pramidex[tw] OR proinsul[tw] OR rastinon[tw] OR SK-tolbutamide[tw] OR tarasina[tw] OR tobutamine[tw] OR tol ortab[tw] OR tolbet[tw] OR tolbugen[tw] OR tolbusal[tw] OR tolbutamid[tw] OR tolbutamida[tw] OR tolbutamide[tw] OR tolbutamidum[tw] OR tolbutone[tw] OR tolbutamte[tw] OR tolbutol[tw] OR tolbutylharnstoff[tw] OR tolbutylurea[tw] OR tolglybutamide[tw] OR tolsiran[tw] OR tolubetin[tw] OR toluran[tw] OR tolurast[tw] OR tosula[tw] OR toluina[tw] OR tolumid[tw] OR toluvan[tw] OR tolylsulfonylbutylurea[tw] OR "U 2043"[tw] OR willbutamide[tw] OR 982XCM1FOI[EC/RN Number]	6637
#32	Search Tolbutamide[mesh]	5173
#31	Search glucobene[tw] OR glucohexal[tw] OR glucolon[tw] OR glucomid[tw] OR gluconic[tw] OR glucoremed[tw] OR glucoven[tw] OR glukoreduct[tw] OR glulo[tw] OR glyamid[tw] OR glyben[tw] OR glybencamidum[tw] OR glybencenamide[tw] OR glybenclamid[tw] OR glybenclamide[tw] OR glybendamine[tw] OR glybenzyclamide[tw] OR glybenzcyclamide[tw] OR glyburide[tw] OR glycolande[tw] OR glycomin[tw] OR glynase[tw] OR "HB 419"[tw] OR "HB 420"[tw] OR hemi-daonil[tw] OR hexaglucon[tw] OR humedia[tw] OR insol[tw] OR lederglib[tw] OR libanil[tw] OR lisaglucon[tw] OR locose[tw] OR lodulce[tw] OR maninil[tw] OR manoglucon[tw] OR med-glionil[tw] OR melix[tw] OR micronase[tw] OR miglucan[tw] OR nadib[tw] OR neogluconin[tw] OR "norglicem 5"[tw] OR normoglucon[tw] OR orabetic[tw] OR pira[tw] OR praeciglucon[tw] OR prodiabet[tw] OR renabetic[tw] OR "RP-1127"[tw] OR semi-daonil[tw] OR semi-euglucon[tw] OR semi-gliben-puren n[tw] OR sugril[tw] OR suraben[tw] OR tiabet[tw] OR "U 26452"[tw] OR "U-26 452"[tw] OR "UR 606"[tw] OR yuglucon[tw] OR xeltic[tw] OR SX6K58TVWC[EC/RN	2434824

Search	Query	Items Found
	Number]	
#30	Search adiab[tw] OR amecladin[tw] OR apo-glibenclamide[tw] OR azuglucon[tw] OR bastiverit[tw] OR benclamin[tw] OR betanase[tw] OR “betanese 5”[tw] OR “BRN 2230085”[tw] OR calabren[tw] OR clamide[tw] OR clibenclamide[tw] OR cytagon[tw] OR dangbinol[tw] OR daonil[tw] OR debtan[tw] OR diabasan[tw] OR diabeta[tw] OR dibelet[tw] OR duraglucon[tw] OR EINECS 233-570-6[tw] OR euclamin[tw] OR euglucan[tw] OR euglucon[tw] OR euglykon[tw] OR “GBN 5”[tw] OR gen-glybe[tw] OR gewaglucon[tw] OR gilemal[tw] OR glamide[tw] OR glencamide[tw] OR gliban[tw] OR glibeclamid[tw] OR glibemid[tw] OR gliben[tw] OR glibenbeta[tw] OR glibenclamid[tw] OR glibenclamida[tw] OR glibenclamide[tw] OR glibenclamidum[tw] OR glibenhexal[tw] OR glibenil[tw] OR glibens[tw] OR glibesyn[tw] OR glibet[tw] OR glibetic[tw] OR glibil[tw] OR gliboral[tw] OR glicem[tw] OR glidiabet[tw] OR gliformin[tw] OR glikeyer[tw] OR glimel[tw] OR glimide[tw] OR glimidstada[tw] OR glisulin[tw] OR glitisol[tw] OR glubate[tw] OR gluben[tw]	7433
#29	Search Glyburide[mesh]	5752
#28	Search glimepiride[tw] OR amaryl[tw] OR amarel[tw] OR “BRN 5365754” [tw] OR “CCRIS 7083” [tw] OR endial[tw] OR euglim[tw] OR glemax[tw] OR glimepirid[tw] OR glimepirida[tw] OR glimepiridum[tw] OR glimerid[tw] OR glorion[tw] OR “HOE 490” [tw] OR HOE490[tw] OR solosa[tw] OR “s 80 8490”[tw] OR 6KY687524K[EC/RN Number]	1092
#27	Search gliclazide[tw] OR diaglyk[tw] OR diaikron[tw] OR diabrezide[tw] OR diamicron[tw] OR “BRN 1657836”[tw] OR EINECS 244-260-5[tw] OR gen-gliclazide[tw] OR gliklazid[tw] OR gliclazida[tw] OR gliclazidum[tw] OR glimicron[tw] OR glyade[tw] OR glyclazide[tw] OR glycazide[tw] OR nordialex[tw] OR predian[tw] OR “S 1702”[tw] OR “S 852”[tw] OR “SE 1702”[tw] OR G4PX8C4HKV[EC/RN Number]	1210
#26	Search Gliclazide[mesh]	767
#25	Search melormin[tw] OR meldian[tw] OR melitase[tw] OR mellinese[tw] OR millinese[tw] OR NCI-C01752[tw] OR “NSC 44634”[tw] OR “NSC 626720”[tw] OR neo-toltinon[tw] OR oradian[tw] OR “P 607”[tw] OR pamidin[tw] OR prodiaben[tw] OR pubetin[tw] OR stabinol[tw] OR tesmel[tw] OR “p chlorobenzolsulphonylglycolic acid nitrile”[tw] OR para chlorobenzenesulfonylglycolic acid nitrile[tw] OR parachlorobenzene sulfonylglycolic acid nitrile[tw] OR “U-3818”[tw] OR “U-9818”[tw] OR WTM2C3IL2X[EC/RN Number]	1843
#24	Search adiaben[tw] OR apo-chlorpropamide[tw] OR apochlorpropamide[tw] OR abemide[tw] OR “arodoc c”[tw] OR asucrol[tw] OR ascurol[tw] OR biabenal[tw] OR bioglumin[tw] OR BRN 2218363[tw] OR catanil[tw] OR “CCRIS 155”[tw] OR chlomide[tw] OR chlormide[tw] OR chlorodiabina[tw] OR chloropropamide[tw] OR chlorpromide[tw] OR clorpropamide[tw] OR copamide[tw] OR chloronase[tw] OR chlorpromide[tw] OR clorpropamide[tw] OR chloropropamide[tw] ORchlorpropamid[tw] OR chlorpropamide[tw] OR chlorpropamidum[tw] OR clorpropamid[tw] OR clorpropamida[tw] OR dabinese[tw] OR deavynfar[tw] OR diabaril[tw] OR diabechlor[tw] OR diabeedol[tw] OR diabemide[tw] OR diabenal[tw] OR diabenese[tw] OR diabeneza[tw] OR diabet-pages[tw] OR diabetoral[tw] OR diabexan[tw] OR diabiclor[tw] OR diabines[tw] OR diabinese[tw] OR diabitex[tw] OR diabitol[tw] OR diamel ex[tw] OR dibecon[tw] OR dynalase[tw] OR EINECS 202-314-5[tw] OR eubetin[tw] OR glicoben[tw] OR glisema[tw] OR glucamide[tw] OR glycemin[tw] OR glymese[tw] OR HSDB 2051[tw] OR hypomide[tw] OR insilange[tw] OR insogen[tw] OR insulase[tw]	2067
#23	Search Chlorpropamide[mesh]	1809
#22	Search sulfonylurea*[tw] OR sulfonurea*[tw] OR sulfonyl urea*[tw] OR sulfonylcarbamide*[tw] OR sulphonurea*[tw] OR sulphonylurea*[tw]	11088
#21	Search Sulfonylurea Compounds[mh:noexp]	5254
#20	Search empagliflozin[tw] OR “BI 10773”[tw] OR BI10773[tw] OR Jardiance[tw] OR HDC1R2M35U[EC/RN Number]	236
#19	Search dapagliflozin[tw] OR “BMS 512148”[tw] OR BMS512148[tw] OR edistride[tw] OR forxiga[tw] OR farxiga[tw] OR 1ULL0QJ8UC[EC/RN Number]	320
#18	Search canagliflozin[tw] OR Invokana[tw] OR JNJ 24831754*[tw] OR “JNJ 28431754”[tw] OR TA 7284[tw] OR Prominad[tw] OR 0SAC974Z85[EC/RN Number]	301
#17	Search Canagliflozin[mesh]	144

Search	Query	Items Found
#16	Search sodium-glucose transporter 2 inhibitor*[tw] OR sodium-glucose cotransporter 2 inhibitor*[tw] OR sodium-glucose co-transporter 2 inhibitor*[tw] OR sodium-glucose co-transporter 2 inhibitor*[tw] OR SGLT-2 inhibitor*[tw] OR SGLT2 inhibitor*[tw] OR sodium dependent glucose transporter 2 inhibitor*[tw] OR sodium dependent glucose cotransporter 2 inhibitor*[tw] OR sodium dependent glucose transporter 2 inhibitor*[tw] OR sodium dependent glucose co-transporter 2 inhibitor*[tw] OR gliflozin[tw] OR gliflozins[tw]	890
#15	Search “sodium glucose transporter 2/antagonists and inhibitors”[MeSH Terms]	515
#14	Search sitagliptin[tw] OR “EC 690-730-1”[tw] OR Glactiv[tw] OR “HSDB 7516”[tw] OR januvia or “mk 0431”[tw] OR mk0431[tw] OR “mk 431”[tw] OR “ono 5435”[tw] OR ristaben[tw] OR sitagliptine[tw] OR tesabel[tw] OR tesavel[tw] OR xelevia[tw] OR TS63EW8X6F[EC/RN Number]	1464
#13	Search Sitagliptin Phosphate[mesh]	812
#12	Search saxagliptin[tw] OR BMS 477118[tw] OR BMS477118[tw] OR HSDB 8199[tw] OR Onglyza[tw] OR “OPC 262”[tw] OR 9GB927LAJW[EC/RN Number]	410
#11	Search linagliptin[tw] OR “BI 1356”[tw] OR ONDERO[tw] OR tradjenta[tw] OR trajenta[tw] OR trayenta[tw] OR trazenta[tw] OR 3X29ZEJ4R2[EC/RN Number]	374
#10	Search Linagliptin[mesh]	194
#9	Search DPP4 inhibitor*[tw] OR DPP 4 inhibitor*[tw] OR DPP IV inhibitor*[tw] OR dipeptidyl-peptidase IV inhibitor*[tw] OR dipeptidyl-peptidase 4 inhibitor*[tw] OR gliptin[tw] OR gliptins[tw] OR alogliptin[tw] OR nesina[tw] OR “SYR 322”[tw] OR SYR322[tw] OR “HSDB 8203”[tw] OR incresina[tw] OR vipidia[tw] OR JHC049LO86[EC/RN Number]	3682
#8	Search Dipeptidyl-Peptidase IV Inhibitors[mesh]	2171
#7	Search antidiabetic*[tw] OR anti-diabetic*[tw] OR antihyperglycemic*[tw] OR antihyperglycaemic*[tw]OR anti-hyperglycemic*[tw] OR anti-hyperglycaemic*[tw] OR hypoglycemic*[tw] OR hypoglycaemic*[tw] OR antidiabetes*[tw] OR anti-diabetes*[tw]	67826
#6	Search Hypoglycemic Agents[mesh]	50724
#5	Search “diabetes mellitus, type 2/drug therapy”[MeSH] AND (Drug Combinations[mh:noexp] OR Drug Therapy, Combination[mh:noexp])	3005
#4	Search #1 OR #2 OR #3	328883
#3	Search MODY[tw] OR NIDDM[tw] OR T2DM[tw]	17648
#2	Search (adult[tw] OR ketosis-resistant[tw] OR matur*[tw] OR late[tw] OR non-insulin depend*[tw] OR noninsulin depend*[tw] OR slow[tw] OR stable[tw] OR “type 2”[tw] OR “type II”[tw] OR lipoatrophic[tw]) AND diabet*[tw]	263664
#1	Search (“Diabetes Mellitus, Type 2” [mesh] OR Diabetes Mellitus [mh:noexp])	191490

Type 2 DM — Metformin/Canagliflozin, Albiglutide

2016 Apr 7

OVID Multifile

Database: Embase Classic+Embase <1947 to 2016 April 06>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy	
1	exp Diabetes Mellitus, Type 2/ (269163)
2	Diabetes Mellitus/ (562571)
3	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or slow or stable or type 2 or type II or lipoatrophic) adj3 diabet*).tw,kw. (278379)

Search Strategy	
4	(MODY or NIDDM or T2DM).tw,kw. (45749)
5	or/1-4 (853960)
6	(metformin adj3 canagliflozin).tw,kw. (30)
7	(invokamet or vokanamet).tw,kw. (12)
8	(albiglutide or albugon or (albumin adj1 GLP 1) or (albumin adj1 glucagon like peptide 1) or eperzan or "gsk 716155" or "gsk 716155a" or gsk716155 or gsk716155a or naliglutide or syncria or tanzeum).tw,kw. (339)
9	bydureon*.tw,kw. (183)
10	or/6-9 (532)
11	5 and 10 (478)
12	(controlled clinical trial or randomized controlled trial).pt. (498240)
13	clinical trials as topic.sh. (175967)
14	(randomi#ed or randomly or RCT$1 or placebo*).tw. (1678922)
15	((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw. (331077)
16	trial.ti. (353740)
17	or/12-16 (2113939)
18	11 and 17 (164)
19	exp Animals/ not (exp Animals/ and Humans/) (14071795)
20	18 not 19 (68)
21	Adolescent/ not (exp Adult/ and Adolescent/) (1008508)
22	exp Child/ not (exp Adult/ and exp Child/) (2907448)
23	exp Infant/ not (exp Adult/ and exp Infant/) (1553718)
24	or/21-23 (3695720)
25	20 not 24 (68)
26	(comment or editorial or interview or news or newspaper article).pt. (1640159)
27	(letter not (letter and randomized controlled trial)).pt. (1835999)
28	25 not (26 or 27) (68)
29	28 use prmz (37)
30	diabetes mellitus/ (562571)
31	non insulin dependent diabetes mellitus/ (268979)
32	lipoatrophic diabetes mellitus/ (434)
33	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or slow or stable or type 2 or type II or lipoatrophic) adj3 diabet*).tw,kw. (278379)
34	(MODY or NIDDM or T2DM).tw,kw. (45749)
35	or/30-34 (854020)
36	canagliflozin plus metformin/ (11)
37	(metformin adj3 canagliflozin).tw,kw. (30)
38	(invokamet or vokanamet).tw,kw. (12)
39	albiglutide/ (428)
40	(albiglutide or albugon or (albumin adj1 GLP 1) or (albumin adj1 glucagon like peptide 1) or eperzan or "gsk 716155" or "gsk 716155a" or gsk716155 or gsk716155a or naliglutide or syncria or tanzeum).tw,kw. (339)
41	782500-75-8.rn. (351)
42	bydureon*.tw,kw. (183)
43	or/36-42 (732)
44	35 and 43 (665)
45	randomized controlled trial/ or controlled clinical trial/ (1038247)
46	exp "clinical trial (topic)"/ (187219)
47	(randomi#ed or randomly or RCT$1 or placebo*).tw. (1678922)

Search Strategy	
48	((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw. (331077)
49	trial.ti. (353740)
50	or/45-49 (2310053)
51	44 and 50 (307)
52	exp animal experimentation/ or exp models animal/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (42446468)
53	exp human/ or exp human experimentation/ or exp human experiment/ (32988838)
54	52 not 53 (9459290)
55	51 not 54 (307)
56	exp Juvenile/ not (exp Adult/ and exp Juvenile/) (2112211)
57	55 not 56 (307)
58	editorial.pt. (902821)
59	letter.pt. not (letter.pt. and randomized controlled trial/) (1831507)
60	57 not (58 or 59) (303)
61	60 use emczd (269)
62	29 or 61 (306)
63	remove duplicates from 62 (272) [TOTAL UNIQUE RECORDS]
64	63 use prmz (37) [MEDLINE UNIQUE RECORDS]
65	63 use emczd (235) [EMBASE UNIQUE RECORDS]

Cochrane Library

ID	Search	Hits
#1	[mh “Diabetes Mellitus, Type 2”]	10504
#2	[mh ^”Diabetes Mellitus”]	2731
#3	((adult or “ketosis-resistant” or matur* or late or (“non-insulin” next depend*) or (noninsulin next depend*) or slow or stable or “type 2” or “type II” or lipoatrophic) near/3 diabet*):ti,ab,kw	20075
#4	(MODY or NIDDM or T2DM):ti,ab,kw	2938
#5	(or #1-#4)	22308
#6	(metformin near/3 canagliflozin):ti,ab,kw	14
#7	(invokamet or vokanamet):ti,ab,kw	0
#8	(albiglutide or albugon or (albumin near/1 GLP 1) or (albumin near/1 “glucagon like peptide 1”) or eperzan or “gsk 716155” or “gsk 716155a” or gsk716155 or gsk716155a or naliglutide or syncria or tanzeum):ti,ab,kw	44
#9	bydureon*:ti,ab,kw	3
#10	(or #6-#9)	60
#11	#5 and #10	58

CENTRAL – 55

PubMed (*newest records only*)

Search	Query	Items Found
#29	Search #27 AND #28	4
#28	Search publisher[sb] OR 2016/04/01:2016/04/07	491128
#27	Search #24 NOT (#25 OR #26)	76
#26	Search letter[pt] NOT (letter[pt] AND randomized controlled trial[pt])	905925
#25	Search comment[pt] OR editorial[pt] OR interview[pt] OR news[pt] OR newspaper article[pt]	1132446

Search	Query	Items Found
#24	Search #19 NOT #23	77
#23	Search #20 OR #21 OR #22	1624995
#22	Search Infant[mesh] not (Adult[mesh] and Infant[mesh])	736446
#21	Search Child[mesh] not (Adult[mesh] and Child[mesh])	1039276
#20	Search Adolescent[mesh] not (Adult[mesh] and Adolescent[mesh])	509692
#19	Search #17 NOT #18	77
#18	Search Animals[mesh] NOT (Animals[mesh] AND humans[mesh])	4194732
#17	Search #10 AND #16	77
#16	Search #11 OR #12 OR #13 OR #14 OR #15	1119773
#15	Search trial [ti]	150082
#14	Search single blind*[tw] OR single mask*[tw] OR single dumm*[tw] OR double blind*[tw] OR double mask*[tw] OR double dumm*[tw] OR triple blind*[tw] OR triple mask*[tw] OR triple dumm*[tw] OR treble blind*[tw] OR treble mask*[tw] OR treble dumm*[tw]	194501
#13	Search randomised[tw] OR randomized[tw] OR randomly[tw] or RCT[tw] OR RCTs[tw] OR placebo*[tw]	874480
#12	Search “clinical trials as topic”[mesh]	288148
#11	Search controlled clinical trial[pt] OR randomized controlled trial[pt]	493795
#10	Search #4 AND #9	158
#9	Search #5 OR #6 OR #7 OR #8	173
#8	Search bydureon*[tw]	9
#7	Search albiglutide[tw] OR albugon[tw] OR “albumin GLP 1”[tw] OR “GLP 1 albumin”[tw] or “albumin glucagon like peptide 1”[tw] OR “glucagon like peptide 1 albumin”[tw] OR eperzan[tw] OR “gsk 716155”[tw] OR “gsk 716155a”[tw] OR gsk716155[tw] OR gsk716155a[tw] OR naliglutide[tw] OR syncria[tw] OR tanzeum[tw]	90
#6	Search invokamet[tw] OR vokanamet[tw]	3
#5	Search metformin[tw] AND canagliflozin[tw]	72
#4	Search #1 OR #2 OR #3	328883
#3	Search MODY[tw] OR NIDDM[tw] OR T2DM[tw]	17759
#2	Search (adult[tw] OR ketosis-resistant[tw] OR matur*[tw] OR late[tw] OR non-insulin depend*[tw] OR noninsulin depend*[tw] OR slow[tw] OR stable[tw] OR “type 2”[tw] OR “type II”[tw] OR lipoatrophic[tw]) AND diabet*[tw]	264674
#1	Search “Diabetes Mellitus, Type 2” [mesh] OR Diabetes Mellitus [mh:noexp]	192175

CADTH

Appendix 2: Research Question 1 — List of Included Studies (and Companion Publications)

1. Merker L, Haring HU, Christiansen AV, et al. Empagliflozin as add-on to metformin in people with Type 2 diabetes. Diabet Med. 2015; 32: 1555-67.

2. Simo R, Guerci B, Schernthaner G, et al. Long-term changes in cardiovascular risk markers during administration of exenatide twice daily or glimepiride: results from the European exenatide study. Cardiovascular Diabetology [electronic resource]. 2015; 14: 116.

3. Weinstock RS, Guerci B, Umpierrez G, Nauck MA, Skrivanek Z and Milicevic Z. Safety and efficacy of once-weekly dulaglutide versus sitagliptin after 2years in metformin-treated patients with type 2 diabetes (AWARD-5): a randomized, phase III study. Diabetes Obes Metab. 2015; 17: 849-58.

4. Ross S, Thamer C, Cescutti J, Meinicke T, Woerle HJ and Broedl UC. Efficacy and safety of empagliflozin twice daily versus once daily in patients with type 2 diabetes inadequately controlled on metformin: a 16-week, randomized, placebo-controlled trial. Diabetes Obes Metab. 2015; 17: 699-702.

5. Schernthaner G, Duran-Garcia S, Hanefeld M, et al. Efficacy and tolerability of saxagliptin compared with glimepiride in elderly patients with type 2 diabetes: a randomized, controlled study (GENERATION). Diabetes Obes Metab. 2015; 17: 630-8.

6. Hansen L, Iqbal N, Ekholm E, Cook W and Hirshberg B. Postprandial dynamics of plasma glucose, insulin, and glucagon in patients with type 2 diabetes treated with saxagliptin plus dapagliflozin add-on to metformin therapy. EndocrPract. 2014; 20: 1187-97.

7. Anholm C, Kumarathurai P, Klit MS, et al. Adding liraglutide to the backbone therapy of biguanide in patients with coronary artery disease and newly diagnosed type-2 diabetes (the AddHope2 study): a randomised controlled study protocol. Bmj open. 2014; 4: e005942, 2014.

8. Moon JS, Ha KS, Yoon JS, et al. The effect of glargine versus glimepiride on pancreatic beta-cell function in patients with type 2 diabetes uncontrolled on metformin monotherapy: open-label, randomized, controlled study. Acta Diabetologica. 2014; 51: 277-85.

9. Grandy S, Langkilde AM, Sugg JE, Parikh S and Sjostrom CD. Health-related quality of life (EQ-5D) among type 2 diabetes mellitus patients treated with dapagliflozin over 2 years. Int J Clin Pract. 2014; 68: 486-94.

10. Gupta S, Khajuria V, Tandon VR, Mahajan A and Gillani ZH. Comparative evaluation of efficacy and safety of combination of metformin-vidagliptin versus metfromin-glimepiride in most frequently used doses in patients of type 2 diabetes mellitus with inadequately controlled metformin monotherapy-A randomised open label study. Perspect Clin Res. 2015; 6: 163-8.

11. Hissa MR, Cavalcante LL, Guimaraes SB and Hissa MN. A 16-week study to compare the effect of vildagliptin versus gliclazide on postprandial lipoprotein concentrations and oxidative stress in patients with type 2 diabetes inadequately controlled with metformin monotherapy. Diabetol Metab Syndr. 2015; 7:62, 2015.

12. Inagaki N, Kondo K, Yoshinari T and Kuki H. Efficacy and safety of canagliflozin alone or as add-on to other oral antihyperglycemic drugs in Japanese patients with type 2 diabetes: A 52-week open-label study. JDiabetesInvestig. 2015; 6: 210-8.

13. Odawara M, Hamada I and Suzuki M. Efficacy and Safety of Vildagliptin as Add-on to Metformin in Japanese Patients with Type 2 Diabetes Mellitus. Diabetes Ther. 2014; 5: 169-81.

14. Chen PH, Tsai YT, Wang JS, et al. Post-meal beta-cell function predicts the efficacy of glycemic control in patients with type 2 diabetes inadequately controlled by metformin monotherapy after addition of glibenclamide or acarbose. Diabetol Metab Syndr. 2014; 6:68, 2014.

15. Kawamori R, Kaku K, Hanafusa T, Oikawa T, Kageyama S and Hotta N. Effect of combination therapy with repaglinide and metformin hydrochloride on glycemic control in Japanese patients with type 2 diabetes mellitus. JDiabetes Investig. 2014; 5: 72-9.

16. Mita T, Katakami N, Shiraiwa T, et al. Rationale, design, and baseline characteristics of a clinical trial for prevention of atherosclerosis in patients with insulin-treated type 2 diabetes mellitus using DPP-4 inhibitor: the Sitagliptin Preventive study of Intima-media thickness Evaluation (SPIKE). Diabetol Metab Syndr. 2014; 6: 35, 2014.

17. White JL, Buchanan P, Li J and Frederich R. A randomized controlled trial of the efficacy and safety of twice-daily saxagliptin plus metformin combination therapy in patients with type 2 diabetes and inadequate glycemic control on metformin monotherapy. BMC Endocr Disord. 2014; 14:17, 2014.

18. Kadowaki T, Tajima N, Odawara M, Nishii M, Taniguchi T and Ferreira JC. Addition of sitagliptin to ongoing metformin monotherapy improves glycemic control in Japanese patients with type 2 diabetes over 52 weeks. Journal of Diabetes Investigation. 2013; 4: 174-81.

19. Neutel JM, Zhao C and Karyekar CS. Adding Saxagliptin to Metformin Extended Release (XR) or Uptitration of Metformin XR: Efficacy on Daily Glucose Measures. Diabetes Ther. 2013; 4: 269-83.

20. Chawla S, Kaushik N, Singh NP, Ghosh RK and Saxena A. Effect of addition of either sitagliptin or pioglitazone in patients with uncontrolled type 2 diabetes mellitus on metformin: A randomized controlled trial. J Pharmacol Pharmacother. 2013; 4: 27-32.

21. Bergenstal RM, Forti A, Chiasson JL, Woloschak M, Boldrin M and Balena R. Efficacy and safety of taspoglutide versus sitagliptin for type 2 diabetes mellitus (T-emerge 4 trial). Diabetes Ther. 2012; 3: 13, 2012.

22. Cho YM, Koo BK, Son HY, et al. Effect of the combination of mitiglinide and metformin on glycemic control in patients with type 2 diabetes mellitus. JDiabetesInvestig. 2010; 1: 143-8.

23. Wang MM, Lin S, Chen YM, et al. Saxagliptin is similar in glycaemic variability more effective in metabolic control than acarbose in aged type 2 diabetes inadequately controlled with metformin. Diabetes Res Clin Pract. 2015; 108: e67-e70.

24. Jin SM, Park SW, Yoon KH, et al. Anagliptin and sitagliptin as add-ons to metformin for patients with type 2 diabetes: a 24-week, multicentre, randomized, double-blind, active-controlled, phase III clinical trial with a 28-week extension. Diabetes Obes Metab. 2015; 17: 511-5.

25. Xiao CC, Ren A, Yang J, et al. Effects of pioglitazone and glipizide on platelet function in patients with type 2 diabetes. European Review for Medical and Pharmacological Sciences. 2015; 19: 963-70.

26. Rosenstock J, Hansen L, Zee P, et al. Dual add-on therapy in type 2 diabetes poorly controlled with metformin monotherapy: a randomized double-blind trial of saxagliptin plus dapagliflozin addition versus single addition of saxagliptin or dapagliflozin to metformin. Diabetes Care. 2015; 38: 376-83.

27. Rosenstock J, Cefalu WT, Lapuerta P, et al. Greater dose-ranging effects on A1C levels than on glucosuria with LX4211, a dual inhibitor of SGLT1 and SGLT2, in patients with type 2 diabetes on metformin monotherapy. Diabetes Care. 2015; 38: 431-8.

28. Leiter LA, Yoon KH, Arias P, et al. Canagliflozin provides durable glycemic improvements and body weight reduction over 104 weeks versus glimepiride in patients with type 2 diabetes on metformin: a randomized, double-blind, phase 3 study. Diabetes Care. 2015; 38: 355-64.

29. Kim MK, Rhee EJ, Han KA, et al. Efficacy and safety of teneligliptin, a dipeptidyl peptidase-4 inhibitor, combined with metformin in Korean patients with type 2 diabetes mellitus: a 16-week, randomized, double-blind, placebo-controlled phase III trial. Diabetes Obes Metab. 2015; 17: 309-12.

30. Gallwitz B, Rosenstock J, Patel S, et al. Regardless of the degree of glycaemic control, linagliptin has lower hypoglycaemia risk than all doses of glimepiride, at all time points, over the course of a 2-year trial. Diabetes Obes Metab. 2015; 17: 276-84.

31. Kashiwagi A, Kazuta K, Goto K, Yoshida S, Ueyama E and Utsuno A. Ipragliflozin in combination with metformin for the treatment of Japanese patients with type 2 diabetes: ILLUMINATE, a randomized, double-blind, placebo-controlled study. Diabetes Obes Metab. 2015; 17: 304-8.

32. Aaboe K, Akram S, Deacon CF, Holst JJ, Madsbad S and Krarup T. Restoration of the insulinotropic effect of glucose-dependent insulinotropic polypeptide contributes to the antidiabetic effect of dipeptidyl peptidase-4 inhibitors. Diabetes Obes Metab. 2015; 17: 74-81.

33. Schumm-Draeger PM, Burgess L, Koranyi L, Hruba V, Hamer-Maansson JE and de Bruin TW. Twice-daily dapagliflozin co-administered with metformin in type 2 diabetes: a 16-week randomized, placebo-controlled clinical trial. Diabetes Obes Metab. 2015; 17: 42-51.

34. Ji L, Han P, Liu Y, et al. Canagliflozin in Asian patients with type 2 diabetes on metformin alone or metformin in combination with sulphonylurea. Diabetes Obes Metab. 2015; 17: 23-31.

35. Gurkan E, Tarkun I, Sahin T, Cetinarslan B and Canturk Z. Evaluation of exenatide versus insulin glargine for the impact on endothelial functions and cardiovascular risk markers. Diabetes Res Clin Pract. 2014; 106: 567-75.

36. Derosa G, Bonaventura A, Bianchi L, et al. Comparison of vildagliptin and glimepiride: effects on glycaemic control, fat tolerance and inflammatory markers in people with type 2 diabetes. Diabet Med. 2014; 31: 1515-23.

37. Del Prato S, Camisasca R, Wilson C and Fleck P. Durability of the efficacy and safety of alogliptin compared with glipizide in type 2 diabetes mellitus: a 2-year study. Diabetes Obes Metab. 2014; 16: 1239-46.

38. Nandy D, Johnson C, Basu R, et al. The effect of liraglutide on endothelial function in patients with type 2 diabetes. Diab Vasc Dis Res. 2014; 11: 419-30.

39. Forst T, Anastassiadis E, Diessel S, Loffler A and Pfutzner A. Effect of linagliptin compared with glimepiride on postprandial glucose metabolism, islet cell function and vascular function parameters in patients with type 2 diabetes mellitus receiving ongoing metformin treatment. Diabetes/Metabolism Research and Reviews. 2014; 30: 582-9.

40. Dungan KM, Povedano ST, Forst T, et al. Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial. Lancet. 2014; 384: 1349-57.

41. Ridderstrale M, Andersen KR, Zeller C, et al. Comparison of empagliflozin and glimepiride as add-on to metformin in patients with type 2 diabetes: a 104-week randomised, active-controlled, double-blind, phase 3 trial. Lancet Diabetes Endocrinol. 2014; 2: 691-700.

42. Bolinder J, Ljunggren O, Johansson L, et al. Dapagliflozin maintains glycaemic control while reducing weight and body fat mass over 2 years in patients with type 2 diabetes mellitus inadequately controlled on metformin. Diabetes Obes Metab. 2014; 16: 159-69.

43. Ohira M, Yamaguchi T, Saiki A, et al. Metformin reduces circulating malondialdehyde-modified low-density lipoprotein in type 2 diabetes mellitus. Clin Invest Med. 2014; 37: E243-E51.

44. Ahren B, Johnson SL, Stewart M, et al. HARMONY 3: 104-week randomized, double-blind, placebo- and active-controlled trial assessing the efficacy and safety of albiglutide compared with placebo, sitagliptin, and glimepiride in patients with type 2 diabetes taking metformin. Diabetes Care. 2014; 37: 2141-8.

45. Grandy S, Hashemi M, Langkilde AM, Parikh S and Sjostrom CD. Changes in weight loss-related quality of life among type 2 diabetes mellitus patients treated with dapagliflozin. Diabetes Obes Metab. 2014; 16: 645-50.

46. Derosa G, Bonaventura A, Bianchi L, et al. Vildagliptin compared to glimepiride on post-prandial lipemia and on insulin resistance in type 2 diabetic patients. Metabolism. 2014; 63: 957-67.

47. Diamant M, van GL, Guerci B, et al. Exenatide once weekly versus insulin glargine for type 2 diabetes (DURATION-3): 3-year results of an open-label randomised trial. Lancet Diabetes Endocrinol. 2014; 2: 464-73.

48. Haring HU, Merker L, Seewaldt-Becker E, et al. Empagliflozin as add-on to metformin in patients with type 2 diabetes: a 24-week, randomized, double-blind, placebo-controlled trial. Diabetes Care. 2014; 37: 1650-9.

49. Mintz ML and Minervini G. Saxagliptin versus glipizide as add-on therapy to metformin: assessment of hypoglycemia. Curr Med Res Opin. 2014; 30: 761-70.

50. Bolli GB, Munteanu M, Dotsenko S, et al. Efficacy and safety of lixisenatide once daily vs. placebo in people with Type 2 diabetes insufficiently controlled on metformin (GetGoal-F1). Diabet Med. 2014; 31: 176-84.

51. Berndt-Zipfel C, Michelson G, Dworak M, et al. Vildagliptin in addition to metformin improves retinal blood flow and erythrocyte deformability in patients with type 2 diabetes mellitus - results from an exploratory study. Cardiovascular Diabetology [electronic resource]. 2013; 12: 59.

52. Rosenstock J, Gross JL, Aguilar-Salinas C, et al. Long-term 4-year safety of saxagliptin in drug-naive and metformin-treated patients with Type 2 diabetes. Diabet Med. 2013; 30: 1472-6.

53. Ridderstrale M, Svaerd R, Zeller C, et al. Rationale, design and baseline characteristics of a 4-year (208-week) phase III trial of empagliflozin, an SGLT2 inhibitor, versus glimepiride as add-on to metformin in patients with type 2 diabetes mellitus with insufficient glycemic control. Cardiovascular Diabetology. 2013; 12: 129.

54. Liebl A, Davidson J, Mersebach H, Dykiel P, Tack CJ and Heise T. A novel insulin combination of insulin degludec and insulin aspart achieves a more stable overnight glucose profile than insulin glargine: results from continuous glucose monitoring in a proof-of-concept trial. J Diabetes Sci Technol. 2013; 7: 1328-36.

55. Engel SS, Seck TL, Golm GT, Meehan AG, Kaufman KD and Goldstein BJ. Assessment of AACE/ACE recommendations for initial dual antihyperglycemic therapy using the fixed-dose combination of sitagliptin and metformin versus metformin. EndocrPract. 2013; 19: 751-7.

56. Genovese S, Passaro A, Brunetti P, et al. Pioglitazone Randomised Italian Study on Metabolic Syndrome (PRISMA): effect of pioglitazone with metformin on HDL-C levels in Type 2 diabetic patients. J Endocrinol Invest. 2013; 36: 606-16.

57. Derosa G, Carbone A, D'Angelo A, et al. Variations in inflammatory biomarkers following the addition of sitagliptin in patients with type 2 diabetes not controlled with metformin. Intern Med. 2013; 52: 2179-87.

58. Rosenstock J, Raccah D, Koranyi L, et al. Efficacy and safety of lixisenatide once daily versus exenatide twice daily in type 2 diabetes inadequately controlled on metformin: a 24-week, randomized, open-label, active-controlled study (GetGoal-X). Diabetes Care. 2013; 36: 2945-51.

59. Kim HS, Shin JA, Lee SH, et al. A comparative study of the effects of a dipeptidyl peptidase-IV inhibitor and sulfonylurea on glucose variability in patients with type 2 diabetes with inadequate glycemic control on metformin. Diabetes Technol Ther. 2013; 15: 810-6.

60. Cefalu WT, Leiter LA, Yoon KH, et al. Efficacy and safety of canagliflozin versus glimepiride in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. Lancet. 2013; 382: 941-50.

61. Derosa G, Cicero AF, Franzetti IG, et al. Effects of exenatide and metformin in combination on some adipocytokine levels: a comparison with metformin monotherapy. Canadian Journal of Physiology and Pharmacology. 2013; 91: 724-32.

62. Henry RR, Rosenstock J, Logan DK, Alessi TR, Luskey K and Baron MA. Randomized trial of continuous subcutaneous delivery of exenatide by ITCA 650 versus twice-daily exenatide injections in metformin-treated type 2 diabetes. Diabetes Care. 2013; 36: 2559-65.

63. Ahren B, Leguizamo DA, Miossec P, Saubadu S and Aronson R. Efficacy and safety of lixisenatide once-daily morning or evening injections in type 2 diabetes inadequately controlled on metformin (GetGoal-M). Diabetes Care. 2013; 36: 2543-50.

64. Derosa G, Franzetti IG, Querci F, et al. Variation in inflammatory markers and glycemic parameters after 12 months of exenatide plus metformin treatment compared with metformin alone: a randomized placebo-controlled trial. Pharmacotherapy. 2013; 33: 817-26.

65. Nathan DM, Buse JB, Kahn SE, et al. Rationale and design of the glycemia reduction approaches in diabetes: a comparative effectiveness study (GRADE). Diabetes Care. 2013; 36: 2254-61.

66. Lapuerta P, Rosenstock J, Zambrowicz B, et al. Study design and rationale of a dose-ranging trial of LX4211, a dual inhibitor of SGLT1 and SGLT2, in type 2 diabetes inadequately controlled on metformin monotherapy. Clin Cardiol. 2013; 36: 367-71.

67. Kapitza C, Forst T, Coester HV, Poitiers F, Ruus P and Hincelin-Mery A. Pharmacodynamic characteristics of lixisenatide once daily versus liraglutide once daily in patients with type 2 diabetes insufficiently controlled on metformin. Diabetes Obes Metab. 2013; 15: 642-9.

68. Charbonnel B, Steinberg H, Eymard E, et al. Efficacy and safety over 26 weeks of an oral treatment strategy including sitagliptin compared with an injectable treatment strategy with liraglutide in patients with type 2 diabetes mellitus inadequately controlled on metformin: a randomised clinical trial. Diabetologia. 2013; 56: 1503-11.

69. Bader G, Geransar P and Schweizer A. Vildagliptin more effectively achieves a composite endpoint of HbA1c < 7.0% without hypoglycaemia and weight gain compared with glimepiride after 2 years of treatment. Diabetes Res Clin Pract. 2013; 100: e78-e81.

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Appendix 3: Research Question 2 — List of Included Studies (and Companion Publications)

1. Masmiquel L, Leiter LA, Vidal J, Bain S, Petrie J, Franek E, et al. LEADER 5: prevalence and cardiometabolic impact of obesity in cardiovascular high-risk patients with type 2 diabetes mellitus: baseline global data from the LEADER trial. Cardiovascular Diabetology [electronic resource]. 2016;15(1):29.

2. Cavender MA, Scirica BM, Raz I, Gabriel SP, McGuire DK, Leiter LA, et al. Cardiovascular Outcomes of Patients in SAVOR-TIMI 53 by Baseline Hemoglobin A1c. Am J Med. 2016;129(3):340-8.

3. Erdmann E, Harding S, Lam H, Perez A. Ten-year observational follow-up of PROactive: a randomized cardiovascular outcomes trial evaluating pioglitazone in type 2 diabetes. Diabetes Obes Metab. 2016;18(3):266-73.

4. Mosenzon O, Wei C, Davidson J, Scirica BM, Yanuv I, Rozenberg A, et al. Incidence of Fractures in Patients With Type 2 Diabetes in the SAVOR-TIMI 53 Trial. Diabetes Care. 2015;38(11):2142-50.

5. Fulcher G, Matthews DR, Perkovic V, de ZD, Mahaffey KW, Mathieu C, et al. Efficacy and safety of canagliflozin when used in conjunction with incretin-mimetic therapy in patients with type 2 diabetes. Diabetes Obes Metab. 2016;18(1):82-91.

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7. Haering HU, Merker L, Christiansen AV, Roux F, Salsali A, Kim G, et al. Empagliflozin as add-on to metformin plus sulphonylurea in patients with type 2 diabetes. Diabetes Res Clin Pract. 2015;110(1):82-90.

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10. Bethel MA, Green JB, Milton J, Tajar A, Engel SS, Califf RM, et al. Regional, age and sex differences in baseline characteristics of patients enrolled in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS). Diabetes Obes Metab. 2015;17(4):395-402.

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13. Pfeffer MA, Claggett B, Diaz R, Dickstein K, Gerstein HC, Kober LV, et al. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. N Engl J Med. 2015;373(23):2247-57.

14. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015;373(22):2117-28.

15. Leiter LA, Teoh H, Braunwald E, Mosenzon O, Cahn A, Kumar KM, et al. Efficacy and safety of saxagliptin in older participants in the SAVOR-TIMI 53 trial. Diabetes Care. 2015;38(6):1145-53.

16. Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, et al. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015;373(3):232-42.

17. Zannad F, Cannon CP, Cushman WC, Bakris GL, Menon V, Perez AT, et al. Heart failure and mortality outcomes in patients with type 2 diabetes taking alogliptin versus placebo in EXAMINE: a multicentre, randomised, double-blind trial. Lancet. 2015;385(9982):2067-76.

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23. Raz I, Bhatt DL, Hirshberg B, Mosenzon O, Scirica BM, Umez-Eronini A, et al. Incidence of pancreatitis and pancreatic cancer in a randomized controlled multicenter trial (SAVOR-TIMI 53) of the dipeptidyl peptidase-4 inhibitor saxagliptin. Diabetes Care. 2014;37(9):2435-41.

24. Zinman B, Inzucchi SE, Lachin JM, Wanner C, Ferrari R, Fitchett D, et al. Rationale, design, and baseline characteristics of a randomized, placebo-controlled cardiovascular outcome trial of empagliflozin (EMPA-REG OUTCOMETM). Cardiovascular Diabetology [electronic resource]. 2014;13:102.

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Appendix 4: Research Question 1 — Study Characteristics of Included Studies

Study Design and Interventions

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Nauck et al.	2014	United States, Canada, France, Germany, India, Republic of Korea, Mexico, Poland, Puerto Rico, Romania, Russian Federation, Spain, Taiwan	Parallel	≥ 6 weeks	1,098	104 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + DUL 0.75	MET ≥ 1,500 + DUL 1.5	
Ross et al.	2015	Europe, North America, Latin America	Parallel	≥ 12 weeks	983	16 weeks	MET 1,976+ PLA	MET 1,973 + EMP 5 b.i.d.	MET 1,984 + EMP 10 q.d.	MET 1,967 + EMP 12.5 b.i.d.	MET 1,909 + EMP 25 q.d.
Moon et al.	2014	Korea	Parallel	> 3 months	75	48 weeks	MET 1,425.5 + GLM 4.3	MET 1,365.1 + IGA 22.8 IU	NA		
Gupta et al.	2015	India	Parallel	4 months	90	12 weeks	MET 1,000 + GLM 4	MET 1,000 + VID 100	NA		
Hissa et al.	2015	Brazil	Parallel	≥ 3 months	36	16 weeks	MET 1,457 + GLL 86.8	MET 1,584 + VIL 100	NA		
Inagak et al.	2015	Japan	Parallel	NR	148	52 weeks	MET + CAN 100	MET + CAN 200	NA		
Odawara et al.	2014	Japan	Parallel	≥ 10 weeks	139	12 weeks	MET 750.0 + PLA	MET 753.6 + VIL 100	NA		
Chen et al.	2014	Taiwan	Parallel	8 weeks	55	16 weeks	MET 1,500 + GLY 15	MET 1,500 + ACA 300	NA		
Kawamori et al.	2014	Japan	Parallel	12 weeks	130	16 weeks	MET 1,500 + PLA	MET 1,500 + REP 1.5	NA		
White et al.	2014	US, Germany, Hungary, Puerto Rice	Parallel	At least 8 weeks	160	12 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SAX 5	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Kadowaki et al.	2013	Japan	Parallel	≥ 12 weeks	149	12 weeks	MET 500 to 750 + PLA	MET 500 to 750 + SIT 50	NA		
Neutel et al.	2013	US, Israel, Mexico, Argentina	Parallel	4 to 8 weeks	93	4 weeks	MET 2,000	MET 1,500 + SAX 5	NA		
Chawla et al.	2013	India	Parallel	1 month	52	16 weeks	MET 1,865.38 + SIT 100	MET 1,830 + PIO 30	NA		
Bergenstal et al.	2012	23 countries	Parallel	12 weeks	666	156 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + TAS 10 q.w.	MET ≥ 1,500 + TAS 10 to 20 q.w.	NA
Cho et al.	2010	Korea	Parallel	8 weeks	145	16 weeks	MET 1,500 + PLA	MET 1,500 + MIT 30	NA		
Wang et al.	2015	NR	Parallel	6 months	90	1 yr	MET + SAX 5	MET + ACA 150	NA		
Jin et al.	2015	Republic of Korea	Parallel	≥ 4 weeks	180	24 weeks	MET 1,500 to 2,000 + SIT 100	MET 1,500 to 2,000 + ANA 200	NA		
Xiao et al.	2015	China	Parallel	≥ 4 weeks	120	24 weeks	MET ≥ 1,500 + GLI 5 to 10	MET ≥ 1,500 + PIO 15 to 45	NA		
Rosenstock et al.	2015	Multi-centre	Parallel	8 weeks	534	24 weeks	MET 1,500 or 2,000 + SAX 5	MET 1,500 or 2,000 + DAP 10	NA		
Rosenstock et al.	2015	US	Parallel		299	12 weeks	MET + PLA	MET + SOT 75	MET + SOT 200	MET + SOT 400 q.d.	MET + SOT 200 b.i.d.
Kim et al.	2015	Korea	Parallel	≥ 8 weeks	204	16 weeks	MET 1,407 + PLA	MET 1,486 + TEN 20	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Kashiwagi et al.	2015	Japan	Parallel	6 weeks	169	24 weeks double-blind, up to 52 weeks with open-label extension	MET + PLA	MET + IPR 50	NA		
Aaboe et al.	2015	Denmark	Parallel	3 months	25	12 weeks	MET ≥ 1,000 + PLA	MET ≥ 1,000 + SIT 100	NA		
Schumm-Draeger et al.	2015	Europe, South Africa	Parallel	≥ 10 weeks	400	16 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + DAP 5	MET ≥ 1,500 + DAP 10 q.d.	MET ≥ 1,500 + DAP 5 b.i.d.	NA
Han et al.	2015	China, Malaysia, Vietnam,	Parallel	8 weeks	678	18 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + CAN 100	MET ≥ 1,500 + CAN 300	NA	
Gurkan et al.	2014	NR	Parallel	2 months	34	26 weeks	MET 2,000 + EXE 20 mcg	MET 2,000 + IGA	NA		
Del Prato et al.	2014	North and South America, Europe, Asia, South Africa, Australia, New Zealand	Parallel	4 weeks	2,639	104 weeks	MET 1,823.4 + GLI 5 to 20	MET 1,825.2 + ALO 12.5	MET 1,837.2 + ALO 25	NA	
Nandy et al.	2014	US	Parallel	3 months	49	12 weeks	MET + GLM 4	MET + PLA	MET + LIR 1.8	NA	
Forst et al.	2014	Germany	Parallel	NR	40	12 weeks	MET + GLM 1 to 4	MET + LIN 5	NA		
Dungan et al.	2014	US, Czech Republic, Hungary, Mexico, Slovakia, Puerto Rico, Poland, Spain, Romania, Germany	Parallel	3 months	599	26 weeks	MET 2,068 + LIR 0.6 to 1.8	MET 2,021 + DUL 1.5 q.w.	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Ridderstrale et al.	2014	Argentina, Austria, Canada, Colombia, Czech Republic, Finland, Hong Kong, India, Italy, Malaysia, Mexico, the Netherlands, Norway, Philippines, Portugal, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, UK, US	Parallel	12 weeks	1,549	104 weeks	MET ≥ 1,500 + GLM 1 to 4	MET ≥ 1,500 + EMP 25	NA		
Ohira et al.	2014	Japan	Parallel	NR	70	6 mo	MET 1,000	MET 500 + SIT 50	NA		
Ahren et al.	2014	United States, Albania, Germany, Hong Kong, Mexico, Peru, Philippines, Russian Federation, South Africa, Spain, United Kingdom	Parallel	3 months	1,049	104 weeks	MET ≥ 1,500 + GLM 2 to 4	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + ALB 30 q.w.	NA
Derosa et al.	2014	Italy	Parallel	≥ 1 month	167	6 months	MET + GLM 6	MET + VIL 100	NA		
Diamant et al.	2014	Multinational (72 sites)	Parallel	≥ 8 weeks	467	156 weeks (3 years)	MET 2,000 + EXE 2 q.w.	MET 2,000 + IGA	NA		
Haring et al.	2014	Canada, China, France, Germany, India, Korea, Mexico, Slovakia, Slovenia, Taiwan, Turkey, and US	Parallel	≥ 12 weeks	1,307	76 weeks (24 + 52 weeks extension)	MET ≥ 1,500 + PLA	MET ≥ 1,500 + EMP 10	MET ≥ 1,500 + EMP 25	NA	
Bolli et al.	2014	US, Brazil, Chile, Colombia, Estonia, Germany, Italy, Lithuania, Malaysia, Mexico, Philippines, Poland, Romania, Slovakia, Ukraine	Parallel	NR	482	≥ 76 weeks	MET 1,943 + PLA	MET 1,968 + LIX 20 mcg 1 STEP	MET2036 + LIX 20 mcg 2 STEP	NA	
Berndt-Zipfel et al.	2013	Germany	Parallel	NR	44	24 weeks	MET + GLM 0.5 to 4	MET + VIL 100	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Genovese et al.	2013	Italy	Parallel	3 months	213	24 weeks	MET2550 + PLA	MET2550 + PIO 30 to 45	NA		
Rosenstock et al.	2013	United States, Argentina, Austria, Brazil, Colombia, Denmark, Finland, Germany, Greece, Hungary, Italy, Netherlands, Norway, Poland, Puerto Rico, Russian Federation, Spain, Sweden	Parallel	NR	639	24 weeks, then 52-week safety extension	MET 2,058 + EXE 20 mcg	MET 2,020 + LIX 20 mcg	NA		
Kim et al.	2013	Korea	Parallel	≥ 2 months	34	4 weeks	MET ≥ 1,000 + GLM 2	MET ≥ 1,000 + SIT 100	NA		
Cefalu et al.	2013	United States, Argentina, Bulgaria, Canada, Costa Rica, Denmark, Finland, Germany, India, Israel, Korea, Republic of, Mexico, Norway, Philippines, Poland, Puerto Rico, Romania, Russian Federation, Slovakia, Ukraine	Parallel	≥ 10 weeks	1,452	104 weeks total; primary outcome: 52 weeks	MET + GLM 5.6	MET + CAN 100	MET + CAN 300	NA	
Derosa et al.	2013	Italy	Parallel	8 ± 2 months	171	12 months	MET 2,500 + PLA	MET 2,500 + EXE 20 mcg	NA		
Henry et al.	2013	US	Parallel	≥ 3 months	155	Period 1 only: 12-week “active-controlled period”	MET 1,236.8 + EXE 10 to 20 mcg	MET 1,403.9 + EXE 20 mcg	MET 1,470.6 + EXE 40 mcg		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Ahrén et al.	2013	Australia, Canada, Chile, Czech Republic, Germany, Croatia, Mexico, Morocco, the Philippines, Romania, Russian Federation, South Africa, Spain, Ukraine, US, and Venezuela	Parallel	NR	680	24 weeks	MET 2,001 + PLA	MET 1,969 + LIX 20 AM	MET 1,943 + LIX 20 PM	NA	
Kapitza et al.	2013	Germany	Parallel	≥ 2 weeks	148	28 days	MET ≥ 1,500 + LIR 0.6 to 1.8	MET ≥ 1,500 + LIX 10 to 20 mcg	NA		
Charbonnel et al.	2013	21 countries	Parallel	≥ 12 weeks	653	12 weeks in phase 1 and 14 weeks in phase 2, total 26 weeks	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + LIR 1.2	NA		
Forst et al.	2013	Germany	Parallel	≥ 3 months	44	24 weeks	MET 2,000 + GLM 1 to 4	MET 2,000 + VIL 100	NA		
Rhee et al.	2013	Korea, India	Parallel	4 weeks	425	24 weeks	MET ≥ 1,000 + SIT 100	MET ≥ 1,000 + GEM 50 q.d.	MET ≥ 1,000 + GEM 25 b.i.d.	NA	
Wilding et al.	2012	Hungary, Poland, Romania, UK, Italy, US	Parallel	≥ 6 weeks	343	12 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + IPR 12.5	MET ≥ 1,500 + IPR 50	MET ≥ 1,500 + IPR 150	MET ≥ 1,500 + IPR 300
Derosa et al.	2012	Italy	Parallel	8 ± 2 months	167	12 months	MET 2,500 + PLA	MET 2,500 + VIL 100	NA		
Hermans et al.	2012	Belgium, France, Germany, Italy, Spain, Turkey, UK	Parallel	4 weeks	286	24 weeks	MET 2,000 or 2,500	MET 1,500 + SAX 5	NA		
Derosa et al.	2012	Italy	Parallel	8 months	178	12 months	MET 2,500 + PLA	MET 2,500 + SIT 100	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Guerci et al.	2012	NR	Parallel	3 months	38	8 weeks	MET 2,113 + SIT 100	MET 2,115 + VIL 100	NA		
Monnier et al.	2012	France	Parallel	≥ 12 weeks	21	12 weeks	MET 2,000 + GLM 1 to 4	MET 2,000 + ROS 4 to 8	NA		
Rizzo et al.	2012	Italy	Parallel	8 weeks	90	12 weeks	MET 2,000 + SIT 100	MET 2,000 + VIL 100	NA		
Seino et al.	2012	Japan	Parallel	12 weeks	288	12 weeks double-blind, with 40 weeks open-label extension for AEs	MET 500 or 750 + PLA	MET 500 or 750 + ALO 12.5	MET 500 or 750 + ALO 25	NA	
Yang et al.	2012	NR	Parallel	10 weeks	395	24 weeks	MET 1,000or 1,700 + PLA	MET 1,000 or 1,700 + SIT 100	NA		
Gallwitz et al.	2012	Bulgaria, Denmark, France, Germany, Hong Kong, Hungary, India, Ireland, Italy, Netherlands, Norway, Poland, South Africa, Sweden, UK, US	Parallel	NR	1,552	104 weeks	MET + GLM	MET + LIN 5	NA		
Srivastava et al.	2012	India	Parallel	≥ 3 months	50	18 weeks	MET + GLM 1 to 4	MET + SIT 50 to 200	NA		
Koren et al.	2012	Isreal	Crossover	NR	40	28	MET + GLY 5	MET + SIT 100	NA		
Pan et al.	2012	China	Parallel	≥ 4 weeks	438	24 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + VIL 50	MET ≥ 1,500 + VIL 100	NA	
Gallwitz et al.	2012	Austria, Czech Republic, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Mexico, Poland, Spain, Switzerland, and the UK	Parallel	NR	1,029	Time to treatment failure or 3 years	MET 1,989 + GLM ≥ 1	MET 1,956 + EXE 10 or 20 mcg	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Aschner et al.	2012	Austria, Brazil, Colombia, Egypt, Greece, Hong Kong, India, Israel, Korea, Lebanon, Mexico, Netherlands, Portugal, Spain, Turkey, UK, US	Parallel	NR	515	6 months	MET 1,835 + SIT 100	MET 1,852 + IGA	NA		
Rosenstock et al.	2012	Argentina, Bulgaria, Canada, Czech Republic, India, Malaysia, Mexico, Poland, Romania, Russia, UK, US	Parallel	3 months	451	12 weeks	MET 1,919 + PLA	MET 1,885 + SIT 100	MET 1,870 + CAN 50	MET 1,903 + CAN 100	MET 1,904 + CAN 200
DeFronzo et al.	2012	United States, Australia, Brazil, Bulgaria, Chile, Croatia, Estonia, Guatemala, India, Israel, Latvia, Mexico, New Zealand, Peru, Romania, Russian Federation, Serbia, South Africa, Ukraine	Parallel	≥ 2 months	1,554	26 weeks	MET 1,937 + PLA	MET 1,902 + ALO 12.5	MET 1,851 + ALO 25	MET 1,893 + PIO 15	MET 1,854 + PIO 30
Bolinder et al.	2012	Bulgaria, Czech Republic, Hungary, Poland, Sweden	Parallel	≥ 12 weeks	182	24 weeks (primary outcome), 102 weeks (extension phase)	MET 1,901 + PLA	MET 1,989 + DAP10	NA		
Fonseca et al.	2012	US, Latin America	Parallel	8 weeks	282	18 weeks	MET 2,000	MET 1,500 + SAX 5	NA		
Wang et al.	2011	Taiwan	Parallel	8 weeks	55	16 weeks	MET 1,500 + GLY	MET 1,500 + ACA	NA		
Yang et al.	2011	China, India and South Korea	Parallel	8 weeks	570	24 weeks	MET 1,606 + PLA	MET 1,620 + SAX 5	NA		
Stephens et al.	2011	UK	Parallel	NR	25	8 weeks	MET 1,500 to 3,000 + GLY 2.5	MET 1,500 to 3,000 + REP 3	NA		
Petrica et al.	2011	Romania	Parallel	≥ 6 months	78	12 months	MET 1,700 + GLM4	MET 1,700 + PIO 30	NA		
Lin et al.	2011	Taiwan	Parallel	At least 8 weeks	51	16 weeks	MET 1,500 + GLY 15	MET 1,500 + ACA 300	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Terra et al.	2011	Colombia, Germany, Italy, Spain, Sweden, US	Parallel	2 months	302	12 weeks	MET + PLA	MET + GOS 2	MET + GOS 5	MET + GOS 10	MET + GOS 20
Derosa et al.	2011	Italy	Parallel	NR	111	12 months	MET 1,000 to 2,000 + GLM 3 to 6	MET 1,000 to 2,000 + EXE 10 to 20 mcg	NA		
Derosa et al.	2011	Italy	Parallel	NR	201	12 months	MET + GLY 15	MET + PIO 45	NA		
Pfutzner et al.	2011	Germany	Parallel	NR	305	24 weeks	MET 1,700 + GLM 2	MET 1,700 + PIO 30	NA		
Zinman et al.	2011	Canada, India, South Africa, US	Parallel	1 week (metformin maintenance period)	245	16 weeks	MET 2,000 + IGA	MET 2,000 + IND 3.1 q.d.	MET 2,000 + IND 4.5 q.d.	MET 2,000 + IND 3.4 Three times a week	NA
Heise et al.	2011	France, Germany, Norway, Romania, Spain	Parallel	1 week	178	16 weeks	MET 1,500or 2,000 + IGA	MET 1,500 or 2,000 + DSP 70/30	MET 1,500 or 2,000 + DSP 55/45	NA	
Gallwitz et al.	2011	Germany	Parallel	NR	363	26 weeks	MET + EXE 20 mcg	MET + IAM 28.4	NA		
Arechavaleta et al.	2011	Austria, Brazil, Chile, Colombia, Costa Rica, Denmark, Ecuador, France, Germany, Guatemala, India, Italy, Korea, Republic of, Malaysia, Mexico, New Zealand, Panama, Peru, Poland, Spain, Switzerland, United Kingdom	Parallel	12 weeks	1035	30 weeks	MET ≥ 1,500 + GLM 1 to 6	MET ≥ 1,500 + SIT 100	NA		
Yang et al.	2011	China, South Korea and India	Parallel	≥ 6 week metformin run-in and maintenance period	929	16 weeks	MET 2,000 + GLM 4	MET 2,000 + LIR 0.6	MET 2,000 + LIR 1.2	MET 2,000 + LIR 1.8	NA

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Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Taskinen et al.	2011	Czech Republic, Finland, Greece, India, Israel, Mexico, New Zealand, Russia, Sweden, US	Parallel	12 weeks	701	24 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + LIN 5	NA		
Forst et al.	2010	UK, Germany, France, Slovakia, Ukraine, Sweden	Parallel	NR	333	12 weeks	MET + GLM	MET + PLA	MET + LIN1	MET + LIN 5	MET + LIN 10
Goke et al.	2010	International	Parallel	8 weeks	858	52 weeks	MET 1,500 to 3,000 + GLI 5 to 20	MET 1,500 to 3,000 + SAX 5	NA		
Scheen et al.	2010	Argentina, Belgium, Denmark, France, Italy, Mexico, Norway, South Africa, Sweden	Parallel	8 weeks	801	18 weeks	MET 1,831.5 + SAX 5	MET 1,826.2 + SIT 100	NA		
Stenlof et al.	2010	United States, Israel, Sweden, Mexico, Puerto Rico, Argentina, Italy, and the Philippines	Parallel	≥ 8 weeks before enrolment and a 4-week MET XR lead-in period before randomization	93	4 weeks	MET 1,500 to 2,000 + PLA	MET 1,500 to 2,000 + SAX 5	NA		
Ratner et al.	2010	Brazil, Canada, Poland, Romania, Russian, Ukraine, and US	Parallel	At least 3 months prior to enrolment	542	13 weeks	MET ≥ 1,000 + PLA	MET ≥ 1,000 + LIX 5 mcg q.d.	MET ≥ 1,000 + LIX 5 mcg b.i.d.	MET ≥ 1,000 + LIX 10 mcg q.d.	MET ≥ 1,00 0 + LIX 10 mcg b.i.d.
Bergenstal et al.	2010	United States, India, Mexico	Parallel	2 months	514	26 weeks	MET 1,583 + SIT 100	MET 1,504 + EXE 2 q.w.	MET 1,480 + PIO 45	NA	
Bailey et al.	2010	United States, Canada, Argentina, Mexico, Brazil	Parallel	8 weeks	546	102 weeks (24 weeks with 78 weeks extension)	MET 1,861 + PLA	MET 1,792 + DAP 2.5	MET 1,854 + DAP 5	MET 1,800 + DAP 10	NA
Filozof et al.	2010	NR	Parallel	4 weeks	1,007	52 weeks	MET ≥ 1,500 + GLL	MET ≥ 1,500 + VIL 100	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
DeFronzo et al.	2010	US	Parallel	6 weeks	141	20 weeks	MET + EXE 20 mcg	MET + ROS 4 to 8	NA		
Pratley et al.	2010	Croatia, Germany, Ireland, Italy, Netherlands, Romania, Serbia, Slovakia, Slovenia, Spain, UK, US, Canada	Parallel	≥ 3 months	665	52 weeks	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + LIR 1.2	MET ≥ 1,500 + LIR 1.8	NA	
Apovian et al.	2010	US	Parallel	6 weeks	196	24 weeks	MET + PLA	MET + EXE 10 to 20 mcg	MET + SUL + PLA	MET + SUL + EXE10 to 20 mcg	NA
Kadoglou et al.	2010	NR	Parallel	4 months	97	14 weeks	MET2550	MET 850 + ROS 8	NA		
Petrica et al.	2009	NR	Parallel	6 months	44	12 months	MET 1,700 + GLM4	MET 1,700 + ROS4	NA		
Scheen et al.	2009	Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Italy, Latvia, Lithuania, Netherlands, Norway, Poland, Slovakia, Sweden, Switzerland, United Kingdom	Parallel	NR	NR	Up to 48 months	MET 1,721 + PLA	MET 1,687 + PIO 15 to 45	NA		
Blonde et al.	2009	US	Parallel	≥ 4 weeks	2664	12 weeks	MET ≥ 1,000 + VIL 100	MET ≥ 1,000 + TZD	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Defronzo et al.	2009	US, Brazil	Parallel	≥ 8 weeks	745	24 weeks; rescued patients (hypoglycemia) and completers were eligible to continue 42-month long-term phase	MET 1,500 to 2,500 + PBO	MET 1,500 to 2,500 + SAX 2.5	MET 1,500 to 2,500 + SAX 5	MET 1,500 to 2,500 + SAX 10	NA
Home et al.	2007	23 countries in Europe, Australia and New Zealand	Parallel	≥ 8 weeks	524	18 months	MET ≤ 2,550 + SUL	MET ≤ 2,550 + ROS 4 to 8	NA		
Papathanassiou et al.	2009	Greece	Parallel	NR	28	6 months	MET + GLM 4	MET + PIO 30	NA		
Goodman et al.	2009	Multinational	Parallel	≥ 3 months	370	24 weeks (6 months)	MET ≥ 1,500 + PLA	MET≥ 1,500 + VIL am 100	MET ≥ 1,500 + VIL pm 100	MET ≥ 1,500 + VIL total 100	NA
Bunck et al.	2009	Sweden, Finland, and the Netherlands	Parallel	≥ 2 months	69	156 weeks	MET 2,058 + EXE 10 to 60 mcg	MET 1,798 + IGA 33.6	NA		
Kaku et al.	2009	NR	Parallel	NR (12 weeks observation period before randomization)	169	28 weeks	MET 500 or 750 + PLA	MET 500 or 750 + PIO	NA		
Nauck et al.	2008	Multinational ("115 sites in 15 countries")	Parallel	≥ 3 months	524	26 weeks	MET 1,847 + PLA	MET 1,847 + ALO 12.5	MET 1,847 + ALO 25	NA	
Ferrannini et al.	2009	Canada, US, Europe, and multinational	Parallel	≥ 4 weeks	2,789	2 years	MET 1,893 + GLM 4.5	MET 11,904 + VIL 100	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Gao et al.	2009	China, India, Korea, Taiwan	Parallel	3 months	472	16 weeks	MET 1,000 to 3,000 + PLA (Note: MET + SU + PLA also mixed in. See comments)	MET 1,000 to 3,000 + EXE 10 to 20 mcg	NA		
Nauck et al.	2009	Argentina, Australia, Belgium, Bulgaria, Croatia, Denmark, Germany, Hungary, India, Ireland, Italy, Netherlands, New Zealand, Norway, Romania, Russian Federation, Slovakia, South Africa, Spain, Sweden, United Kingdom	Parallel		385	26 weeks	MET 1,500 to 2,000 + PLA	MET 1,500 to 2,000 + GLM4	MET 1,500 to 2,000 + LIR 0.6	MET 1,500 to 2,000 + LIR 1.2	MET 1,500 to 2,000 + LIR 1.8
Scott et al.	2008	Multinational	Parallel	10 weeks	273	18 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + ROS 8	NA	
Komajda et al.	2008	23 countries in Europe and Australasia	Parallel	NR	926	12 months	MET ≤ 2,550 + SUL	MET ≤ 2,550 + ROS 4 to 8	NA		
Khanolkar et al.	2008	United Kingdom	Parallel	≥ 4 weeks	50	24 weeks	MET 2,000 + GLC 80	MET 2,000 + ROS 4	NA		
Garcia-Soria et al.	2008	US, Mexico, Australia	Parallel	4 weeks	174	4 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + DUT 100	MET ≥ 1,500 + DUT 200	MET ≥ 1,500 + DUT 400	NA
Raz et al.	2008	Austria, Israel, Mexico, Peru and United States	Parallel	NR or 6-week run-in	190	30 weeks	MET 1,500 to 2,550 + PLA	MET 1,500 to 2,550 + SIT 100	NA		
Hamann et al.	2008	Multinational (Europe and Mexico)	Parallel	8 weeks	596	52 weeks	MET 2,000 + SUL	MET 2,000 + ROS 4	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Bolli et al.	2008	Germany, UK, US, Spain, Italy, Switzerland, Austria, South Africa and Australia	Parallel	NR	576	52 weeks (24 weeks + 28 weeks extension)	MET ≥ 1,500 + VIL 100	MET ≥ 1,500 + PIO 30	NA		
Bosi et al.	2007	US, France, Italy, Sweden	Parallel	4 weeks	544	24 weeks	MET 2,102 + PLA	MET 2,126 + VIL 50	MET 2,126 + VIL 100	NA	
Nauck et al.	2007	NR	Parallel	NR or 8 weeks	1172	52 weeks	MET ≥ 1,500 + GLI 10.6	MET ≥ 1,500 + SIT 100	NA		
Brazg et al.	2007	NR	Crossover	≥ 6 weeks	28	4 weeks × 2	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SIT 100	NA		
Derosa et al.	2007	Italy	Parallel	NR	103	12 months	MET 2,250 + ROS 4	MET 2,250 + PIO 15	NA		
Charbonnel et al.	2006	France, Israel, US	Parallel	Up to 19 weeks	464	24 weeks	MET > 1,500 + PLA	MET > 1,500 + SIT 100	NA		
Nauck et al.	2006	Europe and Austrlia	Parallel	2 weeks	144	5 weeks	MET 2,000 + PLA	MET 2,000 + GLM 3.75	MET 2,000 + LIR 1.96	NA	
Weissman et al.	2005	US	Parallel	4 to 7 weeks	766	24 weeks	MET 2,000	MET 1,000 + ROS 8			
Bakris et al.	2006	North America, South America and Europe	Parallel	NR	389	32 weeks	MET 1,986 + GLY 13.7	MET 1,958 + ROS 7.2	NA		
Ristic et al.	2006	Canada, France, Italy, Spain, Austria	Parallel	≥ 2 months	262	1 year	MET 1,812 + GLC 80 to 240	MET 1,921 + NAT 180 to 540	NA		
Umpierrez et al.	2006	US	Parallel	2 months	210	26 weeks	MET 1,470 to 1,490 + GLM 2 to 8	MET 1,540 to 1,570 + PIO 30 to 45	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Garber et al.	2006	US	Parallel	≥ 8 weeks	318	24 weeks	MET 1,509 + GLY 7.6 (combination tablet)	MET 1,819 + ROS 7.1	NA		
Kvapil et al.	2006	Croatia, Czech Republic, Denmark, France, Greece, Hungary, Norway, Poland, Portugal, Russia, Spain		≥ 1 month			MET 1,660 + GLY 1.75 to 10.75	MET 1,660 + IAS	NA		
Poon et al.	2005	US	Parallel	≥ 3 months	156	28 days	MET + PBO	MET + EXE 5 mcg	MET + EXE 10 mcg	MET + EXE 15 mcg	MET + EXE 20 mcg
Feinglos et al.	2005	United States	Parallel	≥ 3 months	122	16 weeks	MET 1,509 + GLI 2.5	MET 1,513 + PLA	NA		
DeFronzo et al.	2005	United States	Parallel	3 months	336	30 weeks	MET + PLA	MET + EXE 10 mcg	MET + EXE 20 mcg	NA	
Matthews et al.	2005	Multinational	Parallel	NR	630	52 weeks (ID #6199) and 2 years (ID #6104)	MET + GLC 212	MET + PIO 39	NA		
Ahrén et al.	2004	Sweden, Spain, Germany and Switzerland	Parallel	≥ 3 months	107	52 weeks	MET 1,500 to 3,000 + PLA	MET 1,500 to 3,000 + VIL 50	NA		
Schernthaner et al.	2004	10 European countries	Parallel	≥ 3 months	845	27 weeks	MET + GLM 2.9	MET + GLL 76.2	NA		
Raskin et al.	2003	US	Parallel	NR	192	16 weeks	MET 2,000 + REP 3 to 12	MET 2,000 + NAT 180 to 360	NA		
Phillips et al.	2003	Australia and New Zealand	Parallel	4-weeks	83	24 weeks	MET 1,700 + PLA	MET 1,700 + ACA 100 or 200	NA		
Marre et al.	2002	Multinational	Parallel	2 weeks	411	16 weeks	MET 1,650	MET 1,250 + GLY 6.25	MET 1,150 + GLY 11.5		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Marre et al.	2002	Multinational	Parallel	≥ 4 weeks	467	24 weeks	MET 2,000 + PLA	MET 2,000 + NAT 180	MET 2,000 + NAT 360	NA	
Gomez-Perez et al.	2002	Mexico	Parallel	NR	116	6 months	MET 2,500 + PLA	MET 2,500 + ROS 4	MET 2,500 + ROS 8	NA	
Van Gaal et al.	2001	Belgium, Israel, Astria, Czech	Parallel	≥ 3 months	153	32 weeks	MET 1,500 or 1,700 or 2,550 + PLA	MET 1,500 or 1,700 or 2,550 + MIG 75 to 300	NA		
Charpentier et al.	2001	France	Parallel	≥ 4 weeks	379	5 months	MET 2,550 + GLM 1 to 6	MET 2,550 + PLA	NA		
Halimi et al.	2000	France	Parallel	850 mg/day for at least 2 months	152	6 months	MET 1,700 or 2,550 + PLA	MET 1,700 or 2,550 + ACA 150 or 300	NA		
Einhorn et al.	2000	US	Parallel	≥ 30 days	328	16 weeks	MET + PLA	MET + PIO 30	NA		
Fonseca et al.	2000	US	Parallel	MET maintenance period phase: for at least 4 weeks (2,500 mg/d)	348	26 weeks	MET 2,500 + PLA	MET 2,500 + ROS 4	MET 2,500 + ROS 8	NA	
Moses	1999	Australia	Parallel	4 to 5 weeks	83	4 to 5 months	MET 1,000 to 3,000 + PLA	MET 1,000 to 3,000 + REP 1.5 to 12	PLA + REP 1.5 to 12	NA	
Rosenstock et al.	1998	US	Parallel	56 days	84	24 weeks	MET 2,000 to 2,500 + PLA	MET 2,000 to 2,500 + ACA 150 to 300	NA		
Wolever et al.	1997	Canada	Parallel	NR	83	12 months	MET + PLA	MET + ACA 150 to 600	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Strozik et al.	2015	Poland	Parallel	≥ 3 months	61	12 weeks	MET 1,500	MET 3,000	MET 1,500 + VIL 100	MET 3,000 + VIL 100	NA
Qiu et al.	2014	Canada, Czech Republic, Mexico, Romania, Russia, Slovakia, US	Parallel	≥ 8 weeks	279	18 weeks	MET 2,131 + PLA	MET 2,137 + CAN 100	MET 2,128 + CAN 300	NA	
Gaal et al.	2014	United States, Australia, Brazil, Canada, Chile, Germany, Guatemala, Mexico, Peru, Poland, Romania, Russian Federation, Ukraine	Parallel	≥ 3 months	319	24 weeks	MET 1,937 + SIT 100	MET 1,985 + LIX 20 mcg	NA		
Bhandare et al.	2013	India	Parallel	≥ 2 months	73	12 weeks	MET 2,000	MET 1,000 + VIL 100	NA		
Raskin	2007	US	Parallel	≥ 3 months	157	28 weeks	MET 1,500 to 2,550 + IAS 80	MET 1,500 to 2,550 + IGA 49	NA		
Leiter	2005	Canada	Parallel	≥ 3 months	236	32 weeks	MET 1,500 to 2,000	MET 1,500 + ROS 4 to 8	NA		
Kilo et al.	2003	US	Parallel	4 weeks	140	12 weeks	MET 2,200 + NIN	MET 2,200 + IAM	MET 2,200 + NIR	NA	
Ohira et al.	2014	Japan	Parallel	NR	60	6 months	MET 500 + GLM 1	MET 500 + PIO 15	NA		
Yang et al.	2015	China, India, South Korea	Parallel	≥ 8 weeks	445	24 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + DAP 5	MET ≥ 1,500 + DAP 10	NA	
Merck Sharp & Dohme Corp.	2015	Argentina, Canada, Croatia, Estonia, Georgia, Hungary, Israel, Malaysia, Philippines, Poland, Romania, South Africa, US	Parallel	12 weeks	642	24 weeks	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + OMA 25 q.w.	NA		

Author	Year	Country	Design	Duration of Stable Background Therapy	Number Random-ized	Treatment Duration	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Daiichi Sankyo Inc.	2009	Colombia, Mexico, US	Parallel	NR	169	16 weeks	MET + SIT 100	MET + ROS 4	NA		
Merck Sharp & Dohme Corp.	2012	Croatia, Germany, Hungary, South Korea, Lebanon, Lithuania, Malaysia, Poland, Romania, US	Parallel	12 weeks	751	54 weeks	MET ≥ 1,500 + GLM 1 to 6	MET ≥ 1,500 + OMA 25 q.w.	NA		
NCT record	2010 (last updated)	"Not provided", France is listed as a "Removed Location Countries"	Parallel	NR	84	36 months	MET 2,000 + GLC 80 to 320	MET 2,000 + ROS 4 to 8	NA		
NCT record	2015 last update	Republic of Korea	Parallel	NR	228	16 weeks	MET + VIL 100	MET + PIO 30	NA		
NCT record	2015 (last update)	EUROPE: Czech Republic, Finland, France, Germany, Hungary, Italy, Latvia, Lithuania, United Kingdom	Parallel	≥ 90 days	404	26 weeks	MET 1,000 to 3,000 + LIR 1.8	MET 1,000 to 3,000 + 20 mcg	NA		
NCT record	2016 (last update)	China, Beijing	Parallel	60 days	368	26 weeks	MET > 1,000 + SIT 100	MET > 1,000 + LIR 1.8	NA		
Lavalle-Gonzalez et al.	2013	Argentina, Bulgaria, Colombia, Czech Republic, Estonia, Greece, India, Italy, Latvia, Malaysia, Mexico, Peru, Poland, Portugal, Russia, Singapore, Slovakia, Sweden, Thailand, Turkey, Ukraine, US	Parallel	8 weeks	1,284	52 weeks	MET ≥ 1,500 + PLA	MET ≥ 1,500 + SIT 100	MET ≥ 1,500 + CAN 100	MET ≥ 1,500 + CAN 300	NA
Chen et al.	NA	China	Parallel	≥ 12 weeks	120	12 weeks	MET 1,500 + PLA	MET 1,500 + PGL 0.1	MET 1,500 + PGL 0.2	NA	

ACA = acarbose; AE = adverse event; ALB = albiglutide; ALO = alogliptin; b.i.d. = twice daily; CAN = canagliflozin; DAP = dapagliflozin; DSP = insulin degludec/insulin aspart mix; DUL = dulaglutide; DUT = dutaglutide (PHX1149); EMP = empagliflozin; EXE = exenatide; IAM = insulin aspart/aspart protamine mixture; IAS = insulin aspart; IGA = insulin insulin glargine; IPR = ipragliflozin; GLC = glicazide / glicazide MR; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; GLY = glyburide; LIN = linagliptin; LIR = liraglutide; MET = metformin; MIT = mitiglinide; LIX = lixisenatide; NA = not applicable; NAT = nateglinide; NIN = neutral protamine Hagedorn insulin; NR = not reported; OMA = omarigliptin; PIO = pioglitazone; PLA = placebo; PGL = polyethylene glycol loxenatide; q.d. = daily; q.w. = every week; REP = repaglinide; ROS = rosiglitazone; SAX = saxagliptin; SIT = sitagliptin; SOT = sotagliflozin; SU = sulfonylurea; TAS = taspoglutide; TEN = tenegliptan; VIL = vildagliptin; XR = extended release.

Note: All doses are given in milligrams, unless otherwise indicated.

Funding Information

Author	Year	Registration Number	Country	Sponsor
Nauck et al.	2014	NCT00734474	United States, Canada, France, Germany, India, Republic of Korea, Mexico, Poland, Puerto Rico, Romania, Russian Federation, Spain, Taiwan	Eli Lilly and Company
Ross et al.	2015	EudraCT number 2012–000905-53	Europe, North America, Latin America	Boehringer Ingelheim and Eli Lilly and Company
Moon et al.	2014	NCT00562172	Korea	NR
Gupta et al.	2015	NR	India	NR
Hissa et al.	2015	NR	Brazil	Novartis
Inagak et al.	2015	NCT01387737	Japan	Mitsubishi Tanabe Pharma Corporation
Odawara et al.	2014	NCT01497522	Japan	Novartis Pharma K.K
Chen et al.	2014	NCT00417729	Taiwan	Taichung Veterans General Hospital, Taichung, Taiwan and Bayer Schering Pharma, Taiwan Branch.
Kawamori et al.	2014	JapicCTI-101202 and JapicCTI-101203	Japan	Dainippon Sumitomo Pharma Co., Ltd.
White et al.	2014	NCT00885378	US, Germany, Hungary, Puerto Rico	Bristol-Myers Squibb and AstraZeneca
Kadowaki et al.	2013	NCT00363948	Japan	Ono Pharmaceutical Co. Ltd
Neutel et al.	2013	NCT00918138	US, Israel, Mexico, Argentina	Bristol-Myers Squibb and AstraZeneca
Chawla et al.	2013	NR	India	NR
Bergenstal et al.	2012	NCT00754988	23 countries	NR
Cho et al.	2010	NCT01037842	Korea	Choongwae Pharma Corporation, Korea
Wang et al.	2015	NR	NR	NR
Jin et al.	2015	NCT01529541	Republic of Korea	JW Pharmaceutical
Xiao et al.	2015	NR	China	The National Science Foundation of Anhui Province
Rosenstock et al.	2015	NCT01606007	Multi-centre	Bristol-Myers Squibb and AstraZeneca
Rosenstock et al.	2015	NCT01376557	US	Lexicon Pharmaceuticals
Kim et al.	2015	NCT01805830	Korea	Handok Inc., Seoul, Republic of Korea
Kashiwagi et al.	2015	NCT01135433	Japan	Astellas Pharma Inc.

Author	Year	Registration Number	Country	Sponsor
Aaboe et al.	2015	NCT00411411	Denmark	Merck & Co., Inc.
Schumm-Draege et al.r	2015	NCT01217892	Europe, South Africa	Bristol-Myers Squibb and AstraZeneca
Han et al.	2015	NCT01381900	China, Malaysia, Vietnam,	Janssen Research & Development, LLC
Gurkan et al.	2014	NR	NR	NR
Del Prato et al.	2014	NCT00856284	North and South America, Europe, Asia, South Africa, Australia, New Zealand	Takeda Developmnet Center Americas, Inc.
Nandy et al.	2014	NCT00620282	US	
Forst et al.	2014	NCT01547104	Germany	Marcus Borchert
Dungan et al.	2014	NCT01624259	US, Czech Republic, Hungary, Mexico, Slovakia, Puerto Rico, Poland, Spain, Romania, Germany	Eli Lilly and Company
Ridderstrale et al.	2014	NCT01167881	Argentina, Austria, Canada, Colombia, Czech Republic, Finland, Hong Kong, India, Italy, Malaysia, Mexico, the Netherlands, Norway, Philippines, Portugal, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, UK, US	Boehringer Ingelheim and Eli Lilly
Ohira et al.	2014	NR	Japan	NR
Ahren et al.	2014	NCT00838903	United States, Albania, Germany, Hong Kong, Mexico, Peru, Philippines, Russian Federation, South Africa, Spain, United Kingdom	GlaxoSmithKline
Derosa et al.	2014	NR	Italy	NR
Diamant et al.	2014	NCT00641056	Multinational (72 sites)	Amylin Pharmaceuticals and Eli Lilly
Haring et al.	2014	NCT01159600, NCT01289990 (extension)	Canada, China, France, Germany, India, Korea, Mexico, Slovakia, Slovenia, Taiwan, Turkey, and the US	Boehringer Ingelheim and Eli Lilly
Bolli et al.	2014	NCT 00763451	United States, Brazil, Chile, Colombia, Estonia, Germany, Italy, Lithuania, Malaysia, Mexico, Philippines, Poland, Romania, Slovakia, Ukraine	Sanofi
Berndt-Zipfel et al.	2013	NR	Germany	Novartis
Genovese et al.	2013	NCT00772174	Italy	Takeda Italia SpA
Rosenstock et al.	2013	NCT00707031	United States, Argentina, Austria, Brazil, Colombia, Denmark, Finland, Germany, Greece, Hungary, Italy, Netherlands, Norway, Poland, Puerto Rico, Russian Federation, Spain, Sweden	Sanofi
Kim et al.	2013	NCT00699322	Korea	Merck
Cefalu et al.	2013	NCT00968812	United States, Argentina, Bulgaria, Canada, Costa Rica, Denmark, Finland, Germany, India, Israel, Korea, Republic of, Mexico, Norway, Philippines, Poland, Puerto Rico, Romania, Russian Federation, Slovakia, Ukraine	Janssen Research & Development, LLC

Author	Year	Registration Number	Country	Sponsor
Derosa et al.	2013	NR	Italy	NR
Henry et al.	2013	NCT00943917	US	Intarcia Therapeutics
Ahrén et al.	2013	NCT00712673	Australia, Canada, Chile, Czech Republic, Germany, Croatia, Mexico, Morocco, the Philippines, Romania, Russian Federation, South Africa, Spain, Ukraine, US, and Venezuela	Sanofi
Kapitza et al.	2013	NCT01175473	Germany	Sanofi
Charbonnel et al.	2013	NCT01296412	21 countries	Merck Sharp & Dohme Corp.
Forst et al.	2013	NCT01565096	Germany	Novartis Pharma GmbH Nurnberg
Rhee et al.	2013	NCT00562172	Korea, India	LG Life Sciences Ltd.
Wilding et al.	2012	NCT01117584	Hungary, Poland, Romania, UK, Italy, US	Astellas Pharma Inc. and Kotobuki Pharmaceutical Co. Ltd.
Derosa et al.	2012	NR	Italy	NR
Hermans et al.	2012	NCT01006590	Belgium, France, Germany, Italy, Spain, Turkey, UK	AstraZeneca, Bristol-Myers Squibb
Derosa et al.	2012	NR	Italy	NR
Guerci et al.	2012	NCT01193296	NR	Novartis
Monnier et al.	2012	NCT00318656	France	GlaxoSmithKline Laboratories
Rizzo et al.	2012	NR	Italy	NR
Seino et al.	2012	NCT01318109	Japan	Takeda
Yang et al.	2012	NCT00813995	NR	Merck Sharp & Dohme Corp.
Gallwitz et al.	2012	NCT00622284	Bulgaria, Denmark, France, Germany, Hong Kong, Hungary, India, Ireland, Italy, Netherlands, Norway, Poland, South Africa, Sweden, UK, US	Boehringer Ingelheim
Srivastava et al.	2012	NR	India	NR
Koren et al.	2012	NR	Isreal	NR
Pan et al.	2012	NR	China	Novartis Beijing, China
Gallwitz et al.	2012	NCT00359762	Austria, Czech Republic, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Mexico, Poland, Spain, Switzerland, and the UK	AstraZeneca
Aschner et al.	2012	NCT00751114	Austria, Brazil, Colombia, Egypt, Greece, Hong Kong, India, Israel, Korea, Lebanon, Mexico, Netherlands, Portugal, Spain, Turkey, UK, US	Sanofi
Rosenstock et al.	2012	NCT00642278	Argentina, Bulgaria, Canada, Czech Republic, India, Malaysia, Mexico, Poland, Romania, Russia, UK, US	Janssen Global Services, LLC

Author	Year	Registration Number	Country	Sponsor
DeFronzo et al.	2012	NCT00328627	United States, Australia, Brazil, Bulgaria, Chile, Croatia, Estonia, Guatemala, India, Israel, Latvia, Mexico, New Zealand, Peru, Romania, Russian Federation, Serbia, South Africa, Ukraine	Takeda
Bolinder et al.	2012	NCT00855166	Bulgaria, Czech Republic, Hungary, Poland, Sweden	AstraZeneca
Fonseca et al.	2012	NCT00960076	US, Latin America	AstraZeneca, Bristol-Myers Squibb
Wang et al.	2011	NR	Taiwan	Research grant from the National Science Council (Taiwan), Veterans General Hospitals University System of Taiwan Joint Research Program, and Bayer Schering Pharma
Yang et al.	2011	NCT00661362	China, India and South Korea	AstraZeneca LP and Bristol-Myers Squibb
Stephens et al.	2011	NR	UK	Novo Nordisk
Petrica et al.	2011	NR	Romania	NR
Lin et al.	2011	NR	Taiwan	The National Science Council, Taiwan; Veterans General Hospitals University System of Taiwan Joint Research Program; and Bayer Schering Pharma, Taiwan Branch
Terra et al.	2011	NCT00473525	Colombia, Germany, Italy, Spain, Sweden, US	Pfizer Inc.
Derosa et al.	2011	NR	Italy	NR
Derosa et al.	2011	NR	Italy	NR
Pfutzner et al.	2011	NCT00770653	Germany	Takeda Pharma
Zinman et al.	2011	NCT00611884	Canada, India, South Africa, US	Novo Nordisk A/S
Heise et al.	2011	NCT00614055	France, Germany, Norway, Romania, Spain	Novo Nordisk A/S
Gallwitz et al.	2011	NCT00434954	Germany	AstraZeneca
Arechavaleta et al.	2011	NCT00701090	Austria, Brazil, Chile, Colombia, Costa Rica, Denmark, Ecuador, France, Germany, Guatemala, India, Italy, Korea, Republic of, Malaysia, Mexico, New Zealand, Panama, Peru, Poland, Spain, Switzerland, United Kingdom	Merck Sharp & Dohme Corp.
Yang et al.	2011	NR	China, South Korea and India	Novo Nordisk
Taskinen et al.	2011	NCT00601250	Czech Republic, Finland, Greece, India, Israel, Mexico, New Zealand, Russia, Sweden, US	Boehringer Ingelheim
Forst et al.	2010	NCT00309608	UK, Germany, France, Slovakia, Ukraine, Sweden	Boehringer Ingelheim

Author	Year	Registration Number	Country	Sponsor
Goke et al.	2010	NR	International	Bristol-Myers Squibb and AstraZeneca
Scheen et al.	2010	NCT00666458	Argentina, Belgium, Denmark, France, Italy, Mexico, Norway, South Africa, Sweden	AstraZeneca and Bristol-Myers Squibb
Stenlof et al.	2010	NR	the United States, Israel, Sweden, Mexico, Puerto Rico, Argentina, Italy, and the Philippines.	Bristol-Myers Squibb and AstraZeneca
Ratner et al.	2010	NR	Brazil, Canada, Poland, Romania, Russian, Ukraine, and US	sanofi-aventis
Bergenstal et al.	2010	NCT00637273	United States, India, Mexico	Amylin Pharmaceuticals and Eli Lilly
Bailey et al.	2010	NCT00528879	US, Canada, Argentina, Mexico, Brazil	Bristol-Myers Squibb and AstraZeneca
Filozof et al.	2010	NR	NR	Novartis
DeFronzo et al.	2010	NCT00135330	US	AstraZeneca, Eli Lilly
Pratley et al.	2010	NCT00700817	Croatia, Germany, Ireland, Italy, Netherlands, Romania, Serbia, Slovakia, Slovenia, Spain, UK, US, Canada	Novo Nordisk
Apovian et al.	2010	NR	US	Lilly USA, LLC
Kadoglou et al.	2010	NCT00373178	NR	European Social Fund and National Resources- (EPEAEK II) "PYTHAGORAS II" and Alexander S Onassis Public Benefit Foundation
Petrica et al.	2009	NR	NR	NR
Scheen et al.	2009	ISRCTN, NCT00174993	Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Italy, Latvia, Lithuania, Netherlands, Norway, Poland, Slovakia, Sweden, Switzerland, United Kingdom	Takeda
Blonde et al.	2009	NCT00396227	US	Novartis
Defronzo et al.	2009	NCT00121667	US, Brazil	Bristol-Myers Squibb; AstraZeneca
Home et al.	2007	NR	23 countries in Europe, Australia and New Zealand	GlaxoSmithKline
Papathanassiou et al.	2009	NR	Greece	University of Ioannina
Goodman et al.	2009	NR	Multinational	Supported by Novartis Pharmaceuticals Corporation
Bunck et al.	2009	NCT00097500	Sweden, Finland, and the Netherlands	Amylin Pharmaceuticals and Eli Lilly and Company
Kaku et al.	2009	UMIN000001110	NR	Takeda
Nauck et al.	2008	NCT00286442	Multinational ("115 sites in 15 countries")	Takeda Global Research & Development Cente
Ferrannini et al.	2009	NCT00106340	Canada, US, Europe, and multinational	Novartis Pharmaceuticals

Author	Year	Registration Number	Country	Sponsor
Gao et al.	2009	NCT00324363	China, India, Korea, Taiwan	Amylin Pharmaceuticals; Eli Lilly and Company
Nauck et al.	2009	NCT00318461	Argentina, Australia, Belgium, Bulgaria, Croatia, Denmark, Germany, Hungary, India, Ireland, Italy, Netherlands, New Zealand, Norway, Romania, Russian Federation, Slovakia, South Africa, Spain, Sweden, United Kingdom	Novo Nordisk
Scott et al.	2008	NCT00541775	Multinational	Merck
Komajda et al.	2008	NCT00379769	23 countries in Europe and Australasia	GlaxoSmithKline
Khanolkar et al.	2008	NR	United Kingdom	NR
Garcia-Soria et al.	2008	NR	US, Mexico, Australia	Phenomix Corporation
Raz et al.	2008	NCT00337610	Austria, Israel, Mexico, Peru and United States	Merck & Co., Inc.
Hamann et al.	2008	NR	Multinational (Europe and Mexico)	NR
Bolli et al.	2008	NCT 00237237	Germany, UK, US, Spain, Italy, Switzerland, Austria, South Africa and Australia	Novartis Pharmaceuticals Corporation
Bosi et al.	2007	NCT00099892	US, France, Italy, Sweden	Novartis Pharmaceuticals Corporation
Nauck et al.	2007	NCT00094770	NR	Merck & Co.
Brazg et al.	2007	NR	NR	byMerck & Co., Inc.
Derosa et al.	2007	NR	Italy	NR
Charbonnel et al.	2006	NCT00086515 (note: NCT in publication is missing a zero)	France, Israel, US	Sponsored by Merck Research Laboratory
Nauck et al.	2006	NR	Europe and Austrlia	NR
Weissman et al.	2005	NR	US	GlaxoSmithKline Pharmaceuticals
Bakris et al.	2006	NR	North America, South America and Europe	GlaxoSmithKline Pharmaceuticals
Ristic et al.	2006	NR	Canada, France, Italy, Spain, Austria	Sponsored by Novartis Pharma
Umpierrez et al.	2006	NR	US	Sanofi-Aventis
Garber et al.	2006	NR	US	Authors from Bristol-Meyers Squibb
Kvapil et al.	2006	NR	Croatia, Czech Republic, Denmark, France, Greece, Hungary, Norway, Poland, Portugal, Russia, Spain	
Poon et al.	2005	NR	US	Amylin Pharmaceuticals
Feinglos et al.	2005	NR	United States	Pfizer Inc

Author	Year	Registration Number	Country	Sponsor
DeFronzo et al.	2005	Nr	United States	Amylin pharmaceuticals; Eli Lilly and Co.
Matthews et al.	2005	NR	Multinational	Takeda Euro R&D; Eli Lilly and Co.
Ahrén et al.	2004	NR	Sweden, Spain, Germany and Switzerland	Swedish Research Council
Schernthaner et al.	2004	NR	10 European countries	Grant from the Institut de Recherches Internationales Servier, Courbevoie, France
Raskin	2003	NR	US	NovoNordisk Pharmaceuticals
Phillips et al.	2003	NR	Australia and New Zealand	Bayer AG, Leverkusen, Germany
Marre et al.	2002	NR	Multinational	Merck Lipha
Marre et al.	2002	NR	Multinational	Novartis Pharma AG
Gomez-Perez et al.	2002	NR	Mexico	NR
Van Gaal et al.	2001	NR	Belgium, Israel, Astria, Czech	Bayer and Sanofi-Synthelab
Charpentier et al.	2001	NR	France	Hoechst Marion Roussel
Halimi et al.	2000	NR	France	Authors from Bayer
Einhorn et al.	2000		US	Takeda Pharmaceuticals America
Fonseca et al.	2000	NR	US	SmithKline Beecham Pharmaceuticals
Moses	1999	NR	Australia	Novo Nordisk
Rosenstock et al.	1998	NR	US	Bayer Corporation
Wolever et al.	1997	NR	Canada	Bayer Canada, Inc.
Strozik et al.	2015	NR	Poland	“This study was not founded by any pharmaceuticals corporation”
Qiu et al.	2014	NCT01340664	Canada, Czech Republic, Mexico, Romania, Russia, Slovakia, US	Janssen Research & Development LLC
Gaal et al.	2014	NCT00976937	United States, Australia, Brazil, Canada, Chile, Germany, Guatemala, Mexico, Peru, Poland, Romania, Russian Federation, Ukraine	Sanofi
Bhandare et al.	2013	NR	India	NR
Raskin	2007	NR	US	Support from Novo Nordisk
Leiter	2005	NR	Canada	GlaxoSmithKline
Kilo et al.	2003	NR	US	Novo Nordisk
Ohira et al.	2014	NR	Japan	NR

Author	Year	Registration Number	Country	Sponsor
Yang et al.	2015	NCT01095666	China, India, South Korea	Bristol-Myers Squibb and AstraZeneca
Merck Sharp & Dohme Corp.	2015	NCT01841697	Argentina, Canada, Croatia, Estonia, Georgia, Hungary, Israel, Malaysia, Philippines, Poland, Romania, South Africa, US	Merck Sharp & Dohme Corp.
Daiichi Sankyo Inc.	2009	NCT00484419	Colombia, Mexico, US	Daiichi Sankyo Inc.
Merck Sharp & Dohme Corp.	2012	NCT01682759	Croatia, Germany, Hungary, South Korea, Lebanon, Lithuania, Malaysia, Poland, Romania, US	Merck Sharp & Dohme Corp.
NCT record	2010 (last update)	NCT00367055	"Not provided", France is listed as a "Removed Location Countries"	GlaxoSmithKline
NCT record	2015 (last update)	NCT01882907	Republic of Korea	Pusan National University Hospital
NCT record	2015 (last update)	NCT01973231	EUROPE: Czech Republic, Finland, France, Germany, Hungary, Italy, Latvia, Lithuania, United Kingdom	Novo Nordisk A/S
NCT record	2016 (last update)	NCT02008682	China, Beijing	Novo Nordisk A/S
Lavalle-Gonzalez et al.	2013	NCT01106677	Argentina, Bulgaria, Colombia, Czech Republic, Estonia, Greece, India, Italy, Latvia, Malaysia, Mexico, Peru, Poland, Portugal, Russia, Singapore, Slovakia, Sweden, Thailand, Turkey, Ukraine, US	Janssen Research & Development, LLC
Chen et al.	NA	NCT01965509	China	Hansoh Pharmaceutical Co., Ltd. (Jiangsu)

EudraCT = European Union Drug Regulating Authorities Clinical Trials; ISRCTN = International Standard Randomised Controlled Trial Number; JapicCTI = Japan Pharmaceutical Information Center - Clinical Trials Information; NA = not available; NCT = clinicaltrials.gov identifier; NR = not reported; UMIN = University Hospital Medical Information Network.

Appendix 5: Research Question 1 — Inclusion Criteria and Criteria for Inadequate Control for Included Randomized Controlled Trials

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Nauck et al.	2014	18 to 75 years, T2DM, A1C > 8% and ≤ 9.5% (diet and exercise alone) or ≥ 7% and ≤ 9.5% (on oral antihyperglycemic medication monotherapy or combination therapy), BMI 25 to 40 kg/m^2, stable weight during the 3-month period before study	An A1C value of 0.8% (64 mmol/mol) and 9.5% (80 mmol/mol) on diet and exercise alone or 7% (53 mmol/mol) and 9.5% (80 mmol/mol) on oral antihyperglycemic drug (OAD) monotherapy or combination therapy (metformin plus another OAD)
Ross et al.	2015	Adults with T2DM, BMI ≤ 45 kg/m^2, A1C ≥ 7% and ≤ 10% on diet and exercise with stable metformin IR (≥ 1,500 mg/d)	A1C 7% to 10% on metformin at screening
Moon et al.	2014	18 to 75 years, T2DM, A1C 7.5% to 12.0% on metformin (> 1,000 mg/d), BMI < 35 kg/m^2	A1C 7.5% to 12.0% on metformin
Gupta et al.	2015	Uncomplicated T2DM with or without stable comorbid conditions, A1C ≥ 6.5% on metformin (1,000 to 2,500 mg/d), fasting blood glucose ≥ 126 mg/dL, post-prandial blood glucose ≥ 200 mg/dL	A1C ≥ 6.5% on metformin
Hissa et al.	2015	18 to 70 years, T2DM, A1C > 7.5% on metformin (≥ 1,000 mg/d), BMI ≥ 22 and ≤ 40 kg/m^2	A1C > 7.5%
Inagak et al.	2015	Outpatients, ≥ 20 years, T2DM for at least 3 months, A1C ≥ 7.0% to ≤ 10.0% (monotherapy) or ≥ 7.0% to ≤ 10.6% (combination therapy) were eligible for the present study. Patients who had used a sulfonylurea (glimepiride, gliclazide, or glibenclamide), a glinide (nateglinide or mitiglinide), an alpha-glucosidase inhibitor (voglibose, miglitol or acarbose), a biguanide (metformin), a thiazolidinedione (pioglitazone) or a dipeptidyl peptidase-4 inhibitor (sitagliptin, vildagliptin, or alogliptin) for ≥ 83 days before week 0 were eligible for combination therapy in the present study.	≥ 7.0% to ≤ 10.0% (monotherapy, baseline diet/exercise only) or ≥ 7.0% to ≤ 10.6% (combination therapy, baseline diet/exercise + 1 OAD)
Odawara et al.	2014	≥ 20 to < 75 years, T2DM, BMI ≥ 20 kg/m^2 to ≤ 35 kg/m^2, A1C ≥ 7.0% to ≤ 10.0%, inadequately controlled on diet, exercise and metformin	A1C 7% to 10% on metformin
Chen et al.	2014	Outpatients, 30 to 70 years, T2DM, A1C 7.0% to 11.0% on mono- or dual-OAD therapy	A1C 7% to 11% on metformin
Kawamori et al.	2014	> 20 years, T2DM, A1C 6.9% to 9.4% on metformin (750, 1,500 or 2,250 mg/d) in addition to diet and exercise	A1C 6.9% to 9.4% on metformin
White et al.	2014	18 to 78 years, A1C level 7.0% to 10.0%, stable metformin IR monotherapy (≥ 1,500 mg/d), fasting C-peptide value ≥ 0.8 ng/mL, BMI ≤ 45.0 kg/m^2	A1C 7.0% to 10.0%
Kadowaki et al.	2013	20 to < 75 years, T2DM	A1C > 6.9% and < 10.5%
Neutel et al.	2013	18 to 78 years, T2DM, A1C 7.5% to 11.5% (metformin IR or XR ≥ 850 and ≤ 1,500 mg), fasting C-peptide ≥ 1.0 ng/mL, BMI ≤ 40 kg/m^2 at screening	A1C 7.5% to 11.5%

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Chawla et al.	2013	≥ 18 years, T2DM, A1C 7.5% to 11% (metformin monotherapy ≥ 1,500 mg/d), fasting plasma glucose ≥ 140 mg/dL	A1C 7.5% to 11%
Bergenstal et al.	2012	18 to 75 years, T2DM, A1C ≥ 7.0% to ≤ 10.0% (metformin ≥ 1,500 mg/d or maximally tolerated dose, BMI ≥ 25 kg/m^2 (23 for Asians) to ≤ 45 kg/m^2	A1C 7.0% to 10.0%
Cho et al.	2010	30 to 70 years, T2DM, duration of diabetes of < 10 years, BMI 20 to 35 kg/m^2, A1C 7.5% to 11%	A1C > 7.0% at the end of the metformin run-in phase
Wang et al.	2015	Outpatients, > 60 years, fasting blood glucose > 8.5 mmol/L, A1C > 7.5% on metformin	NR
Jin et al.	2015	19 to 75 years, T2DM for at least 3 months, A1C 7.0% to 10.0% (metformin ≥ 1,000 mg/d), fasting blood glucose of ≤ 270 mg/dL	A1C between 7.0% and 10.0% on metformin monotherapy of ≥ 1,000 mg/day for ≥ 4 weeks
Xiao et al.	2015	T2DM, A1C ≥ 7.0% on metformin	A1C ≥ 7% on metformin
Rosenstock et al.	2015	≥ 18 years, T2DM, A1C ≥ 8.0% and ≤ 12.0% on metformin (≥ 1,500 mg/day), C-peptide concentrations ≥ 1.0 ng/mL, BMI ≤ 45.0 kg/m^2	A1C ≥ 8.0% and ≤ 12.0%
Rosenstock et al.	2015	18 to 75 years, T2DM, fasting plasma glucose < 270 mg/dL, metformin (> 1,500 mg/d)	A1C 7% to 10.5%
Kim et al.	2015	T2DM, A1C 7.0% to 10.0%, metformin (≥ 1,000 mg/day)	A1C 7% to 10% on metformin
Kashiwagi et al.	2015	≥ 20 years, T2DM, A1C 7.4% to 9.9% on metformin, BMI 20.0 kg/m^2 to 45.0 kg/m^2	A1C 7.4% to 9.9% and a BMI 20.0 kg/m^2 to 45.0 kg/m^2
Aaboe et al.	2015	Outpatients, ≥ 18 years; A1C 7.0% to 10.0%, metformin (≥ 1,000 mg/d), BMI ≥ 25 kg/m^2	A1C 7.0% to 10.0%
Schumm-Draeger et al.	2015	18 to 77 years, T2DM, A1C ≥ 6.7% and ≤ 10.5%, metformin (≥ 1,500 mg/d)	A1C 6.7% to 10.5%
Han et al.	2015	Women, ≥ 18 and ≤ 80 years, T2DM A1C ≥ 7.0% and ≤ 10.5%, metformin or metformin + sulphonylurea (both at maximum or near-maximum effective doses)	A1C ≥ 7.0% and ≤ 10.5%
Gurkan et al.	2014	40 to 70 years, T2DM, A1C 7% to 9.5%, BMI 25 kg/m^2 to 45 kg/m^2, metformin (2.1 g/d)	NR
Del Prato et al.	2014	18 to 80 years, T2DM, BMI ≥ 23 kg/m^2 and ≤ 45 kg/m^2 (Asian ≥ 20 kg/m^2 and ≤ 35 kg/m^2), A1C 7.0% to 9.0% with fasting plasma glucose < 15.3 mmol/L on stable metformin (≥ 1,500 mg or maximum tolerated dose [MTD]), or A1C of 7.5% to 10% on metformin < 1,500 mg without documented MTD, with A1C values 7.0% to 9.0% and fasting blood glucose < 15.3 mmol/L after metformin stabilization (≥ 1,500 mg or MTD)	(i) glycated haemoglobin (A1C) level 7.0% to 9.0% with fasting plasma glucose < 15.3 mmol/L on stable metformin (≥ 1,500 mg or MTD), or (ii) A1C of 7.5% to 10% on metformin < 1,500 mg without documented MTD, with A1C values 7.0% to 9.0% and fasting blood glucose < 15.3 mmol/L after metformin stabilization (≥ 1,500 mg or MTD) for 8 weeks.
Nandy et al.	2014	40 to 70 years, BMI ≥ 40 kg/m^2, T2DM, A1C of 6.5% to 9.0%, lifestyle changes alone or metformin	NR
Forst et al.	2014	45 to 75 years, T2DM, A1C 6.5% to 8.5% on metformin	A1C 6.5% to 8.5% on metformin
Dungan et al.	2014	≥ 18 years of age, T2DM, diet and exercise and metformin (≥ 1,500 mg/d), A1C value of ≥ 7·0% to ≤ 10.0%, stable weight (± 5%) for at least 3 months, BMI ≤ 45 kg/m^2	NR

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Ridderstrale et al.	2014	≥ 18 years T2DM, BMI ≤ 45 kg/m², A1C 7% to 10%, metformin immediate release (≥ 1,500 mg/d, maximum tolerated dose, or maximum dose according to the local label)	A1C 7% to 10%
Ohira et al.	2014	T2DM, inadequately controlled despite ongoing treatment with metformin 500 mg/d	NR
Ahren et al.	2014	≥ 18 years, T2DM, inadequate glycemic control on metformin (≥ 1,500 mg or maximum tolerated dose), A1C 7.0% to 10.0%, BMI 20 kg/m^2 to 45 kg/m^2; creatinine clearance > 60 mL/min, and normal thyoid-stimulating hormone concentration or were clinically euthyroid	A1C 7.0% to 10.0% on metformin
Derosa et al.	2014	≥ 18 years, T2DM, inadequately controlled T2DM, A1C 7.0% to 9.0% on metformin	A1C 7.0% to 9.0% on metformin
Diamant et al.	2014	≥ 18 years, T2DM, suboptimum glycemic control, A1C 7.1% to 11.0% on maximum tolerated doses of metformin alone or with a sulfonylurea, stable body weight for at least 3 months, BMI 25 kg/m^2 to 45 kg/m² (23 kg/m^2 to 45 kg/m² in South Korea and Taiwan)	A1C 7.1% to 11.0%
Haring et al.	2014	≥ 18 years, BMI ≤ 45 kg/m^2, inadequately controlled T2DM, A1C ≥ 7% to ≤ 10% despite diet and exercise program and stable immediate release metformin	A1C ≥ 7% to ≤ 10% on diet and exercise program and metformin
Bolli et al.	2014	24 to 79 years, T2DM (≥ 1 year since diagnosis), metformin (1.5 g/d), A1C 7% to 10%	A1C 7% to 10%, inclusive, on metformin
Berndt-Zipfel et al.	2013	30 to 80 years, A1C 6.5% to 9.5% on metformin	A1C 6.5% to 9.5% on metformin
Genovese et al.	2013	35 to 75 years, T2DM taking metformin (2,000 to 3,000 mg/d), reduced HDL-C levels (< 40 mg/dL in males, < 50 mg/dL in females), irrespective of statin treatment, central obesity (waist circumference ≥ 94 cm for men, ≥ 80 cm for women)	NR
Rosenstock et al.	2013	21 to 84 years, T2DM, taking metformin (≥ 1.5 g/d), A1C 7% to 10%	A1C 7% to 10% (between 53 and 86 mmol/mol) on metformin
Kim et al.	2013	18 to 80 years, T2DM for < 10 years, A1C 6.5% to 8.0%, BMI 20 kg/m^2 to 30 kg/m^2	A1C 6.5% to 8.0% on metformin
Cefalu et al.	2013	18 to 80 years, T2DM, A1C 7.0% to 9.5%, metformin (≥ 2,000 mg/d or ≥ 1,500 mg/d if unable to tolerate a higher dose). Participants takin metformin in combination with one other oral non-thiazolidinedione antihyperglycemic drug at screening discontinued the second antihyperglycemic drug and, if needed, had their metformin dose increased	A1C 7% to 9.5% on metformin
Derosa et al.	2013	> 18 years, T2DM, naive to treatment, poor glycemic control (A1C > 7.5%), BMI ≥ 25, weight < 34.9 kg/m^2	A1C > 7.5%
Henry et al.	2013	18 to 70 years, T2DM for a minimum of 6 months, stable dose of metformin for at least 3 months, A1C ≥ 7% and ≤ 10%, fasting blood glucose < 240 mg/dL, BMI ≤ 40 kg/m^2, stable body weight for 3 months before study entry	NR
Ahrén et al.	2013	T2DM, inadequately controlled on metformin (≥ 1.5 g/d), A1C 7% to 10%	A1C 7% to 10% on metformin

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Kapitza et al.	2013	37 to 74 years, T2DM, A1C 6.5% to 9.0%, on meformin ≥ 1.5 g/d	A1C 6.5% to 9.0% on metformin
Charbonnel et al.	2013	18 to 79 years, T2DM on metformin (≥ 1,500 mg/d), A1C ≥ 7.0% and ≤ 11.0%, fasting finger stick glucose < 15 mmol/L	A1C 7% to 11% on metformin
Forst et al.	2013	30 to 80 years, T2DM, A1C > 6.5% to ≤ 9.5%. Patients with cardiovascular preconditions (CHD or MI): A1C > 7.0% ≤ 9.5%, metformin at maximal or maximal tolerated dosage	A1C > 6.5% and ≤ 9.5% on metformin; A1C > 7.0% and ≤ 9.5% for patients with cardiovascular preconditions
Rhee et al.	2013	18 to 75 years, T2DM, metformin (1,000 mg/d or higher)	NR
Wilding et al.	2012	≥ 18 years, T2DM for ≥ 6 months, A1C of 7.0% to 9.5%, metformin (≥ 1,500 mg/d), had received routine advice about diet and exercise as part of their usual clinical care, BMI 20 kg/m^2 to 45 kg/m^2	A1C 7.0% to 9.5%
Derosa et al.	2012	"Caucasian", > 18 years, T2DM for 6 months, treatment naive, poor glycemic control, A1C level > 63.9 mmol/mol to < 96.7 mmol/mol, BMI ≥ 25 to < 30 kg/m^2	A1C 63.9 mmol/mol to 96.7 mmol/mol
Hermans et al.	2012	> 18 years, T2DM, insufficient glycemic control on submaximal metformin (1,500 to 1,700 mg/d; A1C 7.0% to 10.0%)	A1C 7.0% to 10.0%
Derosa et al.	2012	"Caucasian", > 18 years, T2DM drug-naive, poor glycemic control, A1C level > 8.0%, BMI ≥ 25, and < 30 kg/m^2	A1C > 8.0%
Guerci et al.	2012	18 to 80 years, BMI 22 kg/m^2 to 45 kg/m^2, T2DM, A1C 6.5% to 8.0% on metformin (maximum tolerated daily dose of at least 1,500 mg)	A1C 6.5% to 8.0%
Monnier et al.	2012	T2DM, inadequate glycemic control, A1C level > 7% on metformin monotherapy (1,700 to 3,000 mg/d) provided that A1C was not greater than 9%	A1C level > 7% on metformin
Rizzo et al.	2012	T2DM, without adequate glycemic control (A1C > 7.5%) on metformin treatment at maximal dose (2,000 mg/d)	A1C > 7.5%
Seino et al.	2012	≥ 20 and < 65 years, T2DM, A1C value ≥ 6.9% to < 10.4% on metformin plus specific dietary and exercise therapies.	A1C 6.9% to 10.4%
Yang et al.	2012	Chinese, 18 to 78 years, T2DM, inadequate glycemic control (i.e., A1C ≥ 7.5% and ≤ 11.0%) while on metformin monotherapy (1,000 or 1,700 mg⁄d)	A1C 7.5% to 11%
Gallwitz et al.	2012	18 to 80 years, T2DM, metformin at a stable dose (1,500 mg/d or more or a maximum tolerated dose less than 1,500 mg/d) alone or with one other oral antidiabetic drug, A1C 6.5% to 10.0% (on metformin alone) or 6.0% to 9.0% (on metformin and one additional oral antidiabetic drug), BMI 40 kg/m^2 or less	A1C 6.0% to 9.0%
Srivastava et al.	2012	> 18 years, T2DM, using metformin with inadequate glycemic control (A1C > 7% and < 10%)	A1C levels > 7% and < 10% on metformin
Koren et al.	2012	18 to 75 years, T2DM, inadequate glycemic control (A1C > 7%) on metformin	A1C > 7%
Pan et al.	2012	18 to 78 years, T2DM, inadequately controlled by metformin, A1C 7.0T to 10.0% (at least 1,500 mg/d), BMI 20 kg/m^2 to 40 kg/m^2, fasting plasma glucose < 270 mg/dL (15 mmol/L)	A1C 7.0% to 10.0%

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Gallwitz et al.	2012	18 to 85 years, T2DM, BMI ≥ 25 kg/m² to < 40 kg/m², maximum tolerated doses of metformin, and suboptimum glycemic control, A1C 6.5% and more or 9.0% and less	A1C 6.5% and more or 9.0% and less
Aschner et al.	2012	35 to 70 years, T2DM for at least 6 months, A1C of 7% or greater and less than 11%, BMI 25 kg/m² to 45 kg/m²	A1C 7% to 11%
Rosenstock et al.	2012	18 to 65 years, T2DM for at least 3 months, A1C ≥ 7% and ≤ 10.5%, metformin monotherapy (≥ 1,500 mg/d),stable body weight, BMI 25 kg/m^2 to 45 kg/m^2 (24 kg/m^2 to 45 kg/m^2 for those of Asian descent), serum creatinine levels < 1.5 mg/dL for men and < 1.4 mg/dL for women	A1C 7% to 10.5%
DeFronzo et al.	2012	18 to 80 years, BMI 23 kg/m^2 to 45 kg/m^2; fasting C-peptide ≥ 0.26 nmol/L, T2DM, inadequately controlled by metformin monotherapy (≥ 1,500 mg/d), systolic/diastolic blood pressure no greater than 160/100 mm Hg, hemoglobin of at least 12 g/dL for men and at least 10 g/dL for women, alanine aminotransferase no more than 2.5 times the upper limit of normal, TSH no greater than the upper limit of normal, serum creatinine below 133 µmol/L (for men) or below 124 µmol/L (for women)	A1C 7.5 to 10%, on metformin
Bolinder et al.	2012	Women aged 55 to 75 years who were postmenopausal for at least 5 years or men aged 30 to 75 years; T2DM, A1C 6.5% to 8.5%; fasting plasma glucose ≤ 240 mg/dL, BMI 25 kg/m^2 or higher; weight no higher than 120 kg, metformin (at least 1,500 mg/d)	A1C ≥ 6.5% and ≤ 8.5%
Fonseca et al.	2012	Adults, T2DM, inadequate glycemic control, A1C 7.5% to 11.0%, metformin (850 mg/d to 1,500 mg/d), fasting C-peptide levels ≥ 1.0 ng/mL, BMI ≤ 45 kg/m^2	A1C 7.5% to 11.0%
Wang et al.	2011	Outpatients, 30 to 70 years, T2DM, mono- or dual-OAD therapy A1C 7.0% to 11.0%	A1C 7.0% to 11.0%
Yang et al.	2011	≥ 18 years, T2DM, A1C 7.0% to 10.0% on metformin (1,500 mg/d), C-peptide level 0.33 nmol/L	A1C 7.0% to 10.0%
Stephens et al.	2011	40 to 70 years, T2DM (diagnosed after the age of 40 years with no history of ketosis), nonsmokers (≥ 12 months), monotherapy with metformin (1.5 g/d to 3.0 g/d), A1C 7.5% to 10.5%	A1C 7.5% to 10.5% on metformin
Petrica et al.	2011	T2DM for at least 5 years, poor glycemic control (A1C > 7%) on metformin	A1C > 7%
Lin et al.	2011	Outpatients, 30 to 70 years, T2DM, treated with one or two oral antidiabetic drugs, A1C 7.0% to 11.0%.	A1C 7% to 11% on one or two oral antidiabetic drugs The baseline A1C level and reduction of A1C value during this 8-week run-in period were not different between the two groups.
Terra et al.	2011	18 to 70 years, T2DM, inadequate glycemic control, A1C > 7% to < 11% on metformin, BMI > 25 kg/m^2 and < 45 kg/m^2	A1C 7% to 11%

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Derosa et al.	2011	≥ 18 years, T2DM, poor glycemic control, A1C > 8.0%, BMI ≥ 25 and < 30 kg/m^2, metformin (1,000 to 2,000 mg/day) and were intolerant to metformin at the highest dosages (2,500 to 3,000 mg/day)	A1C > 8.0%
Derosa et al.	2011	"Caucasian", ≥ 18 years, T2DM, uncontrolled T2DM, A1C > 7.0% on diet, physical activity, and metformin (mean dosage: 1,700 ± 850 mg/d). "	A1C > 7.0%
Pfutzner et al.	2011	18 to 75 years, T2DM, metformin (individually maximal tolerated dosage), A1C of ≥ 6.5%, HDL cholesterol ≤ 1.03 mmol/L (40 mg/dL) and/or triglycerides ≥ 1.7 mmol/L (150 mg/dL)	NR
Zinman et al.	2011	18 to 75 years, T2DM for at least 3 months, A1C 7.0% to 11.0%, BMI 23 kg/m^2 to 42 kg/m^2, insulin-naive, treated with one or two oral antidiabetic drugs (metformin, alpha-glucosidase inhibitors, sulphonylurea, or meglitindes) for more than 2 months at stable half-maximum to maximum allowed doses	A1C 7% to 10% on one or two oral antidiabetic drugs (metformin, alpha-glucosidase inhibitors, sulfonylurea, or meglitindes)
Heise et al.	2011	18 to 75 years, T2DM, A1C 7% to 11%, BMI of 25 to 37 kg/m^2, insulin-naive (no previous insulin treatment or insulin treatment for ≤ 14 days in the 3 months before trial), treated with up to two OADs in the 2 months before trial at stable maximum doses or at least half maximum allowed doses	A1C of 7% to 11%
Gallwitz et al.	2011	Adults, T2DM, A1C 6.5% to 10.0%	A1C 6.5% to 10.0% on metformin
Arechavaleta et al.	2011	≥ 18 years, T2DM, with inadequate glycemic control, A1C ≥ 6.5% and ≤ 9.0% on metformin (≥ 1,500 mg/d) as well as diet and exercise	A1C 6.5% to 9.0% on metformin
Yang et al.	2011	18 to 80 years (18 to 75 years for Chinese subjects), T2DM, one or more oral antidiabetic drugs (OADs) for at least 3 months, A1C level ≥ 7.0% and ≤ 11.0% for subjects on OAD monotherapy or ≥ 7.0% and ≤ 10.0% for subjects on OAD combination therapy, BMI ≤ 45.0 kg/m^2	A1C ≥ 7.0% and ≤ 11.0% on metformin
Taskinen et al.	2011	18 to 80 years, T2DM, BMI ≤ 40 kg/m^2, metformin (≥ 1,500 mg/day or maximum tolerated dose) and not more than one other oral antidiabetes medication, A1C 7.0% to 10.0%	A1C 7.0% to 10.0% on metformin and not more than one other OAD
Forst et al.	2010	21 to 75 years, T2DM for at least 3 months, BMI 25 to 40 kg/m^2, inadequate glycemic control despite treated with metformin alone or with metformin and one other oral hypoglycemic drug other than rosiglitazone or pioglitazone. For patients previously treated with metformin and one other OAD, inadequate glycemic control was defined as A1C level 7.0% to 9.0%; for patients previously treated with metformin alone, inadequate glycemic control was defined as A1C from 7.5% to 10.0%	A1C 7.5% to 10%
Goke et al.	2010	≥ 18 years, T2DM, A1C > 6.5% to 10.0% on metformin ≥ 1,500 mg/d)	A1C 6.5% to 10.0%
Scheen et al.	2010	≥ 18 years, T2DM, uncontrolled (A1C 6.5% to 10.0%) despite metformin (≥ 1,500 mg)	A1C 6.5% to 10.0%

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Stenlof et al.	2010	18 to 77 years, T2DM, inadequate glycemic control (A1C 7% to 10%) on metformin IR or metformin XR 1,500 mg/d, BMI ≤ 40 kg/m^2, fasting C-peptide concentration 1 ng/mL (0.33 nmol/L)	A1C 7% to 10% on metformin
Ratner et al.	2010	30 to 75 years, T2DM of at least 1 year's duration, inadequately controlled (A1C ≥ 7.0 and < 9.0% on metformin, ≥ 1,000 mg/d	A1C ≥ 7.0% and < 9.0% on metformin
Bergenstal et al.	2010	≥ 18 years T2DM, otherwise healthy, A1C of 7.1% to 11.0% on metformin, BMI 25 kg/m^2 to 45 kg/m^2	A1C of 7.1% to 11.0% on metformin
Bailey et al.	2010	18 to 77 years, T2DM, A1C 7% to 10%, C-peptide concentration 0.34 nmol/L or more, BMI 45 kg/m^2 or less, metformin (≥ 1,500 mg/d)	A1C 7% to 10%
Filozof et al.	2010	18 to 78 years, T2DM, A1C 7.5% to 11.0%, metformin (≥ 1,500 mg/d)	A1C 7.5% to 11.0%
DeFronzo et al.	2010	18 to 75 years, BMI 25 kg/m^2 to 40 kg/m^2, stable body weight for at least 6 months, A1C 6.8 to 10.0%, metformin, absence of islet cell autoantibodies	NR
Pratley et al.	2010	18 to 80 years, T2DM, A1C 7.5% to 10.0%, BMI 45.0 kg/m^2 or lower, metformin (≥ 1,500 mg/d)	A1C 7.5% to 10.0%
Apovian et al.	2010	18 to 75 years, T2DM, metformin or a sulfonylurea, A1C 6.6% to 10.0%, BMI 25 kg/m^2 to 39.9 kg/m^2, stable body weight (not varying by 5% for at least 6 months before screening)	NR
Kadoglou et al.	2010	Inadequaate control on metformin (850 mg/d), A1C > 6.5%, BMI > 25 kg/m^2	A1C > 6.5%
Petrica et al.	2009	T2DM for at least 5 years, poor glycemic control, A1C > 7% on metformin	A1C > 7%
Scheen et al.	2009	35 to 75 years, T2DM, A1C > 6.5% despite diet alone or oral glucose-lowering drugs, with or without insulin	A1C > 6.5%
Blonde et al.	2009	18 to 80 years, T2DM, inadequately controlled A1C of 7% to 10% on metformin (≥ 1,000 mg/day), BMI 22 to 41 kg/m^2, fasting plasma glucose < 270 mg/dL (15 mmol/L)	A1C 7% to 10%
Defronzo et al.	2009	18 to 77 years, T2DM, A1C ≥ 7.0% and ≤ 10.0%; metformin (≥ 1,500 mg/d, but not > 2,550 mg/d), fasting C-peptide concentration ≥ 1.0 ng/mL, BMI ≤ 40 kg/m^2.	A1C ≥ 7.0% and ≤ 10.0%
Home et al.	2007	40 to 75 years, T2DM, inadequately controlled, metformin or sulphonylureas, BMI > 25.0 kg/m^2, A1C > 7.0% to 9.0%	A1C > 7.0% to 9.0%
Papathanassiou et al.	2009	T2DM, A1C > 6.5% on metformin, normal liver enzymes and renal function	A1C > 6.5%
Goodman et al.	2009	18 to 78 years, A1C 7.5% to 11%, metformin (≥ 1,500 mg/d), BMI 22 kg/m^2 to 40 kg/m^2, fasting blood glucose < 270 mg/dL (< 15 mmol/L)	A1C 7.5% to 11%
Bunck et al.	2009	30 to 75 years, A1C 6.5% to 9.5%, BMI 25 kg/m^2 to 40 kg/m^2, metformin	A1C 6.5% to 9.5% on metformin
Kaku et al.	2009	≥ 20 and < 65 years, T2DM, treated with diet and exercise, but no antidiabetic drugs other than metformin	A1C 6.5% to 10%

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Nauck et al.	2008	18 to 80 years, "historical" diagnosis of T2DM, inadequate glycemic control, A1C 7.0% to 10.0% despite metformin (≥ 1,500 mg/d), BMI 23 to 45 kg/m^2, C-peptide concentration ≥ 0.26 nmol/L (0.8 ng/mL), serum creatinine < 1.5 mg/dL (men) or < 1.4 mg/dL (women), fasting plasma glucose < 275 mg/dL (< 15.3 mmol/L)	A1C 7.0% to 10.0%
Ferrannini et al.	2009	18 to 73 years, T2DM, A1C 6.5% to 8.5%, metformin (1,500 mg/d), BMI 22 kg/m^2 to 45 kg/m^2	A1C 6.5% to 8.5%
Gao et al.	2009	21 to 75 years, treated immediate release metformin (≥ 1,000 mg/d) and SU; or SU/metformin combination therapy, A1C 7.1% and 11.0%, BMI > 21 kg/m^2 and < 35 kg/m^2.	A1C ≥ 7% to ≤ 11%
Nauck et al.	2009	18 to 80 years, T2DM, A1C 7% to 11%, BMI ≤ 40 kg/m^2	A1C between 7% and 11%
Scott et al.	2008	18 to 75 years, T2DM, metformin (≥ 1,500 mg/d), inadequate glycemic control (A1C ≥ 7% and ≤ 11%)	A1C 7% to 11%
Komajda et al.	2008	40 to 75 years, T2DM, BMI > 25.0 kg/m^2 and A1C 7.1% to 9.0%, on maximum permitted or tolerated doses of metformin or a sulfonylurea (glibenclamide [glyburide], glimepiride or gliclazide), blood press < 180/105 mm Hg	A1C 7.1% to 9.0% on metformin or sulfonylurea monotherapy
Khanolkar et al.	2008	T2DM, suboptimal glycemic control (A1C > 6.5%) on metformin	A1C > 6.5% on metformin
Garcia-Soria et al.	2008	T2DM for > 6 months but < 10 years, metformin alone (≥ 1,500 mg/d or highest tolerated dose) or in combination with a glitazone (any labelled dose)	NR
Raz et al.	2008	18 to 78 years, T2DM, metformin monotherapy or any other single ODA, or being treated with metformin in combination with another ODA, A1C value 8% to 11%	A1C 8% to 11% on metformin
Hamann et al.	2008	Overweight (BMI ≥ 25 kg/m^2), T2DM, A1C ≥ 7% and < 10%, metformin (≥ 850 mg/day)	A1C 7% to 10%
Bolli et al.	2008	18 to 77 years, T2DM, A1C 7.5% to 11.0%, metformin (≥ 1,500 mg/d), BMI 22 kg/m^2 to 45 kg/m^2, fasting plasma glucose < 15 mmol/L	A1C of 7.5% to 11.0% at the screening visit while receiving a stable dose of metformin ≥ 1,500 mg/day (inadequately controlled with prior metformin monotherapy)
Bosi et al.	2007	18 to 78 years, T2DM, metformin (≥ 1,500 mg/d), A1C 7.5% to 11.0%, BMI 22 kg/m^2 to 45 kg/m^2, fasting blood glucose < 15 mmol/L	A1C 7.5% to 11.0% on metformin
Nauck et al.	2007	18 to 78 years, T2DM, not on an ODA, ODA monotherapy, or metformin in combination with another ODA	A1C 6.5% and 10% after the metformin dose-stable period (8-weeks run-in)
Brazg et al.	2007	25 to 75 years, T2DM, inadequate glycemic control, metformin (≥ 1,500 mg/d), A1C ≥ 6.5% and < 10%, fasting plasma glucose ≤ 240 mg/dL at screening	On a stable dose of 1,500 mg/day for 6 weeks before the screening visit and A1C 6.5% and < 10% and fasting plasma glucose 240 mg/dL

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Derosa et al.	2007	"Caucasian", ≥ 18 years, T2DM, poor glycemic control (A1C > 7.5%) or experienced adverse effects with diet and oral hypoglycemic drugs, such as SU or metformin, and diagnosed metabolic syndrome and triglyceridemia (triglycerides ≥ 1.70 mmol/L10), hypertension (systolic/diastolic blood pressure, ≥ 30/85 mm Hg), fasting C-peptide level > 0.33 nmol/L, BMI 25.0 kg/m^2 to 28.1 kg/m^2	A1C > 7.5%
Charbonnel et al.	2006	18 to 78 years, T2DM, inadequate glycemic control, A1C ≥ 7 and ≤ 10% on metformin (≥ 1,500 mg/d)	A1C ≥ 7 and ≤ 10%
Nauck et al.	2006	18 to 70 years, T2DM for a minimum of 1 year, treated with at least 50% of maximum dose of 1 or 2 ODA(s) (except TZD), BMI 25 kg/m^2 to 40 kg/m^2, A1C 8% to 13%, fasting plasma glucose ≥ 10 mmol/L	At least 50% of maximum dose of one or two ODA(s) (except a TZD)
Weissman et al.	2005	18 to 75 years, T2DM, A1C of 6.5% to 8.5% for subjects having received prior combination treatment (metformin + SU) and 7% to 10% for drug-naive or prior monotherapy subjects; fasting plasma glucose of 7.0 to 15.0 mmol/L (126 to 270 mg/dL); and a BMI ≥ 27 kg/m^2. Previous treatment could include either diet and exercise or oral therapy (acarbose, SU, metformin or metformin + SU). Any subject previously receiving metformin or metformin + SU must have received metformin ≤ 1,000 mg/day for at least 3 months prior to study entry. Subjects must have stopped previous treatment with TZDs at least 3 months prior to screening.	A1C of 6.5% to 8.5% for subjects having received prior combination treatment (metformin + SU) and 7% to 10% for drug-naive or prior monotherapy subjects
Bakris et al.	2006	40 to 80 years, T2DM, previously treated with diet and exercise alone, a single OAD, or combination oral antidiabetic therapy; capillary fasting plasma glucose levels > 6.6 mmol/L at visit 3; able to tolerate netformin at a minimum dose of 1 g/d	Fasting plasma glucose levels > 6 mmol/L on previous treatment with diet and exercise alone, a single OAD, or combination oral antidiabetic therapy, baseline A1C is 8.3% to 8.5%.
Ristic et al.	2006	T2DM for ≥ 6 months, inadequately controlled on metformin (≥ 1,000 mg/d) and diet and exercise, A1C 6.8% to 9.0%, BMI 20 kg/m^2 to 35 kg/m^2	6.8% to 9.0%
Umpierrez et al.	2006	18 to 79 years, T2DM for at least 6 months, metformin (1 g/d to 2.5 g/d) or extended release metformin (0.5 g/d to 2.0 g/d), BMI ≥ 24 kg/m^2, A1C 7.5% to 10%, fasting blood glucose 126 to 235 mg/dL (7 mmol/L to 13 mmol/L), C-peptide concentration ≥ 0.27 nmol/L	A1C 7.5% to 10% on metformin
Garber et al.	2006	20 to 78 years with T2DM requiring oral therapy, metformin (1,500 mg/d), A1C > 7.0% and ≤ 12.0%, BMI ≥ 23 kg/m^2 and ≤ 45 kg/m^2.	A1c > 7.0% to < = ≤ 12% on MET
Kvapil et al.	2006	Not adequately controlled on metformin (850 mg/d), A1C 7.5% to 13.0%	
Poon et al.	2005	18 to 65 years, T2DM, A1C 6.8% to 9.0% on metformin, fasting blood glucose < 240 mg/dL, BMI 27 kg/m^2 to 45 kg/m^2, stable body wieght, no clinically relevant abnormal laboratory test values	NR
Feinglos et al.	2005	30 to 81 years, T2DM for at least 6 months, A1C 7.0% to 8.5%, inadequate controlled metformin (≥ 1,000 mg/d), BMI 27 kg/m^2 to 38 kg/m^2	A1C 7.0% to 8.5% on metformin

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
DeFronzo et al.	2005	19 to 78 years, T2DM, meformin, fasting blood glucose < 13.3 mmol/L (< 240 mg/dL), BMI 27 kg/m^2 to 45 kg/m^2, A1C 7.1% to 11.0%, metformin (≥ 1,500 mg/d), stable weight stable for 3 months, no clinically significant abnormal laboratory test values (> 25% outside normal laboratory values)	A1C 7.1% to 11%
Matthews et al.	2005	35 to 75 years, A1C ≥ 7.5% or ≤ 11.0%; fasting C-peptide of ≥ 1.5 ng/mL (0.50 nmol/L) and stable or worsening glycemic control for ≥ 3 months before screening	Patients inadequately managed with metformin alone (at ≥ 50% of the maximum recommended dose or at the maximum tolerated dose for ≥ 3 months) were screened
Ahrén et al.	2004	≥ 30 years, T2DM for at least 6 months, A1C 7.0% to 9.5% on metformin, BMI 20 kg/m^2 to 35 kg/m^2	A1C 7.0% to 9.5% on metformin
Schernthaner et al.	2004	> 35 years, T2DM, diet alone or in combination with metformin or an alpha-glucosidase inhibitor (acarbose or miglitol), A1C 6.9% to 11.5%	A1C 6.9% to 11.5%, and have been treated for at least 3 months with diet alone or in combination with metformin or an alpha-glucosidase inhibitor (acarbose or miglitol)
Raskin et al.	2003	> 18 years, T2DM for at least 3 months and BMI values of 24 kg/m^2 to 42 kg/m^2. Subjects were stratified by baseline A1C value (9% or 9%). Enrolled patients had A1C values 7% and 12% in previous monotherapy with a sulfonylurea (at 25% of the maximum dose), metformin (1,000 mg/day), or low-dose Glucovance (glyburide 2.5 mg and metformin 500 mg).	A1C values 7% and 12% in previous monotherapy with a sulfonylurea (at 25% of the maximum dose), metformin (1,000 mg/day), or low-dose Glucovance (glyburide 2.5 mg and metformin 500 mg).
Phillips et al.	2003	≥ 40 years, T2DM for 6 months or longer, insufficiently controlled by metformin, BMI 25 kg/m^2 to 35 kg/m^2, A1C 6.8% to 10.2%	A1C 7% to 10% on metformin
Marre et al.	2002	> 18 years, T2DM, fasting blood glucose ≥ 7 mmol/L (126 mg/dL) despite metformin (≥ 850 mg b.i.d. or ≥ 500 mg t.i.d.) and diet and exercise, BMI < 40 kg/m^2	NR
Marre et al.	2002	≥ 30 years, T2DM for ≥ 6 months, metformin (> 1,500 mg/d), BMI 20 to 35 kg/m^2, A1C 6.8% to 11%	6.8% to 11% i
Gomez-Perez et al.	2002	40 to 80 years, T2DM, fasting C-peptide level ≥ 0.8 ng/mL, fasting plasma glucose level ≥ 140 mg/dL and ≤ 300 mg/dL at weeks 0 and 2 of the metformin maintenance period	NR
Van Gaal et al.	2001	30 to 75 years, T2DM of at least 1 year, inadequately controlled by diet and metformin, A1C ≥ 7.5% to ≤ 10.5%, BMI kg/m^2 23 to 40 kg/m^2, stable body weight (< 5% change) over the 3 months preceding enrolment	Metformin > 3 months, A1C ≥ 7.5%
Charpentier et al.	2001	35 to 70 years, newly diagnosed (< 1 year) T2DM, inadequately controlled, metformin monotherapy, fasting blood glucose 7.8 to 13.9 mmol/L, serum creatinine < 110 µmol/L, BMI ≥ 23.0 kg/m^2 (women) or ≥ 25.0 kg/m^2 (men), no evidence or history of spontaneous weight loss or ketonuria associated with glucosuria	Fasting blood glucose criteria (7.8 mmol/L to 13.9 mmol/L)

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Halimi et al.	2000	30 to 70 years, T2DM diagnosed at least 1 year before study, BMI ≥ 25.0 kg/m^2 and ≤ 35.0 kg/m^2, poor glycemic control (A1C ≥ 7.0% and < 11.0%) on metformin (850 mg/d), serum creatinine level < 135 μmol/L, transaminases, alkaline phophatase and bilirubin liver function parameters less than twice the upper limit of normal, a gamma-GT liver function test less than three times the upper limit of normal, and a fasting C-peptide value of ≥ 0.20 μg/L	A1C > 7.0% and ≤ 11.0% for any assay performed during the previous 3 months
Einhorn et al.	2000	A1C value ≥ 8.0% on metformin, BMI 25 kg/m^2 to 45 kg/m^2, fasting C-peptide level > 1.0 ng/mL	A1C ≥ 8.0%, fasting C-peptide ~1.0 ng/mL, patients who had been receiving a stable regimen of metformin for ≥ 30 days.
Fonseca et al.	2000	40 to 80 years, T2DM, FPG concentrations 7.8 to 16.7 mmol/L (140 and 300 mg/dL) on metformin (2.5 g/d), fasting C-peptide ≥ 0.27 nmol/L (0.8 ng/mL), BMI 22 kg/m^2 to 38 kg/m^2, stable weight (no more than 10% change between screening and baseline)	Fasting blood glucose 7.7 mmol/L to 16.7 mmol/L (140 mg/dL to 300 mg/dL)
Moses	1999	40 to 75 years, T2DM, A1C > 7.1% on metformin (1 to 3 g/day), BMI ≥ 21 kg/m^2	A1C > 7.1%
Rosenstock et al.	1998	> 30 years, T2DM, inadequately controlled on diet and metformin (2,000 or 2,500 mg/d), no other pharmacological therapy for type 2 diabetes was allowed for at least 56 days before screening, A1C 7% to 10%, stable body weight (within 3 kg) for at least 4 weeks	A1C 7% to 10%
Wolever et al.	1997	≥ 18 years, T2DM for at least 6 months, A1C > 7%, except for patients in the diet only group (> 6.5%).	A1C > 7.0% for treatment groups, > 6.5% for diet alone subgroup
Strozik et al.	2015	T2DM, A1C 7.5%, metformin (1,500 mg/d), BMI 25 kg/m^2 to 35 kg/m^2	NR
Qiu et al.	2014	18 to 80 years, T2DM, inadequate glycemic control (A1C ≥ 7.0% [53 mmol/mol] and ≤ 10.5% [91 mmol/mol]) on metformin monotherapy (≥ 2,000 mg/day, or ≥ 1,500 mg/d if unable to tolerate a higher dose), fasting plasma glucose < 15 mmol/L at week 2, and fasting fingerstick glucose ≥ 6.1 and < 15 mmol/L on day 1	A1C 7.0% to 10.5%
Gaal et al.	2014	Obese (BMI ≥ 30 kg/m^2), ≥ 18 to < 50 years, T2DM diagnosed at least 1 year before screening, insufficiently controlled with metformin (1.5 g/d), A1C ≥ 7.0% and ≤ 10%	A1C ≥ 7.0% and ≤ 10%
Bhandare et al.	2013	> 18 years, A1C > 6.5%, fasting plasma glucose < 270 mg/dL, metformin (1,000 mg/d), inadequate glycemic control	A1C > 6.5% on metformin
Raskin	2007	18 to 75 years, insulin-naive, BMI < 40 kg/m^2, body weight < 125 kg (275 lbs), A1C ≥ 8%, metformin (≥ 1,000 mg/d) as a single drug or in OAD combination therapy	A1C ≥ 8%, and to have been previously treated with metformin ≥ 1,000 mg/day, as a single drug or in OAD combination therapy, for at least 3 months before the trial
Leiter	2005	20 to 80 years, T2DM, fasting blood glucose ≥ 7 mmol/L, A1C ≤ 9.5%, metformin (≤ 1700 mg/d)	FPG > 7.0 mmol/L and ≤ 14.0 mmol/L plus A1C ≤ 9.5%

Author	Year	Inclusion Criteria	Criteria for Inadequate Control
Kilo et al.	2003	≥ 18 years, T2DM, body weight ≤ 100 kg, BMI ≤ 40 kg/m^2, naive insulin treatment, inadequate glycemic control (A1C ≥ 7.5%), metformin as monotherapy or in combination with a sulfonylurea or repaglinide, fasting blood glucose > 126 mg/dL (> 6.99 mmol/L)	Not able to achieve the fasting blood glucose target of 90 mg/dL to 126 mg/dL on metformin only
Ohira et al.	2014	T2DM, A1C > 7.0%, metformin (500 mg/d)	A1C > 7.0% on metformin
Yang et al.	2015	≥ 18 years, inadequately controlled T2DM (A1C ≥ 7.5% and ≤ 10.5%), metformin monotherapy (≥ 1,500 mg/d)	A1C 7.5% to 10.5%
NCT01841697	2015	T2DM, metformin (≥ 1,500 mg/d)	NR
NCT00484419	2009	A1C 7.0% to 10.0% on metformin, may be withdrawn from other (non-metformin) drugs if A1C is 6.5% to 9.5% at screening	A1C 7% to 10% (6.5% to 9.5% if on other OADs)
NCT01682759	2012	T2DM, metformin (≥ 1,500 mg/d), inadequate glycemic control	NR
NCT00367055	2010 (last updated)	40 to 75 years, T2DM for at least 1 year, metformin (1.5 g to 3 g), A1C > 6.5% and < 8%, BMI > 25 kg/m^2 and < 35 kg/m^2	A1C > 6.5% and < 8% on metformin
NCT01882907	2015 (last update)	18 to 80 years, A1C 7% to 11%, fasting blood glucose < 270 mg/dL (15 mmol/L)	A1C 7% to 11%
NCT01973231	2015 (last update)	T2DM, metformin (at least 1,000 mg/d and up to 3,000 mg/d), A1C 7.5% to 10.5%, BMI ≥ 20 kg/m^2	A1C 7.5% to 10.5%
NCT02008682	2016 (last update)	≥ 18 years, T2DM, metformin (at least 1,500 mg/d or maximum tolerated dose above or equal to 1,000 mg/d), A1C 7.0% to 10.0%, BMI ≤ 45.0 kg/m^2	A1C 7.0% to 10.0%
Lavalle-Gonzalez et al.	2013	≥ 18 to ≤ 80 years, inadequate glycemic control (A1C ≥ 7.0% to ≤ 10.5%), metformin (≥ 2,000 mg/day [or ≥ 1,500 mg/d if unable to tolerate higher dose]), fasting plasma glucose < 15 mmol/L, fasting fingerstick glucose ≥ 6.1 mmol/L and < 15 mmol/L on day 1	A1C 7.0% to 10.5%
Chen et al.	NA	20 to 70 years, BMI 19 kg/m^2 to 35 kg/m^2; T2DM, metformin (≥ 1,500 mg/d), A1C 7.0% to 11%	A1C 7.5% to 11% during screening or A1C 7.0% to 11% before randomization

A1C = glycated hemoglobin; b.i.d. = twice daily; BMI = body mass index; CHD = coronary heart disease; HDL-C = high-density lipoprotein cholesterol; IR = immediate release; MI = myocardial infarction; NA = not available; NR = not reported; OAD = oral antidiabetes drugs; SU = sulfonylurea; T2DM = type 2 diabetes mellitus; t.i.d. = three times daily; TSH = thyroid-stimulating hormone; TZD = thiazolidinediones; XR = extended release.

Appendix 6: Research Question 2 — Study Characteristics

Trial Name	First Author (Last Name)	Year of Publication	Description of Background Therapy Drugs	Trial Registration Number, If Provided	Number of Countries	Primary Outcome of Interest	Funding	Parallel RCT	Double Blind?
ELIZA	Pfeffer	2015	Insulin + oral drug, MET+SUL	NCT01147250	49	Composite (CV death, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina)	Sanofi, ELIXA	YES	YES
TECOS	Green	2015	Medications taken alone or in combination: MET+SUL+TZD+INS	NCT00790205	–	Composite (CV death, nonfatal MI, nonfatal stroke, or unstable angina requiring hospitalization)	Merck Sharp & Dohme Corp.	YES	YES
EMPA-REG	Zinman	2014	Monotherapy: MET, INS; dual therapy: MET+SUL, MET+INS	NCT01131676	–	Composite (CV death, including fatal stroke and fatal MI, nonfatal MI, and nonfatal stroke)	Boehringer Ingelheim Eli Lilly	YES	YES
LEADER	Marso	2013	Monotherapy: insulin (human NPH, long-acting analog, and premix); dual: OADs, INS + OADs	NCT01179048	410 sites in 32 countries	Composite (CV death, nonfatal MI or nonfatal stroke)	Novo Nordisk	YES	YES
EXAMINE	White	2013	"Existing antihyperglycemic... therapy" (other than DPP-4 or GLP-1)	NCT00968708	49 countries	Composite (CV death, nonfatal MI, nonfatal stroke	Takeda Development Centre Americas	YES	YES
SAVOR-TMI	Scirica	2013	Insulin, SU, and or MET (combinations and types not provided)	NCT01107886	26 countries (790 centres)	Composite (CV death, fatal MI or fatal ischemic stroke)	AstraZeneca and Bristol-Myers Squibb	YES	YES

Trial Name	First Author (Last Name)	Year of Publication	Description of Background Therapy Drugs	Trial Registration Number, If Provided	Number of Countries	Primary Outcome of Interest	Funding	Parallel RCT	Double Blind?
CANVAS	Neal	2013	Insulin, SU, MET at baseline	NCT01032629	386 centres in 24 countries	Composite of cardiovascular death, nonfatal MI, and nonfatal stroke	Janssen Global Services, LLC	YES	YES
SPREAD-DIMACD	Hong	2013	SU, MET, TZD, Glinide, INS, but not specified	NCT00513630	Single country, sites NR China	Composite of recurrent cardiovascular events, including nonfatal MI, nonfatal stroke or arterial revascularization by percutaneous transluminal coronary angioplasty or by coronary artery bypass graft, death from a cardiovascular cause, and death from any cause	Shanghai Jiao Tong University School of Medicine	YES	YES
PROactive	Dormandy	2005	Monotherapy: MET only, SU only, INS only; Dual therapy: MET+SUL, MET+INS, SUL+INS; triple therapy: MET+SUL+INS; other combinations of “glucose-lowering drugs and other medications”	NCT00174993	321 centres in 19 European countries	Composite (all-cause mortality, nonfatal MI including silent MI, stroke, acute coronary syndrome, endovascular or surgical intervention on the coronary or leg arteries, or amputation above the ankle)	Takeda Pharmaceutical Company and Eli Lilly and Company	YES	YES
NA	Giles	2008	Pioglitazone or glyburide with or without insulin	NCT00521820	US + non-US sites: Argentina, Colombia, Mexico	Progression of congestive heart failure progression, defined as a composite of CV mortality and hospitalization or ER visit for heart failure	Takeda Pharmaceuticals	YES	YES

Trial Name	First Author (Last Name)	Year of Publication	Description of Background Therapy Drugs	Trial Registration Number, If Provided	Number of Countries	Primary Outcome of Interest	Funding	Parallel RCT	Double Blind?
RECORD	Home	2007	MET or SUL	NCT00379769	Europe and Australasia	The primary end point was hospitalization (for acute MI, congestive heart failure, stroke, unstable angina pectoris, transient ischemic attack, unplanned cardiovascular revascularization, amputation of extremities, or any other definite cardiovascular reason) or death from cardiovascular causes (including heart failure, acute MI, sudden death, and death caused by acute vascular events including stroke); time to first occurrence	GlaxoSmithKline	YES	NO Open label

CV = cardiovascular; DPP-4 = dipeptidyl peptidase 4 inhibitor; GLP-1 = glucagon-like peptide-1 receptor agonist; HR = ; INS = insulin; MET = metformin; MI = myocardial infarction; NCT = clinicaltrials.gov identifier; NPH = neutral protamine Hagedorn; NR = not reported; OAD = oral diabetes drug; SUL = sulfonylurea; TZD = thiazolidinediones.

Appendix 7: Research Question 2 — Patient Characteristics of Included Studies

Trial Name	First Author (Last Name)	Year	Included Population	Treatment (Number Randomized)	Mean Age, Years, Mean (SD)	% Male	% Smoker	BMI	Previous MI
ELIZA	Pfeffer	2015	T2DM and had an acute coronary event within 180 days before screening	PLA (3,034) LIX 20 mcg/d (3,034)	60 (9.7)	0.69	0.12	30.2 (5.7)	44%
TECOS	Green	2015	≥ 50 years, T2DM and cardiovascular disease, A1C 6.5% to 8.0%	PLA (7,339) SIT 100 mg/d (7,332)	65.5 (8.0)	0.70	0.11	30.2 (5.6)	85%
EMPA-REG	Zinman	2014	≥ 18 years with T2DM, ≥ 7.0% and ≤ 9.0% (drug-naive) or with A1C ≥ 7.0% and ≤ 10.0% (any background antidiabetes therapy), high risk of CV events (≥ 1 of the following: history of MI > 2 months earlier; multi-vessel CAD; single-vessel CAD; unstable angina > 2 months earlier with evidence of single- or multi-vessel CAD; stroke > 2 months earlier; occlusive peripheral artery disease)	PLA (2,333) EMP 10 mg/d (2,345) EMP 25 mg/d (2,342)	63.1 (8.6)	0.71	0.13	NR	46%
LEADER	Marso	2013	T2DM, A1C ≥ 7.0%, ≥ 50 and ≥ 1 of coronary heart disease, cerebrovascular disease, peripheral vascular disease, chronic kidney disease stage 3 or greater, or chronic heart failure NYHA Class II or III) or ≥ 60 years and at least one cardiovascular risk factor (microalbuminuria, proteinuria, hypertension, and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction or an ankle-brachial index of less than 0.9)	PLA (4,672) LIR 1.8 mg/d (4,668)	64.3 (7.2)	0.64	0.12	32.5 (6.3)	30%
EXAMINE	White	2013	T2DM and an acute coronary syndrome (acute MI or unstable angina requiring hospitalization) within previous 15 to 90 days. Further criteria for the diagnosis. A1C 6.5% to 11.0% (insulin) or A1C 7.0% to 11.0%	PLA (2,679) ALO 6.25 to 25 mg/d (2,701)	61.0	0.68	0.14	NR	88%
SAVOR-TMI	Scirica	2013	≥ 40 years, T2DM, A1C ≥ 6.5% and ≤ 12.0%, and either a history of established CV disease or multiple risk factors (55 years old [male] or 60 years old [female] and have at least one of the following additional risk factors: dyslipidemia, hypertension, or active smoking) for vascular disease but without established CV disease	PLA (8,212) SAX 5 mg/d (8,280)	65.0 (8.6)	0.67	0.13	Median: 30.5	75%

Trial Name	First Author (Last Name)	Year	Included Population	Treatment (Number Randomized)	Mean Age, Years, Mean (SD)	% Male	% Smoker	BMI	Previous MI
CANVAS	Neal	2013	≥ 30 years, T2DM and a history of cardiovascular events or ≥ 50 years old with T2DM and high risk of CV events, A1C ≥ 7.0% to ≤ 10.5%	PLA (1,442) CAN 100 mg/d (1,445)	62.4 (8.0)	0.66	18.00	32.1 (6.2)	NR
SPREAD-DIMACD	HONG	2013	≤ 80 years, T2DM and diagnosed CAD. Fasting plasma glucose 7 mmol/L and/or 2-hour oral glucose tolerance test 11.1 mmol/L and fasting plasma glucose, 15 mmol/L	MET 1,500 mg/d (156) GLI 30 mg/d (148)	NR	0.78	0.38	25.2 (3.0)	54%
PROactive	Dormandy	2005	35 to 75 years, T2DM, A1C > 6.5% and evidence of extensive macrovascular disease	PLA (2,633) PIO 45 mg/d (2,605)	61.8 (7.7)	0.66	0.14	30.9 (4.8)	94%
NA	Giles	2008	> 18 years age, A1C > 7.0%, BMI < 48 kg/m^2, NYHA functional Class II/III HF, left ventricular systolic dysfunction	GLY 15 mg/d (256) PIO 45 mg/d (262)	63.4 (9.38)	0.77	NR	NR	NR
RECORD	Home	2007	40 to 75 years, T2DM, BMI > 25.0; A1C 7.0% to 9.0%	PLA (2,227) ROS 8 mg/d (2,220)	58.8 (8.3)	0.52	0.15	31.5 (4.9)	5%

A1C = glycated hemoglobin; ALO = alogliptin; BMI = body mass index; CAD = coronary artery disease; CAN = canagliflozin; CV = cardiovascular; EMP = empagliflozin; GLI = glipizide; GLY = glyburide; LIR = liraglutide; LIX = lixisenatide; MET = metformin; MI = myocardial infarction; NA = not available; NR = not reported; NYHA = New York Heart Association; PIO = pioglitazone; PLA = placebo; ROS = rosiglitazone; SAX = saxagliptin; SD = standard deviation; SIT= sitagliptin; T2DM = type 2 diabetes mellitus.

Note: Data are those reported for the whole population. If not reported, characteristics are for control group.

Appendix 8: Research Question 1 — Risk Of Bias Assessment

Studies	Adequate Sequence Generation2	Allocation Concealment	Blinding of Participants, Personnel and Outcome Assessors	Incomplete Outcome Data for Efficacy	Incomplete Outcome Data for Safety
Nauck et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Ross et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Moon et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gupta et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Hissa et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Inagaki et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Odawara et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Chen et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Kawamori et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
White et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Kadowaki et al. 2013	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Neutel et al. 2013	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Chawla et al. 2013	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Bergenstal et al. 2012	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Cho et al. 2010	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Wang et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Jin et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Xiao et al. 2015	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Rosenstock et al. 2015	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Rosenstock et al. 2015	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	Yes (low risk of bias)
Kim et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Kashiwagi et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Aaboe et al. 2015	Unclear	Unclear	Yes (low risk of bias)	Unclear	Not applicable
Schumm-Draeger et al. 2015	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ji et al. 2015	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gurkan et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Unclear	Not applicable
Del Prato et al. 2014	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Nandy et al. 2014	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)

Studies	Adequate Sequence Generation2	Allocation Concealment	Blinding of Participants, Personnel and Outcome Assessors	Incomplete Outcome Data for Efficacy	Incomplete Outcome Data for Safety
Forst et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Dungan et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ridderstrale et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ohira et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Unclear	Not applicable
Ahren et al. 2014	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Derosa et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Unclear	Unclear
Diamant et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Haring et al. 2014	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Bolli et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Berndt-Zipfel et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Genovese et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Rosenstock et al. 2013	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Kim et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Cefalu et al. 2013	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Derosa et al. 2013	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Henry et al. 2013	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ahrén et al. 2013	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Kapitza et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Charbonnel et al. 2013	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Forst et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Rhee et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Wilding et al. 2012	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Derosa et al. 2012	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Hermans et al. 2012	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Derosa et al. 2012	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Guerci et al. 2012	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Monnier et al. 2012	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Rizzo et al. 2012	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Seino et al. 2012	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Yang et al. 2012	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gallwitz et al. 2012	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Srivastava et al. 2012	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Unclear	Unclear

Studies	Adequate Sequence Generation2	Allocation Concealment	Blinding of Participants, Personnel and Outcome Assessors	Incomplete Outcome Data for Efficacy	Incomplete Outcome Data for Safety
Koren et al. 2012	No (high risk of bias)	No (high risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Unclear
Pan et al. 2012	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gallwitz et al. 2012	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Aschner et al. 2012	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Rosenstock et al. 2012	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
DeFronzo et al. 2012	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Bolinder et al. 2012	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Fonseca et al. 2012	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Wang et al. 2011	Yes (low risk of bias)	No (high risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Yang et al. 2011	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Stephens et al. 2011	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Petrica et al. 2011	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Terra et al. 2011	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Derosa et al. 2011	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Derosa et al. 2011	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Pfutzner et al. 2011	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Zinman et al. 2011	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Heise et al. 2011	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gallwitz et al. 2011	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Arechavaleta et al. 2011	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Yang et al. 2011	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Taskinen et al. 2011	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Forst et al. 2010	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Goke et al. 2010	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Scheen et al. 2010	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Stenlof et al. 2010	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ratner et al. 2010	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Bergenstal et al. 2010	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Bailey et al. 2010	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Filozof et al. 2010	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
DeFronzo et al. 2010	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Pratley et al. 2010	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)

Studies	Adequate Sequence Generation2	Allocation Concealment	Blinding of Participants, Personnel and Outcome Assessors	Incomplete Outcome Data for Efficacy	Incomplete Outcome Data for Safety
Apovian et al. 2010	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Kadoglou et al. 2010	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Petrica et al. 2009	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	Not applicable
Scheen et al. 2009	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Blonde et al. 2009	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Defronzo et al. 2009	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Home et al. 2009	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Unclear	Unclear
Papathanassiou et al. 2009	No (high risk of bias)	No (high risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Goodman et al. 2009	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Bunck et al. 2009	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Kaku et al. 2009	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Nauck et al. 2008	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Ferrannini et al. 2009	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gao et al. 2009	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Nauck et al. 2009	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Scott et al. 2008	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Komajda et al. 2008	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	Not applicable
Khanolkar et al. 2008	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Garcia-Soria et al. 2008	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Raz et al. 2008	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Hamann et al. 2008	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Unclear	Yes (low risk of bias)
Bolli et al. 2008	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Home et al. 2007	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Bosi et al. 2007	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Nauck et al. 2007	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Brazg et al. 2007	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
Derosa et al. 2007	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Charbonnel et al. 2006	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Nauck et al. 2006	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Ristic et al. 2006	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Umpierrez et al. 2006	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Garber et al. 2006	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)

Studies	Adequate Sequence Generation2	Allocation Concealment	Blinding of Participants, Personnel and Outcome Assessors	Incomplete Outcome Data for Efficacy	Incomplete Outcome Data for Safety
Kvapil et al. 2006	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Poon et al. 2005	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Feinglos et al. 2005	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
DeFronzo et al. 2005	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Matthews et al. 2005	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ahrén et al. 2004	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Schernthaner et al. 2004	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Phillips et al. 2003	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Marre et al. 2002	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Marre et al. 2002	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gomez-Perez et al. 2002	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Van Gaal et al. 2001	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Charpentier et al. 2001	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Halimi et al. 2000	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Unclear	Unclear
Einhorn et al. 2000	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
Fonseca et al. 2000	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Moses 1999	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Rosenstock et al. 1998	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Wolever et al. 1997	Unclear	Unclear	Yes (low risk of bias)	Unclear	Unclear
Strozik et al. 2015	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Unclear	Unclear
Qiu et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Gaal et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Bhandare et al. 2013	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Raskin 2007	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Leiter 2005	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Kilo et al. 2003	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Ohira et al. 2014	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
Yang et al. 2015	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)

Studies	Adequate Sequence Generation2	Allocation Concealment	Blinding of Participants, Personnel and Outcome Assessors	Incomplete Outcome Data for Efficacy	Incomplete Outcome Data for Safety
21399 Merck Sharp & Dohme Corp. 2015	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
21508 Daiichi Sankyo Inc. 2009	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Not applicable
21509 Merck Sharp & Dohme Corp. 2012	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
21577 NCT record 2010 (last updated)	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
21670 NCT record 2015 last update	Unclear	Unclear	Yes (low risk of bias)	No (high risk of bias)	No (high risk of bias)
21802 NCT record 2015 (last update)	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
21811 NCT record 2016 (last update)	Unclear	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
22053 Lavalle-Gonzalez 2013	Yes (low risk of bias)	Unclear	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)
22343 Chen 2016	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)	Yes (low risk of bias)

NCT = clinicaltrials.gov identifier.

Appendix 9: Research Question 1 — Detailed Network Meta-Analysis Results for the Reference-Case Analysis

Glycated Hemoglobin (A1C)

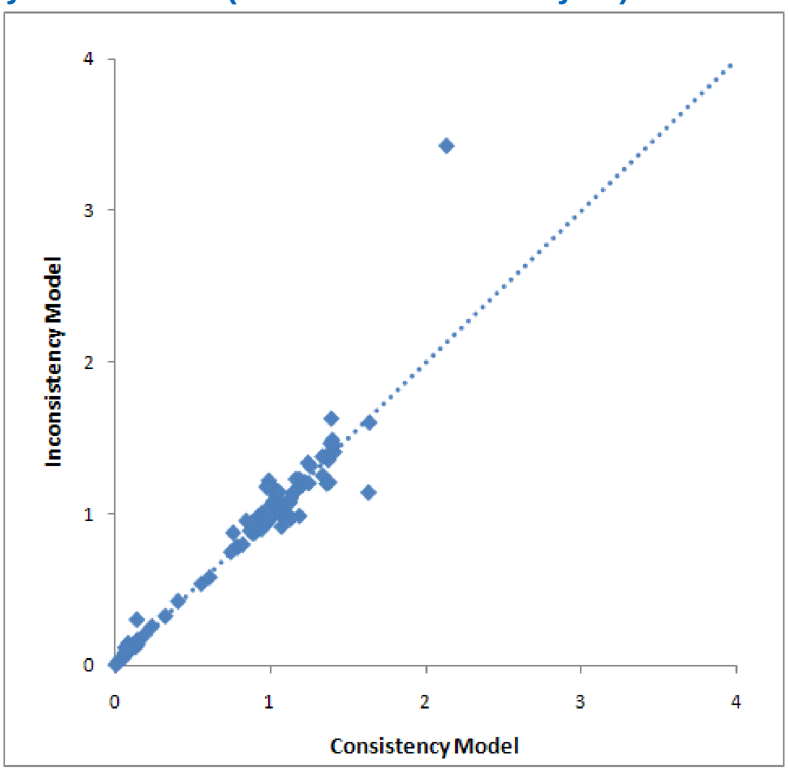
Table 1: A1C: Mean Differences for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	–0.70 (–0.83 to –0.58)
MET + MEG		–0.52 (–0.81 to –0.25)
MET + DPP-4		–0.58 (–0.68 to –0.48)
MET + SGLT-2		–0.67 (–0.84 to –0.49)
MET + GLP-1		–0.88 (–1.05 to –0.71)
MET + AGI		–0.21 (–0.86 to 0.43)
MET + TZD		–0.77 (–0.92 to –0.63)
MET + INS-BA		–0.85 (–1.16 to –0.53)
MET + INS-BI		–0.94 (–1.41 to –0.48)
MET + MEG	MET + SUL	0.18 (–0.11 to 0.47)
MET + DPP-4		0.12 (0.01 to 0.24)
MET + SGLT-2		0.04 (–0.16 to 0.24)
MET + GLP-1		–0.18 (–0.35 to 0.00)
MET + AGI		0.49 (–0.14 to 1.12)
MET + TZD		–0.07 (–0.20 to 0.07)
MET + INS-BA		–0.15 (–0.45 to 0.17)
MET + INS-BI		–0.24 (–0.69 to 0.21)
MET + DPP-4	MET + MEG	–0.06 (–0.34 to 0.24)
MET + SGLT-2		–0.14 (–0.47 to 0.19)
MET + GLP-1		–0.36 (–0.68 to –0.03)
MET + AGI		0.31 (–0.38 to 1.01)
MET + TZD		–0.25 (–0.55 to 0.05)
MET + INS-BA		–0.33 (–0.73 to 0.09)
MET + INS-BI		–0.42 (–0.94 to 0.11)
MET + SGLT-2	MET + DPP-4	–0.09 (–0.28 to 0.10)
MET + GLP-1		–0.30 (–0.46 to –0.13)
MET + AGI		0.37 (–0.28 to 1.00)
MET + TZD		–0.19 (–0.33 to –0.05)
MET + INS-BA		–0.27 (–0.57 to 0.04)
MET + INS-BI		–0.36 (–0.82 to 0.10)
MET + GLP-1	MET + SGLT-2	–0.21 (–0.45 to 0.03)
MET + AGI		0.45 (–0.22 to 1.11)
MET + TZD		–0.11 (–0.32 to 0.11)
MET + INS-BA		–0.18 (–0.53 to 0.18)

Treatment	Reference	MD (95% CrI)
MET + INS-BI		–0.27 (–0.76 to 0.22)
MET + AGI	MET + GLP-1	0.67 (0.00 to 1.32)
MET + TZD		0.11 (–0.09 to 0.30)
MET + INS-BA		0.03 (–0.27 to 0.33)
MET + INS-BI		–0.06 (–0.53 to 0.41)
MET + TZD	MET + AGI	–0.56 (–1.20 to 0.09)
MET + INS-BA		–0.64 (–1.34 to 0.08)
MET + INS-BI		–0.73 (–1.51 to 0.06)
MET + INS-BA	MET + TZD	–0.08 (–0.40 to 0.25)
MET + INS-BI		–0.17 (–0.63 to 0.30)
MET + INS-BI	MET + INS-BA	–0.09 (–0.56 to 0.37)
Random-effects model	Residual deviance	166 vs. 179 data points
	Deviance information criteria	–170.795

AGI = alpha-glucosidase inhibitor; CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; MD = mean difference; MEG = meglitinide; MET = metformin; INS-BA = basal insulin; INS-BI = biphasic insulin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 1: Consistency Plot for A1C (Reference-Case Analysis)



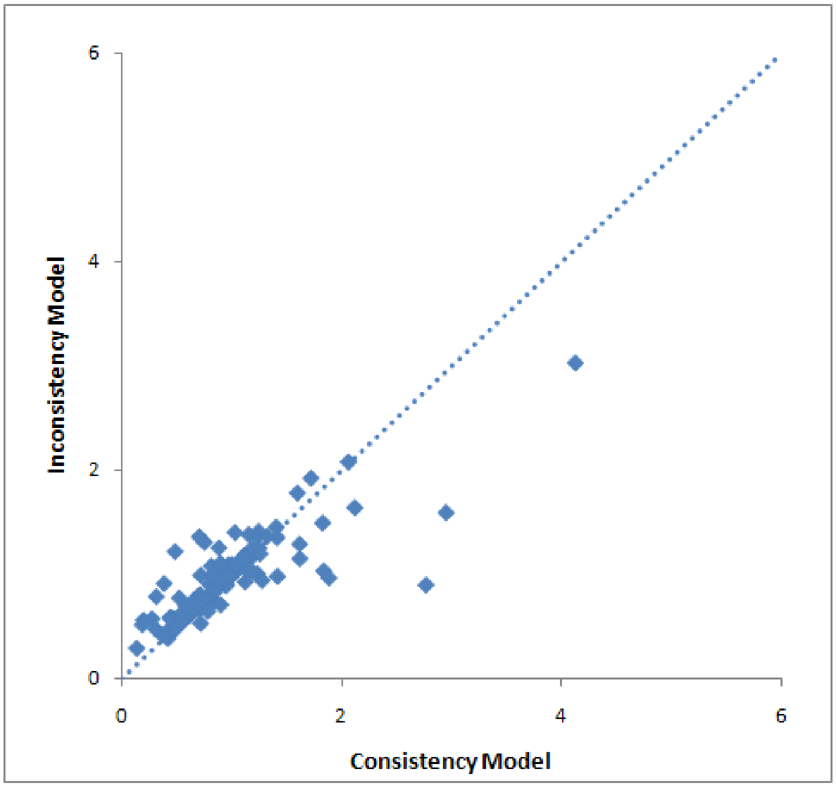
Nonsevere Hypoglycemia

Table 2: Nonsevere Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	7.59 (5.25 to 11.22)	6.88 (4.89 to 9.83)	9.11 (6.16 to 13.10)
MET + MEG		7.08 (3.33 to 15.73)	6.47 (3.20 to 12.97)	8.44 (3.52 to 17.73)
MET + DPP-4		0.77 (0.55 to 1.10)	0.77 (0.55 to 1.10)	–0.35 (–0.80 to 0.13)
MET + SGLT-2		1.00 (0.62 to 1.58)	1.00 (0.63 to 1.57)	–0.01 (–0.63 to 0.81)
MET + GLP-1		0.75 (0.46 to 1.25)	0.75 (0.46 to 1.25)	–0.38 (–0.94 to 0.36)
MET + TZD		0.58 (0.32 to 1.01)	0.58 (0.32 to 1.01)	–0.64 (–1.17 to 0.02)
MET + INS-BA		3.18 (1.73 to 5.80)	3.08 (1.71 to 5.42)	3.21 (1.14 to 6.64)
MET + INS-BI		6.92 (3.34 to 14.52)	6.34 (3.22 to 12.13)	8.25 (3.47 to 16.73)
MET + MEG	MET + SUL	0.93 (0.43 to 2.05)	0.94 (0.47 to 1.86)	–0.64 (-6.56 to 8.45)
MET + DPP-4		0.10 (0.07 to 0.14)	0.11 (0.08 to 0.15)	–9.46 (–13.26 to -6.60)
MET + SGLT-2		0.13 (0.08 to 0.21)	0.14 (0.09 to 0.23)	–9.10 (–13.02 to -6.14)
MET + GLP-1		0.10 (0.06 to 0.16)	0.11 (0.07 to 0.18)	–9.48 (–13.35 to -6.56)
MET + TZD		0.08 (0.04 to 0.14)	0.08 (0.05 to 0.15)	–9.75 (–13.68 to -6.76)
MET + INS-BA		0.42 (0.24 to 0.72)	0.45 (0.26 to 0.74)	-5.79 (–9.52 to –2.46)
MET + INS-BI		0.91 (0.46 to 1.77)	0.92 (0.49 to 1.64)	–0.82 (-5.92 to 6.73)
MET + DPP-4	MET + MEG	0.11 (0.05 to 0.24)	0.12 (0.06 to 0.25)	-8.79 (–18.05 to –3.85)
MET + SGLT-2		0.14 (0.06 to 0.32)	0.15 (0.07 to 0.34)	-8.43 (–17.68 to –3.46)
MET + GLP-1		0.11 (0.04 to 0.25)	0.12 (0.05 to 0.26)	-8.80 (–18.05 to –3.84)
MET + TZD		0.08 (0.03 to 0.20)	0.09 (0.04 to 0.21)	–9.07 (–18.38 to –4.09)
MET + INS-BA		0.45 (0.17 to 1.12)	0.48 (0.20 to 1.11)	–5.15 (–14.60 to 0.65)
MET + INS-BI		0.97 (0.36 to 2.70)	0.98 (0.40 to 2.43)	–0.23 (–10.25 to 9.40)
MET + SGLT-2	MET + DPP-4	1.29 (0.79 to 2.07)	1.28 (0.79 to 2.04)	0.34 (–0.29 to 1.14)
MET + GLP-1		0.97 (0.60 to 1.56)	0.97 (0.61 to 1.55)	–0.03 (–0.54 to 0.63)
MET + TZD		0.74 (0.41 to 1.35)	0.74 (0.41 to 1.34)	–0.30 (–0.85 to 0.37)
MET + INS-BA		4.13 (2.35 to 7.05)	3.98 (2.31 to 6.59)	3.56 (1.55 to 6.88)
MET + INS-BI		8.96 (4.47 to 17.61)	8.17 (4.28 to 14.79)	8.59 (3.89 to 16.99)
MET + GLP-1	MET + SGLT-2	0.75 (0.41 to 1.41)	0.76 (0.42 to 1.41)	–0.37 (–1.25 to 0.48)
MET + TZD		0.58 (0.29 to 1.16)	0.58 (0.29 to 1.16)	–0.64 (–1.53 to 0.19)
MET + INS-BA		3.19 (1.63 to 6.38)	3.09 (1.61 to 5.99)	3.20 (1.09 to 6.63)
MET + INS-BI		6.96 (3.17 to 15.54)	6.36 (3.03 to 13.16)	8.24 (3.47 to 16.74)
MET + TZD	MET + GLP-1	0.77 (0.37 to 1.52)	0.77 (0.38 to 1.51)	–0.26 (–1.06 to 0.47)
MET + INS-BA		4.25 (2.34 to 7.52)	4.09 (2.29 to 7.05)	3.58 (1.62 to 6.80)
MET + INS-BI		9.25 (4.40 to 19.24)	8.43 (4.20 to 16.34)	8.62 (3.93 to 16.99)
MET + INS-BA	MET + TZD	5.56 (2.55 to 11.87)	5.34 (2.50 to 11.11)	3.85 (1.71 to 7.26)
MET + INS-BI		12.13 (5.01 to 28.48)	11.01 (4.77 to 24.15)	8.89 (4.08 to 17.32)
MET + INS-BI	MET + INS-BA	2.18 (1.24 to 3.85)	2.06 (1.22 to 3.44)	4.97 (1.08 to 11.82)
Random-effects model	Residual deviance	128.8 vs. 140 data points		
	Deviance information criteria	678.986		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 2: Consistency Plot for Nonsevere Hypoglycemia (Reference-Case Analysis)



Severe Hypoglycemia

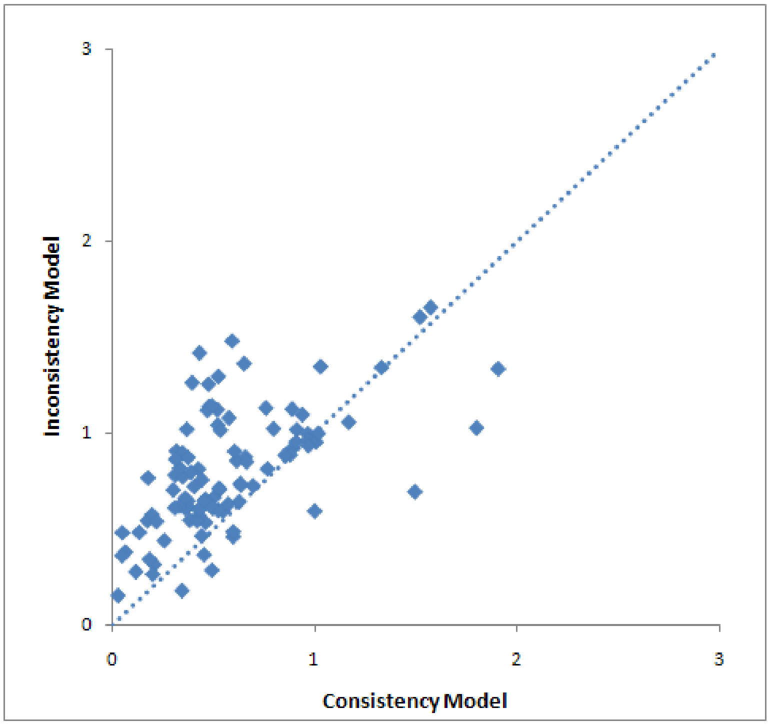
Table 3: Severe Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	6.40 (2.24 to 17.51)	6.30 (2.23 to 17.01)	1.43 (0.43 to 3.56)
MET + MEG		1.16 (0.00 to 838.50)	1.16 (0.00 to 283.50)	0.04 (–0.39 to 61.12)
MET + DPP-4		0.91 (0.34 to 2.41)	0.91 (0.34 to 2.41)	–0.02 (–0.29 to 0.25)
MET + SGLT-2		0.61 (0.13 to 2.36)	0.61 (0.14 to 2.36)	–0.10 (–0.37 to 0.29)
MET + GLP-1		1.80 (0.63 to 5.96)	1.79 (0.63 to 5.90)	0.21 (–0.13 to 1.14)
MET + TZD		2.32 (0.30 to 16.08)	2.31 (0.30 to 15.51)	0.35 (–0.23 to 3.78)
MET + INS-BA		3.08 (0.65 to 27.65)	3.06 (0.65 to 26.17)	0.55 (–0.12 to 5.67)
MET + INS-BI		3.36 (0.33 to 91.77)	3.34 (0.33 to 77.51)	0.64 (–0.23 to 14.82)
MET + MEG	MET + SUL	0.18 (0.00 to 134.80)	0.18 (0.00 to 48.98)	–1.21 (–3.59 to 59.57)
MET + DPP-4		0.14 (0.07 to 0.26)	0.15 (0.07 to 0.26)	–1.46 (–3.45 to –0.58)
MET + SGLT-2		0.09 (0.02 to 0.44)	0.10 (0.02 to 0.45)	–1.52 (–3.68 to –0.47)
MET + GLP-1		0.29 (0.09 to 0.89)	0.29 (0.09 to 0.89)	–1.15 (–3.25 to –0.11)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD		0.36 (0.04 to 2.65)	0.36 (0.05 to 2.59)	–0.98 (–3.14 to 2.24)
MET + INS-BA		0.52 (0.10 to 2.83)	0.53 (0.10 to 2.75)	–0.71 (–2.73 to 3.43)
MET + INS-BI		0.55 (0.06 to 8.71)	0.56 (0.06 to 7.72)	–0.64 (–2.79 to 12.59)
MET + DPP-4	MET + MEG	0.78 (0.00 to 724.70)	0.78 (0.00 to 723.50)	–0.07 (-60.77 to 0.43)
MET + SGLT-2		0.51 (0.00 to 440.00)	0.51 (0.00 to 438.50)	–0.14 (-61.04 to 0.44)
MET + GLP-1		1.54 (0.00 to 1,528.00)	1.54 (0.01 to 1,517.00)	0.15 (-60.61 to 1.26)
MET + TZD		2.19 (0.00 to 2,691.00)	2.17 (0.00 to 2,653.00)	0.22 (-60.69 to 3.58)
MET + INS-BA		2.82 (0.00 to 3,962.00)	2.80 (0.01 to 3,774.00)	0.40 (-60.08 to 4.54)
MET + INS-BI		3.09 (0.01 to 6 to 114.00)	3.03 (0.01 to 5,225.00)	0.35 (-59.18 to 12.48)
MET + SGLT-2	MET + DPP-4	0.66 (0.15 to 2.98)	0.66 (0.15 to 2.97)	–0.08 (–0.38 to 0.34)
MET + GLP-1		2.02 (0.68 to 6.16)	2.01 (0.68 to 6.11)	0.24 (–0.10 to 1.12)
MET + TZD		2.54 (0.32 to 19.19)	2.53 (0.32 to 18.41)	0.37 (–0.22 to 3.81)
MET + INS-BA		3.61 (0.74 to 20.31)	3.59 (0.74 to 19.19)	0.59 (–0.07 to 5.53)
MET + INS-BI		3.92 (0.42 to 60.32)	3.89 (0.42 to 51.22)	0.67 (–0.15 to 14.74)
MET + GLP-1	MET + SGLT-2	2.97 (0.61 to 17.70)	2.96 (0.61 to 17.55)	0.31 (–0.17 to 1.27)
MET + TZD		3.89 (0.33 to 35.21)	3.87 (0.33 to 34.19)	0.45 (–0.25 to 3.90)
MET + INS-BA		5.25 (0.73 to 56.37)	5.21 (0.73 to 53.43)	0.65 (–0.09 to 5.73)
MET + INS-BI		5.54 (0.44 to 139.60)	5.50 (0.44 to 121.50)	0.74 (–0.18 to 14.87)
MET + TZD	MET + GLP-1	1.20 (0.15 to 10.72)	1.19 (0.15 to 10.38)	0.09 (–0.81 to 3.49)
MET + INS-BA		1.73 (0.36 to 12.74)	1.72 (0.36 to 12.04)	0.33 (–0.62 to 5.24)
MET + INS-BI		1.91 (0.18 to 34.90)	1.90 (0.18 to 30.66)	0.41 (–0.77 to 14.53)
MET + INS-BA	MET + TZD	1.37 (0.15 to 30.36)	1.37 (0.15 to 28.60)	0.19 (–3.00 to 5.24)
MET + INS-BI		1.45 (0.09 to 67.31)	1.44 (0.10 to 58.50)	0.22 (–2.56 to 14.49)
MET + INS-BI	MET + INS-BA	1.04 (0.16 to 11.39)	1.04 (0.16 to 9.89)	0.03 (–1.96 to 11.35)
Random-effects model	Residual deviance	57.31 vs. 100 data points		
	Deviance information criteria	299.795		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 3: Consistency Plot for Severe Hypoglycemia (Reference-Case Analysis)



Body Mass Index (BMI)

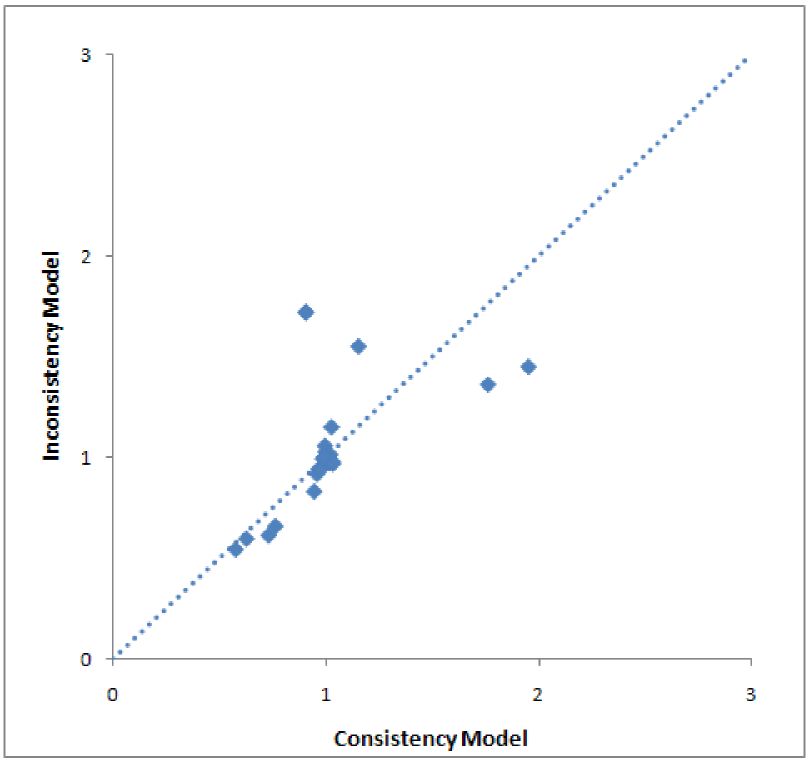
Table 4: BMI: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	0.80 (–0.36 to 2.08)
MET + DPP-4		–0.33 (–1.30 to 0.58)
MET + GLP-1		–1.11 (–2.54 to 0.38)
MET + AGI		0.22 (–2.59 to 3.11)
MET + TZD		1.41 (0.22 to 2.67)
MET + INS-BA		2.57 (–1.04 to 6.20)
MET + DPP-4	MET + SUL	–1.13 (–2.78 to 0.32)
MET + GLP-1		–1.91 (–3.39 to –0.49)
MET + AGI		–0.58 (–3.19 to 2.02)
MET + TZD		0.61 (–0.62 to 1.81)
MET + INS-BA		1.77 (–1.86 to 5.41)
MET + GLP-1	MET + DPP-4	–0.78 (–2.43 to 1.04)
MET + AGI		0.54 (–2.39 to 3.61)
MET + TZD		1.74 (0.28 to 3.36)
MET + INS-BA		2.89 (–0.78 to 6.61)
MET + AGI	MET + GLP-1	1.32 (–1.64 to 4.30)
MET + TZD		2.52 (0.83 to 4.23)

Treatment	Reference	MD (95% CrI)
MET + INS-BA		3.68 (0.36 to 7.01)
MET + TZD	MET + AGI	1.20 (–1.66 to 4.07)
MET + INS-BA		2.35 (–2.14 to 6.82)
MET + INS-BA	MET + TZD	1.16 (–2.58 to 4.91)
Random-effects model	Residual deviance	28.3 vs. 28 data points
	Deviance information criteria	41.431

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; MD = mean difference; MET = metformin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 4: Consistency Plot for BMI (Reference-Case Analysis)



Weight

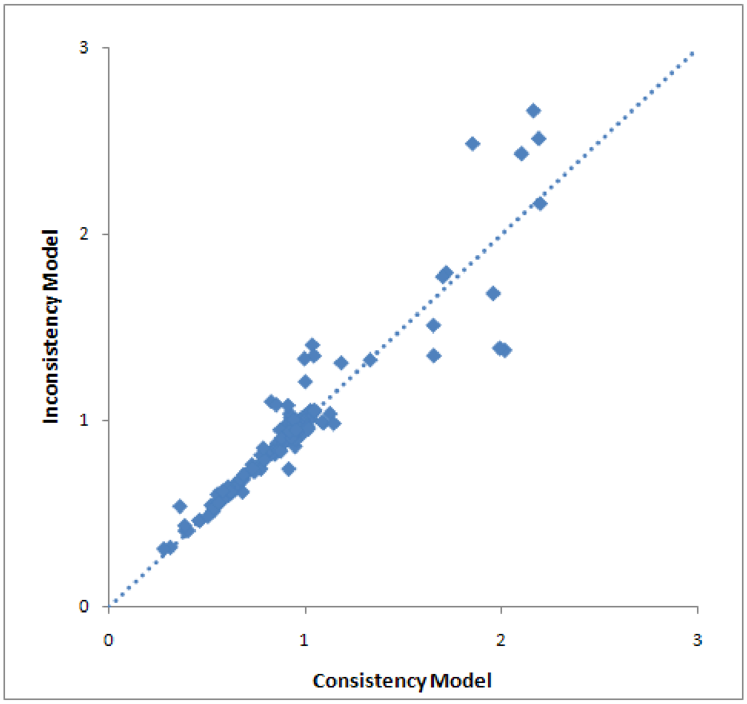
Table 5: Weight: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	2.11 (1.59 to 2.63)
MET + MEG		1.26 (0.28 to 2.28)
MET + DPP-4		0.18 (–0.22 to 0.58)
MET + SGLT-2		–2.21 (–2.75 to –1.67)
MET + GLP-1		–1.44 (–2.07 to –0.81)
MET + TZD		3.20 (2.57 to 3.82)

Treatment	Reference	MD (95% CrI)
MET + INS-BA		2.76 (1.56 to 4.01)
MET + INS-BI		2.91 (0.85 to 5.04)
MET + MEG	MET + SUL	–0.85 (–1.96 to 0.30)
MET + DPP-4		–1.93 (–2.37 to –1.49)
MET + SGLT-2		–4.32 (–5.00 to –3.66)
MET + GLP–1		–3.55 (–4.26 to –2.85)
MET + TZD		1.09 (0.48 to 1.70)
MET + INS-BA		0.65 (–0.57 to 1.95)
MET + INS-BI		0.80 (–1.26 to 2.96)
MET + DPP-4	MET + MEG	–1.08 (–2.18 to –0.02)
MET + SGLT-2		–3.47 (–4.63 to –2.35)
MET + GLP-1		–2.70 (–3.89 to –1.52)
MET + TZD		1.94 (0.77 to 3.10)
MET + INS-BA		1.50 (–0.06 to 3.07)
MET + INS-BI		1.65 (–0.64 to 3.98)
MET + SGLT-2	MET + DPP-4	–2.39 (–2.98 to –1.80)
MET + GLP-1		–1.62 (–2.25 to –0.99)
MET + TZD		3.02 (2.43 to 3.61)
MET + INS-BA		2.59 (1.41 to 3.82)
MET + INS-BI		2.73 (0.70 to 4.84)
MET + GLP-1	MET + SGLT-2	0.78 (–0.02 to 1.57)
MET + TZD		5.41 (4.63 to 6.18)
MET + INS-BA		4.98 (3.68 to 6.31)
MET + INS-BI		5.13 (3.03 to 7.30)
MET + TZD	MET + GLP-1	4.64 (3.85 to 5.42)
MET + INS-BA		4.20 (3.03 to 5.40)
MET + INS-BI		4.35 (2.33 to 6.46)
MET + INS-BA	MET + TZD	–0.44 (–1.70 to 0.90)
MET + INS-BI		–0.29 (–2.39 to 1.90)
MET + INS-BI	MET + INS-BA	0.15 (–1.54 to 1.82)
Random-effects model	Residual deviance	138.4 vs. 148 data points
	Deviance information criteria	307.531

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; MD = mean difference; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 5: Consistency Plot for Weight (Reference-Case Analysis)



Systolic Blood Pressure (SBP)

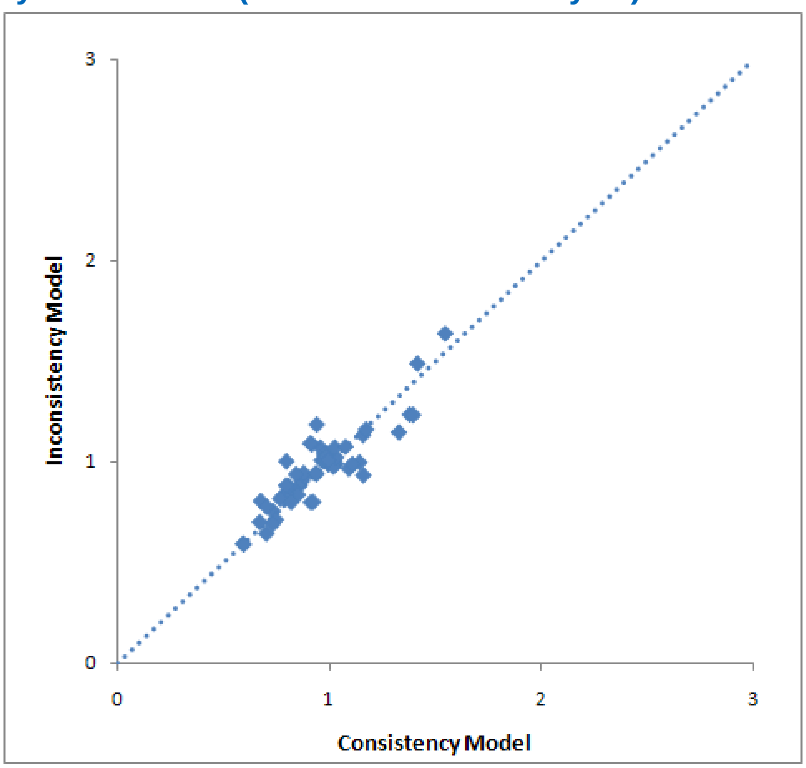
Table 6: Systolic Blood Pressure: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	0.28 (–1.54 to 2.06)
MET + DPP-4		–1.04 (–2.34 to 0.22)
MET + SGLT-2		–4.06 (–5.24 to –2.89)
MET + GLP-1		–2.79 (–4.57 to –1.07)
MET + TZD		–2.02 (–4.02 to –0.11)
MET + INS-BA		1.01 (–3.04 to 5.16)
MET + INS-BI		0.15 (–5.62 to 5.93)
MET + DPP-4	MET + SUL	–1.31 (–3.19 to 0.57)
MET + SGLT-2		–4.33 (–6.17 to –2.47)
MET + GLP-1		–3.07 (–5.35 to –0.78)
MET + TZD		–2.29 (–3.87 to –0.76)
MET + INS-BA		0.73 (–3.61 to 5.10)
MET + INS-BI		–0.13 (–6.10 to 5.84)
MET + SGLT-2	MET + DPP-4	–3.02 (–4.39 to –1.61)
MET + GLP-1		–1.75 (–3.46 to –0.02)
MET + TZD		–0.98 (–3.01 to 1.01)
MET + INS-BA		2.05 (–1.85 to 6.03)

Treatment	Reference	MD (95% CrI)
MET + INS-BI		1.18 (–4.47 to 6.87)
MET + GLP-1	MET + SGLT-2	1.27 (–0.71 to 3.21)
MET + TZD		2.04 (–0.04 to 4.08)
MET + INS-BA		5.07 (0.96 to 9.21)
MET + INS-BI		4.20 (–1.61 to 10.06)
MET + TZD	MET + GLP-1	0.78 (–1.56 to 3.07)
MET + INS-BA		3.80 (–0.43 to 8.12)
MET + INS-BI		2.94 (–2.95 to 8.85)
MET + INS-BA	MET + TZD	3.02(–1.35 to 7.47)
MET + INS-BI		2.16(–3.81 to 8.20)
MET + INS-BI	MET + INS-BA	–0.86(–4.96 to 3.22)
Random-effects model	Residual deviance	58.75 vs. 62 data points
	Deviance information criteria	208.403

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MD = mean difference; MET = metformin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 6: Consistency Plot for SBP (Reference-Case Analysis)



Nocturnal Hypoglycemia

Table 7: Nocturnal Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLP-1	MET + DPP-4	1.45 (0.44 to 5.10)	1.43 (0.45 to 4.59)	1.27 (–1.93 to 9.64)
MET + INS-BA		5.92 (1.82 to 20.08)	5.15 (1.76 to 13.64)	12.38 (2.56 to 32.26)
MET + INS-BI		9.72 (2.37 to 41.27)	7.64 (2.26 to 20.65)	20.11 (4.19 to 50.52)
MET + INS-BA	MET + GLP-1	4.09 (0.73 to 22.49)	3.60 (0.76 to 16.04)	10.90 (–2.21 to 31.18)
MET + INS-BI		6.74 (1.02 to 43.42)	5.35 (1.02 to 23.23)	18.52 (0.16 to 49.09)
MET + INS-BI	MET + INS-BA	1.64 (0.77 to 3.65)	1.48 (0.81 to 2.60)	7.26 (–2.88 to 24.97)
Random-effects model	Residual deviance	10.97 vs. 10 data points		
	Deviance information criteria	61.45		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; vs. = versus.

Diastolic Blood Pressure (DBP)

Table 8: Diastolic Blood Pressure: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	–0.30 (–1.43 to 0.80)
MET + DPP-4		–1.07 (–1.87 to –0.21)
MET + SGLT-2		–2.22 (–2.99 to –1.41)
MET + GLP-1		–1.09 (–2.13 to –0.01)
MET + TZD		–1.61 (–2.91 to –0.36)
MET + DPP-4	MET + SUL	–0.77 (–1.89 to 0.42)
MET + SGLT-2		–1.92 (–3.05 to –0.73)
MET + GLP-1		–0.79 (–2.11 to 0.58)
MET + TZD		–1.31 (–2.20 to –0.45)
MET + SGLT-2	MET + DPP-4	–1.15 (–2.15 to –0.14)
MET + GLP-1		–0.02 (–1.04 to 0.99)
MET + TZD		–0.54 (–1.87 to 0.69)
MET + GLP-1	MET + SGLT-2	1.13 (–0.11 to 2.36)
MET + TZD		0.61 (–0.77 to 1.88)
MET + TZD	MET + GLP-1	–0.52 (–1.98 to 0.85)
Random-effects model	Residual deviance	49.78 vs. 53 data points
	Deviance information criteria	141.401

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; MD = mean difference; MET = metformin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

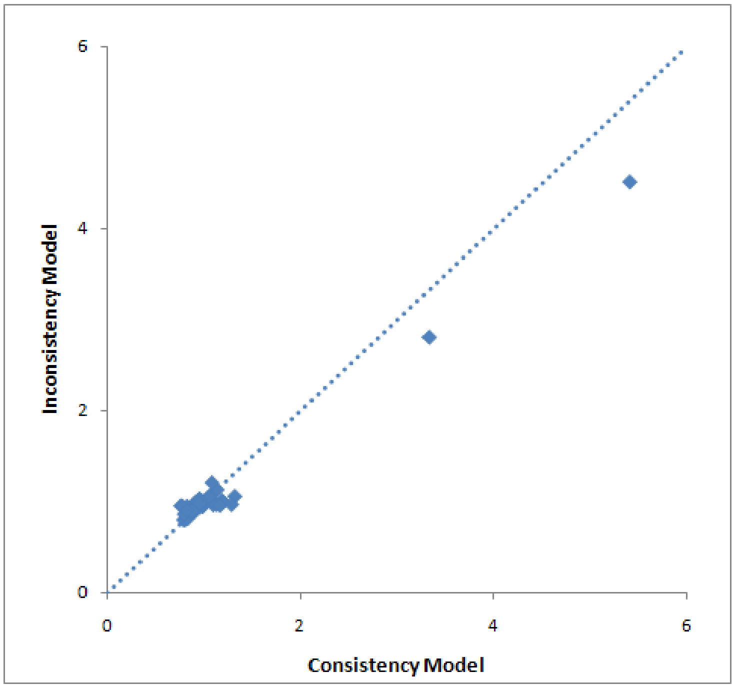
LDL Cholesterol

Table 9: Low-Density Lipoprotein Cholesterol: Mean Difference for All Treatment Comparisons —Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	0.06 (–0.09 to 0.20)
MET + MEG		0.06 (–0.23 to 0.35)
MET + DPP-4		–0.02 (–0.12 to 0.08)
MET + SGLT-2		0.14 (0.02 to 0.27)
MET + GLP-1		–0.02 (–0.17 to 0.13)
MET + TZD		0.23 (0.11 to 0.35)
MET + INS-BA		–0.18 (–0.47 to 0.11)
MET + MEG	MET + SUL	0.00 (–0.32 to 0.33)
MET + DPP-4		–0.07 (–0.22 to 0.07)
MET + SGLT-2		0.08 (–0.10 to 0.27)
MET + GLP-1		–0.08 (–0.27 to 0.11)
MET + TZD		0.17 (0.05 to 0.29)
MET + INS-BA		–0.24 (–0.55 to 0.07)
MET + DPP-4	MET + MEG	–0.08 (–0.39 to 0.23)
MET + SGLT-2		0.08 (–0.24 to 0.40)
MET + GLP-1		–0.08 (–0.41 to 0.25)
MET + TZD		0.17 (–0.14 to 0.48)
MET + INS-BA		–0.24 (–0.65 to 0.17)
MET + SGLT-2	MET + DPP-4	0.16 (0.02 to 0.30)
MET + GLP-1		0.00 (–0.15 to 0.15)
MET + TZD		0.25 (0.13 to 0.37)
MET + INS-BA		–0.16 (–0.43 to 0.11)
MET + GLP-1	MET + SGLT-2	–0.16 (–0.35 to 0.02)
MET + TZD		0.09 (–0.07 to 0.25)
MET + INS-BA		–0.32 (–0.63 to –0.02)
MET + TZD	MET + GLP-1	0.25 (0.08 to 0.42)
MET + INS-BA		–0.16(–0.45 to 0.13)
MET + INS-BA	MET + TZD	–0.41(–0.71 to –0.11)
Random-effects model	Residual deviance	71.91 vs. 68 data points
	Deviance information criteria	–131.999

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; MD = mean difference; MEG = meglitinide; MET = metformin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 7: Consistency Plot for LDL (Reference-Case Analysis)



HDL Cholesterol

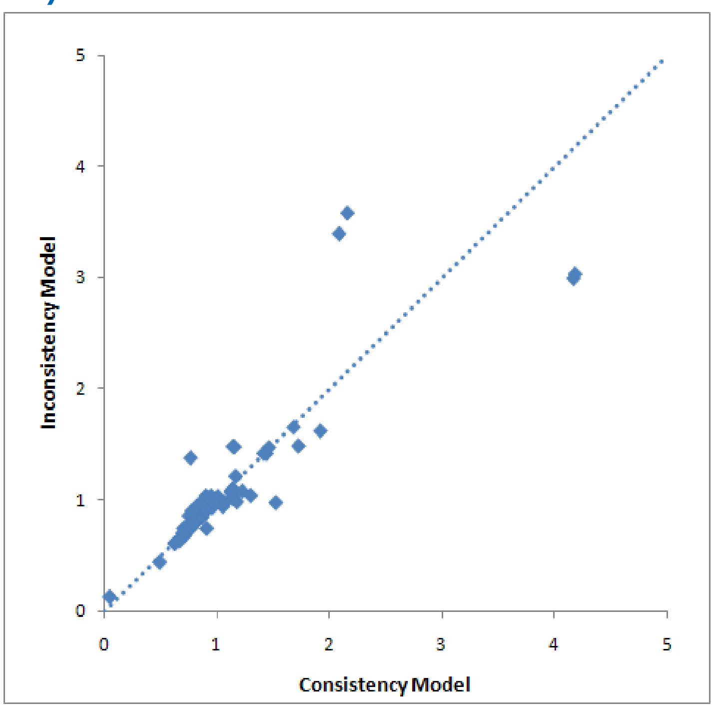
Table 10: High-Density Lipoprotein Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	–0.02 (–0.06 to 0.01)
MET + MEG		0.00 (–0.06 to 0.05)
MET + DPP-4		–0.01 (–0.03 to 0.02)
MET + SGLT-2		0.06 (0.03 to 0.09)
MET + GLP-1		–0.02 (–0.06 to 0.02)
MET + TZD		0.10 (0.07 to 0.13)
MET + INS-BA		–0.02 (–0.09 to 0.06)
MET + INS-BI		0.03 (–0.05 to 0.11)
MET + MEG	MET + SUL	0.02 (–0.04 to 0.08)
MET + DPP-4		0.02 (–0.01 to 0.05)
MET + SGLT-2		0.09 (0.05 to 0.13)
MET + GLP-1		0.01 (–0.04 to 0.05)
MET + TZD		0.12 (0.10 to 0.15)
MET + INS-BA		0.01 (–0.07 to 0.08)
MET + INS-BI		0.05 (–0.02 to 0.12)
MET + DPP-4	MET + MEG	0.00 (–0.06 to 0.06)
MET + SGLT-2		0.07 (0.01 to 0.13)
MET + GLP-1		–0.01 (–0.08 to 0.05)
MET + TZD		0.11 (0.05 to 0.16)
MET + INS-BA		–0.01 (–0.11 to 0.08)

Treatment	Reference	MD (95% CrI)
MET + INS-BI		0.03 (–0.06 to 0.13)
MET + SGLT-2	MET + DPP-4	0.07 (0.04 to 0.10)
MET + GLP-1		–0.01 (–0.04 to 0.03)
MET + TZD		0.11 (0.08 to 0.13)
MET + INS-BA		–0.01 (–0.08 to 0.06)
MET + INS-BI		0.03 (–0.04 to 0.11)
MET + GLP-1	MET + SGLT-2	–0.08 (–0.12 to –0.03)
MET + TZD		0.04 (0.00 to 0.08)
MET + INS-BA		–0.08 (–0.16 to 0.00)
MET + INS-BI		–0.04 (–0.12 to 0.05)
MET + TZD	MET + GLP-1	0.12 (0.08 to 0.16)
MET + INS-BA		0.00 (–0.08 to 0.08)
MET + INS-BI		0.04 (–0.04 to 0.13)
MET + INS-BA	MET + TZD	–0.12 (–0.20 to –0.04)
MET + INS-BI		–0.07 (–0.15 to 0.00)
MET + INS-BI	MET + INS-BA	0.04 (–0.06 to 0.15)
Random-effects model	Residual deviance	84.6 vs. 78 data points
	Deviance information criteria	–333.356

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MD = mean difference; MEG = meglitinide; MET = metformin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 8: Consistency Plot for High-Density Lipoprotein Cholesterol (Reference-Case Analysis)



Total Adverse Events

Table 11: Total Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	1.14 (0.99 to 1.32)	1.07 (1.00 to 1.15)	3.35 (–0.25 to 6.89)
MET + MEG		1.10 (0.72 to 1.66)	1.05 (0.83 to 1.26)	2.36 (-8.04 to 12.52)
MET + DPP-4		0.97 (0.87 to 1.08)	0.98 (0.93 to 1.04)	–0.81 (–3.52 to 1.93)
MET + SGLT-2		1.03 (0.88 to 1.21)	1.02 (0.93 to 1.10)	0.82 (–3.20 to 4.78)
MET + GLP-1		1.38 (1.12 to 1.68)	1.16 (1.06 to 1.27)	7.94 (2.79 to 12.74)
MET + TZD		1.05 (0.87 to 1.28)	1.03 (0.93 to 1.13)	1.30 (–3.43 to 6.16)
MET + INS-BA		2.20 (1.47 to 3.33)	1.39 (1.20 to 1.57)	18.99 (9.55 to 27.38)
MET + INS-BI		2.32 (1.42 to 3.79)	1.42 (1.18 to 1.63)	20.08 (8.70 to 29.83)
MET + MEG	MET + SUL	0.96 (0.62 to 1.50)	0.98 (0.77 to 1.20)	–1.00 (–11.95 to 9.98)
MET + DPP-4		0.85 (0.76 to 0.95)	0.92 (0.87 to 0.97)	–4.16 (–6.93 to –1.33)
MET + SGLT-2		0.90 (0.75 to 1.10)	0.95 (0.86 to 1.05)	–2.55 (–7.28 to 2.27)
MET + GLP-1		1.20 (0.96 to 1.50)	1.09 (0.98 to 1.20)	4.58 (–1.05 to 10.02)
MET + TZD		0.92 (0.77 to 1.10)	0.96 (0.88 to 1.05)	–2.04 (–6.43 to 2.44)
MET + INS-BA		1.93 (1.29 to 2.89)	1.30 (1.12 to 1.48)	15.65 (6.26 to 23.98)
MET + INS-BI		2.03 (1.26 to 3.27)	1.32 (1.11 to 1.52)	16.73 (5.66 to 26.16)
MET + DPP-4	MET + MEG	0.88 (0.57 to 1.36)	0.94 (0.77 to 1.19)	–3.13 (–13.88 to 7.58)
MET + SGLT-2		0.94 (0.60 to 1.47)	0.97 (0.79 to 1.23)	–1.53 (–12.75 to 9.45)
MET + GLP-1		1.25 (0.79 to 1.98)	1.11 (0.90 to 1.41)	5.58 (–5.86 to 16.92)
MET + TZD		0.96 (0.60 to 1.53)	0.98 (0.79 to 1.25)	–1.03 (–12.52 to 10.46)
MET + INS-BA		2.01 (1.12 to 3.59)	1.33 (1.05 to 1.71)	16.58 (2.76 to 29.86)
MET + INS-BI		2.11 (1.10 to 4.05)	1.35 (1.04 to 1.76)	17.70 (2.23 to 32.03)
MET + SGLT-2	MET + DPP-4	1.07 (0.90 to 1.27)	1.03 (0.94 to 1.13)	1.61 (–2.68 to 5.97)
MET + GLP-1		1.42 (1.16 to 1.73)	1.18 (1.08 to 1.29)	8.74 (3.73 to 13.60)
MET + TZD		1.09 (0.91 to 1.31)	1.04 (0.95 to 1.14)	2.10 (–2.44 to 6.71)
MET + INS-BA		2.28 (1.54 to 3.37)	1.42 (1.22 to 1.59)	19.78 (10.67 to 27.82)
MET + INS-BI		2.39 (1.48 to 3.87)	1.44 (1.21 to 1.65)	20.89 (9.81 to 30.34)
MET + GLP-1	MET + SGLT-2	1.33 (1.04 to 1.71)	1.15 (1.02 to 1.28)	7.10 (0.95 to 13.19)
MET + TZD		1.02 (0.81 to 1.29)	1.01 (0.90 to 1.14)	0.49 (–5.35 to 6.37)
MET + INS-BA		2.13 (1.39 to 3.30)	1.37 (1.16 to 1.58)	18.10 (8.21 to 27.27)
MET + INS-BI		2.25 (1.36 to 3.74)	1.39 (1.15 to 1.62)	19.31 (7.63 to 29.52)
MET + TZD	MET + GLP-1	0.77 (0.59 to 1.00)	0.88 (0.78 to 1.00)	–6.65 (–13.13 to 0.05)
MET + INS-BA		1.60 (1.04 to 2.49)	1.20 (1.02 to 1.38)	11.01 (0.89 to 20.44)
MET + INS-BI		1.69 (1.01 to 2.85)	1.22 (1.00 to 1.43)	12.16 (0.23 to 22.88)
MET + INS-BA	MET + TZD	2.10 (1.36 to 3.21)	1.36 (1.15 to 1.57)	17.69 (7.53 to 26.75)
MET + INS-BI		2.20 (1.32 to 3.64)	1.38 (1.14 to 1.61)	18.78 (6.92 to 28.89)
MET + INS-BI	MET + INS-BA	1.06 (0.67 to 1.63)	1.02 (0.87 to 1.16)	1.19 (–8.91 to 10.29)
Random-effects model	Residual deviance	118.5 vs. 120 data points		
	Deviance information criteria	828.862		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

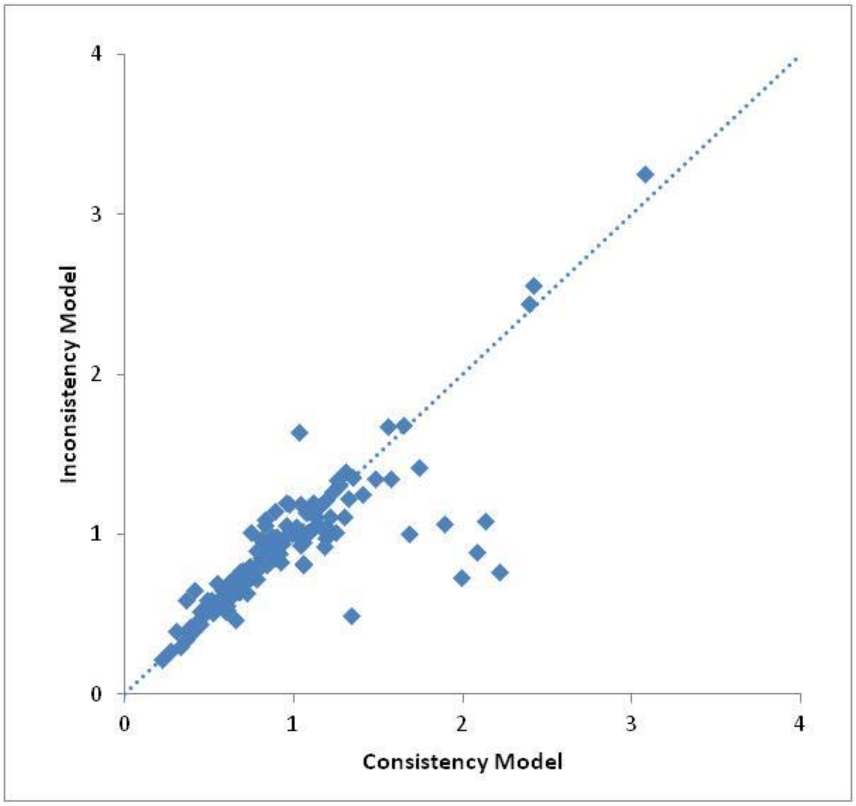
Serious Adverse Events

Table 12: Serious Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	0.96 (0.76 to 1.21)	0.96 (0.76 to 1.21)	–0.10 (–0.62 to 0.44)
MET + MEG		3.81 (1.17 to 23.71)	3.57 (1.16 to 15.92)	5.98 (0.39 to 32.42)
MET + DPP-4		0.91 (0.72 to 1.15)	0.91 (0.73 to 1.14)	–0.21 (–0.71 to 0.31)
MET + SGLT-2		1.11 (0.83 to 1.51)	1.11 (0.84 to 1.49)	0.26 (–0.41 to 1.06)
MET + GLP-1		1.05 (0.71 to 1.51)	1.05 (0.71 to 1.50)	0.11 (–0.70 to 1.11)
MET + TZD		1.05 (0.81 to 1.37)	1.05 (0.81 to 1.36)	0.11 (–0.48 to 0.79)
MET + INS-BA		1.48 (0.63 to 3.74)	1.46 (0.63 to 3.53)	1.06 (–0.88 to 5.75)
MET + INS-BI		1.73 (0.42 to 8.43)	1.70 (0.43 to 7.18)	1.63 (–1.36 to 14.28)
MET + MEG	MET + SUL	3.96 (1.23 to 24.36)	3.71 (1.22 to 16.34)	6.06 (0.52 to 32.43)
MET + DPP-4		0.95 (0.82 to 1.10)	0.95 (0.82 to 1.10)	–0.12 (–0.44 to 0.20)
MET + SGLT-2		1.17 (0.87 to 1.55)	1.16 (0.87 to 1.53)	0.36 (–0.31 to 1.11)
MET + GLP-1		1.10 (0.74 to 1.61)	1.09 (0.75 to 1.59)	0.21 (–0.61 to 1.21)
MET + TZD		1.09 (0.89 to 1.37)	1.09 (0.89 to 1.36)	0.19 (–0.26 to 0.77)
MET + INS-BA		1.54 (0.67 to 3.83)	1.52 (0.68 to 3.61)	1.15 (–0.72 to 5.77)
MET + INS-BI		1.83 (0.45 to 8.70)	1.80 (0.45 to 7.43)	1.75 (–1.25 to 14.36)
MET + DPP-4	MET + MEG	0.24 (0.04 to 0.79)	0.26 (0.06 to 0.79)	–6.17 (–32.56 to –0.58)
MET + SGLT-2		0.29 (0.05 to 0.93)	0.31 (0.07 to 0.93)	–5.67 (–32.09 to –0.19)
MET + GLP-1		0.28 (0.04 to 0.96)	0.29 (0.06 to 0.96)	–5.83 (–32.34 to –0.10)
MET + TZD		0.28 (0.04 to 0.92)	0.29 (0.06 to 0.92)	–5.86 (–32.24 to –0.22)
MET + INS-BA		0.39 (0.05 to 1.72)	0.41 (0.07 to 1.68)	–4.70 (–31.69 to 2.51)
MET + INS-BI		0.43 (0.04 to 3.24)	0.45 (0.06 to 2.94)	–4.13 (-31.66 to 9.21)
MET + SGLT-2	MET + DPP-4	1.23 (0.91 to 1.66)	1.23 (0.91 to 1.64)	0.48 (–0.21 to 1.26)
MET + GLP-1		1.16 (0.80 to 1.66)	1.15 (0.80 to 1.64)	0.32 (–0.44 to 1.28)
MET + TZD		1.15 (0.92 to 1.47)	1.15 (0.92 to 1.46)	0.31 (–0.17 to 0.93)
MET + INS-BA		1.63 (0.72 to 4.02)	1.60 (0.72 to 3.79)	1.26 (–0.58 to 5.85)
MET + INS-BI		1.93 (0.47 to 9.13)	1.89 (0.47 to 7.77)	1.85 (–1.14 to 14.41)
MET + GLP-1	MET + SGLT-2	0.94 (0.60 to 1.49)	0.94 (0.61 to 1.47)	–0.16 (–1.19 to 1.03)
MET + TZD		0.93 (0.69 to 1.33)	0.93 (0.70 to 1.32)	–0.18 (–0.96 to 0.70)
MET + INS-BA		1.33 (0.55 to 3.34)	1.32 (0.56 to 3.16)	0.82 (–1.25 to 5.46)
MET + INS-BI		1.57 (0.38 to 7.77)	1.54 (0.38 to 6.64)	1.39 (–1.68 to 14.04)
MET + TZD	MET + GLP-1	1.00 (0.67 to 1.51)	1.00 (0.67 to 1.50)	–0.01 (–1.06 to 0.91)
MET + INS-BA		1.41 (0.61 to 3.46)	1.40 (0.62 to 3.27)	0.95 (–1.03 to 5.43)
MET + INS-BI		1.68 (0.39 to 7.83)	1.65 (0.40 to 6.75)	1.55 (–1.60 to 14.04)
MET + INS-BA	MET + TZD	1.41 (0.58 to 3.48)	1.40 (0.59 to 3.29)	0.96 (–1.08 to 5.50)
MET + INS-BI		1.67 (0.40 to 7.99)	1.64 (0.41 to 6.79)	1.54 (–1.53 to 14.13)
MET + INS-BI	MET + INS-BA	1.18 (0.37 to 4.11)	1.17 (0.38 to 3.67)	0.54 (–2.73 to 11.25)
Random-effects model	Residual deviance	129.3 vs. 140 data points		
	Deviance information criteria	701.988		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 9: Consistency Plot for Serious Adverse Events (Reference-Case Analysis)



Withdrawals Due to Adverse Events

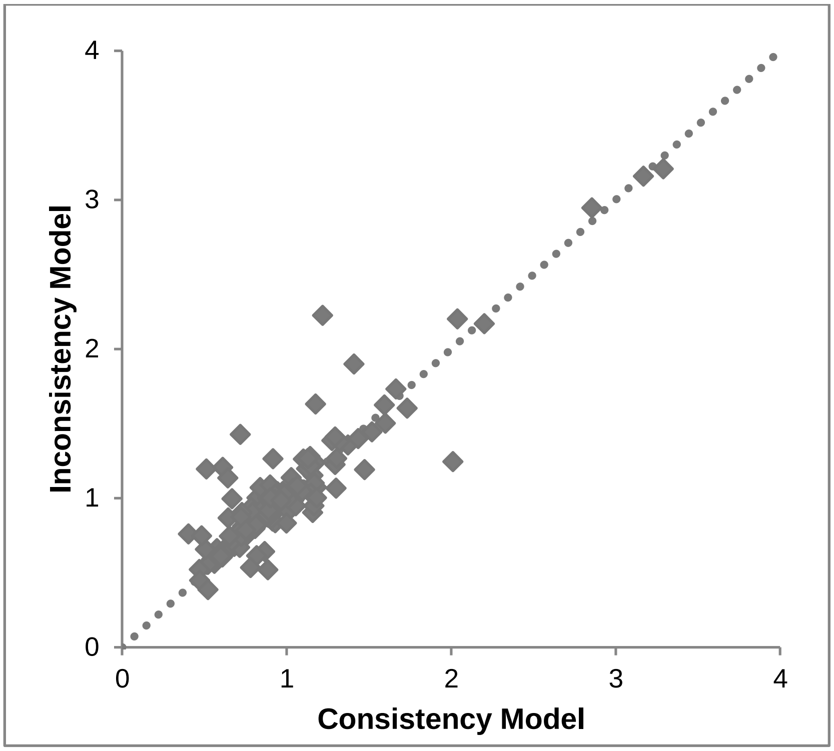
Table 13: Withdrawals Due to Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	0.74 (0.51 to 1.11)	0.75 (0.52 to 1.10)	–0.72 (–1.51 to 0.28)
MET + MEG		0.72 (0.21 to 2.42)	0.72 (0.21 to 2.33)	–0.79 (–2.36 to 3.77)
MET + DPP-4		0.78 (0.56 to 1.09)	0.78 (0.57 to 1.08)	–0.63 (–1.36 to 0.22)
MET + SGLT-2		1.00 (0.61 to 1.66)	1.00 (0.62 to 1.63)	–0.01 (–1.15 to 1.71)
MET + GLP-1		1.81 (1.12 to 2.99)	1.77 (1.11 to 2.84)	2.20 (0.34 to 5.06)
MET + TZD		1.00 (0.64 to 1.64)	1.00 (0.65 to 1.61)	0.00 (–1.09 to 1.64)
MET + INS-BA		0.33 (0.07 to 1.40)	0.34 (0.07 to 1.39)	–1.88 (–2.88 to 1.10)
MET + INS-BI		3.27 (0.41 to 54.86)	3.07 (0.42 to 21.39)	5.93 (–1.67 to 59.10)
MET + MEG	MET + SUL	0.96 (0.27 to 3.34)	0.97 (0.27 to 3.19)	–0.08 (–1.83 to 4.48)
MET + DPP-4		1.04 (0.76 to 1.45)	1.04 (0.76 to 1.44)	0.09 (–0.66 to 0.77)
MET + SGLT-2		1.34 (0.76 to 2.39)	1.33 (0.77 to 2.34)	0.70 (–0.62 to 2.42)
MET + GLP-1		2.42 (1.46 to 4.10)	2.35 (1.45 to 3.88)	2.90 (1.07 to 5.68)
MET + TZD		1.35 (0.91 to 2.04)	1.34 (0.91 to 2.00)	0.71 (–0.22 to 2.03)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BA		0.45 (0.09 to 1.90)	0.45 (0.09 to 1.87)	–1.15 (–2.37 to 1.76)
MET + INS-BI		4.38 (0.56 to 75.00)	4.07 (0.56 to 29.26)	6.63 (–0.96 to 59.76)
MET + DPP-4	MET + MEG	1.09 (0.32 to 3.88)	1.08 (0.33 to 3.81)	0.17 (–4.40 to 1.85)
MET + SGLT-2		1.39 (0.38 to 5.32)	1.38 (0.39 to 5.17)	0.77 (–3.89 to 3.08)
MET + GLP-1		2.51 (0.68 to 9.70)	2.44 (0.69 to 9.15)	2.91 (–1.89 to 6.32)
MET + TZD		1.39 (0.39 to 5.25)	1.38 (0.40 to 5.11)	0.78 (–3.82 to 3.00)
MET + INS-BA		0.46 (0.06 to 3.16)	0.47 (0.07 to 3.10)	–1.03 (–5.55 to 2.17)
MET + INS-BI		4.72 (0.41 to 94.24)	4.34 (0.42 to 41.27)	6.51 (–2.27 to 59.31)
MET + SGLT-2	MET + DPP-4	1.28 (0.74 to 2.22)	1.27 (0.75 to 2.17)	0.62 (–0.66 to 2.34)
MET + GLP-1		2.33 (1.44 to 3.79)	2.26 (1.42 to 3.58)	2.82 (1.01 to 5.57)
MET + TZD		1.29 (0.84 to 2.02)	1.28 (0.84 to 1.98)	0.63 (–0.40 to 2.07)
MET + INS-BA		0.43 (0.09 to 1.78)	0.44 (0.09 to 1.74)	–1.25 (–2.31 to 1.65)
MET + INS-BI		4.21 (0.53 to 72.11)	3.93 (0.54 to 28.14)	6.54 (–1.07 to 59.75)
MET + GLP-1	MET + SGLT-2	1.82 (0.93 to 3.56)	1.77 (0.93 to 3.37)	2.19 (–0.26 to 5.24)
MET + TZD		1.01 (0.54 to 1.91)	1.01 (0.55 to 1.88)	0.02 (–1.88 to 1.87)
MET + INS-BA		0.33 (0.07 to 1.51)	0.34 (0.07 to 1.49)	–1.82 (–3.69 to 1.20)
MET + INS-BI		3.29 (0.38 to 57.58)	3.08 (0.39 to 22.51)	5.89 (–2.01 to 59.10)
MET + TZD	MET + GLP-1	0.55 (0.31 to 1.00)	0.57 (0.33 to 1.00)	–2.17 (–5.00 to –0.02)
MET + INS-BA		0.19 (0.04 to 0.77)	0.19 (0.04 to 0.78)	–3.95 (–6.89 to –0.97)
MET + INS-BI		1.80 (0.22 to 31.25)	1.73 (0.23 to 12.65)	3.65 (–4.52 to 56.64)
MET + INS-BA	MET + TZD	0.33 (0.07 to 1.43)	0.34 (0.07 to 1.41)	–1.83 (–3.60 to 1.05)
MET + INS-BI		3.25 (0.40 to 57.58)	3.05 (0.41 to 22.34)	5.88 (–1.87 to 58.97)
MET + INS-BI	MET + INS-BA	9.89 (1.32 to 161.30)	8.90 (1.31 to 77.99)	7.59 (0.36 to 60.08)
Random-effects model	Residual deviance	146 vs. 149 data points		
	Deviance information criteria	773.773		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 10: Consistency Plot for Withdrawals Due to Adverse Events(Reference-Case Analysis)



Urogenital Adverse Events

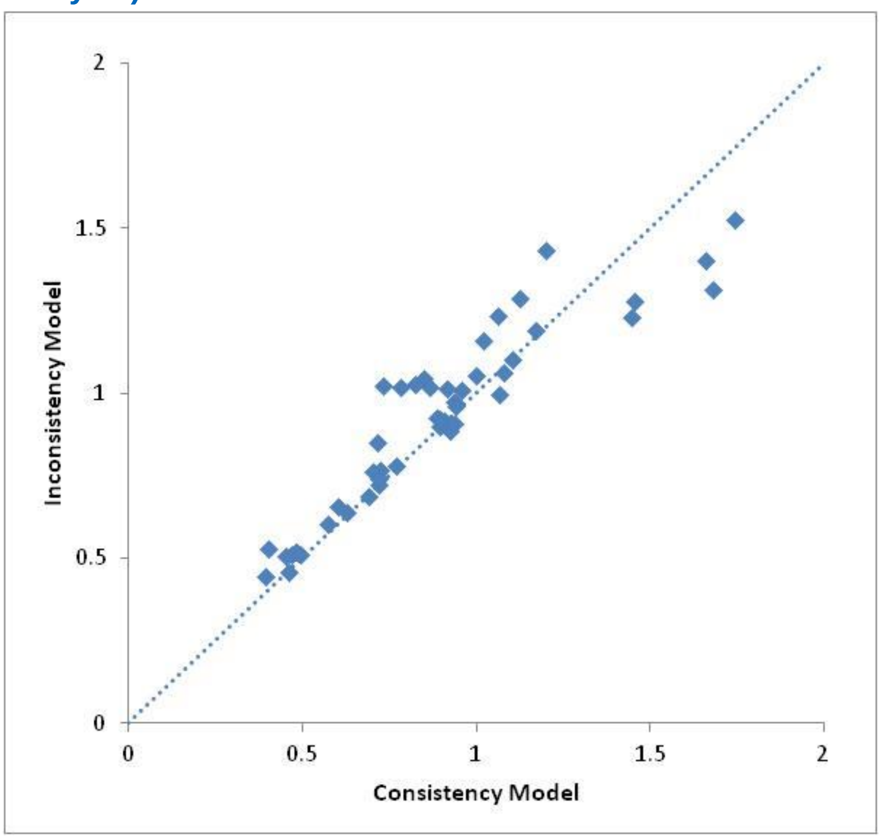
Table 14: Urogenital Adverse Events (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	1.02 (0.69 to 1.49)	1.02 (0.70 to 1.48)	0.06 (–0.90 to 1.12)
MET + DPP-4		1.23 (0.90 to 1.72)	1.22 (0.90 to 1.69)	0.59 (–0.30 to 1.59)
MET + SGLT-2		1.06 (0.70 to 1.58)	1.05 (0.70 to 1.56)	0.14 (–0.89 to 1.38)
MET + GLP-1		1.17 (0.59 to 2.27)	1.16 (0.59 to 2.20)	0.42 (–1.18 to 3.05)
MET + TZD		0.71 (0.23 to 2.06)	0.71 (0.24 to 2.01)	–0.75 (–2.22 to 2.55)
MET + INS-BA		0.87 (0.07 to 6.51)	0.88 (0.07 to 5.67)	–0.32 (–2.70 to 12.13)
MET + DPP-4	MET + SUL	1.21 (0.91 to 1.66)	1.20 (0.91 to 1.64)	0.54 (–0.31 to 1.39)
MET + SGLT-2		1.03 (0.71 to 1.55)	1.03 (0.72 to 1.53)	0.07 (–0.89 to 1.25)
MET + GLP-1		1.13 (0.59 to 2.27)	1.13 (0.59 to 2.21)	0.35 (–1.27 to 2.99)
MET + TZD		0.69 (0.22 to 2.08)	0.70 (0.23 to 2.03)	–0.80 (–2.41 to 2.56)
MET + INS-BA		0.86 (0.07 to 6.43)	0.86 (0.07 to 5.61)	–0.37 (–2.79 to 12.18)
MET + SGLT-2	MET + DPP-4	0.85 (0.57 to 1.30)	0.86 (0.57 to 1.29)	–0.46 (–1.59 to 0.87)
MET + GLP-1		0.95 (0.50 to 1.79)	0.95 (0.51 to 1.75)	–0.17 (–1.70 to 2.36)
MET + TZD		0.57 (0.19 to 1.61)	0.58 (0.20 to 1.57)	–1.34 (–2.80 to 1.87)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BA		0.71 (0.06 to 5.19)	0.71 (0.06 to 4.55)	–0.93 (–3.29 to 11.51)
MET + GLP-1	MET + SGLT-2	1.11 (0.52 to 2.30)	1.10 (0.53 to 2.23)	0.28 (–1.62 to 2.98)
MET + TZD		0.68 (0.21 to 2.04)	0.68 (0.21 to 1.99)	–0.86 (–2.73 to 2.51)
MET + INS-BA		0.83 (0.07 to 6.24)	0.83 (0.07 to 5.46)	–0.46 (–3.07 to 11.96)
MET + TZD	MET + GLP-1	0.61 (0.21 to 1.68)	0.62 (0.22 to 1.65)	–1.11 (–3.65 to 1.71)
MET + INS-BA		0.75 (0.07 to 4.81)	0.76 (0.07 to 4.25)	–0.70 (–3.81 to 10.86)
MET + INS-BA	MET + TZD	1.22 (0.09 to 11.70)	1.22 (0.09 to 10.28)	0.38 (–3.51 to 12.81)
Random-effects model	Residual deviance	41.08 vs. 46 data points		
	Deviance information criteria	247.955		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 11: Consistency Plot for Urogenital Adverse Events (People) (Reference-Case Analysis)



Renal Adverse Events

Table 15: Renal Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	1.29 (0.45 to 3.60)	1.29 (0.45 to 3.55)	0.26 (–0.77 to 1.57)
MET + DPP-4		1.50 (0.53 to 4.85)	1.49 (0.54 to 4.75)	0.44 (–0.65 to 2.14)
MET + SGLT-2		0.98 (0.41 to 2.36)	0.98 (0.41 to 2.34)	–0.02 (–0.80 to 0.83)
MET + GLP-1		0.87 (0.01 to 18.31)	0.87 (0.01 to 16.10)	–0.11 (–1.31 to 10.97)
MET + TZD		0.75 (0.24 to 2.90)	0.76 (0.24 to 2.87)	–0.21 (–1.09 to 1.19)
MET + DPP-4	MET + SUL	1.16 (0.59 to 2.48)	1.16 (0.60 to 2.45)	0.17 (–0.71 to 1.34)
MET + SGLT-2		0.74 (0.29 to 1.99)	0.74 (0.29 to 1.98)	–0.28 (–1.50 to 0.68)
MET + GLP-1		0.67 (0.01 to 10.85)	0.68 (0.01 to 9.73)	–0.34 (–1.72 to 10.39)
MET + TZD		0.57 (0.29 to 1.57)	0.57 (0.29 to 1.56)	–0.46 (–1.29 to 0.53)
MET + SGLT-2	MET + DPP-4	0.63 (0.21 to 1.82)	0.64 (0.22 to 1.81)	–0.47 (–2.10 to 0.65)
MET + GLP-1		0.58 (0.01 to 8.72)	0.59 (0.01 to 7.77)	–0.49 (–2.05 to 10.06)
MET + TZD		0.49 (0.19 to 1.43)	0.50 (0.20 to 1.42)	–0.64 (–1.94 to 0.44)
MET + GLP-1	MET + SGLT-2	0.93 (0.01 to 17.84)	0.93 (0.01 to 15.73)	–0.06 (–1.32 to 10.80)
MET + TZD		0.77 (0.25 to 2.97)	0.78 (0.25 to 2.94)	–0.18 (–1.07 to 1.16)
MET + TZD	MET + GLP-1	0.86 (0.06 to 54.60)	0.86 (0.06 to 54.05)	–0.10 (–10.70 to 1.21)

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

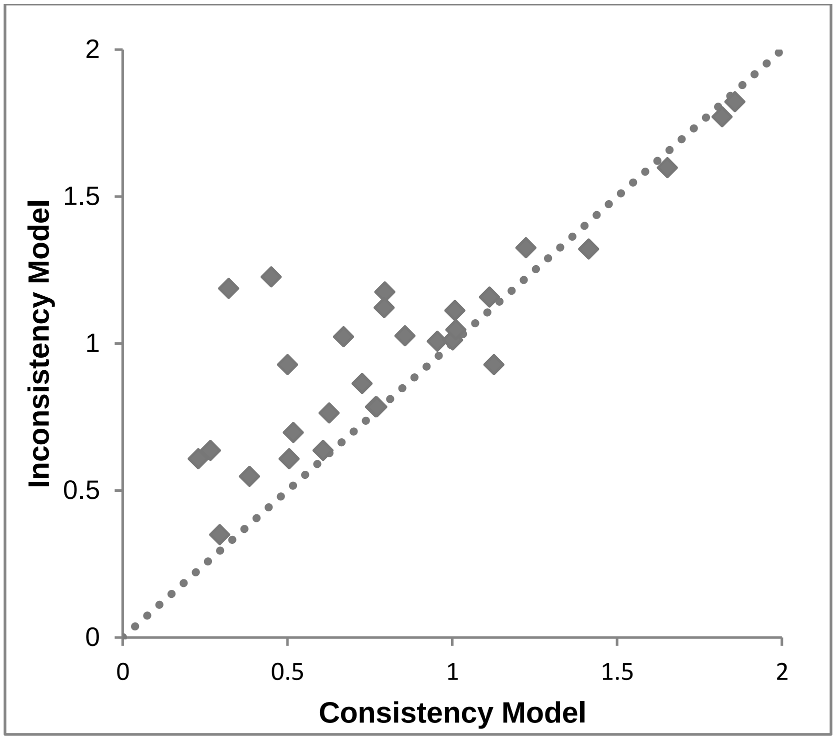
Unstable Angina

Table 16: Unstable Angina: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	0.94 (0.24 to 3.56)	0.94 (0.24 to 3.54)	–0.03 (–0.66 to 0.73)
MET + DPP-4		0.98 (0.32 to 3.10)	0.98 (0.32 to 3.08)	–0.01 (–0.58 to 0.56)
MET + SGLT-2		0.81 (0.15 to 3.58)	0.81 (0.15 to 3.55)	–0.08 (–0.71 to 0.90)
MET + TZD		0.70 (0.14 to 3.13)	0.70 (0.14 to 3.11)	–0.14 (–0.75 to 0.69)
MET + DPP-4	MET + SUL	1.08 (0.43 to 2.93)	1.08 (0.43 to 2.92)	0.03 (–0.55 to 0.48)
MET + SGLT-2		0.88 (0.22 to 3.20)	0.88 (0.22 to 3.19)	–0.05 (–0.67 to 0.78)
MET + TZD		0.75 (0.29 to 1.86)	0.75 (0.29 to 1.86)	–0.10 (–0.53 to 0.38)
MET + SGLT-2	MET + DPP-4	0.80 (0.18 to 3.64)	0.80 (0.18 to 3.61)	–0.09 (–0.66 to 0.90)
MET + TZD		0.70 (0.18 to 2.32)	0.70 (0.18 to 2.30)	–0.13 (–0.62 to 0.55)
MET + TZD	MET + SGLT-2	0.84 (0.18 to 4.40)	0.84 (0.18 to 4.38)	–0.05 (–0.94 to 0.69)
Random-effects model	Residual deviance	24.26 vs. 29 data points		
	Deviance information criteria	107.69		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 12: Consistency Plot for Unstable Angina (Reference-Case Analysis)



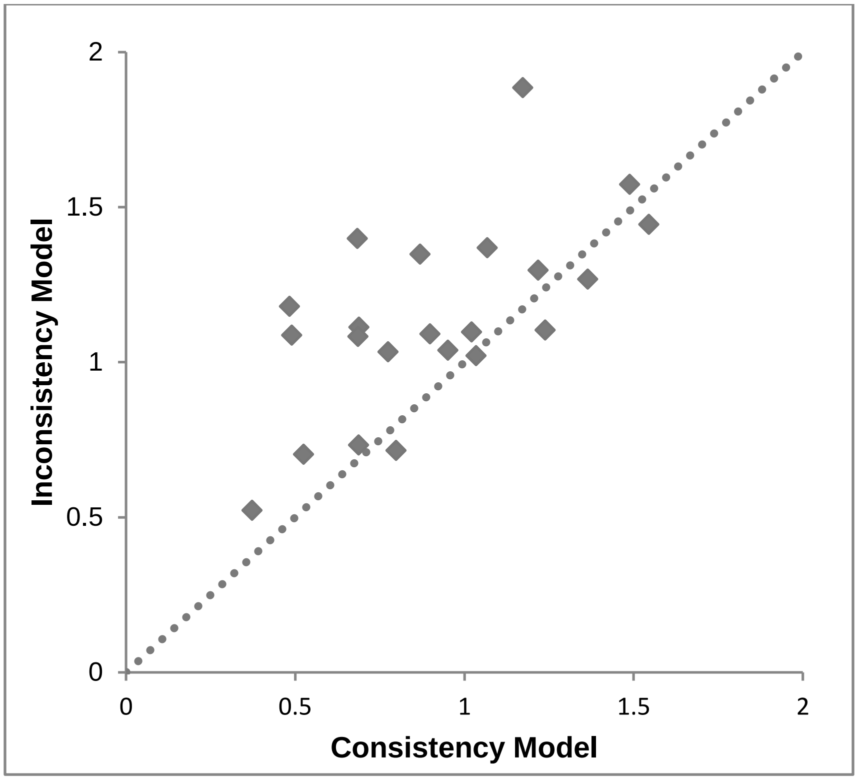
Transient Ischemic Attack (TIA)

Table 17: Transient Ischemic Attack: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	0.84 (0.07 to 6.94)	0.84 (0.07 to 6.77)	–0.09 (–1.31 to 2.49)
MET + DPP-4		0.57 (0.05 to 5.46)	0.58 (0.05 to 5.39)	–0.25 (–1.42 to 1.49)
MET + SGLT-2		0.66 (0.09 to 4.84)	0.66 (0.09 to 4.80)	–0.21 (–1.35 to 1.19)
MET + TZD		0.71 (0.05 to 7.28)	0.71 (0.06 to 7.05)	–0.16 (–1.35 to 2.86)
MET + DPP-4	MET + SUL	0.69 (0.24 to 2.06)	0.69 (0.24 to 2.05)	–0.12 (–1.75 to 0.53)
MET + SGLT-2		0.84 (0.13 to 5.60)	0.84 (0.14 to 5.57)	–0.06 (–2.38 to 0.89)
MET + TZD		0.86 (0.32 to 2.72)	0.86 (0.32 to 2.67)	–0.05 (–1.09 to 1.41)
MET + SGLT-2	MET + DPP-4	1.19 (0.19 to 8.02)	1.19 (0.19 to 7.97)	0.05 (–1.39 to 1.12)
MET + TZD		1.25 (0.30 to 5.27)	1.25 (0.31 to 5.18)	0.06 (–0.78 to 2.23)
MET + TZD	MET + SGLT-2	1.05 (0.13 to 8.63)	1.05 (0.13 to 8.43)	0.02 (–1.04 to 2.80)
Random-effects model	Residual deviance	20.07 vs. 22 data points		
	Deviance information criteria	87.956		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 13: Consistency Plot for Transient Ischemic Attack (Reference-Case Analysis)



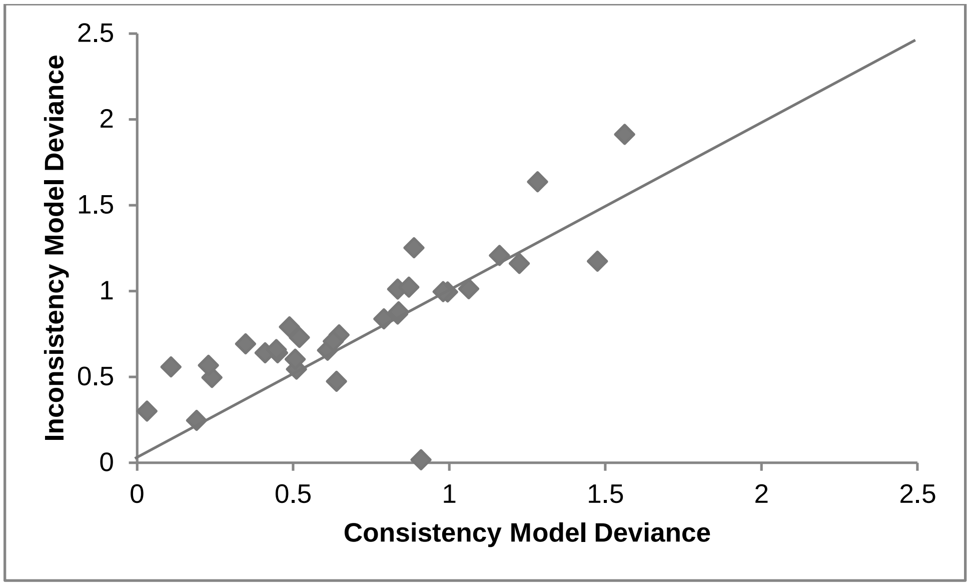
Fractures (People)

Table 18: Fractures Adverse Events (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	1.15 (0.35 to 3.89)	1.15 (0.35 to 3.86)	0.04 (–0.31 to 0.62)
MET + DPP-4		2.02 (0.63 to 6.75)	2.02 (0.63 to 6.69)	0.30 (–0.17 to 1.19)
MET + SGLT-2		1.35 (0.48 to 4.20)	1.35 (0.48 to 4.17)	0.10 (–0.24 to 0.72)
MET + TZD		1.09 (0.30 to 3.95)	1.09 (0.30 to 3.92)	0.02 (–0.30 to 0.74)
MET + DPP-4	MET + SUL	1.73 (0.58 to 5.09)	1.72 (0.58 to 5.04)	0.24 (–0.29 to 1.05)
MET + SGLT-2		1.18 (0.53 to 2.70)	1.18 (0.53 to 2.69)	0.06 (–0.32 to 0.47)
MET + TZD		0.95 (0.18 to 4.48)	0.96 (0.19 to 4.45)	–0.01 (–0.65 to 0.75)
MET + SGLT-2	MET + DPP-4	0.67 (0.21 to 2.31)	0.68 (0.21 to 2.29)	–0.18 (–1.06 to 0.45)
MET + TZD		0.54 (0.11 to 2.44)	0.54 (0.11 to 2.43)	–0.26 (–1.17 to 0.53)
MET + TZD	MET + SGLT-2	0.80 (0.17 to 3.65)	0.80 (0.17 to 3.63)	–0.07 (–0.74 to 0.71)
Random-effects model	Residual deviance	22.74 vs. 32 data points		
	Deviance information criteria	109.921		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Figure 14: Consistency Plot for Fractures (People) (Reference-Case Analysis)



Appendix 10: Detailed Network Meta-Analysis Results for the Dose-Stratified Analysis

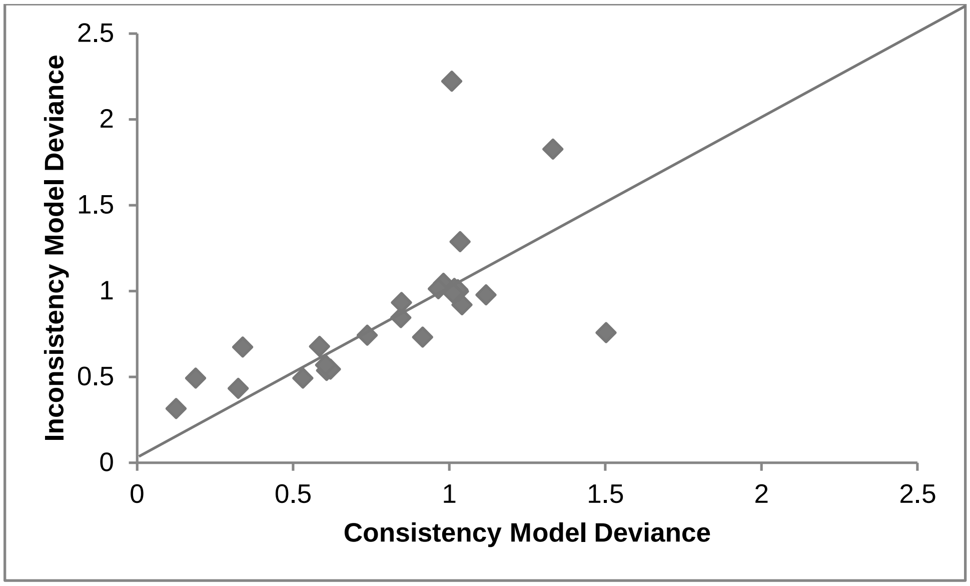
Fracture (People)

Table 19: Fractures (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	0.98 (0.27 to 3.73)	0.98 (0.27 to 3.70)	–0.01 (–0.55 to 0.85)
MET + DPP-L		6.72 (0.27 to 688.30)	6.54 (0.27 to 227.30)	2.62 (–0.44 to 64.94)
MET + DPP-H		1.81 (0.53 to 6.30)	1.80 (0.53 to 6.20)	0.36 (–0.34 to 1.62)
MET + SGL-L		0.90 (0.24 to 3.53)	0.90 (0.24 to 3.50)	–0.04 (–0.57 to 0.88)
MET + SGL-H		1.24 (0.40 to 4.05)	1.24 (0.40 to 4.02)	0.10 (–0.44 to 0.96)
MET + TZD-H		1.04 (0.21 to 5.38)	1.04 (0.21 to 5.28)	0.02 (–0.50 to 1.99)
MET + DPP-L	MET + SUL-T	6.86 (0.24 to 644.90)	6.65 (0.24 to 224.90)	2.59 (–0.57 to 64.90)
MET + DPP-H		1.82 (0.61 to 5.91)	1.81 (0.61 to 5.84)	0.35 (–0.35 to 1.43)
MET + SGL-L		0.92 (0.21 to 4.12)	0.92 (0.21 to 4.09)	–0.03 (–0.84 to 0.86)
MET + SGL-H		1.25 (0.56 to 3.09)	1.25 (0.56 to 3.07)	0.10 (–0.41 to 0.68)
MET + TZD-H		1.06 (0.13 to 8.67)	1.06 (0.13 to 8.49)	0.02 (–0.92 to 2.12)
MET + DPP-H	MET + DPP-L	0.27 (0.00 to 6.87)	0.28 (0.01 to 6.80)	–2.19 (–64.52 to 1.10)
MET + SGL-L		0.13 (0.00 to 4.49)	0.14 (0.00 to 4.46)	–2.63 (–65.01 to 0.65)
MET + SGL-H		0.18 (0.00 to 5.29)	0.19 (0.01 to 5.25)	–2.49 (-64.79 to 0.76)
MET + TZD-H		0.16 (0.00 to 5.88)	0.16 (0.00 to 5.78)	–2.47 (–64.88 to 1.29)
MET + SGL-L	MET + DPP-H	0.50 (0.11 to 2.36)	0.51 (0.11 to 2.34)	–0.38 (–1.66 to 0.64)
MET + SGL-H		0.69 (0.21 to 2.31)	0.69 (0.21 to 2.29)	–0.24 (–1.42 to 0.63)
MET + TZD-H		0.58 (0.07 to 4.39)	0.58 (0.07 to 4.31)	–0.31 (–1.66 to 1.80)
MET + SGL-H	MET + SGL-L	1.37 (0.38 to 5.17)	1.37 (0.38 to 5.13)	0.14 (–0.67 to 0.89)
MET + TZD-H		1.16 (0.13 to 9.47)	1.15 (0.13 to 9.30)	0.05 (–0.97 to 2.14)
MET + TZD-H	MET + SGL-H	0.84 (0.11 to 6.28)	0.84 (0.11 to 6.16)	–0.08 (–1.04 to 2.03)
Random-effects model	Residual deviance	20.36 vs. 25 data points		
	Deviance information criteria	97.939		

CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; -H = high-dose; -L = low-dose; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Figure 15: Consistency Plot for Fracture (People) (Dose-Case Analysis)



High-Density Lipoprotein Cholesterol

Table 20: High-Density Lipoprotein Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-H	MET	–0.03 (–0.17 to 0.11)
MET + SUL-L		–0.80 (–1.06 to –0.53)
MET + SUL-T		–0.05 (–0.16 to 0.06)
MET + MEG-L		0.00 (–0.30 to 0.30)
MET + MEG-T		0.05 (–0.20 to 0.29)
MET + MEG-H		0.00 (–0.30 to 0.30)
MET + DPP-L		–0.03 (–0.19 to 0.12)
MET + DPP-H		0.00 (–0.08 to 0.08)
MET + SGL-L		0.04 (–0.06 to 0.15)
MET + SGL-H		0.06 (–0.04 to 0.17)
MET + GLP-T		0.10 (–0.12 to 0.33)
MET + GLP-L		–0.01 (–0.26 to 0.24)
MET + GLP-H		–0.02 (–0.14 to 0.09)
MET + AGI-L		0.01 (–0.23 to 0.25)
MET + TZD-L		0.08 (–0.07 to 0.23)
MET + TZD-H		0.10 (0.01 to 0.19)
MET + TZD-T		0.09 (–0.08 to 0.27)
MET + INS-BA-T		–0.01 (–0.24 to 0.21)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		0.01 (–0.21 to 0.24)
MET + SUL-L	MET + SUL-H	–0.77 (–1.06 to –0.47)
MET + SUL-T		–0.02 (–0.19 to 0.15)
MET + MEG-L		0.03 (–0.30 to 0.37)
MET + MEG-T		0.08 (–0.20 to 0.35)
MET + MEG-H		0.03 (–0.31 to 0.36)
MET + DPP-L		0.00 (–0.21 to 0.20)
MET + DPP-H		0.03 (–0.11 to 0.17)
MET + SGL-L		0.07 (–0.10 to 0.24)
MET + SGL-H		0.09 (–0.07 to 0.26)
MET + GLP-T		0.13 (–0.12 to 0.39)
MET + GLP-L		0.02 (–0.26 to 0.30)
MET + GLP-H		0.01 (–0.15 to 0.16)
MET + AGI-L		0.04 (–0.19 to 0.27)
MET + TZD-L		0.11 (–0.09 to 0.31)
MET + TZD-H		0.13 (–0.01 to 0.27)
MET + TZD-T		0.12 (–0.09 to 0.34)
MET + INS-BA-T		0.02 (–0.24 to 0.27)
MET + INS-BI-T		0.04 (–0.21 to 0.30)
MET + SUL-T	MET + SUL-L	0.74 (0.46 to 1.03)
MET + MEG-L		0.79 (0.39 to 1.20)
MET + MEG-T		0.84 (0.48 to 1.20)
MET + MEG-H		0.80 (0.39 to 1.20)
MET + DPP-L		0.76 (0.46 to 1.06)
MET + DPP-H		0.80 (0.52 to 1.07)
MET + SGL-L		0.84 (0.55 to 1.12)
MET + SGL-H		0.86 (0.58 to 1.14)
MET + GLP-T		0.90 (0.55 to 1.25)
MET + GLP-L		0.78 (0.42 to 1.15)
MET + GLP-H		0.77 (0.48 to 1.05)
MET + AGI-L		0.81 (0.45 to 1.16)
MET + TZD-L		0.87 (0.65 to 1.09)
MET + TZD-H		0.89 (0.63 to 1.16)
MET + TZD-T		0.89 (0.57 to 1.20)
MET + INS-BA-T		0.78 (0.43 to 1.13)
MET + INS-BI-T		0.81 (0.46 to 1.16)
MET + MEG-L	MET + SUL-T	0.05 (–0.27 to 0.38)
MET + MEG-T		0.10 (–0.15 to 0.35)
MET + MEG-H		0.05 (–0.27 to 0.37)
MET + DPP-L		0.02 (–0.17 to 0.21)
MET + DPP-H		0.05 (–0.06 to 0.17)
MET + SGL-L		0.09 (–0.05 to 0.23)

Treatment	Reference	MD (95% CrI)
MET + SGL-H		0.12 (–0.02 to 0.25)
MET + GLP-T		0.15 (–0.08 to 0.39)
MET + GLP-L		0.04 (–0.23 to 0.31)
MET + GLP-H		0.03 (–0.11 to 0.16)
MET + AGI-L		0.06 (–0.19 to 0.32)
MET + TZD-L		0.13 (–0.06 to 0.32)
MET + TZD-H		0.15 (0.02 to 0.28)
MET + TZD-T		0.14 (0.01 to 0.28)
MET + INS-BA-T		0.04 (–0.20 to 0.28)
MET + INS-BI-T		0.07 (–0.16 to 0.29)
MET + MEG-T	MET + MEG-L	0.05 (–0.34 to 0.44)
MET + MEG-H		0.00 (–0.30 to 0.30)
MET + DPP-L		–0.03 (–0.38 to 0.31)
MET + DPP-H		0.00 (–0.31 to 0.32)
MET + SGL-L		0.04 (–0.28 to 0.36)
MET + SGL-H		0.06 (–0.26 to 0.39)
MET + GLP-T		0.10 (–0.27 to 0.48)
MET + GLP-L		–0.01 (–0.40 to 0.38)
MET + GLP-H		–0.02 (–0.35 to 0.30)
MET + AGI-L		0.01 (–0.38 to 0.40)
MET + TZD-L		0.08 (–0.26 to 0.42)
MET + TZD-H		0.10 (–0.22 to 0.42)
MET + TZD-T		0.09 (–0.26 to 0.44)
MET + INS-BA-T		–0.02 (–0.40 to 0.37)
MET + INS-BI-T		0.01 (–0.37 to 0.39)
MET + MEG-H	MET + MEG-T	–0.05 (–0.44 to 0.34)
MET + DPP-L		–0.08 (–0.37 to 0.21)
MET + DPP-H		–0.05 (–0.30 to 0.21)
MET + SGL-L		0.00 (–0.27 to 0.26)
MET + SGL-H		0.02 (–0.24 to 0.28)
MET + GLP-T		0.06 (–0.27 to 0.38)
MET + GLP-L		–0.06 (–0.41 to 0.29)
MET + GLP-H		–0.07 (–0.33 to 0.19)
MET + AGI-L		–0.03 (–0.38 to 0.31)
MET + TZD-L		0.03 (–0.25 to 0.32)
MET + TZD-H		0.05 (–0.21 to 0.31)
MET + TZD-T		0.05 (–0.24 to 0.33)
MET + INS-BA-T		–0.06 (–0.39 to 0.27)
MET + INS-BI-T		–0.03 (–0.36 to 0.29)
MET + DPP-L	MET + MEG-H	–0.03 (–0.37 to 0.31)
MET + DPP-H		0.00 (–0.31 to 0.31)
MET + SGL-L		0.04 (–0.28 to 0.37)

Treatment	Reference	MD (95% CrI)
MET + SGL-H		0.06 (–0.25 to 0.39)
MET + GLP-T		0.10 (–0.27 to 0.48)
MET + GLP-L		–0.01 (–0.40 to 0.38)
MET + GLP-H		–0.02 (–0.35 to 0.30)
MET + AGI-L		0.01 (–0.37 to 0.40)
MET + TZD-L		0.08 (–0.26 to 0.42)
MET + TZD-H		0.10 (–0.22 to 0.41)
MET + TZD-T		0.09 (–0.26 to 0.44)
MET + INS-BA-T		–0.02 (–0.39 to 0.36)
MET + INS-BI-T		0.01 (–0.37 to 0.40)
MET + DPP-H	MET + DPP-L	0.03 (–0.13 to 0.20)
MET + SGL-L		0.08 (–0.11 to 0.26)
MET + SGL-H		0.10 (–0.09 to 0.28)
MET + GLP-T		0.13 (–0.13 to 0.41)
MET + GLP-L		0.02 (–0.27 to 0.31)
MET + GLP-H		0.01 (–0.18 to 0.19)
MET + AGI-L		0.04 (–0.24 to 0.32)
MET + TZD-L		0.11 (–0.09 to 0.31)
MET + TZD-H		0.13 (–0.04 to 0.30)
MET + TZD-T		0.13 (–0.11 to 0.36)
MET + INS-BA-T		0.02 (–0.25 to 0.29)
MET + INS-BI-T		0.05 (–0.23 to 0.32)
MET + SGL-L	MET + DPP-H	0.04 (–0.08 to 0.16)
MET + SGL-H		0.06 (–0.05 to 0.18)
MET + GLP-T		0.10 (–0.12 to 0.33)
MET + GLP-L		–0.01 (–0.27 to 0.24)
MET + GLP-H		–0.02 (–0.14 to 0.09)
MET + AGI-L		0.01 (–0.22 to 0.24)
MET + TZD-L		0.08 (–0.08 to 0.24)
MET + TZD-H		0.10 (0.00 to 0.20)
MET + TZD-T		0.09 (–0.09 to 0.27)
MET + INS-BA-T		–0.02 (–0.24 to 0.20)
MET + INS-BI-T		0.01 (–0.22 to 0.24)
MET + SGL-H	MET + SGL-L	0.02 (–0.08 to 0.13)
MET + GLP-T		0.06 (–0.18 to 0.30)
MET + GLP-L		–0.05 (–0.33 to 0.21)
MET + GLP-H		–0.07 (–0.22 to 0.08)
MET + AGI-L		–0.03 (–0.29 to 0.23)
MET + TZD-L		0.03 (–0.15 to 0.22)
MET + TZD-H		0.06 (–0.08 to 0.19)
MET + TZD-T		0.05 (–0.15 to 0.24)
MET + INS-BA-T		–0.06 (–0.30 to 0.19)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		–0.03 (–0.28 to 0.22)
MET + GLP-T	MET + SGL-H	0.04 (–0.20 to 0.28)
MET + GLP-L		–0.07 (–0.35 to 0.19)
MET + GLP-H		–0.09 (–0.23 to 0.05)
MET + AGI-L		–0.05 (–0.31 to 0.20)
MET + TZD-L		0.01 (–0.17 to 0.20)
MET + TZD-H		0.03 (–0.10 to 0.16)
MET + TZD-T		0.03 (–0.16 to 0.22)
MET + INS-BA-T		–0.08 (–0.32 to 0.16)
MET + INS-BI-T		–0.05 (–0.30 to 0.20)
MET + GLP-L	MET + GLP-T	–0.11 (–0.45 to 0.22)
MET + GLP-H		–0.13 (–0.37 to 0.11)
MET + AGI-L		–0.09 (–0.41 to 0.23)
MET + TZD-L		–0.02 (–0.29 to 0.24)
MET + TZD-H		0.00 (–0.24 to 0.23)
MET + TZD-T		–0.01 (–0.28 to 0.26)
MET + INS-BA-T		–0.12 (–0.38 to 0.15)
MET + INS-BI-T		–0.09 (–0.40 to 0.22)
MET + GLP-H	MET + GLP-L	–0.01 (–0.27 to 0.24)
MET + AGI-L		0.02 (–0.32 to 0.36)
MET + TZD-L		0.09 (–0.20 to 0.38)
MET + TZD-H		0.11 (–0.15 to 0.37)
MET + TZD-T		0.10 (–0.20 to 0.40)
MET + INS-BA-T		0.00 (–0.33 to 0.33)
MET + INS-BI-T		0.02 (–0.30 to 0.36)
MET + AGI-L	MET + GLP-H	0.04 (–0.22 to 0.29)
MET + TZD-L		0.10 (–0.08 to 0.29)
MET + TZD-H		0.12 (0.00 to 0.25)
MET + TZD-T		0.12 (–0.07 to 0.31)
MET + INS-BA-T		0.01 (–0.22 to 0.24)
MET + INS-BI-T		0.04 (–0.18 to 0.26)
MET + TZD-L	MET + AGI-L	0.07 (–0.21 to 0.35)
MET + TZD-H		0.09 (–0.16 to 0.33)
MET + TZD-T		0.08 (–0.21 to 0.37)
MET + INS-BA-T		–0.03 (–0.34 to 0.29)
MET + INS-BI-T		0.00 (–0.32 to 0.33)
MET + TZD-H	MET + TZD-L	0.02 (–0.14 to 0.18)
MET + TZD-T		0.01 (–0.21 to 0.24)
MET + INS-BA-T		–0.09 (–0.36 to 0.18)
MET + INS-BI-T		–0.06 (–0.34 to 0.21)
MET + TZD-T	MET + TZD-H	–0.01 (–0.20 to 0.18)
MET + INS-BA-T		–0.11 (–0.35 to 0.12)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		–0.08 (–0.32 to 0.15)
MET + INS-BA-T	MET + TZD-T	–0.11 (–0.38 to 0.17)
MET + INS-BI-T		–0.08 (–0.34 to 0.18)
MET + INS-BI-T	MET + INS-BA-T	0.03 (–0.28 to 0.34)
Random-effects model	Residual deviance	142.7 vs. 139 data points
	Deviance information criteria	–535.729

AGI = alpha-glucosidase inhibitor; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

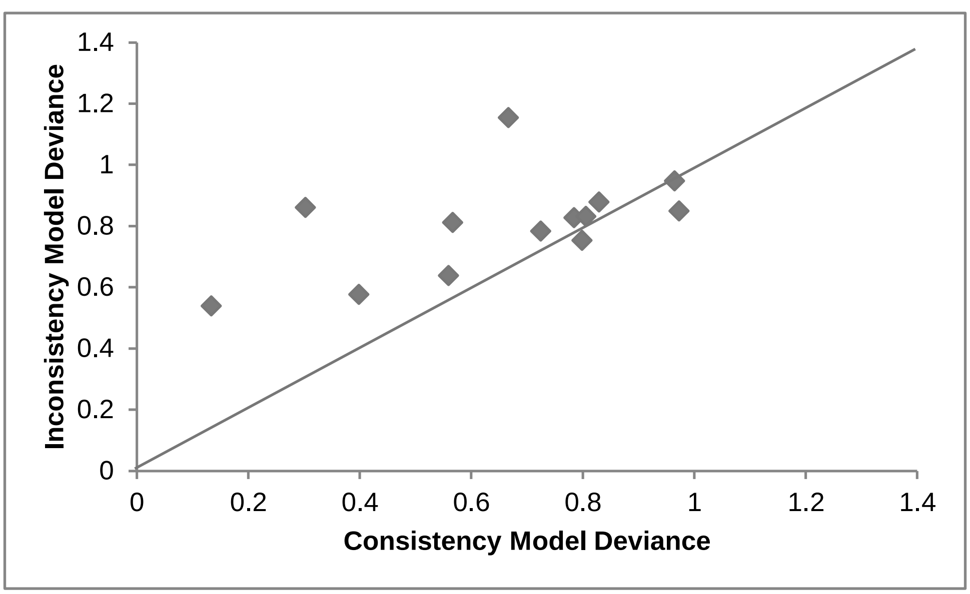
Nonfatal Myocardial Infarction (MI)

Table 21: Nonfatal Myocardial Infarction Dose: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	5.37 (0.41 to 205.90)	5.32 (0.41 to 201.30)	0.60 (–0.43 to 3.17)
MET + DPP-H		4.09 (0.35 to 139.00)	4.06 (0.36 to 137.70)	0.42 (–0.53 to 1.72)
MET + DPP-L		0.81 (0.01 to 45.51)	0.81 (0.01 to 45.07)	–0.02 (–0.92 to 1.19)
MET + DPP-H	MET + SUL-T	0.75 (0.32 to 1.79)	0.75 (0.32 to 1.79)	–0.17 (–1.92 to 0.37)
MET + DPP-L		0.15 (0.00 to 1.22)	0.15 (0.00 to 1.22)	–0.61 (–2.86 to 0.12)
MET + DPP-L	MET + DPP-H	0.20 (0.01 to 1.60)	0.20 (0.01 to 1.60)	–0.42 (–1.55 to 0.38)
Random-effects model	Residual deviance	8.507 vs. 13 data points		
	Deviance information criteria	50.986		

CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SUL = sulfonylurea; vs. = versus.

Figure 16: Consistency Plot for Nonfatal Myocardial Infarction (Dose-Case Analysis)



Nonfatal Stroke

Table 22: Nonfatal Stroke: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	10.00 (1.13 to 113.30)	9.88 (1.13 to 110.70)	1.06 (0.05 to 4.01)
MET + DPP-L		4.46 (0.37 to 55.87)	4.43 (0.37 to 55.52)	0.38 (–0.29 to 1.65)
MET + DPP-H		4.58 (0.64 to 52.28)	4.56 (0.64 to 51.81)	0.40 (–0.17 to 1.29)
MET + TZD-H		10.24 (0.26 to 341.30)	10.10 (0.26 to 280.10)	1.00 (–0.26 to 18.88)
MET + DPP-L	MET + SUL-T	0.43 (0.08 to 1.64)	0.43 (0.08 to 1.64)	–0.63 (–3.35 to 0.42)
MET + DPP-H		0.45 (0.17 to 1.18)	0.45 (0.17 to 1.18)	–0.64 (–3.13 to 0.09)
MET + TZD-H		0.94 (0.05 to 18.27)	0.94 (0.05 to 15.12)	–0.06 (–2.69 to 17.39)
MET + DPP-H	MET + DPP-L	1.06 (0.28 to 5.22)	1.06 (0.28 to 5.18)	0.03 (–1.09 to 0.87)
MET + TZD-H		2.33 (0.11 to 51.04)	2.31 (0.11 to 42.87)	0.57 (–1.04 to 18.36)
MET + TZD-H	MET + DPP-H	2.05 (0.14 to 38.87)	2.04 (0.14 to 32.15)	0.55 (–0.59 to 18.24)
Random-effects model	Residual deviance	12.92 vs. 19 data points		
	Deviance information criteria	68.493		

CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; -L = low-dose; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Nonsevere Hypoglycemia

Table 23: Nonsevere Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	5.59 (3.74 to 8.59)	5.15 (3.54 to 7.60)	7.79 (4.99 to 11.67)
MET + SUL-L		5.74 (0.85 to 54.40)	5.26 (0.86 to 27.41)	8.02 (–0.27 to 48.86)
MET + SUL-H		11.20 (3.26 to 40.20)	9.38 (3.13 to 23.47)	15.75 (4.01 to 41.31)
MET + MEG-L		3.49 (1.08 to 11.98)	3.33 (1.08 to 10.01)	4.38 (0.15 to 16.27)
MET + MEG-H		5.67 (2.14 to 15.45)	5.21 (2.09 to 12.26)	7.92 (2.11 to 20.34)
MET + DPP-T		2.13 (0.32 to 13.59)	2.09 (0.32 to 11.04)	2.04 (–1.30 to 18.67)
MET + DPP-L		0.99 (0.47 to 2.07)	0.99 (0.48 to 2.03)	–0.02 (–1.06 to 1.82)
MET + DPP-H		0.72 (0.49 to 1.09)	0.72 (0.49 to 1.09)	–0.52 (–1.08 to 0.14)
MET + SGL-L		0.92 (0.54 to 1.59)	0.92 (0.55 to 1.58)	–0.15 (–0.93 to 1.02)
MET + SGL-H		0.88 (0.53 to 1.46)	0.88 (0.53 to 1.45)	–0.23 (–0.95 to 0.79)
MET + GLP-T		1.11 (0.45 to 2.76)	1.11 (0.46 to 2.68)	0.21 (–1.06 to 3.07)
MET + GLP-L		1.03 (0.43 to 2.45)	1.03 (0.44 to 2.39)	0.06 (–1.11 to 2.53)
MET + GLP-H		0.95 (0.57 to 1.59)	0.95 (0.57 to 1.58)	–0.10 (–0.87 to 1.02)
MET + TZD-T		0.59 (0.29 to 1.23)	0.60 (0.29 to 1.22)	–0.75 (–1.45 to 0.39)
MET + TZD-L		1.04 (0.21 to 4.73)	1.04 (0.22 to 4.43)	0.07 (–1.55 to 6.28)
MET + TZD-H		0.74 (0.40 to 1.39)	0.75 (0.41 to 1.38)	–0.47 (–1.20 to 0.67)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + AGI-L		0.24 (0.01 to 2.64)	0.24 (0.01 to 2.56)	–1.39 (–2.10 to 2.90)
MET + AGI-T		0.39 (0.01 to 6.79)	0.39 (0.01 to 6.14)	–1.12 (–2.05 to 9.47)
MET + INS-BA-T		2.72 (1.34 to 5.56)	2.64 (1.34 to 5.15)	3.07 (0.64 to 7.49)
MET + INS-BI-T		4.87 (2.21 to 10.90)	4.53 (2.16 to 9.27)	6.65 (2.22 to 15.13)
MET + SUL-L	MET + SUL-T	1.03 (0.15 to 10.19)	1.03 (0.16 to 5.60)	0.28 (–9.41 to 41.06)
MET + SUL-H		1.99 (0.56 to 7.29)	1.82 (0.59 to 4.65)	7.87 (–4.29 to 33.37)
MET + MEG-L		0.63 (0.18 to 2.17)	0.65 (0.20 to 1.97)	–3.32 (–9.24 to 8.68)
MET + MEG-H		1.01 (0.38 to 2.69)	1.01 (0.41 to 2.34)	0.12 (–6.56 to 12.28)
MET + DPP-T		0.38 (0.06 to 2.30)	0.41 (0.06 to 2.04)	–5.55 (–10.55 to 10.16)
MET + DPP-L		0.18 (0.08 to 0.37)	0.19 (0.09 to 0.39)	–7.74 (–11.56 to –4.75)
MET + DPP-H		0.13 (0.09 to 0.19)	0.14 (0.10 to 0.20)	–8.31 (–11.97 to –5.65)
MET + SGL-L		0.16 (0.09 to 0.29)	0.18 (0.10 to 0.31)	–7.92 (–11.67 to –5.05)
MET + SGL-H		0.16 (0.09 to 0.27)	0.17 (0.10 to 0.28)	–8.00 (–11.73 to –5.23)
MET + GLP-T		0.20 (0.08 to 0.49)	0.22 (0.09 to 0.51)	–7.46 (–11.28 to –4.06)
MET + GLP-L		0.19 (0.07 to 0.44)	0.20 (0.08 to 0.46)	–7.63 (–11.58 to –4.33)
MET + GLP-H		0.17 (0.10 to 0.29)	0.19 (0.11 to 0.30)	–7.85 (–11.56 to –5.12)
MET + TZD-T		0.11 (0.05 to 0.20)	0.12 (0.06 to 0.21)	–8.51 (–12.06 to –5.91)
MET + TZD-L		0.19 (0.04 to 0.88)	0.20 (0.04 to 0.89)	–7.50 (–11.92 to –0.99)
MET + TZD-H		0.13 (0.07 to 0.25)	0.15 (0.08 to 0.27)	–8.23 (–12.02 to –5.37)
MET + AGI-L		0.04 (0.00 to 0.47)	0.05 (0.00 to 0.49)	–8.95 (–12.90 to –4.47)
MET + AGI-T		0.07 (0.00 to 1.25)	0.08 (0.00 to 1.23)	–8.53 (–12.80 to 1.99)
MET + INS-BA-T		0.49 (0.24 to 0.95)	0.51 (0.27 to 0.96)	–4.64 (–8.59 to –0.38)
MET + INS-BI-T		0.87 (0.41 to 1.87)	0.88 (0.43 to 1.73)	–1.13 (–6.16 to 6.82)
MET + SUL-H	MET + SUL-L	1.97 (0.15 to 18.70)	1.77 (0.25 to 13.20)	6.84 (–33.70 to 34.43)
MET + MEG-L		0.60 (0.05 to 6.06)	0.63 (0.08 to 5.40)	–3.38 (–44.18 to 11.38)
MET + MEG-H		0.98 (0.09 to 8.53)	0.98 (0.15 to 7.31)	–0.17 (–41.01 to 15.38)
MET + DPP-T		0.36 (0.02 to 5.41)	0.39 (0.03 to 4.76)	–5.38 (–45.92 to 12.54)
MET + DPP-L		0.17 (0.02 to 1.31)	0.19 (0.03 to 1.30)	–7.96 (–48.69 to 0.53)
MET + DPP-H		0.13 (0.01 to 0.89)	0.14 (0.02 to 0.89)	–8.54 (–49.44 to –0.18)
MET + SGL-L		0.16 (0.02 to 1.14)	0.18 (0.03 to 1.14)	–8.14 (–48.99 to 0.24)
MET + SGL-H		0.15 (0.02 to 1.09)	0.17 (0.03 to 1.09)	–8.24 (–49.06 to 0.15)
MET + GLP-T		0.19 (0.02 to 1.62)	0.21 (0.03 to 1.60)	–7.67 (–48.60 to 1.15)
MET + GLP-L		0.18 (0.02 to 1.44)	0.20 (0.03 to 1.43)	–7.85 (–48.58 to 0.79)
MET + GLP-H		0.17 (0.02 to 1.18)	0.18 (0.03 to 1.17)	–8.08 (–48.89 to 0.30)
MET + TZD-T		0.10 (0.01 to 0.79)	0.11 (0.02 to 0.79)	–8.75 (–49.51 to –0.34)
MET + TZD-L		0.18 (0.01 to 1.99)	0.20 (0.02 to 1.94)	–7.57 (–48.20 to 2.42)
MET + TZD-H		0.13 (0.01 to 0.95)	0.14 (0.02 to 0.95)	–8.47 (–49.34 to –0.08)
MET + AGI-L		0.04 (0.00 to 0.98)	0.05 (0.00 to 0.98)	–9.08 (–49.67 to –0.03)
MET + AGI-T		0.07 (0.00 to 2.33)	0.08 (0.00 to 2.20)	–8.48 (–49.16 to 4.18)
MET + INS-BA-T		0.47 (0.04 to 3.65)	0.50 (0.08 to 3.47)	–4.83 (–45.48 to 4.86)
MET + INS-BI-T		0.84 (0.08 to 6.75)	0.86 (0.14 to 6.05)	–1.33 (–41.99 to 11.09)
MET + MEG-L	MET + SUL-H	0.31 (0.06 to 1.82)	0.36 (0.08 to 1.70)	–10.80 (–36.77 to 5.60)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + MEG-H		0.51 (0.11 to 2.44)	0.56 (0.16 to 2.19)	–7.52 (–33.70 to 9.29)
MET + DPP-T		0.19 (0.02 to 1.76)	0.23 (0.03 to 1.62)	–12.76 (–38.80 to 5.94)
MET + DPP-L		0.09 (0.02 to 0.36)	0.11 (0.03 to 0.38)	–15.69 (–41.28 to –3.83)
MET + DPP-H		0.06 (0.02 to 0.22)	0.08 (0.03 to 0.24)	–16.27 (–41.72 to –4.53)
MET + SGL-L		0.08 (0.02 to 0.31)	0.10 (0.04 to 0.33)	–15.87 (–41.42 to –4.07)
MET + SGL-H		0.08 (0.02 to 0.29)	0.09 (0.03 to 0.30)	–15.93 (–41.45 to –4.18)
MET + GLP-T		0.10 (0.02 to 0.45)	0.12 (0.03 to 0.47)	–15.38 (–40.91 to –3.35)
MET + GLP-L		0.09 (0.03 to 0.31)	0.11 (0.04 to 0.33)	–15.57 (–40.51 to –4.23)
MET + GLP-H		0.08 (0.02 to 0.28)	0.10 (0.04 to 0.29)	–15.84 (–41.10 to –4.29)
MET + TZD-T		0.05 (0.01 to 0.21)	0.06 (0.02 to 0.22)	–16.46 (–42.00 to –4.72)
MET + TZD-L		0.09 (0.01 to 0.65)	0.11 (0.02 to 0.67)	–15.19 (–40.67 to –2.44)
MET + TZD-H		0.07 (0.02 to 0.25)	0.08 (0.03 to 0.27)	–16.18 (–41.63 to –4.40)
MET + AGI-L		0.02 (0.00 to 0.26)	0.03 (0.00 to 0.29)	–16.75 (–42.16 to –5.00)
MET + AGI-T		0.03 (0.00 to 0.79)	0.04 (0.00 to 0.81)	–15.99 (–41.91 to –1.79)
MET + INS-BA-T		0.24 (0.06 to 0.92)	0.28 (0.10 to 0.93)	–12.46 (–37.81 to –0.47)
MET + INS-BI-T		0.44 (0.11 to 1.78)	0.49 (0.16 to 1.68)	–8.85 (–34.13 to 4.85)
MET + MEG-H	MET + MEG-L	1.62 (0.48 to 5.45)	1.56 (0.51 to 4.81)	3.27 (–6.95 to 13.98)
MET + DPP-T		0.60 (0.07 to 5.36)	0.62 (0.07 to 4.59)	–2.09 (–14.36 to 14.23)
MET + DPP-L		0.28 (0.07 to 1.12)	0.30 (0.08 to 1.12)	–4.33 (–16.26 to 0.28)
MET + DPP-H		0.21 (0.06 to 0.71)	0.22 (0.07 to 0.72)	–4.89 (–16.78 to –0.58)
MET + SGL-L		0.26 (0.07 to 0.96)	0.28 (0.08 to 0.96)	–4.50 (–16.37 to –0.09)
MET + SGL-H		0.25 (0.07 to 0.90)	0.26 (0.08 to 0.90)	–4.57 (–16.52 to –0.21)
MET + GLP-T		0.32 (0.07 to 1.41)	0.33 (0.08 to 1.39)	–4.08 (–15.99 to 0.96)
MET + GLP-L		0.30 (0.07 to 1.26)	0.31 (0.08 to 1.25)	–4.22 (–16.25 to 0.61)
MET + GLP-H		0.27 (0.07 to 0.98)	0.28 (0.09 to 0.98)	–4.45 (–16.34 to –0.05)
MET + TZD-T		0.17 (0.04 to 0.67)	0.18 (0.05 to 0.68)	–5.09 (–17.00 to –0.72)
MET + TZD-L		0.30 (0.04 to 2.06)	0.31 (0.05 to 1.98)	–4.04 (–16.23 to 3.11)
MET + TZD-H		0.21 (0.05 to 0.82)	0.22 (0.06 to 0.83)	–4.81 (–16.75 to –0.39)
MET + AGI-L		0.07 (0.00 to 0.99)	0.07 (0.00 to 0.99)	–5.48 (–17.46 to –0.02)
MET + AGI-T		0.11 (0.00 to 2.51)	0.12 (0.00 to 2.36)	–4.98 (–17.04 to 5.44)
MET + INS-BA-T		0.78 (0.19 to 3.03)	0.79 (0.22 to 2.88)	–1.26 (–13.44 to 4.92)
MET + INS-BI-T		1.39 (0.33 to 5.64)	1.35 (0.37 to 5.07)	2.13 (–10.41 to 11.69)
MET + DPP-T	MET + MEG-H	0.37 (0.05 to 2.94)	0.40 (0.05 to 2.59)	–5.38 (–18.26 to 11.12)
MET + DPP-L		0.17 (0.05 to 0.57)	0.19 (0.06 to 0.58)	–7.87 (–20.35 to –1.83)
MET + DPP-H		0.13 (0.05 to 0.35)	0.14 (0.06 to 0.36)	–8.44 (–20.84 to –2.60)
MET + SGL-L		0.16 (0.05 to 0.48)	0.18 (0.07 to 0.49)	–8.02 (–20.50 to –2.15)
MET + SGL-H		0.15 (0.05 to 0.45)	0.17 (0.06 to 0.46)	–8.13 (–20.52 to –2.26)
MET + GLP-T		0.20 (0.05 to 0.72)	0.21 (0.07 to 0.74)	–7.58 (–19.97 to –1.29)
MET + GLP-L		0.18 (0.05 to 0.63)	0.20 (0.06 to 0.65)	–7.74 (–20.22 to –1.62)
MET + GLP-H		0.17 (0.06 to 0.48)	0.18 (0.07 to 0.49)	–7.98 (–20.44 to –2.10)
MET + TZD-T		0.11 (0.03 to 0.33)	0.12 (0.04 to 0.34)	–8.62 (–21.01 to –2.76)
MET + TZD-L		0.18 (0.03 to 1.09)	0.20 (0.03 to 1.09)	–7.47 (–20.04 to 0.48)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD-H		0.13 (0.04 to 0.40)	0.14 (0.05 to 0.42)	–8.36 (–20.76 to –2.45)
MET + AGI-L		0.04 (0.00 to 0.56)	0.05 (0.00 to 0.58)	–8.98 (–21.51 to –2.37)
MET + AGI-T		0.07 (0.00 to 1.41)	0.08 (0.00 to 1.37)	–8.42 (–21.09 to 2.56)
MET + INS-BA-T		0.48 (0.15 to 1.53)	0.51 (0.18 to 1.49)	–4.71 (–17.20 to 2.42)
MET + INS-BI-T		0.86 (0.25 to 2.88)	0.87 (0.29 to 2.62)	–1.20 (–14.14 to 8.81)
MET + DPP-L	MET + DPP-T	0.47 (0.07 to 3.45)	0.48 (0.08 to 3.39)	–2.02 (–18.53 to 1.78)
MET + DPP-H		0.34 (0.05 to 2.27)	0.35 (0.07 to 2.25)	–2.55 (–19.05 to 0.79)
MET + SGL-L		0.43 (0.06 to 3.10)	0.44 (0.08 to 3.06)	–2.16 (–18.65 to 1.38)
MET + SGL-H		0.41 (0.06 to 2.88)	0.42 (0.08 to 2.85)	–2.23 (–18.75 to 1.20)
MET + GLP-T		0.52 (0.07 to 4.26)	0.53 (0.09 to 4.15)	–1.76 (–18.13 to 2.62)
MET + GLP-L		0.49 (0.06 to 3.78)	0.50 (0.08 to 3.70)	–1.90 (–18.36 to 2.20)
MET + GLP-H		0.45 (0.07 to 3.04)	0.46 (0.08 to 3.00)	–2.10 (–18.64 to 1.36)
MET + TZD-T		0.28 (0.04 to 2.00)	0.29 (0.05 to 1.99)	–2.75 (–19.24 to 0.69)
MET + TZD-L		0.49 (0.04 to 5.55)	0.50 (0.05 to 5.28)	–1.77 (–18.37 to 4.97)
MET + TZD-H		0.35 (0.05 to 2.53)	0.36 (0.06 to 2.50)	–2.48 (–19.01 to 1.03)
MET + AGI-L		0.11 (0.00 to 2.37)	0.11 (0.00 to 2.32)	–3.17 (–19.55 to 1.72)
MET + AGI-T		0.18 (0.00 to 5.93)	0.19 (0.00 to 5.45)	–2.67 (–19.02 to 7.37)
MET + INS-BA-T		1.27 (0.19 to 9.34)	1.26 (0.22 to 8.79)	0.97 (–15.26 to 6.53)
MET + INS-BI-T		2.29 (0.33 to 16.84)	2.17 (0.37 to 15.23)	4.24 (–11.67 to 13.30)
MET + DPP-H	MET + DPP-L	0.73 (0.36 to 1.51)	0.73 (0.37 to 1.50)	–0.49 (–2.22 to 0.50)
MET + SGL-L		0.93 (0.39 to 2.22)	0.93 (0.40 to 2.19)	–0.13 (–2.02 to 1.33)
MET + SGL-H		0.89 (0.38 to 2.06)	0.89 (0.39 to 2.04)	–0.20 (–2.08 to 1.14)
MET + GLP-T		1.13 (0.38 to 3.45)	1.12 (0.38 to 3.35)	0.22 (–1.90 to 3.18)
MET + GLP-L		1.05 (0.35 to 3.08)	1.05 (0.35 to 3.00)	0.08 (–2.01 to 2.66)
MET + GLP-H		0.96 (0.41 to 2.21)	0.96 (0.42 to 2.19)	–0.07 (–1.95 to 1.32)
MET + TZD-T		0.60 (0.23 to 1.54)	0.61 (0.24 to 1.53)	–0.71 (–2.54 to 0.64)
MET + TZD-L		1.05 (0.19 to 5.65)	1.05 (0.19 to 5.30)	0.08 (–2.33 to 6.32)
MET + TZD-H		0.75 (0.30 to 1.86)	0.76 (0.31 to 1.85)	–0.44 (–2.32 to 0.96)
MET + AGI-L		0.24 (0.01 to 2.81)	0.25 (0.01 to 2.73)	–1.28 (–3.23 to 2.77)
MET + AGI-T		0.40 (0.01 to 7.51)	0.40 (0.01 to 6.81)	–1.00 (–3.10 to 9.35)
MET + INS-BA-T		2.76 (1.07 to 7.04)	2.67 (1.07 to 6.57)	3.04 (0.18 to 7.52)
MET + INS-BI-T		4.93 (1.80 to 13.43)	4.59 (1.75 to 11.64)	6.61 (1.95 to 15.04)
MET + SGL-L	MET + DPP-H	1.28 (0.71 to 2.27)	1.27 (0.71 to 2.24)	0.37 (–0.47 to 1.51)
MET + SGL-H		1.22 (0.70 to 2.08)	1.21 (0.70 to 2.06)	0.29 (–0.49 to 1.27)
MET + GLP-T		1.54 (0.63 to 3.77)	1.53 (0.63 to 3.65)	0.72 (–0.55 to 3.50)
MET + GLP-L		1.44 (0.59 to 3.38)	1.43 (0.59 to 3.29)	0.58 (–0.62 to 2.97)
MET + GLP-H		1.32 (0.77 to 2.20)	1.31 (0.78 to 2.16)	0.42 (–0.36 to 1.46)
MET + TZD-T		0.83 (0.40 to 1.65)	0.83 (0.40 to 1.64)	–0.23 (–0.95 to 0.81)
MET + TZD-L		1.44 (0.28 to 6.72)	1.43 (0.29 to 6.28)	0.58 (–1.09 to 6.75)
MET + TZD-H		1.04 (0.53 to 1.96)	1.04 (0.53 to 1.94)	0.05 (–0.76 to 1.14)
MET + AGI-L		0.33 (0.01 to 3.56)	0.33 (0.01 to 3.44)	–0.87 (–1.63 to 3.34)
MET + AGI-T		0.54 (0.01 to 9.53)	0.55 (0.01 to 8.60)	–0.60 (–1.64 to 9.97)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BA-T		3.77 (1.89 to 7.38)	3.63 (1.86 to 6.83)	3.58 (1.21 to 7.86)
MET + INS-BI-T		6.76 (3.05 to 14.71)	6.26 (2.97 to 12.55)	7.16 (2.76 to 15.53)
MET + SGL-H	MET + SGL-L	0.95 (0.58 to 1.57)	0.95 (0.58 to 1.56)	–0.08 (–1.02 to 0.76)
MET + GLP-T		1.21 (0.44 to 3.34)	1.20 (0.45 to 3.24)	0.34 (–1.28 to 3.24)
MET + GLP-L		1.12 (0.42 to 2.95)	1.12 (0.42 to 2.87)	0.20 (–1.36 to 2.70)
MET + GLP-H		1.03 (0.51 to 2.04)	1.03 (0.52 to 2.01)	0.06 (–1.24 to 1.29)
MET + TZD-T		0.65 (0.27 to 1.50)	0.65 (0.28 to 1.49)	–0.59 (–1.84 to 0.65)
MET + TZD-L		1.13 (0.21 to 5.42)	1.13 (0.21 to 5.08)	0.21 (–1.77 to 6.42)
MET + TZD-H		0.81 (0.37 to 1.77)	0.81 (0.37 to 1.75)	–0.32 (–1.63 to 0.97)
MET + AGI-L		0.26 (0.01 to 2.98)	0.26 (0.01 to 2.90)	–1.19 (–2.51 to 3.01)
MET + AGI-T		0.43 (0.01 to 7.79)	0.43 (0.01 to 7.04)	–0.93 (–2.42 to 9.65)
MET + INS-BA-T		2.96 (1.29 to 6.71)	2.86 (1.28 to 6.25)	3.19 (0.61 to 7.62)
MET + INS-BI-T		5.30 (2.14 to 13.20)	4.92 (2.08 to 11.30)	6.75 (2.25 to 15.19)
MET + GLP-T	MET + SGL-H	1.27 (0.47 to 3.47)	1.26 (0.48 to 3.37)	0.42 (–1.10 to 3.30)
MET + GLP-L		1.17 (0.45 to 3.07)	1.17 (0.46 to 2.99)	0.28 (–1.18 to 2.77)
MET + GLP-H		1.08 (0.56 to 2.09)	1.08 (0.57 to 2.07)	0.13 (–1.00 to 1.33)
MET + TZD-T		0.68 (0.30 to 1.52)	0.68 (0.30 to 1.51)	–0.52 (–1.61 to 0.67)
MET + TZD-L		1.19 (0.22 to 5.86)	1.18 (0.23 to 5.47)	0.29 (–1.60 to 6.53)
MET + TZD-H		0.85 (0.40 to 1.84)	0.85 (0.40 to 1.82)	–0.24 (–1.40 to 1.02)
MET + AGI-L		0.27 (0.01 to 3.08)	0.28 (0.01 to 2.98)	–1.12 (–2.29 to 3.11)
MET + AGI-T		0.44 (0.01 to 8.09)	0.45 (0.01 to 7.28)	–0.87 (–2.23 to 9.65)
MET + INS-BA-T		3.11 (1.39 to 6.92)	3.00 (1.38 to 6.42)	3.27 (0.75 to 7.68)
MET + INS-BI-T		5.53 (2.30 to 13.47)	5.14 (2.24 to 11.54)	6.83 (2.37 to 15.30)
MET + GLP-L	MET + GLP-T	0.93 (0.27 to 3.05)	0.93 (0.28 to 2.98)	–0.14 (–3.13 to 2.49)
MET + GLP-H		0.86 (0.32 to 2.22)	0.86 (0.33 to 2.20)	–0.29 (–3.12 to 1.25)
MET + TZD-T		0.53 (0.18 to 1.56)	0.54 (0.18 to 1.55)	–0.93 (–3.80 to 0.62)
MET + TZD-L		0.93 (0.16 to 5.27)	0.93 (0.16 to 4.96)	–0.14 (–3.36 to 6.08)
MET + TZD-H		0.67 (0.24 to 1.89)	0.67 (0.24 to 1.87)	–0.67 (–3.52 to 0.93)
MET + AGI-L		0.21 (0.01 to 2.68)	0.22 (0.01 to 2.61)	–1.46 (–4.44 to 2.68)
MET + AGI-T		0.35 (0.01 to 6.85)	0.36 (0.01 to 6.20)	–1.17 (–4.21 to 9.12)
MET + INS-BA-T		2.45 (0.88 to 6.52)	2.37 (0.89 to 6.15)	2.78 (–0.43 to 7.03)
MET + INS-BI-T		4.39 (1.44 to 13.03)	4.08 (1.41 to 11.40)	6.29 (1.45 to 14.69)
MET + GLP-H	MET + GLP-L	0.92 (0.42 to 2.06)	0.92 (0.43 to 2.03)	–0.15 (–2.33 to 1.09)
MET + TZD-T		0.58 (0.20 to 1.68)	0.58 (0.20 to 1.67)	–0.79 (–3.30 to 0.70)
MET + TZD-L		1.00 (0.17 to 5.74)	1.00 (0.17 to 5.40)	0.00 (–2.90 to 6.20)
MET + TZD-H		0.72 (0.26 to 1.98)	0.72 (0.27 to 1.96)	–0.53 (–2.95 to 1.00)
MET + AGI-L		0.23 (0.01 to 2.74)	0.23 (0.01 to 2.67)	–1.33 (–3.84 to 2.74)
MET + AGI-T		0.38 (0.01 to 7.32)	0.38 (0.01 to 6.69)	–1.05 (–3.71 to 9.39)
MET + INS-BA-T		2.64 (0.97 to 7.22)	2.55 (0.97 to 6.75)	2.93 (–0.10 to 7.31)
MET + INS-BI-T		4.72 (1.60 to 14.11)	4.39 (1.56 to 12.31)	6.47 (1.73 to 14.83)
MET + TZD-T	MET + GLP-H	0.63 (0.28 to 1.40)	0.63 (0.28 to 1.39)	–0.64 (–1.83 to 0.55)
MET + TZD-L		1.10 (0.21 to 5.31)	1.10 (0.21 to 4.97)	0.17 (–1.78 to 6.35)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD-H		0.79 (0.39 to 1.58)	0.79 (0.39 to 1.57)	–0.37 (–1.54 to 0.79)
MET + AGI-L		0.25 (0.01 to 2.80)	0.25 (0.01 to 2.70)	–1.23 (–2.50 to 2.93)
MET + AGI-T		0.41 (0.01 to 7.40)	0.42 (0.01 to 6.69)	–0.98 (–2.45 to 9.53)
MET + INS-BA-T		2.87 (1.44 to 5.82)	2.77 (1.43 to 5.42)	3.13 (0.84 to 7.33)
MET + INS-BI-T		5.12 (2.37 to 11.19)	4.76 (2.31 to 9.68)	6.71 (2.44 to 14.93)
MET + TZD-L	MET + TZD-T	1.75 (0.32 to 9.14)	1.74 (0.32 to 8.58)	0.81 (–1.09 to 7.02)
MET + TZD-H		1.25 (0.52 to 3.08)	1.25 (0.52 to 3.04)	0.27 (–0.93 to 1.48)
MET + AGI-L		0.40 (0.01 to 4.82)	0.40 (0.01 to 4.65)	–0.61 (–1.82 to 3.62)
MET + AGI-T		0.66 (0.02 to 12.71)	0.66 (0.02 to 11.45)	–0.35 (–1.77 to 10.24)
MET + INS-BA-T		4.57 (1.85 to 11.52)	4.38 (1.82 to 10.70)	3.77 (1.29 to 8.14)
MET + INS-BI-T		8.19 (3.11 to 22.09)	7.55 (3.00 to 19.18)	7.36 (2.88 to 15.75)
MET + TZD-H	MET + TZD-L	0.72 (0.16 to 3.46)	0.72 (0.17 to 3.42)	–0.53 (–6.60 to 1.26)
MET + AGI-L		0.22 (0.01 to 4.18)	0.22 (0.01 to 4.04)	–1.31 (–7.41 to 2.95)
MET + AGI-T		0.38 (0.01 to 10.16)	0.38 (0.01 to 9.18)	–0.96 (–7.24 to 9.29)
MET + INS-BA-T		2.62 (0.50 to 15.03)	2.54 (0.52 to 14.07)	2.85 (–3.48 to 7.59)
MET + INS-BI-T		4.68 (0.87 to 27.63)	4.36 (0.88 to 24.32)	6.24 (–0.79 to 14.91)
MET + AGI-L	MET + TZD-H	0.32 (0.01 to 3.65)	0.32 (0.01 to 3.53)	–0.88 (–2.16 to 3.34)
MET + AGI-T		0.52 (0.01 to 9.72)	0.53 (0.01 to 8.72)	–0.62 (–2.09 to 9.87)
MET + INS-BA-T		3.65 (1.54 to 8.79)	3.51 (1.53 to 8.16)	3.50 (0.96 to 7.88)
MET + INS-BI-T		6.51 (2.57 to 16.92)	6.03 (2.49 to 14.55)	7.08 (2.61 to 15.53)
MET + AGI-T	MET + AGI-L	1.67 (0.02 to 124.30)	1.66 (0.02 to 115.30)	0.20 (–3.75 to 10.47)
MET + INS-BA-T		11.51 (0.99 to 335.60)	10.97 (0.99 to 316.70)	4.23 (–0.07 to 8.72)
MET + INS-BI-T		20.75 (1.69 to 613.40)	18.91 (1.64 to 551.50)	7.75 (2.19 to 16.29)
MET + INS-BA-T	MET + AGI-T	6.97 (0.37 to 288.00)	6.65 (0.39 to 270.80)	3.84 (–6.43 to 8.58)
MET + INS-BI-T		12.43 (0.66 to 528.70)	11.39 (0.68 to 472.20)	7.20 (–3.21 to 15.92)
MET + INS-BI-T	MET + INS-BA-T	1.78 (0.91 to 3.53)	1.71 (0.92 to 3.20)	3.46 (–0.49 to 10.24)
Random-effects model	Residual deviance	180 vs. 196 data points		
	Deviance information criteria	997.41		

AGI = alpha-glucosidase inhibitor; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Renal Adverse Events (People)

Table 24: Renal Adverse Events (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + DPP-L	MET	0.91 (0.24 to 3.48)	0.91 (0.24 to 3.45)	–0.06 (–1.18 to 1.02)
MET + DPP-H		0.26 (0.04 to 1.19)	0.26 (0.04 to 1.19)	–0.53 (–1.65 to 0.08)
MET + GLP-H		0.19 (0.01 to 9.45)	0.19 (0.01 to 8.91)	–0.51 (–1.66 to 5.34)
MET + TZD-H		0.32 (0.01 to 13.94)	0.33 (0.01 to 12.82)	–0.41 (–1.59 to 7.92)
MET + DPP-H	MET + DPP-L	0.28 (0.04 to 1.37)	0.28 (0.04 to 1.37)	–0.47 (–1.51 to 0.13)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLP-H		0.22 (0.01 to 10.40)	0.22 (0.01 to 9.86)	–0.44 (–1.53 to 5.37)
MET + TZD-H		0.39 (0.02 to 15.74)	0.39 (0.02 to 14.46)	–0.34 (–1.44 to 8.09)
MET + GLP-H	MET + DPP-H	0.87 (0.04 to 22.29)	0.87 (0.04 to 21.16)	–0.02 (–0.46 to 5.68)
MET + TZD-H		1.42 (0.09 to 38.39)	1.42 (0.09 to 35.11)	0.06 (–0.37 to 8.39)
MET + TZD-H	MET + GLP-H	1.69 (0.20 to 19.22)	1.68 (0.20 to 18.85)	0.06 (–1.41 to 4.90)
Random-effects model	Residual deviance	10.21 vs. 14 data points		
	Deviance information criteria	47.105		

CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; -L = low-dose; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Serious Adverse Events (SAE)

Table 25: Serious Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	1.00 (0.80 to 1.25)	1.00 (0.80 to 1.24)	–0.01 (–0.55 to 0.57)
MET + SUL-L		1.47 (0.25 to 10.26)	1.46 (0.26 to 8.33)	1.17 (–1.96 to 18.32)
MET + SUL-H		1.38 (0.46 to 4.42)	1.37 (0.46 to 4.07)	0.95 (–1.43 to 7.64)
MET + MEG-H		5.26 (1.09 to 36.41)	4.74 (1.08 to 19.20)	9.65 (0.21 to 45.95)
MET + DPP-L		0.92 (0.67 to 1.30)	0.93 (0.68 to 1.29)	–0.19 (–0.89 to 0.71)
MET + DPP-H		0.96 (0.77 to 1.18)	0.96 (0.78 to 1.18)	–0.11 (–0.63 to 0.41)
MET + SGL-L		0.95 (0.69 to 1.30)	0.95 (0.69 to 1.29)	–0.12 (–0.85 to 0.71)
MET + SGL-H		0.97 (0.75 to 1.26)	0.97 (0.75 to 1.25)	–0.07 (–0.69 to 0.61)
MET + GLP-T		5.50 (0.89 to 47.40)	4.93 (0.89 to 22.36)	10.07 (–0.29 to 51.98)
MET + GLP-L		0.73 (0.36 to 1.32)	0.73 (0.36 to 1.31)	–0.68 (–1.71 to 0.77)
MET + GLP-H		0.99 (0.74 to 1.33)	0.99 (0.75 to 1.32)	–0.02 (–0.70 to 0.77)
MET + TZD-T		1.00 (0.73 to 1.41)	1.00 (0.74 to 1.40)	0.00 (–0.72 to 0.96)
MET + TZD-L		0.78 (0.33 to 1.69)	0.78 (0.34 to 1.66)	–0.56 (–1.78 to 1.64)
MET + TZD-H		1.26 (0.95 to 1.70)	1.25 (0.95 to 1.67)	0.65 (–0.13 to 1.65)
MET + AGI-T		2.44 (0.88 to 7.22)	2.35 (0.88 to 6.23)	3.45 (–0.30 to 13.26)
MET + INS-BA-T		1.83 (0.82 to 4.14)	1.79 (0.83 to 3.83)	2.03 (–0.45 to 7.14)
MET + INS-BI-T		2.22 (0.55 to 9.82)	2.15 (0.56 to 8.02)	2.98 (–1.15 to 17.70)
MET + SUL-L	MET + SUL-T	1.48 (0.25 to 10.32)	1.46 (0.25 to 8.41)	1.18 (–2.02 to 18.33)
MET + SUL-H		1.40 (0.45 to 4.34)	1.39 (0.46 to 4.00)	0.97 (–1.46 to 7.55)
MET + MEG-H		5.32 (1.05 to 37.23)	4.78 (1.05 to 19.78)	9.66 (0.13 to 46.05)
MET + DPP-L		0.93 (0.69 to 1.25)	0.93 (0.70 to 1.25)	–0.18 (–0.84 to 0.60)
MET + DPP-H		0.96 (0.83 to 1.10)	0.96 (0.83 to 1.10)	–0.10 (–0.47 to 0.24)
MET + SGL-L		0.95 (0.71 to 1.29)	0.95 (0.71 to 1.28)	–0.12 (–0.80 to 0.67)
MET + SGL-H		0.97 (0.75 to 1.25)	0.98 (0.76 to 1.24)	–0.06 (–0.67 to 0.56)
MET + GLP-T		5.50 (0.91 to 46.91)	4.93 (0.91 to 22.04)	10.09 (–0.23 to 52.00)
MET + GLP-L		0.73 (0.36 to 1.32)	0.74 (0.37 to 1.31)	–0.67 (–1.70 to 0.77)
MET + GLP-H		0.99 (0.75 to 1.32)	0.99 (0.75 to 1.31)	–0.01 (–0.69 to 0.75)
MET + TZD-T		1.00 (0.78 to 1.29)	1.00 (0.79 to 1.29)	0.01 (–0.56 to 0.73)
MET + TZD-L		0.78 (0.34 to 1.71)	0.78 (0.34 to 1.68)	–0.56 (–1.79 to 1.66)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD-H		1.27 (0.94 to 1.74)	1.26 (0.94 to 1.71)	0.65 (–0.16 to 1.71)
MET + AGI-T		2.45 (0.85 to 7.41)	2.37 (0.85 to 6.42)	3.48 (–0.39 to 13.31)
MET + INS-BA-T		1.84 (0.83 to 4.08)	1.80 (0.84 to 3.79)	2.04 (–0.42 to 7.14)
MET + INS-BI-T		2.24 (0.55 to 9.64)	2.17 (0.56 to 7.87)	2.99 (–1.16 to 17.65)
MET + SUL-H	MET + SUL-L	0.90 (0.11 to 8.31)	0.90 (0.13 to 7.79)	–0.35 (–16.69 to 7.43)
MET + MEG-H		3.46 (0.32 to 52.60)	3.10 (0.36 to 33.14)	7.57 (–9.95 to 43.20)
MET + DPP-L		0.62 (0.09 to 3.84)	0.63 (0.11 to 3.77)	–1.37 (–18.45 to 1.98)
MET + DPP-H		0.65 (0.09 to 3.85)	0.66 (0.11 to 3.78)	–1.28 (–18.45 to 1.89)
MET + SGL-L		0.64 (0.09 to 3.87)	0.65 (0.12 to 3.79)	–1.30 (–18.35 to 1.99)
MET + SGL-H		0.66 (0.10 to 3.99)	0.67 (0.12 to 3.90)	–1.25 (–18.41 to 1.98)
MET + GLP-T		3.86 (0.23 to 73.60)	3.39 (0.26 to 41.74)	8.36 (–12.28 to 50.92)
MET + GLP-L		0.49 (0.06 to 3.38)	0.50 (0.08 to 3.32)	–1.85 (–18.98 to 1.76)
MET + GLP-H		0.67 (0.09 to 4.09)	0.68 (0.11 to 4.01)	–1.20 (–18.37 to 2.07)
MET + TZD-T		0.68 (0.10 to 4.09)	0.69 (0.12 to 4.00)	–1.17 (–18.30 to 2.14)
MET + TZD-L		0.52 (0.07 to 3.67)	0.53 (0.08 to 3.60)	–1.68 (–18.70 to 2.26)
MET + TZD-H		0.85 (0.12 to 5.21)	0.86 (0.15 to 5.06)	–0.53 (–17.63 to 2.84)
MET + AGI-T		1.69 (0.17 to 14.06)	1.64 (0.20 to 12.47)	2.14 (–15.54 to 13.07)
MET + INS-BA-T		1.22 (0.15 to 9.38)	1.21 (0.18 to 8.83)	0.74 (–16.29 to 7.10)
MET + INS-BI-T		1.57 (0.12 to 15.44)	1.53 (0.15 to 13.48)	1.68 (–15.83 to 16.31)
MET + MEG-H	MET + SUL-H	3.81 (0.92 to 23.73)	3.42 (0.92 to 14.82)	8.42 (–0.31 to 42.75)
MET + DPP-L		0.67 (0.21 to 2.11)	0.68 (0.23 to 2.08)	–1.13 (–7.79 to 1.41)
MET + DPP-H		0.69 (0.22 to 2.11)	0.69 (0.24 to 2.08)	–1.07 (–7.68 to 1.33)
MET + SGL-L		0.69 (0.22 to 2.18)	0.69 (0.24 to 2.15)	–1.09 (–7.65 to 1.44)
MET + SGL-H		0.70 (0.23 to 2.18)	0.71 (0.24 to 2.15)	–1.03 (–7.60 to 1.45)
MET + GLP-T		4.11 (0.39 to 48.39)	3.66 (0.41 to 26.00)	8.83 (–4.13 to 50.29)
MET + GLP-L		0.53 (0.14 to 1.81)	0.53 (0.15 to 1.79)	–1.58 (–8.36 to 1.15)
MET + GLP-H		0.72 (0.22 to 2.26)	0.73 (0.24 to 2.23)	–0.95 (–7.61 to 1.55)
MET + TZD-T		0.72 (0.23 to 2.24)	0.73 (0.25 to 2.21)	–0.96 (–7.54 to 1.56)
MET + TZD-L		0.56 (0.14 to 2.26)	0.57 (0.15 to 2.22)	–1.42 (–8.18 to 1.80)
MET + TZD-H		0.92 (0.30 to 2.78)	0.92 (0.32 to 2.72)	–0.27 (–6.82 to 2.18)
MET + AGI-T		1.81 (0.37 to 8.68)	1.76 (0.39 to 7.76)	2.37 (–5.19 to 12.79)
MET + INS-BA-T		1.35 (0.33 to 5.41)	1.34 (0.35 to 5.09)	1.07 (–5.95 to 6.89)
MET + INS-BI-T		1.70 (0.26 to 10.24)	1.66 (0.27 to 8.63)	2.05 (–5.78 to 16.94)
MET + DPP-L	MET + MEG-H	0.17 (0.03 to 0.91)	0.19 (0.05 to 0.91)	–9.80 (–46.00 to –0.24)
MET + DPP-H		0.18 (0.03 to 0.90)	0.20 (0.05 to 0.91)	–9.76 (–46.08 to –0.27)
MET + SGL-L		0.18 (0.03 to 0.95)	0.20 (0.05 to 0.95)	–9.75 (–45.96 to –0.15)
MET + SGL-H		0.18 (0.03 to 0.93)	0.20 (0.05 to 0.93)	–9.73 (–45.96 to –0.19)
MET + GLP-T		1.03 (0.05 to 20.28)	1.02 (0.08 to 11.12)	0.23 (–41.43 to 44.18)
MET + GLP-L		0.13 (0.02 to 0.81)	0.15 (0.03 to 0.81)	–10.34 (–46.48 to –0.54)
MET + GLP-H		0.19 (0.03 to 0.94)	0.21 (0.05 to 0.94)	–9.68 (–46.00 to –0.16)
MET + TZD-T		0.19 (0.03 to 0.96)	0.21 (0.05 to 0.97)	–9.62 (–45.98 to –0.10)
MET + TZD-L		0.15 (0.02 to 0.91)	0.16 (0.03 to 0.92)	–10.11 (–46.42 to –0.26)
MET + TZD-H		0.24 (0.03 to 1.19)	0.26 (0.06 to 1.18)	–8.97 (–45.26 to 0.51)
MET + AGI-T		0.45 (0.05 to 3.44)	0.49 (0.08 to 3.13)	–6.15 (–43.10 to 8.41)
MET + INS-BA-T		0.34 (0.04 to 2.33)	0.37 (0.07 to 2.23)	–7.48 (–44.49 to 3.95)
MET + INS-BI-T		0.40 (0.03 to 4.53)	0.44 (0.06 to 4.01)	–6.51 (–43.79 to 11.86)
MET + DPP-H	MET + DPP-L	1.03 (0.77 to 1.39)	1.03 (0.77 to 1.38)	0.08 (–0.71 to 0.71)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SGL-L		1.02 (0.69 to 1.54)	1.02 (0.70 to 1.53)	0.05 (–0.90 to 1.04)
MET + SGL-H		1.05 (0.72 to 1.50)	1.05 (0.73 to 1.49)	0.12 (–0.83 to 0.95)
MET + GLP-T		5.94 (1.01 to 52.83)	5.30 (1.01 to 24.56)	10.23 (0.03 to 52.15)
MET + GLP-L		0.79 (0.37 to 1.50)	0.79 (0.38 to 1.48)	–0.50 (–1.71 to 1.02)
MET + GLP-H		1.07 (0.73 to 1.57)	1.07 (0.74 to 1.55)	0.17 (–0.79 to 1.09)
MET + TZD-T		1.09 (0.73 to 1.59)	1.08 (0.74 to 1.57)	0.19 (–0.76 to 1.16)
MET + TZD-L		0.84 (0.35 to 1.91)	0.84 (0.35 to 1.87)	–0.38 (–1.76 to 1.86)
MET + TZD-H		1.37 (0.92 to 2.07)	1.36 (0.93 to 2.02)	0.84 (–0.22 to 2.04)
MET + AGI-T		2.64 (0.88 to 8.35)	2.53 (0.88 to 7.23)	3.65 (–0.30 to 13.50)
MET + INS-BA-T		1.98 (0.86 to 4.61)	1.94 (0.87 to 4.27)	2.22 (–0.35 to 7.35)
MET + INS-BI-T		2.40 (0.59 to 11.05)	2.32 (0.59 to 9.00)	3.15 (–1.02 to 17.95)
MET + SGL-L	MET + DPP-H	1.00 (0.73 to 1.35)	1.00 (0.74 to 1.34)	–0.01 (–0.69 to 0.79)
MET + SGL-H		1.02 (0.78 to 1.31)	1.02 (0.79 to 1.30)	0.04 (–0.57 to 0.70)
MET + GLP-T		5.71 (0.96 to 49.22)	5.11 (0.96 to 22.98)	10.17 (–0.09 to 52.12)
MET + GLP-L		0.76 (0.38 to 1.38)	0.77 (0.39 to 1.37)	–0.56 (–1.57 to 0.88)
MET + GLP-H		1.04 (0.78 to 1.37)	1.04 (0.78 to 1.36)	0.09 (–0.57 to 0.85)
MET + TZD-T		1.05 (0.80 to 1.39)	1.05 (0.80 to 1.37)	0.11 (–0.51 to 0.91)
MET + TZD-L		0.81 (0.35 to 1.78)	0.81 (0.36 to 1.74)	–0.46 (–1.65 to 1.75)
MET + TZD-H		1.32 (0.99 to 1.80)	1.31 (0.99 to 1.77)	0.76 (–0.04 to 1.79)
MET + AGI-T		2.56 (0.89 to 7.68)	2.46 (0.89 to 6.66)	3.58 (–0.29 to 13.40)
MET + INS-BA-T		1.92 (0.88 to 4.23)	1.88 (0.88 to 3.92)	2.14 (–0.29 to 7.23)
MET + INS-BI-T		2.35 (0.58 to 9.96)	2.27 (0.59 to 8.17)	3.10 (–1.03 to 17.76)
MET + SGL-H	MET + SGL-L	1.02 (0.76 to 1.35)	1.02 (0.77 to 1.34)	0.05 (–0.68 to 0.72)
MET + GLP-T		5.74 (0.90 to 50.36)	5.16 (0.91 to 23.47)	10.15 (–0.25 to 52.03)
MET + GLP-L		0.76 (0.37 to 1.47)	0.77 (0.37 to 1.46)	–0.57 (–1.80 to 0.98)
MET + GLP-H		1.04 (0.70 to 1.54)	1.04 (0.71 to 1.52)	0.10 (–0.89 to 1.07)
MET + TZD-T		1.05 (0.72 to 1.56)	1.05 (0.72 to 1.54)	0.13 (–0.82 to 1.12)
MET + TZD-L		0.82 (0.34 to 1.85)	0.82 (0.34 to 1.81)	–0.44 (–1.84 to 1.80)
MET + TZD-H		1.33 (0.90 to 2.00)	1.32 (0.90 to 1.96)	0.77 (–0.31 to 1.96)
MET + AGI-T		2.58 (0.88 to 8.18)	2.48 (0.88 to 7.05)	3.59 (–0.33 to 13.47)
MET + INS-BA-T		1.92 (0.85 to 4.38)	1.88 (0.85 to 4.06)	2.14 (–0.40 to 7.26)
MET + INS-BI-T		2.35 (0.58 to 10.13)	2.28 (0.58 to 8.31)	3.10 (–1.07 to 17.72)
MET + GLP-T	MET + SGL-H	5.71 (0.91 to 49.49)	5.11 (0.91 to 23.39)	10.14 (–0.24 to 52.12)
MET + GLP-L		0.75 (0.36 to 1.39)	0.75 (0.36 to 1.38)	–0.61 (–1.77 to 0.87)
MET + GLP-H		1.02 (0.72 to 1.45)	1.02 (0.73 to 1.44)	0.05 (–0.81 to 0.95)
MET + TZD-T		1.03 (0.74 to 1.49)	1.03 (0.75 to 1.47)	0.07 (–0.72 to 1.04)
MET + TZD-L		0.80 (0.33 to 1.79)	0.81 (0.34 to 1.76)	–0.49 (–1.85 to 1.75)
MET + TZD-H		1.30 (0.92 to 1.89)	1.29 (0.92 to 1.85)	0.71 (–0.24 to 1.86)
MET + AGI-T		2.51 (0.88 to 7.74)	2.42 (0.88 to 6.69)	3.53 (–0.32 to 13.40)
MET + INS-BA-T		1.89 (0.82 to 4.29)	1.85 (0.83 to 3.99)	2.11 (–0.45 to 7.23)
MET + INS-BI-T		2.31 (0.56 to 10.22)	2.24 (0.57 to 8.35)	3.06 (–1.12 to 17.82)
MET + GLP-L	MET + GLP-T	0.13 (0.01 to 0.96)	0.14 (0.03 to 0.96)	–10.77 (-52.51 to –0.09)
MET + GLP-H		0.18 (0.02 to 1.14)	0.20 (0.04 to 1.14)	–10.11 (-52.01 to 0.32)
MET + TZD-T		0.18 (0.02 to 1.10)	0.20 (0.04 to 1.10)	–10.03 (-51.90 to 0.24)
MET + TZD-L		0.14 (0.02 to 0.95)	0.15 (0.03 to 0.95)	–10.57 (-52.41 to –0.12)
MET + TZD-H		0.23 (0.03 to 1.47)	0.25 (0.05 to 1.45)	–9.40 (-51.44 to 1.09)
MET + AGI-T		0.44 (0.04 to 3.26)	0.48 (0.08 to 3.03)	–6.20 (–47.43 to 7.26)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BA-T		0.34 (0.04 to 1.90)	0.38 (0.07 to 1.85)	–7.76 (–48.99 to 2.59)
MET + INS-BI-T		0.41 (0.03 to 3.77)	0.45 (0.06 to 3.36)	–6.61 (–47.87 to 10.07)
MET + GLP-H	MET + GLP-L	1.36 (0.77 to 2.68)	1.35 (0.77 to 2.63)	0.66 (–0.71 to 1.72)
MET + TZD-T		1.38 (0.73 to 2.91)	1.37 (0.73 to 2.85)	0.68 (–0.84 to 1.94)
MET + TZD-L		1.08 (0.40 to 2.91)	1.07 (0.40 to 2.84)	0.13 (–1.67 to 2.44)
MET + TZD-H		1.75 (0.92 to 3.66)	1.72 (0.92 to 3.56)	1.34 (–0.24 to 2.70)
MET + AGI-T		3.39 (1.00 to 12.55)	3.23 (1.00 to 10.87)	4.13 (0.00 to 13.97)
MET + INS-BA-T		2.56 (0.99 to 7.01)	2.48 (0.99 to 6.51)	2.70 (–0.02 to 7.83)
MET + INS-BI-T		3.09 (0.70 to 14.58)	2.97 (0.70 to 12.28)	3.62 (–0.68 to 18.23)
MET + TZD-T	MET + GLP-H	1.01 (0.69 to 1.48)	1.01 (0.70 to 1.46)	0.02 (–0.90 to 1.03)
MET + TZD-L		0.78 (0.34 to 1.76)	0.79 (0.34 to 1.73)	–0.54 (–1.88 to 1.71)
MET + TZD-H		1.27 (0.89 to 1.86)	1.26 (0.89 to 1.83)	0.67 (–0.33 to 1.80)
MET + AGI-T		2.47 (0.85 to 7.50)	2.38 (0.85 to 6.53)	3.49 (–0.42 to 13.28)
MET + INS-BA-T		1.85 (0.80 to 4.28)	1.81 (0.81 to 3.97)	2.05 (–0.53 to 7.20)
MET + INS-BI-T		2.27 (0.54 to 9.82)	2.20 (0.55 to 8.08)	3.01 (–1.23 to 17.67)
MET + TZD-L	MET + TZD-T	0.78 (0.31 to 1.76)	0.78 (0.32 to 1.73)	–0.55 (–2.06 to 1.68)
MET + TZD-H		1.26 (0.86 to 1.86)	1.25 (0.86 to 1.83)	0.64 (–0.43 to 1.80)
MET + AGI-T		2.45 (0.81 to 7.72)	2.36 (0.82 to 6.68)	3.47 (–0.51 to 13.36)
MET + INS-BA-T		1.83 (0.80 to 4.17)	1.79 (0.81 to 3.88)	2.02 (–0.54 to 7.12)
MET + INS-BI-T		2.23 (0.54 to 9.79)	2.16 (0.54 to 8.05)	2.97 (–1.27 to 17.65)
MET + TZD-H	MET + TZD-L	1.63 (0.77 to 3.81)	1.61 (0.77 to 3.72)	1.19 (–0.91 to 2.67)
MET + AGI-T		3.18 (0.82 to 12.57)	3.04 (0.82 to 10.94)	3.95 (–0.57 to 13.86)
MET + INS-BA-T		2.39 (0.72 to 7.23)	2.33 (0.73 to 6.74)	2.56 (–0.92 to 7.58)
MET + INS-BI-T		2.96 (0.54 to 15.10)	2.84 (0.54 to 12.60)	3.55 (–1.45 to 18.04)
MET + AGI-T	MET + TZD-H	1.93 (0.66 to 5.89)	1.87 (0.67 to 5.15)	2.79 (–1.15 to 12.61)
MET + INS-BA-T		1.45 (0.62 to 3.41)	1.43 (0.63 to 3.18)	1.37 (–1.32 to 6.60)
MET + INS-BI-T		1.78 (0.42 to 7.81)	1.74 (0.43 to 6.44)	2.33 (–1.96 to 17.06)
MET + INS-BA-T	MET + AGI-T	0.73 (0.19 to 2.99)	0.75 (0.21 to 2.82)	–1.46 (–11.69 to 5.51)
MET + INS-BI-T		0.87 (0.16 to 6.06)	0.88 (0.18 to 5.20)	–0.67 (–10.62 to 14.41)
MET + INS-BI-T	MET + INS-BA-T	1.21 (0.38 to 4.16)	1.20 (0.39 to 3.61)	0.85 (–3.49 to 13.16)
Random-effects model	Residual deviance	182.8 vs. 201 data points		
	Deviance information criteria	990.564		

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Total Cholesterol

Table 26: Total Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-H	MET	0.12 (–0.09 to 0.31)
MET + SUL-T		0.03 (–0.14 to 0.20)
MET + SUL-L		0.23 (–0.31 to 0.77)
MET + MEG-T		–0.08 (–0.46 to 0.30)
MET + MEG-L		0.00 (–0.47 to 0.46)
MET + MEG-H		0.00 (–0.47 to 0.46)
MET + DPP-L		–0.01 (–0.23 to 0.22)
MET + DPP-H		0.01 (–0.10 to 0.12)
MET + SGL-L		0.21 (–0.03 to 0.44)
MET + SGL-H		0.21 (–0.01 to 0.43)
MET + GLP-L		–0.02 (–1.29 to 1.19)
MET + GLP-T		–0.07 (–0.40 to 0.24)
MET + GLP-H		–0.06 (–0.23 to 0.10)
MET + AGI-L		0.26 (–0.12 to 0.64)
MET + TZD-L		0.24 (0.02 to 0.46)
MET + TZD-H		0.34 (0.19 to 0.48)
MET + TZD-T		0.31 (0.04 to 0.58)
MET + INS-BA-T		–0.09 (–0.47 to 0.29)
MET + SUL-T	MET + SUL-H	–0.08 (–0.33 to 0.16)
MET + SUL-L		0.11 (–0.45 to 0.68)
MET + MEG-T		–0.19 (–0.62 to 0.23)
MET + MEG-L		–0.12 (–0.62 to 0.39)
MET + MEG-H		–0.12 (–0.62 to 0.38)
MET + DPP-L		–0.12 (–0.41 to 0.17)
MET + DPP-H		–0.10 (–0.30 to 0.09)
MET + SGL-L		0.09 (–0.21 to 0.40)
MET + SGL-H		0.09 (–0.19 to 0.38)
MET + GLP-L		–0.14 (–1.42 to 1.09)
MET + GLP-T		–0.19 (–0.56 to 0.17)
MET + GLP-H		–0.18 (–0.41 to 0.05)
MET + AGI-L		0.15 (–0.22 to 0.51)
MET + TZD-L		0.13 (–0.14 to 0.40)
MET + TZD-H		0.22 (0.03 to 0.42)
MET + TZD-T		0.19 (–0.12 to 0.52)
MET + INS-BA-T		–0.21 (–0.62 to 0.22)
MET + SUL-L	MET + SUL-T	0.20 (–0.36 to 0.76)
MET + MEG-T		–0.11 (–0.49 to 0.28)
MET + MEG-L		–0.03 (–0.53 to 0.46)
MET + MEG-H		–0.03 (–0.53 to 0.46)
MET + DPP-L		–0.04 (–0.31 to 0.23)
MET + DPP-H		–0.02 (–0.18 to 0.15)
MET + SGL-L		0.18 (–0.10 to 0.46)
MET + SGL-H		0.18 (–0.09 to 0.45)

Treatment	Reference	MD (95% CrI)
MET + GLP-L		–0.06 (–1.33 to 1.17)
MET + GLP-T		–0.10 (–0.43 to 0.22)
MET + GLP-H		–0.09 (–0.30 to 0.11)
MET + AGI-L		0.23 (–0.17 to 0.64)
MET + TZD-L		0.21 (–0.06 to 0.48)
MET + TZD-H		0.31 (0.10 to 0.51)
MET + TZD-T		0.28 (0.08 to 0.49)
MET + INS-BA-T		–0.12 (–0.52 to 0.28)
MET + MEG-T	MET + SUL-L	–0.31 (–0.96 to 0.35)
MET + MEG-L		–0.23 (–0.94 to 0.48)
MET + MEG-H		–0.23 (–0.94 to 0.48)
MET + DPP-L		–0.23 (–0.80 to 0.34)
MET + DPP-H		–0.22 (–0.76 to 0.33)
MET + SGL-L		–0.02 (–0.60 to 0.56)
MET + SGL-H		–0.02 (–0.59 to 0.56)
MET + GLP-L		–0.25 (–1.64 to 1.08)
MET + GLP-T		–0.30 (–0.93 to 0.32)
MET + GLP-H		–0.29 (–0.85 to 0.27)
MET + AGI-L		0.03 (–0.62 to 0.69)
MET + TZD-L		0.01 (–0.48 to 0.50)
MET + TZD-H		0.11 (–0.43 to 0.65)
MET + TZD-T		0.08 (–0.51 to 0.68)
MET + INS-BA-T		–0.32 (–0.97 to 0.34)
MET + MEG-L	MET + MEG-T	0.08 (–0.52 to 0.68)
MET + MEG-H		0.07 (–0.52 to 0.67)
MET + DPP-L		0.07 (–0.37 to 0.51)
MET + DPP-H		0.09 (–0.30 to 0.48)
MET + SGL-L		0.28 (–0.16 to 0.73)
MET + SGL-H		0.29 (–0.15 to 0.73)
MET + GLP-L		0.05 (–1.27 to 1.32)
MET + GLP-T		0.00 (–0.48 to 0.49)
MET + GLP-H		0.01 (–0.40 to 0.42)
MET + AGI-L		0.34 (–0.19 to 0.87)
MET + TZD-L		0.32 (–0.12 to 0.75)
MET + TZD-H		0.42 (0.01 to 0.82)
MET + TZD-T		0.38 (–0.05 to 0.82)
MET + INS-BA-T		–0.01 (–0.55 to 0.52)
MET + MEG-H	MET + MEG-L	0.00 (–0.46 to 0.46)
MET + DPP-L		0.00 (–0.52 to 0.51)
MET + DPP-H		0.01 (–0.46 to 0.49)
MET + SGL-L		0.21 (–0.31 to 0.73)
MET + SGL-H		0.21 (–0.30 to 0.73)
MET + GLP-L		–0.02 (–1.37 to 1.28)
MET + GLP-T		–0.07 (–0.64 to 0.49)
MET + GLP-H		–0.06 (–0.55 to 0.43)
MET + AGI-L		0.26 (–0.34 to 0.87)
MET + TZD-L		0.24 (–0.27 to 0.75)

Treatment	Reference	MD (95% CrI)
MET + TZD-H		0.34 (–0.14 to 0.83)
MET + TZD-T		0.31 (–0.22 to 0.85)
MET + INS-BA-T		–0.09 (–0.69 to 0.51)
MET + DPP-L	MET + MEG-H	0.00 (–0.52 to 0.51)
MET + DPP-H		0.01 (–0.46 to 0.49)
MET + SGL-L		0.21 (–0.31 to 0.73)
MET + SGL-H		0.21 (–0.30 to 0.73)
MET + GLP-L		–0.02 (–1.36 to 1.27)
MET + GLP-T		–0.07 (–0.63 to 0.49)
MET + GLP-H		–0.06 (–0.55 to 0.43)
MET + AGI-L		0.26 (–0.34 to 0.86)
MET + TZD-L		0.24 (–0.27 to 0.75)
MET + TZD-H		0.34 (–0.14 to 0.82)
MET + TZD-T		0.31 (–0.22 to 0.85)
MET + INS-BA-T		–0.09 (–0.68 to 0.52)
MET + DPP-H	MET + DPP-L	0.02 (–0.21 to 0.25)
MET + SGL-L		0.21 (–0.10 to 0.53)
MET + SGL-H		0.22 (–0.09 to 0.53)
MET + GLP-L		–0.02 (–1.30 to 1.22)
MET + GLP-T		–0.07 (–0.45 to 0.32)
MET + GLP-H		–0.06 (–0.33 to 0.21)
MET + AGI-L		0.27 (–0.16 to 0.70)
MET + TZD-L		0.25 (–0.04 to 0.53)
MET + TZD-H		0.34 (0.10 to 0.59)
MET + TZD-T		0.31 (–0.02 to 0.66)
MET + INS-BA-T		–0.08 (–0.52 to 0.35)
MET + SGL-L	MET + DPP-H	0.20 (–0.05 to 0.44)
MET + SGL-H		0.20 (–0.03 to 0.42)
MET + GLP-L		–0.04 (–1.31 to 1.18)
MET + GLP-T		–0.09 (–0.40 to 0.23)
MET + GLP-H		–0.08 (–0.24 to 0.09)
MET + AGI-L		0.25 (–0.12 to 0.62)
MET + TZD-L		0.23 (0.00 to 0.46)
MET + TZD-H		0.33 (0.17 to 0.48)
MET + TZD-T		0.29 (0.03 to 0.56)
MET + INS-BA-T		–0.10 (–0.47 to 0.27)
MET + SGL-H	MET + SGL-L	0.00 (–0.22 to 0.23)
MET + GLP-L		–0.23 (–1.52 to 1.00)
MET + GLP-T		–0.28 (–0.68 to 0.11)
MET + GLP-H		–0.27 (–0.55 to 0.01)
MET + AGI-L		0.06 (–0.39 to 0.50)
MET + TZD-L		0.03 (–0.28 to 0.35)
MET + TZD-H		0.13 (–0.14 to 0.40)
MET + TZD-T		0.10 (–0.25 to 0.45)
MET + INS-BA-T		–0.30 (–0.73 to 0.14)
MET + GLP-L	MET + SGL-H	–0.24 (–1.52 to 1.00)
MET + GLP-T		–0.28 (–0.67 to 0.10)

Treatment	Reference	MD (95% CrI)
MET + GLP-H		–0.27 (–0.54,–0.01)
MET + AGI-L		0.05 (–0.38 to 0.48)
MET + TZD-L		0.03 (–0.28 to 0.34)
MET + TZD-H		0.13 (–0.13 to 0.38)
MET + TZD-T		0.10 (–0.24 to 0.44)
MET + INS-BA-T		–0.30 (–0.73 to 0.13)
MET + GLP-T	MET + GLP-L	–0.05 (–1.30 to 1.25)
MET + GLP-H		–0.04 (–1.26 to 1.23)
MET + AGI-L		0.29 (–0.99 to 1.61)
MET + TZD-L		0.27 (–0.97 to 1.56)
MET + TZD-H		0.36 (–0.86 to 1.64)
MET + TZD-T		0.33 (–0.91 to 1.62)
MET + INS-BA-T		–0.06 (–1.34 to 1.26)
MET + GLP-H	MET + GLP-T	0.01 (–0.33 to 0.36)
MET + AGI-L		0.33 (–0.15 to 0.83)
MET + TZD-L		0.31 (–0.07 to 0.70)
MET + TZD-H		0.41 (0.07 to 0.76)
MET + TZD-T		0.38 (0.00 to 0.77)
MET + INS-BA-T		–0.02 (–0.46 to 0.44)
MET + AGI-L	MET + GLP-H	0.33 (–0.07 to 0.73)
MET + TZD-L		0.31 (0.04 to 0.57)
MET + TZD-H		0.40 (0.21 to 0.59)
MET + TZD-T		0.37 (0.08 to 0.67)
MET + INS-BA-T		–0.03 (–0.42 to 0.38)
MET + TZD-L	MET + AGI-L	–0.02 (–0.44 to 0.40)
MET + TZD-H		0.08 (–0.31 to 0.46)
MET + TZD-T		0.05 (–0.41 to 0.50)
MET + INS-BA-T		–0.35 (–0.87 to 0.17)
MET + TZD-H	MET + TZD-L	0.10 (–0.13 to 0.32)
MET + TZD-T		0.06 (–0.27 to 0.41)
MET + INS-BA-T		–0.33 (–0.76 to 0.11)
MET + TZD-T	MET + TZD-H	–0.03 (–0.32 to 0.27)
MET + INS-BA-T		–0.43 (–0.82,–0.03)
MET + INS-BA-T	MET + TZD-T	–0.40 (–0.84 to 0.05)
Random-effects model	Residual deviance	109.7 vs. 113 data points
	Deviance information criteria	–151.102

AGI = alpha-glucosidase inhibitor; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; -L = low-dose; MD = mean difference; MEG = meglitinide; MET = metformin; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Glycated Hemoglobin (A1C)

Table 27: A1C: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-T	MET	–0.66 (–0.78 to –0.55)
MET + SUL-L		0.01 (–0.33 to 0.34)
MET + SUL-H		–0.61 (–0.78 to –0.44)
MET + MEG-H		–0.50 (–0.78 to –0.21)
MET + MEG-L		–0.67 (–1.01 to –0.32)
MET + MEG-T		–1.13 (–1.67 to –0.58)
MET + DPP-L		–0.56 (–0.70 to –0.42)
MET + DPP-H		–0.58 (–0.66 to –0.50)
MET + DPP-T		–0.13 (–0.75 to 0.48)
MET + SGL-L		–0.55 (–0.70 to –0.40)
MET + SGL-H		–0.67 (–0.81 to –0.54)
MET + GLP-L		–0.56 (–0.75 to –0.37)
MET + GLP-H		–0.76 (–0.88 to –0.64)
MET + GLP-T		–0.86 (–1.15 to –0.57)
MET + AGI-T		–0.79 (–1.11 to –0.46)
MET + AGI-H		–0.11 (–0.76 to 0.54)
MET + AGI-L		–0.49 (–0.87 to –0.11)
MET + TZD-L		–0.58 (–0.79 to –0.37)
MET + TZD-H		–0.67 (–0.79 to –0.54)
MET + TZD-T		–0.66 (–0.86 to –0.45)
MET + INS-BA-T		–0.81 (–1.07 to –0.55)
MET + INS-BI-T		–0.86 (–1.14 to –0.57)
MET + SUL-L	MET + SUL-T	0.67 (0.32 to 1.02)
MET + SUL-H		0.05 (–0.14 to 0.24)
MET + MEG-H		0.17 (–0.14 to 0.48)
MET + MEG-L		0.00 (–0.36 to 0.36)
MET + MEG-T		–0.46 (–1.01 to 0.09)
MET + DPP-L		0.10 (–0.06 to 0.27)
MET + DPP-H		0.08 (–0.02 to 0.19)
MET + DPP-T		0.53 (–0.07 to 1.13)
MET + SGL-L		0.12 (–0.06 to 0.29)
MET + SGL-H		–0.01 (–0.17 to 0.16)
MET + GLP-L		0.10 (–0.11 to 0.32)
MET + GLP-H		–0.10 (–0.25 to 0.05)
MET + GLP-T		–0.20 (–0.49 to 0.09)
MET + AGI-T		–0.12 (–0.47 to 0.22)
MET + AGI-H		0.55 (–0.10 to 1.21)
MET + AGI-L		0.17 (–0.22 to 0.56)
MET + TZD-L		0.08 (–0.15 to 0.31)

Treatment	Reference	MD (95% CrI)
MET + TZD-H		0.00 (–0.16 to 0.15)
MET + TZD-T		0.01 (–0.17 to 0.18)
MET + INS-BA-T		–0.15 (–0.41 to 0.11)
MET + INS-BI-T		–0.19 (–0.48 to 0.10)
MET + SUL-H	MET + SUL-L	–0.62 (–0.98 to –0.25)
MET + MEG-H		–0.50 (–0.94 to –0.06)
MET + MEG-L		–0.67 (–1.15 to –0.19)
MET + MEG-T		–1.13 (–1.77 to –0.49)
MET + DPP-L		–0.57 (–0.93 to –0.21)
MET + DPP-H		–0.58 (–0.92 to –0.25)
MET + DPP-T		–0.14 (–0.83 to 0.56)
MET + SGL-L		–0.55 (–0.91 to –0.19)
MET + SGL-H		–0.68 (–1.03 to –0.32)
MET + GLP-L		–0.57 (–0.95 to –0.18)
MET + GLP-H		–0.77 (–1.12 to –0.42)
MET + GLP-T		–0.87 (–1.31 to –0.43)
MET + AGI-T		–0.79 (–1.26 to –0.33)
MET + AGI-H		–0.12 (–0.84 to 0.61)
MET + AGI-L		–0.50 (–1.00 to 0.01)
MET + TZD-L		–0.59 (–0.91 to –0.26)
MET + TZD-H		–0.67 (–1.02 to –0.32)
MET + TZD-T		–0.66 (–1.05 to –0.27)
MET + INS-BA-T		–0.82 (–1.24 to –0.39)
MET + INS-BI-T		–0.86 (–1.30 to –0.42)
MET + MEG-H	MET + SUL-H	0.12 (–0.19 to 0.42)
MET + MEG-L		–0.05 (–0.43 to 0.32)
MET + MEG-T		–0.51 (–1.08 to 0.06)
MET + DPP-L		0.05 (–0.16 to 0.26)
MET + DPP-H		0.03 (–0.13 to 0.20)
MET + DPP-T		0.48 (–0.15 to 1.11)
MET + SGL-L		0.07 (–0.15 to 0.29)
MET + SGL-H		–0.06 (–0.27 to 0.15)
MET + GLP-L		0.05 (–0.19 to 0.29)
MET + GLP-H		–0.15 (–0.33 to 0.03)
MET + GLP-T		–0.25 (–0.58 to 0.08)
MET + AGI-T		–0.18 (–0.54 to 0.19)
MET + AGI-H		0.50 (–0.12 to 1.13)
MET + AGI-L		0.12 (–0.26 to 0.51)
MET + TZD-L		0.03 (–0.21 to 0.28)
MET + TZD-H		–0.06 (–0.23 to 0.12)
MET + TZD-T		–0.05 (–0.30 to 0.21)
MET + INS-BA-T		–0.20 (–0.49 to 0.10)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		–0.24 (–0.56 to 0.08)
MET + MEG-L	MET + MEG-H	–0.17 (–0.55 to 0.21)
MET + MEG-T		–0.63 (–1.25 to –0.01)
MET + DPP-L		–0.07 (–0.38 to 0.25)
MET + DPP-H		–0.08 (–0.38 to 0.21)
MET + DPP-T		0.37 (–0.31 to 1.04)
MET + SGL-L		–0.05 (–0.37 to 0.27)
MET + SGL-H		–0.18 (–0.49 to 0.14)
MET + GLP-L		–0.07 (–0.41 to 0.28)
MET + GLP-H		–0.27 (–0.57 to 0.04)
MET + GLP-T		–0.37 (–0.77 to 0.04)
MET + AGI-T		–0.29 (–0.72 to 0.14)
MET + AGI-H		0.38 (–0.31 to 1.08)
MET + AGI-L		0.00 (–0.46 to 0.47)
MET + TZD-L		–0.08 (–0.43 to 0.26)
MET + TZD-H		–0.17 (–0.48 to 0.14)
MET + TZD-T		–0.16 (–0.51 to 0.19)
MET + INS-BA-T		–0.32 (–0.70 to 0.07)
MET + INS-BI-T		–0.36 (–0.76 to 0.04)
MET + MEG-T	MET + MEG-L	–0.46 (–1.10 to 0.19)
MET + DPP-L		0.10 (–0.27 to 0.47)
MET + DPP-H		0.09 (–0.26 to 0.44)
MET + DPP-T		0.54 (–0.17 to 1.23)
MET + SGL-L		0.12 (–0.25 to 0.49)
MET + SGL-H		–0.01 (–0.37 to 0.36)
MET + GLP-L		0.10 (–0.29 to 0.50)
MET + GLP-H		–0.10 (–0.46 to 0.26)
MET + GLP-T		–0.20 (–0.64 to 0.25)
MET + AGI-T		–0.12 (–0.59 to 0.35)
MET + AGI-H		0.55 (–0.18 to 1.29)
MET + AGI-L		0.17 (–0.33 to 0.69)
MET + TZD-L		0.09 (–0.31 to 0.48)
MET + TZD-H		0.00 (–0.36 to 0.36)
MET + TZD-T		0.01 (–0.39 to 0.41)
MET + INS-BA-T		–0.15 (–0.57 to 0.28)
MET + INS-BI-T		–0.19 (–0.64 to 0.25)
MET + DPP-L	MET + MEG-T	0.56 (0.00 to 1.13)
MET + DPP-H		0.55 (0.00 to 1.10)
MET + DPP-T		0.99 (0.18 to 1.81)
MET + SGL-L		0.58 (0.02 to 1.15)
MET + SGL-H		0.45 (–0.11 to 1.02)
MET + GLP-L		0.56 (–0.02 to 1.15)

Treatment	Reference	MD (95% CrI)
MET + GLP-H		0.36 (–0.20 to 0.92)
MET + GLP-T		0.26 (–0.35 to 0.88)
MET + AGI-T		0.34 (–0.30 to 0.98)
MET + AGI-H		1.01 (0.17 to 1.86)
MET + AGI-L		0.63 (–0.03 to 1.30)
MET + TZD-L		0.54 (–0.03 to 1.13)
MET + TZD-H		0.46 (–0.10 to 1.02)
MET + TZD-T		0.47 (–0.11 to 1.04)
MET + INS-BA-T		0.31 (–0.29 to 0.91)
MET + INS-BI-T		0.27 (–0.34 to 0.88)
MET + DPP-H	MET + DPP-L	–0.02 (–0.16 to 0.13)
MET + DPP-T		0.43 (–0.19 to 1.06)
MET + SGL-L		0.02 (–0.19 to 0.22)
MET + SGL-H		–0.11 (–0.30 to 0.08)
MET + GLP-L		0.00 (–0.23 to 0.23)
MET + GLP-H		–0.20 (–0.38 to –0.02)
MET + GLP-T		–0.30 (–0.62 to 0.01)
MET + AGI-T		–0.23 (–0.58 to 0.13)
MET + AGI-H		0.45 (–0.21 to 1.11)
MET + AGI-L		0.07 (–0.33 to 0.47)
MET + TZD-L		–0.02 (–0.26 to 0.22)
MET + TZD-H		–0.11 (–0.28 to 0.07)
MET + TZD-T		–0.10 (–0.34 to 0.14)
MET + INS-BA-T		–0.25 (–0.54 to 0.03)
MET + INS-BI-T		–0.29 (–0.61 to 0.02)
MET + DPP-T	MET + DPP-H	0.45 (–0.16 to 1.06)
MET + SGL-L		0.03 (–0.13 to 0.19)
MET + SGL-H		–0.09 (–0.24 to 0.05)
MET + GLP-L		0.02 (–0.18 to 0.22)
MET + GLP-H		–0.18 (–0.30 to –0.06)
MET + GLP-T		–0.28 (–0.57 to 0.00)
MET + AGI-T		–0.21 (–0.54 to 0.13)
MET + AGI-H		0.47 (–0.18 to 1.11)
MET + AGI-L		0.09 (–0.29 to 0.47)
MET + TZD-L		0.00 (–0.21 to 0.21)
MET + TZD-H		–0.09 (–0.21 to 0.04)
MET + TZD-T		–0.08 (–0.28 to 0.12)
MET + INS-BA-T		–0.23 (–0.49 to 0.02)
MET + INS-BI-T		–0.28 (–0.56 to 0.01)
MET + SGL-L	MET + DPP-T	–0.42 (–1.04 to 0.22)
MET + SGL-H		–0.54 (–1.16 to 0.09)
MET + GLP-L		–0.43 (–1.07 to 0.21)

Treatment	Reference	MD (95% CrI)
MET + GLP-H		–0.63 (–1.25 to –0.01)
MET + GLP-T		–0.73 (–1.40 to –0.06)
MET + AGI-T		–0.66 (–1.35 to 0.04)
MET + AGI-H		0.02 (–0.87 to 0.90)
MET + AGI-L		–0.36 (–1.08 to 0.36)
MET + TZD-L		–0.45 (–1.10 to 0.19)
MET + TZD-H		–0.54 (–1.16 to 0.09)
MET + TZD-T		–0.53 (–1.16 to 0.10)
MET + INS-BA-T		–0.68 (–1.34 to –0.02)
MET + INS-BI-T		–0.73 (–1.39 to –0.06)
MET + SGL-H	MET + SGL-L	–0.13 (–0.27 to 0.02)
MET + GLP-L		–0.02 (–0.26 to 0.23)
MET + GLP-H		–0.22 (–0.40 to –0.03)
MET + GLP-T		–0.32 (–0.64 to 0.01)
MET + AGI-T		–0.24 (–0.60 to 0.12)
MET + AGI-H		0.43 (–0.23 to 1.10)
MET + AGI-L		0.05 (–0.35 to 0.46)
MET + TZD-L		–0.03 (–0.29 to 0.22)
MET + TZD-H		–0.12 (–0.31 to 0.07)
MET + TZD-T		–0.11 (–0.36 to 0.13)
MET + INS-BA-T		–0.27 (–0.56 to 0.03)
MET + INS-BI-T		–0.31 (–0.63 to 0.01)
MET + GLP-L	MET + SGL-H	0.11 (–0.12 to 0.34)
MET + GLP-H		–0.09 (–0.27 to 0.08)
MET + GLP-T		–0.19 (–0.50 to 0.12)
MET + AGI-T		–0.12 (–0.47 to 0.24)
MET + AGI-H		0.56 (–0.10 to 1.22)
MET + AGI-L		0.18 (–0.22 to 0.58)
MET + TZD-L		0.09 (–0.15 to 0.34)
MET + TZD-H		0.00 (–0.18 to 0.18)
MET + TZD-T		0.01 (–0.22 to 0.25)
MET + INS-BA-T		–0.14 (–0.43 to 0.14)
MET + INS-BI-T		–0.18 (–0.49 to 0.13)
MET + GLP-H	MET + GLP-L	–0.20 (–0.39 to –0.02)
MET + GLP-T		–0.30 (–0.64 to 0.04)
MET + AGI-T		–0.23 (–0.60 to 0.15)
MET + AGI-H		0.45 (–0.22 to 1.12)
MET + AGI-L		0.07 (–0.34 to 0.49)
MET + TZD-L		–0.02 (–0.30 to 0.26)
MET + TZD-H		–0.11 (–0.33 to 0.11)
MET + TZD-T		–0.10 (–0.37 to 0.18)
MET + INS-BA-T		–0.25 (–0.56 to 0.06)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		–0.29 (–0.62 to 0.04)
MET + GLP-T	MET + GLP-H	–0.10 (–0.40 to 0.20)
MET + AGI-T		–0.03 (–0.37 to 0.32)
MET + AGI-H		0.65 (0.00 to 1.30)
MET + AGI-L		0.27 (–0.12 to 0.66)
MET + TZD-L		0.18 (–0.05 to 0.42)
MET + TZD-H		0.10 (–0.06 to 0.25)
MET + TZD-T		0.10 (–0.12 to 0.33)
MET + INS-BA-T		–0.05 (–0.31 to 0.21)
MET + INS-BI-T		–0.09 (–0.38 to 0.19)
MET + AGI-T	MET + GLP-T	0.07 (–0.36 to 0.51)
MET + AGI-H		0.75 (0.05 to 1.46)
MET + AGI-L		0.37 (–0.10 to 0.84)
MET + TZD-L		0.28 (–0.07 to 0.63)
MET + TZD-H		0.19 (–0.11 to 0.50)
MET + TZD-T		0.20 (–0.13 to 0.54)
MET + INS-BA-T		0.05 (–0.28 to 0.38)
MET + INS-BI-T		0.01 (–0.36 to 0.38)
MET + AGI-H	MET + AGI-T	0.68 (–0.05 to 1.40)
MET + AGI-L		0.30 (–0.21 to 0.80)
MET + TZD-L		0.21 (–0.18 to 0.60)
MET + TZD-H		0.12 (–0.23 to 0.47)
MET + TZD-T		0.13 (–0.26 to 0.52)
MET + INS-BA-T		–0.02 (–0.44 to 0.39)
MET + INS-BI-T		–0.07 (–0.50 to 0.37)
MET + AGI-L	MET + AGI-H	–0.38 (–1.12 to 0.36)
MET + TZD-L		–0.47 (–1.14 to 0.20)
MET + TZD-H		–0.55 (–1.21 to 0.10)
MET + TZD-T		–0.55 (–1.22 to 0.13)
MET + INS-BA-T		–0.70 (–1.39 to –0.01)
MET + INS-BI-T		–0.74 (–1.45 to –0.04)
MET + TZD-L	MET + AGI-L	–0.09 (–0.52 to 0.34)
MET + TZD-H		–0.18 (–0.57 to 0.21)
MET + TZD-T		–0.17 (–0.59 to 0.26)
MET + INS-BA-T		–0.32 (–0.77 to 0.13)
MET + INS-BI-T		–0.36 (–0.83 to 0.11)
MET + TZD-H	MET + TZD-L	–0.09 (–0.31 to 0.13)
MET + TZD-T		–0.08 (–0.36 to 0.21)
MET + INS-BA-T		–0.23 (–0.56 to 0.10)
MET + INS-BI-T		–0.28 (–0.62 to 0.08)
MET + TZD-T	MET + TZD-H	0.01 (–0.22 to 0.24)
MET + INS-BA-T		–0.15 (–0.42 to 0.13)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		–0.19 (–0.49 to 0.11)
MET + INS-BA-T	MET + TZD-T	–0.15 (–0.47 to 0.16)
MET + INS-BI-T		–0.20 (–0.53 to 0.14)
MET + INS-BI-T	MET + INS-BA-T	–0.04 (–0.30 to 0.21)
Random-effects model	Residual deviance	302.6 vs. 310 data points
	Deviance information criteria	–404.458

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MD = mean difference; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Diastolic Blood Pressure (DBP)

Table 28: Diastolic Blood Pressure: Mean Difference for All Treatment Comparisons — Random-Effects Model

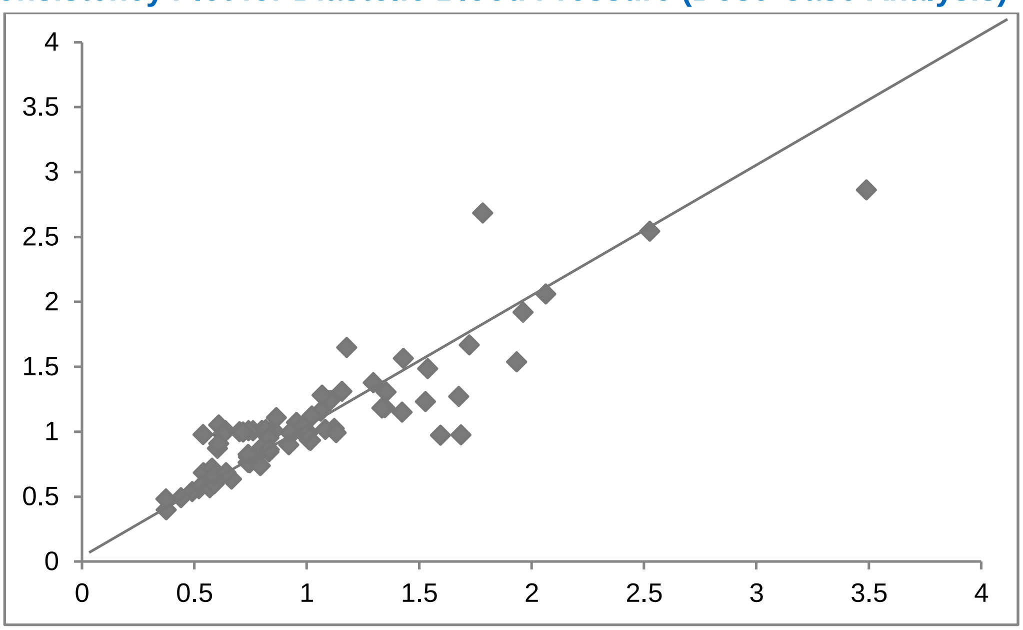
Treatment	Reference	MD (95% CrI)
MET + SUL-H	MET	–1.98 (–3.52 to –0.38)
MET + SUL-L		1.40 (–4.00 to 6.60)
MET + SUL-T		0.18 (–0.55 to 0.89)
MET + DPP-H		–1.20 (–1.83 to –0.54)
MET + SGL-L		–1.48 (–2.08 to –0.85)
MET + SGL-H		–2.12 (–2.72 to –1.51)
MET + GLP-L		–1.06 (–2.22 to 0.06)
MET + GLP-H		–1.22 (–1.94 to –0.46)
MET + GLP-T		–0.95 (–2.49 to 0.54)
MET + TZD-H		–2.79 (–3.87 to –1.71)
MET + TZD-L		–0.67 (–4.64 to 3.19)
MET + TZD-T		–0.35 (–1.53 to 0.78)
MET + SUL-L	MET + SUL-H	3.38 (–1.74 to 8.36)
MET + SUL-T		2.16 (0.53 to 3.74)
MET + DPP-H		0.78 (–0.82 to 2.32)
MET + SGL-L		0.50 (–1.14 to 2.08)
MET + SGL-H		–0.14 (–1.77 to 1.47)
MET + GLP-L		0.93 (–1.01 to 2.76)
MET + GLP-H		0.76 (–0.83 to 2.33)
MET + GLP-T		1.03 (–1.11 to 3.08)
MET + TZD-H		–0.81 (–2.03 to 0.38)
MET + TZD-L		1.31 (–2.34 to 4.90)
MET + TZD-T		1.63 (–0.25 to 3.46)
MET + SUL-T	MET + SUL-L	–1.22 (–6.44 to 4.18)
MET + DPP-H		–2.60 (–7.82 to 2.80)
MET + SGL-L		–2.88 (–8.09 to 2.50)
MET + SGL-H		–3.52 (–8.73 to 1.89)

Treatment	Reference	MD (95% CrI)
MET + GLP-L		–2.45 (–7.77 to 2.96)
MET + GLP-H		–2.62 (–7.82 to 2.80)
MET + GLP-T		–2.35 (–7.81 to 3.19)
MET + TZD-H		–4.19 (–9.26 to 1.06)
MET + TZD-L		–2.07 (–5.84 to 1.73)
MET + TZD-T		–1.75 (–7.03 to 3.74)
MET + DPP-H	MET + SUL-T	–1.38 (–2.29 to –0.55)
MET + SGL-L		–1.66 (–2.40 to –0.89)
MET + SGL-H		–2.30 (–2.96 to –1.60)
MET + GLP-L		–1.24 (–2.51 to –0.01)
MET + GLP-H		–1.40 (–2.39 to –0.50)
MET + GLP-T		–1.13 (–2.68 to 0.36)
MET + TZD-H		–2.97 (–4.07 to –1.84)
MET + TZD-L		–0.85 (–4.94 to 3.05)
MET + TZD-T		–0.53 (–1.43 to 0.36)
MET + SGL-L	MET + DPP-H	–0.28 (–1.06 to 0.56)
MET + SGL-H		–0.92 (–1.66 to –0.10)
MET + GLP-L		0.14 (–1.04 to 1.21)
MET + GLP-H		–0.02 (–0.73 to 0.69)
MET + GLP-T		0.25 (–1.31 to 1.72)
MET + TZD-H		–1.59 (–2.67 to –0.50)
MET + TZD-L		0.53 (–3.45 to 4.41)
MET + TZD-T		0.85 (–0.40 to 2.00)
MET + SGL-H	MET + SGL-L	–0.64 (–1.20 to –0.05)
MET + GLP-L		0.43 (–0.87 to 1.64)
MET + GLP-H		0.26 (–0.68 to 1.14)
MET + GLP-T		0.53 (–1.07 to 2.08)
MET + TZD-H		–1.31 (–2.47 to –0.13)
MET + TZD-L		0.81 (–3.21 to 4.68)
MET + TZD-T		1.13 (–0.08 to 2.27)
MET + GLP-L	MET + SGL-H	1.06 (–0.21 to 2.25)
MET + GLP-H		0.90 (–0.03 to 1.75)
MET + GLP-T		1.17 (–0.42 to 2.69)
MET + TZD-H		–0.67 (–1.80 to 0.49)
MET + TZD-L		1.45 (–2.61 to 5.36)
MET + TZD-T		1.77 (0.60 to 2.87)
MET + GLP-H	MET + GLP-L	–0.17 (–1.21 to 0.99)
MET + GLP-T		0.10 (–1.71 to 1.99)
MET + TZD-H		–1.73 (–3.17 to –0.22)
MET + TZD-L		0.38 (–3.68 to 4.35)
MET + TZD-T		0.71 (–0.82 to 2.24)
MET + GLP-T	MET + GLP-H	0.27 (–1.33 to 1.82)

Treatment	Reference	MD (95% CrI)
MET + TZD-H		–1.57 (–2.70 to –0.46)
MET + TZD-L		0.55 (–3.44 to 4.36)
MET + TZD-T		0.87 (–0.44 to 2.06)
MET + TZD-H	MET + GLP-T	–1.84 (–3.60 to –0.02)
MET + TZD-L		0.28 (–3.94 to 4.41)
MET + TZD-T		0.60 (–1.14 to 2.40)
MET + TZD-L	MET + TZD-H	2.12 (–1.70 to 5.88)
MET + TZD-T		2.44 (0.98 to 3.83)
MET + TZD-T	MET + TZD-L	0.32 (–3.69 to 4.38)
Random-effects model	Residual deviance	83.55 vs. 83 data points
	Deviance information criteria	222.184

CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; -L = low-dose; MD = mean difference; MET = metformin; SGL = sodium-glucose cotransporter-2 inhibitor; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Figure 17: Consistency Plot for Diastolic Blood Pressure (Dose-Case Analysis)



Body Mass Index (BMI)

Table 29: Body Mass Index: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-L	MET	0.55 (–0.81 to 1.94)
MET + SUL-H		0.64 (0.21 to 1.19)
MET + SUL-T		0.25 (–2.48 to 2.83)
MET + MEG-T		0.49 (–4.45 to 5.53)
MET + DPP-L		0.20 (–0.60 to 1.01)
MET + DPP-H		–0.18 (–0.58 to 0.16)
MET + DPP-T		0.03 (–3.18 to 3.22)
MET + SGL-L		–1.35 (–4.19 to 1.35)
MET + SGL-H		–1.35 (–4.19 to 1.33)
MET + GLP-H		–1.19 (–1.83 to –0.49)
MET + AGI-L		–0.16 (–2.33 to 2.09)
MET + AGI-H		0.05 (–2.02 to 2.13)
MET + TZD-L		1.05 (0.05 to 2.03)
MET + TZD-H		1.52 (0.91 to 2.16)
MET + TZD-T		0.27 (–2.56 to 2.91)
MET + INS-BA-T		2.61 (–0.53 to 5.66)
MET + INS-BI-T		0.52 (–0.46 to 1.57)
MET + SUL-H	MET + SUL-L	0.09 (–1.34 to 1.50)
MET + SUL-T		–0.29 (–3.58 to 2.76)
MET + MEG-T		–0.05 (–5.24 to 5.12)
MET + DPP-L		–0.34 (–1.95 to 1.22)
MET + DPP-H		–0.73 (–2.17 to 0.66)
MET + DPP-T		–0.51 (–4.17 to 2.97)
MET + SGL-L		–1.89 (–5.27 to 1.24)
MET + SGL-H		–1.89 (–5.28 to 1.24)
MET + GLP-H		–1.74 (–3.27 to –0.22)
MET + AGI-L		–0.71 (–3.33 to 1.88)
MET + AGI-H		–0.50 (–3.04 to 1.94)
MET + TZD-L		0.51 (–0.90 to 1.81)
MET + TZD-H		0.98 (–0.48 to 2.41)
MET + TZD-T		–0.28 (–3.65 to 2.80)
MET + INS-BA-T		2.06 (–1.35 to 5.37)
MET + INS-BI-T		–0.03 (–1.73 to 1.65)
MET + SUL-T	MET + SUL-H	–0.38 (–3.16 to 2.21)
MET + MEG-T		–0.14 (–5.12 to 4.91)
MET + DPP-L		–0.43 (–1.44 to 0.44)
MET + DPP-H		–0.82 (–1.46 to –0.35)
MET + DPP-T		–0.60 (–3.82 to 2.57)

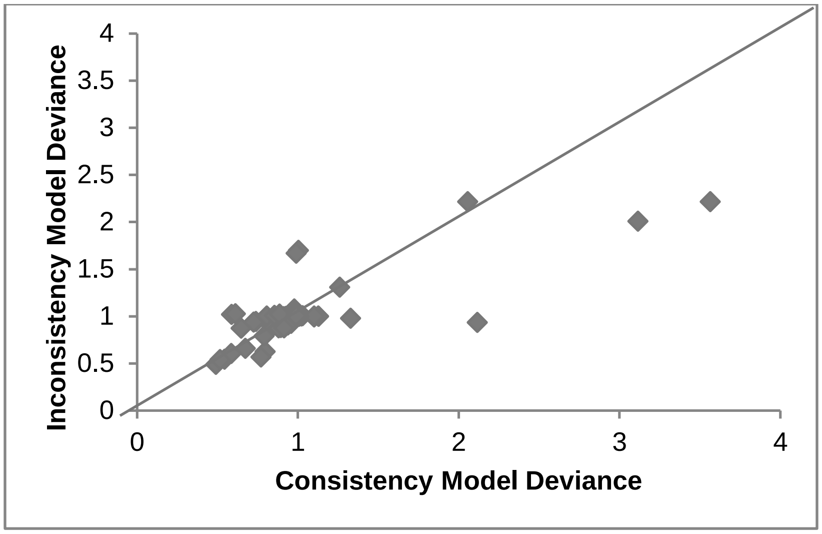
Treatment	Reference	MD (95% CrI)
MET + SGL-L		–1.98 (–4.87 to 0.71)
MET + SGL-H		–1.98 (–4.85 to 0.71)
MET + GLP-H		–1.83 (–2.53 to –1.18)
MET + AGI-L		–0.80 (–2.94 to 1.37)
MET + AGI-H		–0.59 (–2.61 to 1.43)
MET + TZD-L		0.42 (–0.66 to 1.42)
MET + TZD-H		0.89 (0.17 to 1.55)
MET + TZD-T		–0.37 (–3.22 to 2.30)
MET + INS-BA-T		1.97 (–1.18 to 5.05)
MET + INS-BI-T		–0.12 (–1.17 to 0.86)
MET + MEG-T	MET + SUL-T	0.24 (–4.18 to 4.74)
MET + DPP-L		–0.05 (–2.74 to 2.82)
MET + DPP-H		–0.44 (–3.00 to 2.27)
MET + DPP-T		–0.22 (–2.00 to 1.49)
MET + SGL-L		–1.60 (–2.38 to –0.82)
MET + SGL-H		–1.60 (–2.39 to –0.81)
MET + GLP-H		–1.45 (–4.11 to 1.34)
MET + AGI-L		–0.42 (–3.83 to 2.98)
MET + AGI-H		–0.20 (–3.56 to 3.19)
MET + TZD-L		0.80 (–1.95 to 3.67)
MET + TZD-H		1.27 (–1.37 to 4.06)
MET + TZD-T		0.02 (–0.64 to 0.62)
MET + INS-BA-T		2.35 (–1.65 to 6.42)
MET + INS-BI-T		0.27 (–2.49 to 3.15)
MET + DPP-L	MET + MEG-T	–0.29 (–5.41 to 4.71)
MET + DPP-H		–0.68 (–5.73 to 4.26)
MET + DPP-T		–0.46 (–5.28 to 4.38)
MET + SGL-L		–1.84 (–6.40 to 2.58)
MET + SGL-H		–1.84 (–6.43 to 2.59)
MET + GLP-H		–1.69 (–6.76 to 3.30)
MET + AGI-L		–0.66 (–6.13 to 4.81)
MET + AGI-H		–0.44 (–5.90 to 5.02)
MET + TZD-L		0.56 (–4.56 to 5.60)
MET + TZD-H		1.03 (–4.04 to 6.01)
MET + TZD-T		–0.22 (–4.77 to 4.21)
MET + INS-BA-T		2.12 (–3.84 to 7.82)
MET + INS-BI-T		0.03 (–5.09 to 5.08)
MET + DPP-H	MET + DPP-L	–0.39 (–1.30 to 0.48)
MET + DPP-T		–0.17 (–3.49 to 3.11)
MET + SGL-L		–1.55 (–4.51 to 1.24)
MET + SGL-H		–1.55 (–4.51 to 1.23)
MET + GLP-H		–1.40 (–2.41 to –0.32)

Treatment	Reference	MD (95% CrI)
MET + AGI-L		–0.37 (–2.67 to 2.02)
MET + AGI-H		–0.15 (–2.35 to 2.07)
MET + TZD-L		0.85 (–0.41 to 2.12)
MET + TZD-H		1.32 (0.32 to 2.35)
MET + TZD-T		0.07 (–2.88 to 2.82)
MET + INS-BA-T		2.40 (–0.83 to 5.56)
MET + INS-BI-T		0.32 (–0.95 to 1.65)
MET + DPP-T	MET + DPP-H	0.22 (–2.99 to 3.38)
MET + SGL-L		–1.16 (–3.97 to 1.51)
MET + SGL-H		–1.16 (–3.98 to 1.50)
MET + GLP-H		–1.01 (–1.69 to –0.21)
MET + AGI-L		0.02 (–2.15 to 2.29)
MET + AGI-H		0.23 (–1.85 to 2.32)
MET + TZD-L		1.24 (0.19 to 2.30)
MET + TZD-H		1.71 (1.02 to 2.44)
MET + TZD-T		0.45 (–2.35 to 3.08)
MET + INS-BA-T		2.79 (–0.35 to 5.84)
MET + INS-BI-T		0.70 (–0.29 to 1.83)
MET + SGL-L	MET + DPP-T	–1.38 (–3.26 to 0.55)
MET + SGL-H		–1.38 (–3.26 to 0.54)
MET + GLP-H		–1.23 (–4.44 to 2.04)
MET + AGI-L		–0.20 (–4.03 to 3.64)
MET + AGI-H		0.02 (–3.70 to 3.88)
MET + TZD-L		1.02 (–2.26 to 4.36)
MET + TZD-H		1.49 (–1.74 to 4.74)
MET + TZD-T		0.24 (–1.61 to 2.10)
MET + INS-BA-T		2.57 (–1.79 to 7.09)
MET + INS-BI-T		0.49 (–2.80 to 3.82)
MET + SGL-H	MET + SGL-L	0.00 (–0.78 to 0.79)
MET + GLP-H		0.15 (–2.59 to 3.05)
MET + AGI-L		1.18 (–2.31 to 4.70)
MET + AGI-H		1.40 (–2.03 to 4.88)
MET + TZD-L		2.40 (–0.45 to 5.38)
MET + TZD-H		2.87 (0.13 to 5.76)
MET + TZD-T		1.62 (0.58 to 2.59)
MET + INS-BA-T		3.95 (–0.09 to 8.08)
MET + INS-BI-T		1.87 (–0.96 to 4.86)
MET + GLP-H	MET + SGL-H	0.16 (–2.59 to 3.04)
MET + AGI-L		1.18 (–2.31 to 4.69)
MET + AGI-H		1.40 (–2.02 to 4.88)
MET + TZD-L		2.40 (–0.45 to 5.37)
MET + TZD-H		2.87 (0.13 to 5.75)

Treatment	Reference	MD (95% CrI)
MET + TZD-T		1.62 (0.58 to 2.59)
MET + INS-BA-T		3.95 (–0.09 to 8.10)
MET + INS-BI-T		1.87 (–0.97 to 4.85)
MET + AGI-L	MET + GLP-H	1.03 (–1.19 to 3.32)
MET + AGI-H		1.24 (–0.90 to 3.38)
MET + TZD-L		2.25 (1.06 to 3.39)
MET + TZD-H		2.72 (1.83 to 3.58)
MET + TZD-T		1.46 (–1.41 to 4.17)
MET + INS-BA-T		3.80 (0.75 to 6.82)
MET + INS-BI-T		1.71 (0.95 to 2.48)
MET + AGI-H	MET + AGI-L	0.21 (–2.74 to 3.10)
MET + TZD-L		1.22 (–1.21 to 3.58)
MET + TZD-H		1.69 (–0.62 to 3.94)
MET + TZD-T		0.43 (–3.04 to 3.89)
MET + INS-BA-T		2.77 (–1.07 to 6.47)
MET + INS-BI-T		0.69 (–1.72 to 3.02)
MET + TZD-L	MET + AGI-H	1.00 (–1.25 to 3.27)
MET + TZD-H		1.48 (–0.66 to 3.61)
MET + TZD-T		0.22 (–3.24 to 3.62)
MET + INS-BA-T		2.56 (–1.24 to 6.13)
MET + INS-BI-T		0.47 (–1.79 to 2.74)
MET + TZD-H		0.47 (–0.54 to 1.51)
MET + TZD-T	MET + TZD-L	–0.78 (–3.74 to 2.03)
MET + INS-BA-T		1.55 (–1.76 to 4.78)
MET + INS-BI-T		–0.53 (–1.90 to 0.85)
MET + TZD-T	MET + TZD-H	–1.25 (–4.13 to 1.44)
MET + INS-BA-T		1.08 (–2.10 to 4.21)
MET + INS-BI-T		–1.00 (–2.14 to 0.16)
MET + INS-BA-T	MET + TZD-T	2.34 (–1.68 to 6.41)
MET + INS-BI-T		0.25 (–2.55 to 3.22)
MET + INS-BI-T	MET + INS-BA-T	–2.09 (–5.17 to 1.06)
Random-effects model	Residual deviance	63.9 vs. 62 data points
	Deviance information criteria	96.739

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MD = mean difference; MET = metformin; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Figure 18: Consistency Plot for Body Mass Index (Dose-Case Analysis)



LDL Cholesterol

Table 30: Low-Density Lipoprotein Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-H	MET	0.19 (0.02 to 0.35)
MET + SUL-T		0.04 (–0.09 to 0.18)
MET + SUL-L		0.19 (–0.11 to 0.49)
MET + DPP-H		0.00 (–0.09 to 0.08)
MET + MEG-T		0.02 (–0.30 to 0.34)
MET + MEG-L		0.00 (–0.39 to 0.39)
MET + MEG-H		0.10 (–0.29 to 0.49)
MET + SGL-L		0.12 (0.01 to 0.24)
MET + DPP-L		–0.03 (–0.20 to 0.15)
MET + SGL-H		0.15 (0.04 to 0.26)
MET + GLP-H		–0.01 (–0.13 to 0.12)
MET + GLP-T		0.03 (–0.21 to 0.28)
MET + GLP-L		–0.03 (–0.31 to 0.24)
MET + AGI-L		0.29 (–0.01 to 0.60)
MET + TZD-L		0.14 (–0.02 to 0.30)
MET + TZD-H		0.20 (0.11 to 0.30)
MET + TZD-T		0.16 (–0.03 to 0.36)
MET + INS-BA-T		–0.10 (–0.36 to 0.17)
MET + INS-BI-T		0.19 (–0.14 to 0.51)
MET + SUL-T	MET + SUL-H	–0.14 (–0.35 to 0.06)

Treatment	Reference	MD (95% CrI)
MET + SUL-L		0.00 (–0.33 to 0.34)
MET + DPP-H		–0.19 (–0.35 to –0.03)
MET + MEG-T		–0.16 (–0.52 to 0.19)
MET + MEG-L		–0.19 (–0.61 to 0.24)
MET + MEG-H		–0.09 (–0.52 to 0.34)
MET + SGL-L		–0.06 (–0.26 to 0.13)
MET + DPP-L		–0.21 (–0.44 to 0.02)
MET + SGL-H		–0.04 (–0.23 to 0.16)
MET + GLP-H		–0.19 (–0.38 to –0.01)
MET + GLP-T		–0.16 (–0.44 to 0.13)
MET + GLP-L		–0.22 (–0.53 to 0.09)
MET + AGI-L		0.11 (–0.18 to 0.40)
MET + TZD-L		–0.05 (–0.26 to 0.17)
MET + TZD-H		0.02 (–0.15 to 0.19)
MET + TZD-T		–0.02 (–0.27 to 0.23)
MET + INS-BA-T		–0.28 (–0.58 to 0.01)
MET + INS-BI-T		0.00 (–0.36 to 0.35)
MET + SUL-L	MET + SUL-T	0.15 (–0.18 to 0.47)
MET + DPP-H		–0.04 (–0.18 to 0.09)
MET + MEG-T		–0.02 (–0.34 to 0.30)
MET + MEG-L		–0.04 (–0.45 to 0.38)
MET + MEG-H		0.06 (–0.36 to 0.48)
MET + SGL-L		0.08 (–0.08 to 0.24)
MET + DPP-L		–0.07 (–0.28 to 0.14)
MET + SGL-H		0.11 (–0.05 to 0.27)
MET + GLP-H		–0.05 (–0.21 to 0.11)
MET + GLP-T		–0.01 (–0.26 to 0.24)
MET + GLP-L		–0.07 (–0.37 to 0.23)
MET + AGI-L		0.25 (–0.07 to 0.57)
MET + TZD-L		0.10 (–0.10 to 0.30)
MET + TZD-H		0.16 (0.00 to 0.32)
MET + TZD-T		0.12 (–0.02 to 0.26)
MET + INS-BA-T		–0.14 (–0.42 to 0.14)
MET + INS-BI-T		0.14 (–0.20 to 0.49)
MET + DPP-H	MET + SUL-L	–0.19 (–0.49 to 0.12)
MET + MEG-T		–0.17 (–0.60 to 0.27)
MET + MEG-L		–0.19 (–0.68 to 0.31)
MET + MEG-H		–0.09 (–0.58 to 0.41)
MET + SGL-L		–0.07 (–0.39 to 0.26)
MET + DPP-L		–0.22 (–0.55 to 0.12)
MET + SGL-H		–0.04 (–0.36 to 0.28)
MET + GLP-H		–0.20 (–0.52 to 0.13)

Treatment	Reference	MD (95% CrI)
MET + GLP-T		–0.16 (–0.54 to 0.23)
MET + GLP-L		–0.22 (–0.63 to 0.18)
MET + AGI-L		0.10 (–0.32 to 0.53)
MET + TZD-L		–0.05 (–0.31 to 0.21)
MET + TZD-H		0.01 (–0.29 to 0.32)
MET + TZD-T		–0.03 (–0.38 to 0.33)
MET + INS-BA-T		–0.29 (–0.68 to 0.11)
MET + INS-BI-T		0.00 (–0.44 to 0.43)
MET + MEG-T	MET + DPP-H	0.02 (–0.30 to 0.35)
MET + MEG-L		0.00 (–0.40 to 0.41)
MET + MEG-H		0.10 (–0.30 to 0.50)
MET + SGL-L		0.12 (0.00 to 0.25)
MET + DPP-L		–0.03 (–0.20 to 0.15)
MET + SGL-H		0.15 (0.03 to 0.28)
MET + GLP-H		0.00 (–0.13 to 0.12)
MET + GLP-T		0.03 (–0.21 to 0.27)
MET + GLP-L		–0.03 (–0.31 to 0.24)
MET + AGI-L		0.30 (0.00 to 0.59)
MET + TZD-L		0.14 (–0.02 to 0.31)
MET + TZD-H		0.21 (0.10 to 0.31)
MET + TZD-T		0.16 (–0.03 to 0.36)
MET + INS-BA-T		–0.10 (–0.35 to 0.16)
MET + INS-BI-T		0.19 (–0.14 to 0.51)
MET + MEG-L	MET + MEG-T	–0.02 (–0.53 to 0.48)
MET + MEG-H		0.08 (–0.43 to 0.59)
MET + SGL-L		0.10 (–0.24 to 0.43)
MET + DPP-L		–0.05 (–0.41 to 0.31)
MET + SGL-H		0.13 (–0.20 to 0.46)
MET + GLP-H		–0.03 (–0.37 to 0.31)
MET + GLP-T		0.01 (–0.38 to 0.40)
MET + GLP-L		–0.06 (–0.47 to 0.36)
MET + AGI-L		0.27 (–0.17 to 0.71)
MET + TZD-L		0.12 (–0.24 to 0.47)
MET + TZD-H		0.18 (–0.15 to 0.51)
MET + TZD-T		0.14 (–0.21 to 0.49)
MET + INS-BA-T		–0.12 (–0.53 to 0.29)
MET + INS-BI-T		0.16 (–0.29 to 0.61)
MET + MEG-H	MET + MEG-L	0.10 (–0.29 to 0.49)
MET + SGL-L		0.12 (–0.29 to 0.53)
MET + DPP-L		–0.03 (–0.46 to 0.40)
MET + SGL-H		0.15 (–0.26 to 0.56)
MET + GLP-H		–0.01 (–0.42 to 0.41)

Treatment	Reference	MD (95% CrI)
MET + GLP-T		0.03 (–0.43 to 0.49)
MET + GLP-L		–0.03 (–0.51 to 0.45)
MET + AGI-L		0.29 (–0.21 to 0.79)
MET + TZD-L		0.14 (–0.29 to 0.56)
MET + TZD-H		0.20 (–0.20 to 0.61)
MET + TZD-T		0.16 (–0.28 to 0.60)
MET + INS-BA-T		–0.10 (–0.57 to 0.38)
MET + INS-BI-T		0.19 (–0.33 to 0.70)
MET + SGL-L	MET + MEG-H	0.02 (–0.39 to 0.43)
MET + DPP-L		–0.13 (–0.56 to 0.30)
MET + SGL-H		0.05 (–0.36 to 0.46)
MET + GLP-H		–0.11 (–0.52 to 0.31)
MET + GLP-T		–0.07 (–0.53 to 0.39)
MET + GLP-L		–0.13 (–0.61 to 0.35)
MET + AGI-L		0.19 (–0.30 to 0.69)
MET + TZD-L		0.04 (–0.38 to 0.47)
MET + TZD-H		0.10 (–0.30 to 0.51)
MET + TZD-T		0.06 (–0.38 to 0.51)
MET + INS-BA-T		–0.20 (–0.67 to 0.27)
MET + INS-BI-T		0.09 (–0.43 to 0.60)
MET + DPP-L	MET + SGL-L	–0.15 (–0.36 to 0.05)
MET + SGL-H		0.03 (–0.08 to 0.14)
MET + GLP-H		–0.13 (–0.29 to 0.03)
MET + GLP-T		–0.09 (–0.35 to 0.17)
MET + GLP-L		–0.16 (–0.45 to 0.14)
MET + AGI-L		0.17 (–0.15 to 0.49)
MET + TZD-L		0.02 (–0.18 to 0.21)
MET + TZD-H		0.08 (–0.07 to 0.23)
MET + TZD-T		0.04 (–0.17 to 0.25)
MET + INS-BA-T		–0.22 (–0.50 to 0.06)
MET + INS-BI-T		0.06 (–0.28 to 0.41)
MET + SGL-H	MET + DPP-L	0.18 (–0.03 to 0.38)
MET + GLP-H		0.02 (–0.19 to 0.23)
MET + GLP-T		0.06 (–0.23 to 0.35)
MET + GLP-L		–0.01 (–0.33 to 0.32)
MET + AGI-L		0.32 (–0.02 to 0.66)
MET + TZD-L		0.17 (–0.05 to 0.39)
MET + TZD-H		0.23 (0.04 to 0.42)
MET + TZD-T		0.19 (–0.06 to 0.45)
MET + INS-BA-T		–0.07 (–0.38 to 0.24)
MET + INS-BI-T		0.21 (–0.15 to 0.58)
MET + GLP-H	MET + SGL-H	–0.16 (–0.32 to 0.00)

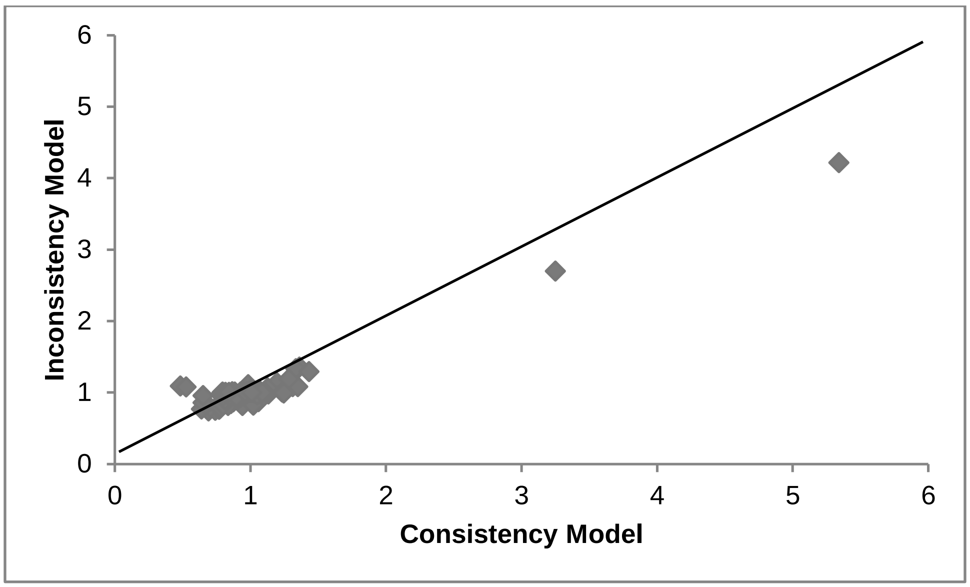
CADTH

Treatment	Reference	MD (95% CrI)
MET + GLP-T		–0.12 (–0.38 to 0.14)
MET + GLP-L		–0.18 (–0.48 to 0.11)
MET + AGI-L		0.14 (–0.18 to 0.46)
MET + TZD-L		–0.01 (–0.20 to 0.18)
MET + TZD-H		0.05 (–0.09 to 0.20)
MET + TZD-T		0.01 (–0.20 to 0.23)
MET + INS-BA-T		–0.25 (–0.53 to 0.03)
MET + INS-BI-T		0.04 (–0.31 to 0.38)
MET + GLP-T	MET + GLP-H	0.04 (–0.22 to 0.30)
MET + GLP-L		–0.03 (–0.31 to 0.26)
MET + AGI-L		0.30 (–0.02 to 0.62)
MET + TZD-L		0.15 (–0.05 to 0.34)
MET + TZD-H		0.21 (0.07 to 0.35)
MET + TZD-T		0.17 (–0.04 to 0.39)
MET + INS-BA-T		–0.09 (–0.36 to 0.19)
MET + INS-BI-T		0.19 (–0.11 to 0.50)
MET + GLP-L	MET + GLP-T	–0.06 (–0.43 to 0.30)
MET + AGI-L		0.26 (–0.12 to 0.64)
MET + TZD-L		0.11 (–0.18 to 0.39)
MET + TZD-H		0.17 (–0.08 to 0.43)
MET + TZD-T		0.13 (–0.15 to 0.42)
MET + INS-BA-T		–0.13 (–0.44 to 0.18)
MET + INS-BI-T		0.16 (–0.25 to 0.55)
MET + AGI-L	MET + GLP-L	0.33 (–0.08 to 0.73)
MET + TZD-L		0.17 (–0.14 to 0.49)
MET + TZD-H		0.24 (–0.05 to 0.52)
MET + TZD-T		0.20 (–0.14 to 0.53)
MET + INS-BA-T		–0.07 (–0.44 to 0.30)
MET + INS-BI-T		0.22 (–0.19 to 0.63)
MET + TZD-L	MET + AGI-L	–0.15 (–0.49 to 0.18)
MET + TZD-H		–0.09 (–0.40 to 0.22)
MET + TZD-T		–0.13 (–0.48 to 0.22)
MET + INS-BA-T		–0.39 (–0.78 to 0.00)
MET + INS-BI-T		–0.11 (–0.55 to 0.33)
MET + TZD-H	MET + TZD-L	0.06 (–0.10 to 0.23)
MET + TZD-T		0.02 (–0.22 to 0.27)
MET + INS-BA-T		–0.24 (–0.54 to 0.06)
MET + INS-BI-T		0.04 (–0.31 to 0.40)
MET + TZD-T	MET + TZD-H	–0.04 (–0.25 to 0.17)
MET + INS-BA-T		–0.30 (–0.57 to –0.03)
MET + INS-BI-T		–0.02 (–0.35 to 0.32)
MET + INS-BA-T	MET + TZD-T	–0.26 (–0.58 to 0.05)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		0.02 (–0.35 to 0.39)
MET + INS-BI-T	MET + INS-BA-T	0.28 (–0.13 to 0.69)
Random-effects model	Residual deviance	136.5 vs. 137 data points
	Deviance information criteria	–239.204

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MD = mean difference; MEG = meglitinide; MET = metformin; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Figure 19: Consistency Plot for Low-Density Lipoprotein Cholesterol (Dose-Case Analysis)



Systolic Blood Pressure (SBP)

Table 31: Systolic Blood Pressure: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-H	MET	1.01 (–2.40 to 4.40)
MET + SUL-T		0.80 (–0.81 to 2.38)
MET + SUL-L		0.95 (–8.24 to 9.92)
MET + DPP-L		–1.14 (–4.93 to 2.64)
MET + DPP-H		–1.32 (–2.58 to –0.07)
MET + SGL-L		–2.96 (–4.21 to –1.75)
MET + SGL-H		–3.97 (–5.13 to –2.83)
MET + GLP-H		–3.31 (–4.97 to –1.69)
MET + GLP-L		–2.20 (–4.87 to 0.47)
MET + GLP-T		–2.35 (–5.52 to 0.82)
MET + AGI-L		3.28 (–4.93 to 11.47)
MET + TZD-H		–2.81 (–4.90 to –0.76)

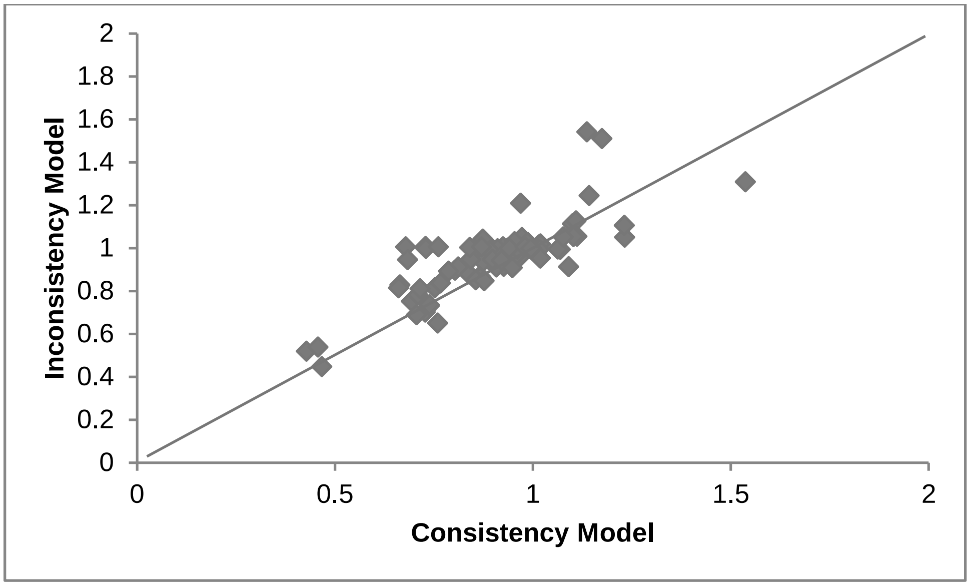
Treatment	Reference	MD (95% CrI)
MET + TZD-L		0.33 (–6.18 to 6.82)
MET + TZD-T		0.28 (–2.71 to 3.19)
MET + INS-BA-T		0.68 (–3.50 to 4.84)
MET + INS-BI-T		–0.23 (–6.01 to 5.56)
MET + SUL-T	MET + SUL-H	–0.20 (–3.73 to 3.31)
MET + SUL-L		–0.06 (–8.64 to 8.39)
MET + DPP-L		–2.15 (–7.15 to 2.92)
MET + DPP-H		–2.33 (–5.76 to 1.14)
MET + SGL-L		–3.96 (–7.50 to –0.44)
MET + SGL-H		–4.98 (–8.46 to –1.48)
MET + GLP-H		–4.32 (–7.87 to –0.75)
MET + GLP-L		–3.20 (–7.36 to 0.98)
MET + GLP-T		–3.35 (–7.88 to 1.19)
MET + AGI-L		2.27 (–5.20 to 9.78)
MET + TZD-H		–3.82 (–6.53 to –1.14)
MET + TZD-L		–0.68 (–6.25 to 4.94)
MET + TZD-T		–0.73 (–5.05 to 3.57)
MET + INS-BA-T		–0.33 (–5.59 to 4.90)
MET + INS-BI-T		–1.24 (–7.89 to 5.35)
MET + SUL-L	MET + SUL-T	0.14 (–9.09 to 9.17)
MET + DPP-L		–1.94 (–5.93 to 2.10)
MET + DPP-H		–2.12 (–3.82 to –0.40)
MET + SGL-L		–3.76 (–5.48 to –2.07)
MET + SGL-H		–4.77 (–6.35 to –3.17)
MET + GLP-H		–4.12 (–6.05 to –2.18)
MET + GLP-L		–3.00 (–5.92 to –0.07)
MET + GLP-T		–3.15 (–6.34 to 0.03)
MET + AGI-L		2.47 (–5.81 to 10.73)
MET + TZD-H		–3.62 (–5.86 to –1.36)
MET + TZD-L		–0.47 (–7.01 to 6.08)
MET + TZD-T		–0.53 (–3.03 to 1.93)
MET + INS-BA-T		–0.12 (–4.46 to 4.20)
MET + INS-BI-T		–1.04 (–6.94 to 4.90)
MET + DPP-L	MET + SUL-L	–2.08 (–11.84 to 7.85)
MET + DPP-H		–2.26 (–11.30 to 6.94)
MET + SGL-L		–3.90 (–12.94 to 5.30)
MET + SGL-H		–4.92 (–13.96 to 4.29)
MET + GLP-H		–4.26 (–13.33 to 5.01)
MET + GLP-L		–3.14 (–12.51 to 6.36)
MET + GLP-T		–3.29 (–12.79 to 6.40)
MET + AGI-L		2.33 (–9.00 to 13.69)
MET + TZD-H		–3.76 (–12.59 to 5.21)
MET + TZD-L		–0.61 (–7.02 to 5.84)
MET + TZD-T		–0.67 (–10.07 to 8.90)
MET + INS-BA-T		–0.27 (–10.19 to 9.73)
MET + INS-BI-T		–1.18 (–11.92 to 9.55)

Treatment	Reference	MD (95% CrI)
MET + DPP-H	MET + DPP-L	–0.18 (–3.92 to 3.53)
MET + SGL-L		–1.82 (–5.72 to 2.08)
MET + SGL-H		–2.83 (–6.70 to 1.03)
MET + GLP-H		–2.18 (–6.18 to 1.82)
MET + GLP-L		–1.06 (–5.59 to 3.43)
MET + GLP-T		–1.21 (–6.06 to 3.64)
MET + AGI-L		4.42 (–4.58 to 13.42)
MET + TZD-H		–1.68 (–5.95 to 2.53)
MET + TZD-L		1.47 (–6.02 to 8.96)
MET + TZD-T		1.42 (–3.36 to 6.10)
MET + INS-BA-T		1.82 (–3.62 to 7.27)
MET + INS-BI-T		0.91 (–5.83 to 7.67)
MET + SGL-L	MET + DPP-H	–1.64 (–3.09 to –0.23)
MET + SGL-H		–2.65 (–3.99 to –1.30)
MET + GLP-H		–2.00 (–3.64 to –0.35)
MET + GLP-L		–0.88 (–3.52 to 1.78)
MET + GLP-T		–1.03 (–4.20 to 2.12)
MET + AGI-L		4.60 (–3.66 to 12.85)
MET + TZD-H		–1.50 (–3.68 to 0.67)
MET + TZD-L		1.65 (–4.89 to 8.21)
MET + TZD-T		1.60 (–1.45 to 4.57)
MET + INS-BA-T		2.00 (–1.99 to 5.97)
MET + INS-BI-T		1.09 (–4.57 to 6.75)
MET + SGL-H	MET + SGL-L	–1.02 (–2.11 to 0.12)
MET + GLP-H		–0.36 (–2.22 to 1.53)
MET + GLP-L		0.76 (–2.06 to 3.60)
MET + GLP-T		0.61 (–2.66 to 3.91)
MET + AGI-L		6.23 (–2.01 to 14.51)
MET + TZD-H		0.14 (–2.12 to 2.44)
MET + TZD-L		3.29 (–3.30 to 9.89)
MET + TZD-T		3.23 (0.22 to 6.22)
MET + INS-BA-T		3.64 (–0.58 to 7.88)
MET + INS-BI-T		2.72 (–3.08 to 8.58)
MET + GLP-H	MET + SGL-H	0.66 (–1.16 to 2.47)
MET + GLP-L		1.78 (–1.01 to 4.57)
MET + GLP-T		1.62 (–1.62 to 4.87)
MET + AGI-L		7.25 (–1.00 to 15.50)
MET + TZD-H		1.16 (–1.07 to 3.38)
MET + TZD-L		4.30 (–2.24 to 10.87)
MET + TZD-T		4.25 (1.28 to 7.15)
MET + INS-BA-T		4.65 (0.44 to 8.83)
MET + INS-BI-T		3.74 (–2.07 to 9.56)
MET + GLP-L	MET + GLP-H	1.12 (–1.45 to 3.70)
MET + GLP-T		0.97 (–2.44 to 4.36)
MET + AGI-L		6.59 (–1.66 to 14.87)
MET + TZD-H		0.50 (–1.82 to 2.82)
MET + TZD-L		3.65 (–2.93 to 10.24)

Treatment	Reference	MD (95% CrI)
MET + TZD-T		3.59 (0.42 to 6.71)
MET + INS-BA-T		4.00 (–0.31 to 8.30)
MET + INS-BI-T		3.08 (–2.81 to 8.97)
MET + GLP-T	MET + GLP-L	–0.15 (–4.16 to 3.86)
MET + AGI-L		5.47 (–3.07 to 14.10)
MET + TZD-H		–0.62 (–3.82 to 2.58)
MET + TZD-L		2.53 (–4.42 to 9.48)
MET + TZD-T		2.47 (–1.39 to 6.28)
MET + INS-BA-T		2.88 (–1.91 to 7.64)
MET + INS-BI-T		1.96 (–4.29 to 8.23)
MET + AGI-L	MET + GLP-T	5.62 (–3.12 to 14.36)
MET + TZD-H		–0.47 (–4.12 to 3.16)
MET + TZD-L		2.68 (–4.52 to 9.88)
MET + TZD-T		2.62 (–1.44 to 6.65)
MET + INS-BA-T		3.03 (–2.04 to 8.13)
MET + INS-BI-T		2.11 (–4.34 to 8.62)
MET + TZD-H	MET + AGI-L	–6.09 (–14.05 to 1.85)
MET + TZD-L		–2.95 (–12.31 to 6.42)
MET + TZD-T		–3.00 (–11.61 to 5.63)
MET + INS-BA-T		–2.60 (–11.75 to 6.52)
MET + INS-BI-T		–3.51 (–13.50 to 6.51)
MET + TZD-L	MET + TZD-H	3.15 (–3.06 to 9.40)
MET + TZD-T		3.09 (–0.29 to 6.41)
MET + INS-BA-T		3.49 (–1.06 to 7.99)
MET + INS-BI-T		2.58 (–3.48 to 8.63)
MET + TZD-T	MET + TZD-L	–0.06 (–7.12 to 6.96)
MET + INS-BA-T		0.35 (–7.33 to 7.96)
MET + INS-BI-T		–0.56 (–9.22 to 8.08)
MET + INS-BA-T	MET + TZD-T	0.40 (–4.58 to 5.42)
MET + INS-BI-T		–0.51 (–6.89 to 5.92)
MET + INS-BI-T	MET + INS-BA-T	–0.91 (–4.98 to 3.17)
Random-effects model	Residual deviance	85.05 vs. 93 data points
	Deviance information criteria	326.648

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MD = mean difference; MET = metformin; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Figure 20: Consistency Plot for Systolic Blood Pressure (Dose-Case Analysis)



Total Adverse Events

Table 32: Total Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	1.15 (1.02 to 1.31)	1.07 (1.01 to 1.14)	3.53 (0.42 to 6.68)
MET + SUL-L		1.74 (0.74 to 4.50)	1.27 (0.85 to 1.65)	13.47 (–7.35 to 32.02)
MET + SUL-H		1.59 (0.70 to 3.69)	1.23 (0.82 to 1.59)	11.32 (–8.93 to 28.86)
MET + MEG-L		1.27 (0.86 to 1.94)	1.12 (0.92 to 1.33)	5.87 (–3.78 to 16.04)
MET + MEG-H		1.12 (0.74 to 1.68)	1.06 (0.85 to 1.26)	2.76 (–7.46 to 12.75)
MET + DPP-L		1.04 (0.89 to 1.22)	1.02 (0.94 to 1.10)	1.06 (–2.90 to 4.88)
MET + DPP-H		0.96 (0.87 to 1.06)	0.98 (0.93 to 1.03)	–0.97 (–3.47 to 1.45)
MET + SGL-L		1.05 (0.89 to 1.23)	1.02 (0.94 to 1.11)	1.09 (–3.00 to 5.25)
MET + SGL-H		1.04 (0.89 to 1.20)	1.02 (0.94 to 1.09)	0.94 (–2.86 to 4.60)
MET + GLP-T		1.55 (0.63 to 4.03)	1.22 (0.78 to 1.61)	10.79 (–11.17 to 30.30)
MET + GLP-L		1.05 (0.80 to 1.36)	1.02 (0.89 to 1.15)	1.21 (–5.50 to 7.58)
MET + GLP-H		1.43 (1.18 to 1.72)	1.18 (1.08 to 1.27)	8.90 (4.21 to 13.20)
MET + TZD-T		0.99 (0.76 to 1.30)	1.00 (0.86 to 1.13)	–0.15 (–6.93 to 6.53)
MET + TZD-L		1.18 (0.73 to 1.96)	1.08 (0.84 to 1.33)	4.14 (–7.75 to 16.29)
MET + TZD-H		1.13 (0.92 to 1.39)	1.06 (0.96 to 1.17)	3.06 (–2.07 to 8.24)
MET + AGI-T		1.65 (1.05 to 2.61)	1.25 (1.02 to 1.46)	12.25 (1.13 to 22.49)
MET + INS-BA-T		1.93 (1.33 to 2.81)	1.32 (1.14 to 1.48)	15.94 (6.98 to 23.85)
MET + INS-BI-T		2.18 (1.36 to 3.53)	1.37 (1.15 to 1.57)	18.53 (7.56 to 28.14)
MET + SUL-L	MET + SUL-T	1.51 (0.64 to 3.92)	1.19 (0.79 to 1.54)	9.93 (–11.16 to 28.59)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-H		1.37 (0.60 to 3.19)	1.15 (0.77 to 1.48)	7.76 (–12.50 to 25.28)
MET + MEG-L		1.10 (0.73 to 1.71)	1.05 (0.85 to 1.25)	2.43 (–7.92 to 12.91)
MET + MEG-H		0.97 (0.63 to 1.50)	0.99 (0.79 to 1.19)	–0.77 (–11.46 to 9.84)
MET + DPP-L		0.90 (0.76 to 1.07)	0.95 (0.88 to 1.03)	–2.52 (–6.79 to 1.67)
MET + DPP-H		0.83 (0.75 to 0.92)	0.92 (0.87 to 0.96)	–4.52 (–7.19 to –1.95)
MET + SGL-L		0.91 (0.76 to 1.09)	0.95 (0.87 to 1.04)	–2.47 (–6.98 to 2.15)
MET + SGL-H		0.90 (0.76 to 1.06)	0.95 (0.88 to 1.03)	–2.65 (–6.73 to 1.42)
MET + GLP-T		1.35 (0.55 to 3.51)	1.14 (0.72 to 1.51)	7.27 (–14.93 to 26.86)
MET + GLP-L		0.91 (0.68 to 1.20)	0.96 (0.83 to 1.09)	–2.34 (–9.47 to 4.44)
MET + GLP-H		1.24 (1.01 to 1.52)	1.10 (1.00 to 1.20)	5.33 (0.16 to 10.26)
MET + TZD-T		0.86 (0.67 to 1.11)	0.93 (0.81 to 1.05)	–3.71 (–10.04 to 2.54)
MET + TZD-L		1.02 (0.63 to 1.72)	1.01 (0.79 to 1.25)	0.57 (–11.58 to 12.95)
MET + TZD-H		0.98 (0.80 to 1.22)	0.99 (0.89 to 1.09)	–0.48 (–5.71 to 4.86)
MET + AGI-T		1.43 (0.89 to 2.30)	1.16 (0.95 to 1.37)	8.71 (–2.86 to 19.33)
MET + INS-BA-T		1.68 (1.16 to 2.43)	1.23 (1.07 to 1.39)	12.34 (3.61 to 20.33)
MET + INS-BI-T		1.89 (1.19 to 3.01)	1.28 (1.08 to 1.46)	15.08 (4.26 to 24.22)
MET + SUL-H	MET + SUL-L	0.90 (0.27 to 3.30)	0.96 (0.60 to 1.58)	–2.41 (-28.98 to 26.98)
MET + MEG-L		0.74 (0.26 to 1.78)	0.88 (0.64 to 1.32)	–7.33 (-28.45 to 14.25)
MET + MEG-H		0.65 (0.22 to 1.60)	0.84 (0.59 to 1.26)	–10.28 (-32.61 to 11.57)
MET + DPP-L		0.60 (0.23 to 1.43)	0.80 (0.61 to 1.21)	–12.48 (-31.48 to 8.81)
MET + DPP-H		0.55 (0.21 to 1.30)	0.77 (0.59 to 1.15)	–14.48 (-33.13 to 6.47)
MET + SGL-L		0.60 (0.23 to 1.43)	0.80 (0.61 to 1.21)	–12.43 (-31.34 to 8.94)
MET + SGL-H		0.60 (0.23 to 1.42)	0.80 (0.61 to 1.21)	–12.64 (-31.35 to 8.66)
MET + GLP-T		0.89 (0.25 to 3.14)	0.96 (0.58 to 1.55)	–2.61 (-30.77 to 25.26)
MET + GLP-L		0.60 (0.22 to 1.46)	0.81 (0.60 to 1.22)	–12.26 (-32.22 to 9.31)
MET + GLP-H		0.82 (0.31 to 1.95)	0.93 (0.71 to 1.39)	–4.67 (-23.71 to 16.52)
MET + TZD-T		0.57 (0.21 to 1.40)	0.78 (0.58 to 1.19)	–13.66 (-33.26 to 8.31)
MET + TZD-L		0.68 (0.24 to 1.83)	0.85 (0.60 to 1.34)	–9.16 (-31.44 to 14.81)
MET + TZD-H		0.65 (0.25 to 1.54)	0.84 (0.63 to 1.25)	–10.30 (-29.44 to 10.77)
MET + AGI-T		0.94 (0.33 to 2.61)	0.98 (0.71 to 1.52)	–1.51 (-22.94 to 22.98)
MET + INS-BA-T		1.10 (0.40 to 2.84)	1.04 (0.77 to 1.58)	2.24 (–18.17 to 24.95)
MET + INS-BI-T		1.24 (0.43 to 3.38)	1.08 (0.78 to 1.64)	4.88 (–16.97 to 28.13)
MET + MEG-L	MET + SUL-H	0.80 (0.32 to 2.07)	0.91 (0.67 to 1.43)	–5.51 (-25.02 to 17.81)
MET + MEG-H		0.70 (0.28 to 1.80)	0.86 (0.62 to 1.34)	–8.72 (-28.64 to 14.42)
MET + DPP-L		0.66 (0.28 to 1.48)	0.83 (0.64 to 1.24)	–10.27 (-27.98 to 9.67)
MET + DPP-H		0.61 (0.26 to 1.36)	0.80 (0.62 to 1.19)	–12.26 (-29.54 to 7.62)
MET + SGL-L		0.66 (0.28 to 1.52)	0.83 (0.64 to 1.26)	–10.27 (-28.35 to 10.40)
MET + SGL-H		0.65 (0.28 to 1.50)	0.83 (0.63 to 1.25)	–10.52 (-28.39 to 10.10)
MET + GLP-T		0.98 (0.30 to 3.26)	0.99 (0.60 to 1.61)	–0.49 (-28.13 to 27.10)
MET + GLP-L		0.67 (0.28 to 1.54)	0.84 (0.63 to 1.26)	–9.96 (-28.36 to 10.62)
MET + GLP-H		0.90 (0.38 to 2.07)	0.96 (0.74 to 1.44)	–2.41 (-20.34 to 17.96)
MET + TZD-T		0.62 (0.26 to 1.48)	0.81 (0.60 to 1.23)	–11.59 (-30.26 to 9.64)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD-L		0.74 (0.29 to 2.00)	0.88 (0.62 to 1.40)	–7.11 (-28.25 to 16.95)
MET + TZD-H		0.72 (0.30 to 1.67)	0.87 (0.66 to 1.31)	–8.19 (-26.37 to 12.68)
MET + AGI-T		1.04 (0.40 to 2.67)	1.02 (0.74 to 1.56)	1.00 (–19.71 to 23.61)
MET + INS-BA-T		1.22 (0.48 to 2.90)	1.08 (0.80 to 1.61)	4.67 (–14.95 to 25.47)
MET + INS-BI-T		1.38 (0.53 to 3.45)	1.12 (0.82 to 1.69)	7.33 (–13.18 to 28.93)
MET + MEG-H	MET + MEG-L	0.88 (0.55 to 1.37)	0.94 (0.76 to 1.15)	–3.22 (–14.41 to 7.65)
MET + DPP-L		0.82 (0.52 to 1.25)	0.91 (0.76 to 1.12)	–4.88 (–15.77 to 5.62)
MET + DPP-H		0.76 (0.49 to 1.13)	0.88 (0.73 to 1.07)	–6.89 (–17.37 to 3.09)
MET + SGL-L		0.82 (0.52 to 1.26)	0.91 (0.76 to 1.12)	–4.86 (–15.70 to 5.73)
MET + SGL-H		0.82 (0.52 to 1.24)	0.91 (0.75 to 1.12)	–5.06 (–15.96 to 5.43)
MET + GLP-T		1.23 (0.47 to 3.48)	1.09 (0.68 to 1.54)	4.95 (–18.61 to 27.03)
MET + GLP-L		0.83 (0.50 to 1.31)	0.91 (0.73 to 1.14)	–4.75 (–16.94 to 6.75)
MET + GLP-H		1.13 (0.71 to 1.73)	1.05 (0.87 to 1.29)	2.93 (–8.16 to 13.53)
MET + TZD-T		0.78 (0.47 to 1.27)	0.89 (0.71 to 1.12)	–6.14 (–18.40 to 5.86)
MET + TZD-L		0.93 (0.50 to 1.80)	0.97 (0.72 to 1.29)	–1.89 (–17.16 to 14.27)
MET + TZD-H		0.89 (0.56 to 1.39)	0.95 (0.78 to 1.17)	–2.89 (–14.01 to 8.14)
MET + AGI-T		1.30 (0.70 to 2.41)	1.11 (0.86 to 1.43)	6.22 (–8.59 to 20.73)
MET + INS-BA-T		1.52 (0.86 to 2.62)	1.18 (0.94 to 1.47)	9.92 (–3.62 to 22.57)
MET + INS-BI-T		1.72 (0.90 to 3.21)	1.23 (0.96 to 1.55)	12.61 (–2.54 to 26.50)
MET + DPP-L	MET + MEG-H	0.93 (0.60 to 1.45)	0.97 (0.80 to 1.21)	–1.73 (–12.54 to 9.13)
MET + DPP-H		0.86 (0.57 to 1.31)	0.93 (0.77 to 1.16)	–3.76 (–14.00 to 6.73)
MET + SGL-L		0.93 (0.60 to 1.46)	0.97 (0.80 to 1.22)	–1.72 (–12.36 to 9.40)
MET + SGL-H		0.93 (0.60 to 1.44)	0.96 (0.80 to 1.21)	–1.92 (–12.61 to 9.12)
MET + GLP-T		1.39 (0.52 to 3.89)	1.15 (0.71 to 1.64)	7.99 (–16.23 to 29.86)
MET + GLP-L		0.94 (0.57 to 1.52)	0.97 (0.77 to 1.24)	–1.58 (–13.75 to 10.37)
MET + GLP-H		1.28 (0.81 to 2.01)	1.11 (0.92 to 1.40)	5.99 (–4.99 to 17.29)
MET + TZD-T		0.89 (0.54 to 1.45)	0.94 (0.75 to 1.21)	–2.98 (–15.16 to 9.22)
MET + TZD-L		1.05 (0.57 to 2.05)	1.02 (0.76 to 1.38)	1.28 (–13.99 to 17.49)
MET + TZD-H		1.01 (0.64 to 1.61)	1.01 (0.82 to 1.27)	0.27 (–10.97 to 11.85)
MET + AGI-T		1.47 (0.81 to 2.71)	1.18 (0.91 to 1.54)	9.35 (–5.14 to 23.77)
MET + INS-BA-T		1.72 (0.99 to 3.01)	1.25 (1.00 to 1.60)	12.93 (–0.27 to 26.07)
MET + INS-BI-T		1.94 (1.05 to 3.73)	1.30 (1.02 to 1.69)	15.56 (1.21 to 30.15)
MET + DPP-H	MET + DPP-L	0.92 (0.80 to 1.07)	0.96 (0.89 to 1.04)	–2.02 (–5.70 to 1.74)
MET + SGL-L		1.00 (0.81 to 1.25)	1.00 (0.90 to 1.12)	0.06 (–5.35 to 5.57)
MET + SGL-H		1.00 (0.81 to 1.22)	1.00 (0.90 to 1.10)	–0.09 (–5.27 to 4.96)
MET + GLP-T		1.49 (0.61 to 3.96)	1.19 (0.76 to 1.60)	9.73 (–12.27 to 29.92)
MET + GLP-L		1.01 (0.74 to 1.35)	1.00 (0.86 to 1.16)	0.21 (–7.43 to 7.52)
MET + GLP-H		1.37 (1.09 to 1.73)	1.15 (1.04 to 1.28)	7.83 (2.12 to 13.40)
MET + TZD-T		0.95 (0.71 to 1.29)	0.98 (0.83 to 1.13)	–1.21 (–8.65 to 6.29)
MET + TZD-L		1.13 (0.69 to 1.93)	1.06 (0.82 to 1.32)	3.06 (–9.20 to 15.94)
MET + TZD-H		1.09 (0.85 to 1.40)	1.04 (0.92 to 1.17)	2.02 (–3.98 to 8.39)
MET + AGI-T		1.58 (0.98 to 2.57)	1.22 (0.99 to 1.46)	11.19 (–0.41 to 22.20)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BA-T		1.85 (1.24 to 2.76)	1.29 (1.10 to 1.48)	14.88 (5.40 to 23.50)
MET + INS-BI-T		2.09 (1.28 to 3.40)	1.35 (1.12 to 1.56)	17.57 (6.03 to 27.43)
MET + SGL-L	MET + DPP-H	1.09 (0.91 to 1.30)	1.04 (0.95 to 1.14)	2.07 (–2.34 to 6.62)
MET + SGL-H		1.08 (0.92 to 1.27)	1.04 (0.96 to 1.12)	1.90 (–2.09 to 5.89)
MET + GLP-T		1.61 (0.66 to 4.20)	1.24 (0.79 to 1.65)	11.75 (–10.24 to 31.30)
MET + GLP-L		1.09 (0.83 to 1.41)	1.05 (0.91 to 1.18)	2.19 (–4.63 to 8.60)
MET + GLP-H		1.49 (1.23 to 1.79)	1.20 (1.11 to 1.30)	9.85 (5.25 to 14.25)
MET + TZD-T		1.03 (0.79 to 1.35)	1.02 (0.88 to 1.15)	0.84 (–5.86 to 7.41)
MET + TZD-L		1.23 (0.75 to 2.05)	1.11 (0.86 to 1.36)	5.09 (–7.09 to 17.36)
MET + TZD-H		1.18 (0.96 to 1.45)	1.08 (0.98 to 1.19)	4.06 (–1.03 to 9.20)
MET + AGI-T		1.72 (1.08 to 2.73)	1.27 (1.04 to 1.49)	13.28 (1.82 to 23.56)
MET + INS-BA-T		2.01 (1.40 to 2.91)	1.35 (1.17 to 1.51)	16.91 (8.33 to 24.76)
MET + INS-BI-T		2.26 (1.43 to 3.62)	1.40 (1.18 to 1.60)	19.53 (8.83 to 28.77)
MET + SGL-H	MET + SGL-L	0.99 (0.86 to 1.15)	1.00 (0.93 to 1.07)	–0.20 (–3.86 to 3.41)
MET + GLP-T		1.48 (0.59 to 3.87)	1.19 (0.75 to 1.59)	9.66 (–12.85 to 29.41)
MET + GLP-L		1.00 (0.73 to 1.37)	1.00 (0.85 to 1.16)	0.05 (–7.68 to 7.72)
MET + GLP-H		1.37 (1.07 to 1.74)	1.15 (1.03 to 1.29)	7.78 (1.65 to 13.62)
MET + TZD-T		0.95 (0.70 to 1.29)	0.97 (0.83 to 1.13)	–1.27 (–8.91 to 6.24)
MET + TZD-L		1.12 (0.68 to 1.94)	1.06 (0.82 to 1.32)	2.90 (–9.39 to 16.00)
MET + TZD-H		1.08 (0.84 to 1.40)	1.04 (0.92 to 1.17)	2.00 (–4.49 to 8.31)
MET + AGI-T		1.58 (0.98 to 2.57)	1.22 (0.99 to 1.45)	11.14 (–0.40 to 22.13)
MET + INS-BA-T		1.85 (1.24 to 2.76)	1.29 (1.10 to 1.48)	14.77 (5.27 to 23.57)
MET + INS-BI-T		2.09 (1.27 to 3.40)	1.35 (1.11 to 1.56)	17.49 (5.90 to 27.39)
MET + GLP-T	MET + SGL-H	1.50 (0.60 to 3.89)	1.20 (0.76 to 1.59)	9.95 (–12.45 to 29.51)
MET + GLP-L		1.01 (0.75 to 1.37)	1.01 (0.86 to 1.16)	0.28 (–7.34 to 7.78)
MET + GLP-H		1.38 (1.09 to 1.74)	1.16 (1.04 to 1.28)	7.95 (2.10 to 13.62)
MET + TZD-T		0.96 (0.71 to 1.28)	0.98 (0.84 to 1.13)	–1.03 (–8.42 to 6.16)
MET + TZD-L		1.13 (0.69 to 1.94)	1.06 (0.82 to 1.33)	3.12 (–9.16 to 16.07)
MET + TZD-H		1.09 (0.85 to 1.40)	1.04 (0.92 to 1.17)	2.18 (–4.05 to 8.36)
MET + AGI-T		1.59 (0.99 to 2.57)	1.22 (0.99 to 1.45)	11.33 (–0.27 to 22.11)
MET + INS-BA-T		1.86 (1.26 to 2.78)	1.30 (1.11 to 1.49)	14.96 (5.65 to 23.69)
MET + INS-BI-T		2.10 (1.29 to 3.42)	1.35 (1.12 to 1.56)	17.66 (6.23 to 27.45)
MET + GLP-L	MET + GLP-T	0.68 (0.25 to 1.72)	0.84 (0.61 to 1.34)	–9.65 (-30.52 to 13.39)
MET + GLP-H		0.92 (0.35 to 2.29)	0.97 (0.72 to 1.52)	–1.96 (-21.89 to 20.37)
MET + TZD-T		0.64 (0.23 to 1.63)	0.82 (0.59 to 1.31)	–11.00 (-31.87 to 11.99)
MET + TZD-L		0.75 (0.27 to 2.17)	0.89 (0.61 to 1.47)	–6.86 (-29.31 to 18.96)
MET + TZD-H		0.73 (0.27 to 1.82)	0.87 (0.64 to 1.38)	–7.71 (-28.04 to 14.77)
MET + AGI-T		1.06 (0.37 to 2.91)	1.02 (0.73 to 1.64)	1.38 (-20.96 to 25.72)
MET + INS-BA-T		1.24 (0.44 to 3.24)	1.08 (0.79 to 1.72)	5.04 (–16.58 to 28.13)
MET + INS-BI-T		1.40 (0.46 to 3.90)	1.13 (0.80 to 1.81)	7.54 (–15.67 to 31.80)
MET + GLP-H	MET + GLP-L	1.36 (1.06 to 1.77)	1.15 (1.03 to 1.31)	7.67 (1.41 to 14.10)
MET + TZD-T		0.95 (0.65 to 1.38)	0.97 (0.81 to 1.18)	–1.36 (–10.59 to 8.02)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD-L		1.13 (0.64 to 2.01)	1.06 (0.80 to 1.36)	3.02 (–10.87 to 16.87)
MET + TZD-H		1.08 (0.78 to 1.51)	1.04 (0.89 to 1.22)	1.83 (–6.04 to 10.17)
MET + AGI-T		1.57 (0.93 to 2.68)	1.22 (0.97 to 1.50)	11.06 (–1.71 to 23.24)
MET + INS-BA-T		1.84 (1.19 to 2.90)	1.29 (1.08 to 1.55)	14.68 (4.17 to 25.04)
MET + INS-BI-T		2.07 (1.23 to 3.58)	1.34 (1.09 to 1.62)	17.22 (5.01 to 28.86)
MET + TZD-T	MET + GLP-H	0.69 (0.50 to 0.96)	0.85 (0.72 to 0.98)	–9.02 (–16.90 to –1.01)
MET + TZD-L		0.82 (0.50 to 1.44)	0.92 (0.71 to 1.15)	–4.75 (–17.21 to 8.57)
MET + TZD-H		0.79 (0.60 to 1.04)	0.90 (0.80 to 1.02)	–5.78 (–12.33 to 0.90)
MET + AGI-T		1.15 (0.71 to 1.89)	1.06 (0.86 to 1.26)	3.41 (–8.51 to 14.47)
MET + INS-BA-T		1.35 (0.90 to 2.03)	1.12 (0.96 to 1.29)	6.99 (–2.63 to 15.99)
MET + INS-BI-T		1.52 (0.92 to 2.51)	1.17 (0.97 to 1.35)	9.64 (–1.98 to 19.92)
MET + TZD-L	MET + TZD-T	1.19 (0.69 to 2.09)	1.09 (0.82 to 1.39)	4.34 (–9.21 to 17.93)
MET + TZD-H		1.14 (0.82 to 1.59)	1.07 (0.91 to 1.26)	3.24 (–4.83 to 11.46)
MET + AGI-T		1.66 (0.98 to 2.85)	1.25 (0.99 to 1.55)	12.41 (–0.44 to 24.76)
MET + INS-BA-T		1.94 (1.25 to 3.05)	1.32 (1.10 to 1.59)	16.00 (5.49 to 26.18)
MET + INS-BI-T		2.21 (1.30 to 3.72)	1.38 (1.12 to 1.66)	18.84 (6.41 to 29.82)
MET + TZD-H	MET + TZD-L	0.96 (0.58 to 1.58)	0.98 (0.80 to 1.26)	–1.14 (–13.08 to 11.26)
MET + AGI-T		1.40 (0.70 to 2.70)	1.15 (0.87 to 1.54)	8.10 (–8.41 to 23.72)
MET + INS-BA-T		1.64 (0.84 to 3.07)	1.22 (0.94 to 1.61)	11.80 (–4.09 to 26.62)
MET + INS-BI-T		1.85 (0.89 to 3.63)	1.27 (0.96 to 1.68)	14.40 (–2.79 to 29.68)
MET + AGI-T	MET + TZD-H	1.46 (0.88 to 2.42)	1.17 (0.94 to 1.42)	9.16 (–3.19 to 20.72)
MET + INS-BA-T		1.71 (1.12 to 2.61)	1.24 (1.05 to 1.44)	12.81 (2.78 to 22.13)
MET + INS-BI-T		1.93 (1.16 to 3.24)	1.29 (1.07 to 1.53)	15.50 (3.69 to 26.25)
MET + INS-BA-T	MET + AGI-T	1.17 (0.64 to 2.11)	1.06 (0.86 to 1.33)	3.59 (–9.97 to 17.28)
MET + INS-BI-T		1.32 (0.68 to 2.56)	1.10 (0.88 to 1.40)	6.27 (–8.51 to 20.91)
MET + INS-BI-T	MET + INS-BA-T	1.13 (0.74 to 1.76)	1.04 (0.89 to 1.20)	2.63 (–7.03 to 12.02)
Random-effects model	Residual deviance	176.5 vs. 180 data points		
	Deviance information criteria	1,212.8		

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Urogenital Adverse Events (People)

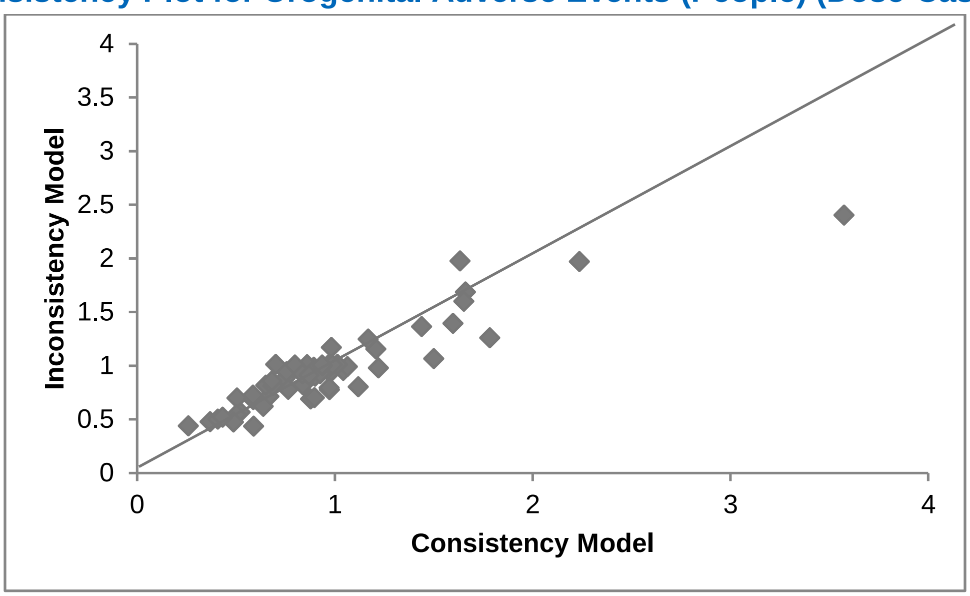
Table 33: Urogenital Adverse Events (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	1.07 (0.73 to 1.60)	1.07 (0.73 to 1.58)	0.19 (–0.81 to 1.38)
MET + DPP-L		1.35 (0.66 to 2.74)	1.34 (0.66 to 2.63)	0.90 (–0.99 to 3.99)
MET + DPP-H		1.19 (0.86 to 1.67)	1.19 (0.87 to 1.64)	0.50 (–0.42 to 1.48)
MET + SGL-L		1.07 (0.68 to 1.72)	1.07 (0.69 to 1.69)	0.19 (–0.90 to 1.73)
MET + SGL-H		1.05 (0.70 to 1.62)	1.05 (0.71 to 1.60)	0.13 (–0.86 to 1.47)
MET + GLP-L		1.54 (0.69 to 3.33)	1.52 (0.70 to 3.15)	1.38 (–0.85 to 5.48)
MET + GLP-H		1.12 (0.56 to 2.20)	1.11 (0.57 to 2.14)	0.30 (–1.26 to 2.84)
MET + GLP-T		0.82 (0.43 to 1.53)	0.82 (0.44 to 1.51)	–0.47 (–1.67 to 1.28)
MET + TZD-H		0.65 (0.22 to 1.83)	0.66 (0.23 to 1.79)	–0.90 (–2.27 to 2.01)
MET + INS-BA-T		0.54 (0.05 to 4.22)	0.55 (0.06 to 3.89)	–1.19 (–2.81 to 7.58)
MET + DPP-L	MET + SUL-T	1.25 (0.58 to 2.63)	1.24 (0.59 to 2.53)	0.69 (–1.39 to 3.83)
MET + DPP-H		1.11 (0.82 to 1.50)	1.11 (0.82 to 1.49)	0.30 (–0.65 to 1.14)
MET + SGL-L		1.00 (0.59 to 1.68)	1.00 (0.60 to 1.65)	0.00 (–1.38 to 1.62)
MET + SGL-H		0.98 (0.66 to 1.49)	0.98 (0.66 to 1.47)	–0.06 (–1.16 to 1.19)
MET + GLP-L		1.43 (0.63 to 3.17)	1.42 (0.63 to 3.00)	1.18 (–1.18 to 5.28)
MET + GLP-H		1.04 (0.51 to 2.06)	1.04 (0.52 to 2.01)	0.10 (–1.61 to 2.63)
MET + GLP-T		0.76 (0.41 to 1.37)	0.77 (0.42 to 1.36)	–0.65 (–1.94 to 0.94)
MET + TZD-H		0.61 (0.20 to 1.68)	0.62 (0.21 to 1.65)	–1.08 (–2.67 to 1.76)
MET + INS-BA-T		0.50 (0.05 to 3.85)	0.51 (0.05 to 3.55)	–1.36 (–3.17 to 7.30)
MET + DPP-H	MET + DPP-L	0.89 (0.44 to 1.83)	0.89 (0.46 to 1.80)	–0.39 (–3.47 to 1.53)
MET + SGL-L		0.80 (0.35 to 1.85)	0.80 (0.36 to 1.82)	–0.70 (–3.96 to 1.72)
MET + SGL-H		0.78 (0.36 to 1.76)	0.79 (0.37 to 1.73)	–0.74 (–3.95 to 1.48)
MET + GLP-L		1.14 (0.41 to 3.17)	1.14 (0.42 to 3.01)	0.48 (–3.27 to 4.93)
MET + GLP-H		0.83 (0.32 to 2.11)	0.83 (0.34 to 2.06)	–0.58 (–3.91 to 2.46)
MET + GLP-T		0.61 (0.25 to 1.50)	0.62 (0.26 to 1.48)	–1.34 (–4.52 to 1.06)
MET + TZD-H		0.49 (0.14 to 1.57)	0.49 (0.14 to 1.55)	–1.74 (–4.99 to 1.42)
MET + INS-BA-T		0.40 (0.04 to 3.38)	0.41 (0.04 to 3.14)	–1.93 (–5.44 to 6.74)
MET + SGL-L	MET + DPP-H	0.90 (0.54 to 1.51)	0.90 (0.55 to 1.49)	–0.31 (–1.64 to 1.39)
MET + SGL-H		0.88 (0.57 to 1.39)	0.88 (0.58 to 1.37)	–0.36 (–1.50 to 1.06)
MET + GLP-L		1.29 (0.59 to 2.72)	1.28 (0.60 to 2.58)	0.89 (–1.32 to 4.90)
MET + GLP-H		0.94 (0.49 to 1.75)	0.94 (0.50 to 1.71)	–0.19 (–1.69 to 2.22)
MET + GLP-T		0.69 (0.38 to 1.22)	0.70 (0.39 to 1.21)	–0.96 (–2.11 to 0.64)
MET + TZD-H		0.55 (0.19 to 1.45)	0.56 (0.19 to 1.43)	–1.39 (–2.77 to 1.36)
MET + INS-BA-T		0.45 (0.05 to 3.46)	0.46 (0.05 to 3.21)	–1.68 (–3.33 to 7.02)
MET + SGL-H	MET + SGL-L	0.98 (0.65 to 1.50)	0.98 (0.66 to 1.48)	–0.05 (–1.32 to 1.09)
MET + GLP-L		1.44 (0.58 to 3.43)	1.42 (0.59 to 3.24)	1.18 (–1.48 to 5.39)
MET + GLP-H		1.04 (0.46 to 2.27)	1.04 (0.47 to 2.21)	0.10 (–2.02 to 2.80)
MET + GLP-T		0.76 (0.36 to 1.59)	0.77 (0.37 to 1.57)	–0.66 (–2.47 to 1.26)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + TZD-H		0.61 (0.19 to 1.84)	0.62 (0.20 to 1.80)	–1.08 (–3.04 to 1.93)
MET + INS-BA-T		0.50 (0.05 to 4.07)	0.51 (0.05 to 3.76)	–1.35 (–3.55 to 7.37)
MET + GLP-L	MET + SGL-H	1.46 (0.61 to 3.37)	1.44 (0.62 to 3.19)	1.23 (–1.29 to 5.39)
MET + GLP-H		1.06 (0.49 to 2.23)	1.06 (0.50 to 2.16)	0.16 (–1.78 to 2.80)
MET + GLP-T		0.78 (0.39 to 1.53)	0.78 (0.39 to 1.51)	–0.60 (–2.20 to 1.19)
MET + TZD-H		0.62 (0.20 to 1.78)	0.63 (0.21 to 1.74)	–1.02 (–2.79 to 1.87)
MET + INS-BA-T		0.51 (0.05 to 4.04)	0.52 (0.05 to 3.74)	–1.31 (–3.29 to 7.39)
MET + GLP-H	MET + GLP-L	0.72 (0.32 to 1.65)	0.73 (0.34 to 1.63)	–1.06 (–4.75 to 1.57)
MET + GLP-T		0.53 (0.20 to 1.38)	0.54 (0.22 to 1.36)	–1.82 (–6.01 to 0.82)
MET + TZD-H		0.42 (0.12 to 1.38)	0.44 (0.13 to 1.37)	–2.19 (–6.29 to 0.99)
MET + INS-BA-T		0.35 (0.03 to 3.16)	0.36 (0.04 to 2.96)	–2.38 (–6.83 to 6.22)
MET + GLP-T	MET + GLP-H	0.73 (0.31 to 1.73)	0.74 (0.32 to 1.71)	–0.75 (–3.42 to 1.36)
MET + TZD-H		0.58 (0.20 to 1.62)	0.59 (0.20 to 1.60)	–1.16 (–3.53 to 1.44)
MET + INS-BA-T		0.49 (0.05 to 4.02)	0.49 (0.05 to 3.73)	–1.38 (–4.41 to 7.17)
MET + TZD-H	MET + GLP-T	0.80 (0.24 to 2.50)	0.80 (0.24 to 2.43)	–0.41 (–2.48 to 2.51)
MET + INS-BA-T		0.66 (0.07 to 4.68)	0.67 (0.08 to 4.32)	–0.68 (–2.66 to 7.65)
MET + INS-BA-T	MET + TZD-H	0.84 (0.07 to 8.12)	0.84 (0.07 to 7.42)	–0.25 (–3.43 to 8.41)
Random-effects model	Residual deviance	57.39 vs. 59 data points		
	Deviance information criteria	314.836		

CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; -L = low-dose; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Figure 21: Consistency Plot for Urogenital Adverse Events (People) (Dose-Case Analysis)



Withdrawal Due to Adverse Events

Table 34: Withdrawal Due to Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL-T	MET	0.90 (0.66 to 1.24)	0.91 (0.67 to 1.23)	–0.26 (–0.96 to 0.59)
MET + SUL-L		0.48 (0.02 to 8.30)	0.49 (0.02 to 6.93)	–1.38 (–2.85 to 15.52)
MET + SUL-H		0.91 (0.49 to 1.77)	0.91 (0.49 to 1.73)	–0.23 (–1.43 to 1.94)
MET + MEG-L		1.09 (0.33 to 3.69)	1.09 (0.33 to 3.45)	0.25 (–1.85 to 6.54)
MET + MEG-H		0.73 (0.23 to 2.16)	0.74 (0.24 to 2.10)	–0.70 (–2.15 to 2.93)
MET + DPP-L		1.01 (0.64 to 1.63)	1.01 (0.65 to 1.61)	0.03 (–1.01 to 1.56)
MET + DPP-H		0.89 (0.69 to 1.17)	0.90 (0.69 to 1.16)	–0.28 (–0.91 to 0.41)
MET + SGL-L		1.05 (0.68 to 1.62)	1.04 (0.68 to 1.59)	0.12 (–0.90 to 1.55)
MET + SGL-H		1.02 (0.69 to 1.53)	1.02 (0.69 to 1.51)	0.04 (–0.89 to 1.32)
MET + GLP-T		1.54 (0.72 to 3.40)	1.52 (0.72 to 3.19)	1.41 (–0.76 to 5.81)
MET + GLP-L		1.22 (0.52 to 2.86)	1.21 (0.53 to 2.73)	0.58 (–1.30 to 4.57)
MET + GLP-H		2.26 (1.53 to 3.39)	2.18 (1.51 to 3.19)	3.21 (1.41 to 5.76)
MET + TZD-T		0.81 (0.47 to 1.42)	0.81 (0.48 to 1.40)	–0.50 (–1.49 to 1.05)
MET + TZD-L		1.36 (0.62 to 2.97)	1.35 (0.63 to 2.83)	0.94 (–1.04 to 4.81)
MET + TZD-H		1.13 (0.76 to 1.72)	1.12 (0.76 to 1.69)	0.33 (–0.68 to 1.77)
MET + AGI-T		2.81 (1.34 to 6.02)	2.68 (1.33 to 5.32)	4.54 (0.90 to 11.54)
MET + AGI-L		1.35 (0.19 to 13.37)	1.34 (0.19 to 10.10)	0.91 (–2.25 to 24.20)
MET + AGI-H		0.19 (0.00 to 6.19)	0.19 (0.00 to 5.41)	–2.14 (–3.02 to 12.13)
MET + INS-BA-T		0.24 (0.07 to 0.78)	0.25 (0.07 to 0.79)	–2.02 (–2.74 to –0.56)
MET + INS-BI-T		0.67 (0.20 to 2.24)	0.67 (0.20 to 2.17)	–0.88 (–2.26 to 3.10)
MET + SUL-L	MET + SUL-T	0.53 (0.02 to 9.05)	0.54 (0.02 to 7.60)	–1.11 (–2.78 to 15.73)
MET + SUL-H		1.01 (0.53 to 2.03)	1.01 (0.54 to 1.98)	0.02 (–1.30 to 2.20)
MET + MEG-L		1.22 (0.35 to 4.35)	1.21 (0.36 to 4.04)	0.51 (–1.78 to 6.88)
MET + MEG-H		0.81 (0.25 to 2.50)	0.81 (0.25 to 2.41)	–0.46 (–2.08 to 3.24)
MET + DPP-L		1.12 (0.70 to 1.84)	1.11 (0.71 to 1.81)	0.28 (–0.83 to 1.79)
MET + DPP-H		0.99 (0.76 to 1.30)	0.99 (0.76 to 1.29)	–0.03 (–0.71 to 0.61)
MET + SGL-L		1.16 (0.73 to 1.86)	1.15 (0.73 to 1.82)	0.37 (–0.77 to 1.79)
MET + SGL-H		1.13 (0.74 to 1.74)	1.12 (0.74 to 1.72)	0.30 (–0.73 to 1.57)
MET + GLP-T		1.71 (0.78 to 3.74)	1.68 (0.79 to 3.52)	1.66 (–0.55 to 5.93)
MET + GLP-L		1.35 (0.56 to 3.26)	1.34 (0.57 to 3.10)	0.83 (–1.16 to 4.84)
MET + GLP-H		2.50 (1.64 to 3.89)	2.41 (1.61 to 3.66)	3.46 (1.65 to 5.97)
MET + TZD-T		0.90 (0.56 to 1.46)	0.90 (0.57 to 1.44)	–0.25 (–1.12 to 1.06)
MET + TZD-L		1.51 (0.67 to 3.36)	1.49 (0.67 to 3.19)	1.20 (–0.89 to 5.04)
MET + TZD-H		1.25 (0.80 to 1.97)	1.24 (0.81 to 1.93)	0.58 (–0.55 to 2.02)
MET + AGI-T		3.10 (1.39 to 7.13)	2.95 (1.37 to 6.27)	4.78 (1.02 to 11.89)
MET + AGI-L		1.50 (0.20 to 15.00)	1.48 (0.21 to 11.32)	1.17 (–2.06 to 24.42)
MET + AGI-H		0.21 (0.00 to 6.80)	0.21 (0.00 to 5.96)	–1.85 (–2.99 to 12.31)
MET + INS-BA-T		0.27 (0.07 to 0.87)	0.28 (0.07 to 0.87)	–1.75 (–2.70 to –0.30)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BI-T		0.73 (0.22 to 2.48)	0.74 (0.22 to 2.39)	–0.64 (–2.11 to 3.33)
MET + SUL-H	MET + SUL-L	1.88 (0.11 to 54.19)	1.85 (0.13 to 52.77)	1.05 (–15.56 to 3.76)
MET + MEG-L		2.26 (0.10 to 77.80)	2.22 (0.12 to 73.44)	1.37 (–15.09 to 7.82)
MET + MEG-H		1.49 (0.07 to 50.37)	1.48 (0.08 to 48.45)	0.56 (–16.16 to 4.60)
MET + DPP-L		2.10 (0.12 to 56.76)	2.07 (0.15 to 55.05)	1.36 (–15.46 to 3.51)
MET + DPP-H		1.87 (0.11 to 49.50)	1.84 (0.13 to 48.42)	1.10 (–15.83 to 2.63)
MET + SGL-L		2.18 (0.12 to 58.67)	2.14 (0.15 to 56.87)	1.46 (–15.43 to 3.54)
MET + SGL-H		2.13 (0.12 to 57.05)	2.09 (0.14 to 55.47)	1.39 (–15.54 to 3.37)
MET + GLP-T		3.20 (0.18 to 91.32)	3.10 (0.21 to 86.55)	2.52 (–13.78 to 7.29)
MET + GLP-L		2.53 (0.14 to 73.76)	2.48 (0.16 to 70.37)	1.74 (–14.64 to 6.14)
MET + GLP-H		4.68 (0.27 to 125.00)	4.46 (0.31 to 117.20)	4.39 (–12.29 to 7.54)
MET + TZD-T		1.69 (0.10 to 46.20)	1.67 (0.11 to 45.01)	0.85 (–15.80 to 2.98)
MET + TZD-L		2.80 (0.16 to 74.43)	2.74 (0.19 to 71.08)	2.04 (–14.29 to 6.25)
MET + TZD-H		2.33 (0.14 to 63.82)	2.28 (0.16 to 61.86)	1.65 (–15.10 to 3.79)
MET + AGI-T		5.77 (0.32 to 170.40)	5.41 (0.36 to 153.90)	5.40 (–10.96 to 12.88)
MET + AGI-L		2.84 (0.08 to 171.80)	2.75 (0.10 to 137.00)	1.85 (–14.46 to 25.01)
MET + AGI-H		0.35 (0.00 to 48.62)	0.36 (0.00 to 42.12)	–0.56 (–16.82 to 12.66)
MET + INS-BA-T		0.49 (0.02 to 16.12)	0.49 (0.03 to 15.89)	–0.63 (–17.39 to 1.40)
MET + INS-BI-T		1.33 (0.07 to 46.19)	1.32 (0.08 to 44.52)	0.37 (–16.13 to 4.53)
MET + MEG-L	MET + SUL-H	1.20 (0.30 to 4.61)	1.20 (0.31 to 4.32)	0.48 (–2.54 to 6.78)
MET + MEG-H		0.80 (0.22 to 2.64)	0.81 (0.23 to 2.56)	–0.46 (–2.98 to 3.14)
MET + DPP-L		1.11 (0.52 to 2.33)	1.11 (0.53 to 2.28)	0.26 (–2.00 to 2.07)
MET + DPP-H		0.98 (0.51 to 1.82)	0.98 (0.52 to 1.80)	–0.05 (–2.18 to 1.16)
MET + SGL-L		1.15 (0.53 to 2.39)	1.14 (0.54 to 2.34)	0.35 (–1.96 to 2.13)
MET + SGL-H		1.12 (0.52 to 2.29)	1.12 (0.54 to 2.25)	0.28 (–2.02 to 1.95)
MET + GLP-T		1.70 (0.62 to 4.47)	1.67 (0.63 to 4.22)	1.63 (–1.40 to 6.07)
MET + GLP-L		1.34 (0.51 to 3.45)	1.33 (0.52 to 3.30)	0.79 (–1.72 to 4.62)
MET + GLP-H		2.47 (1.30 to 4.71)	2.38 (1.28 to 4.47)	3.38 (1.11 to 5.86)
MET + TZD-T		0.89 (0.39 to 1.97)	0.89 (0.40 to 1.93)	–0.27 (–2.54 to 1.56)
MET + TZD-L		1.50 (0.57 to 3.70)	1.48 (0.58 to 3.52)	1.15 (–1.56 to 4.98)
MET + TZD-H		1.24 (0.64 to 2.34)	1.23 (0.65 to 2.29)	0.56 (–1.49 to 2.11)
MET + AGI-T		3.08 (1.14 to 8.29)	2.93 (1.13 to 7.38)	4.69 (0.47 to 11.86)
MET + AGI-L		1.49 (0.20 to 15.06)	1.47 (0.20 to 11.22)	1.13 (–2.54 to 24.15)
MET + AGI-H		0.21 (0.00 to 6.25)	0.21 (0.00 to 5.47)	–1.72 (–3.96 to 11.86)
MET + INS-BA-T		0.27 (0.06 to 0.97)	0.27 (0.06 to 0.97)	–1.75 (–3.97 to –0.06)
MET + INS-BI-T		0.73 (0.19 to 2.68)	0.73 (0.20 to 2.60)	–0.63 (–3.07 to 3.27)
MET + MEG-H	MET + MEG-L	0.66 (0.18 to 2.38)	0.67 (0.18 to 2.33)	–0.89 (–6.37 to 2.19)
MET + DPP-L		0.92 (0.25 to 3.44)	0.93 (0.27 to 3.36)	–0.22 (–6.57 to 2.41)
MET + DPP-H		0.81 (0.23 to 2.79)	0.82 (0.25 to 2.75)	–0.54 (–6.88 to 1.66)
MET + SGL-L		0.96 (0.26 to 3.46)	0.96 (0.28 to 3.37)	–0.13 (–6.48 to 2.46)
MET + SGL-H		0.93 (0.26 to 3.30)	0.93 (0.28 to 3.23)	–0.21 (–6.60 to 2.31)
MET + GLP-T		1.41 (0.34 to 5.95)	1.39 (0.36 to 5.63)	1.09 (–5.39 to 6.06)

CADTH

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLP-L		1.13 (0.25 to 4.82)	1.12 (0.27 to 4.61)	0.34 (–6.22 to 4.84)
MET + GLP-H		2.06 (0.57 to 7.33)	2.00 (0.59 to 6.89)	2.89 (–3.62 to 6.36)
MET + TZD-T		0.74 (0.19 to 2.85)	0.75 (0.20 to 2.79)	–0.74 (–7.09 to 1.92)
MET + TZD-L		1.24 (0.29 to 5.20)	1.23 (0.31 to 4.97)	0.65 (–5.92 to 5.20)
MET + TZD-H		1.03 (0.29 to 3.72)	1.03 (0.31 to 3.62)	0.07 (–6.27 to 2.70)
MET + AGI-T		2.56 (0.62 to 10.73)	2.44 (0.64 to 9.66)	4.07 (–2.88 to 11.60)
MET + AGI-L		1.26 (0.12 to 15.06)	1.25 (0.13 to 11.53)	0.63 (–6.09 to 23.57)
MET + AGI-H		0.17 (0.00 to 6.80)	0.18 (0.00 to 5.88)	–2.05 (–8.33 to 11.58)
MET + INS-BA-T		0.22 (0.04 to 1.20)	0.22 (0.04 to 1.20)	–2.22 (–8.51 to 0.24)
MET + INS-BI-T		0.60 (0.11 to 3.43)	0.61 (0.12 to 3.33)	–1.08 (–7.45 to 3.42)
MET + DPP-L	MET + MEG-H	1.38 (0.43 to 4.78)	1.37 (0.44 to 4.65)	0.73 (–2.98 to 2.82)
MET + DPP-H		1.22 (0.40 to 3.93)	1.22 (0.42 to 3.86)	0.43 (–3.25 to 1.97)
MET + SGL-L		1.42 (0.45 to 4.84)	1.41 (0.46 to 4.71)	0.81 (–2.93 to 2.83)
MET + SGL-H		1.39 (0.44 to 4.70)	1.38 (0.45 to 4.59)	0.75 (–2.97 to 2.68)
MET + GLP-T		2.10 (0.56 to 8.52)	2.06 (0.58 to 7.99)	2.03 (–2.02 to 6.73)
MET + GLP-L		1.68 (0.43 to 6.98)	1.65 (0.44 to 6.66)	1.23 (–2.69 to 5.45)
MET + GLP-H		3.08 (0.99 to 10.42)	2.95 (0.99 to 9.81)	3.83 (–0.07 to 6.92)
MET + TZD-T		1.11 (0.33 to 4.01)	1.11 (0.34 to 3.92)	0.21 (–3.53 to 2.30)
MET + TZD-L		1.88 (0.48 to 7.48)	1.84 (0.49 to 7.11)	1.60 (–2.47 to 5.72)
MET + TZD-H		1.54 (0.50 to 5.20)	1.52 (0.51 to 5.04)	1.02 (–2.63 to 3.07)
MET + AGI-T		3.88 (1.04 to 15.12)	3.66 (1.03 to 13.62)	5.10 (0.16 to 12.27)
MET + AGI-L		1.89 (0.18 to 22.87)	1.85 (0.19 to 17.34)	1.53 (–3.25 to 24.69)
MET + AGI-H		0.26 (0.00 to 9.92)	0.26 (0.00 to 8.71)	–1.20 (–4.96 to 12.53)
MET + INS-BA-T		0.33 (0.06 to 1.63)	0.33 (0.06 to 1.62)	–1.27 (–4.93 to 0.58)
MET + INS-BI-T		0.90 (0.18 to 4.69)	0.90 (0.19 to 4.52)	–0.18 (–3.92 to 3.95)
MET + DPP-H	MET + DPP-L	0.89 (0.56 to 1.38)	0.89 (0.57 to 1.37)	–0.30 (–1.75 to 0.70)
MET + SGL-L		1.04 (0.56 to 1.89)	1.04 (0.56 to 1.86)	0.10 (–1.69 to 1.79)
MET + SGL-H		1.00 (0.56 to 1.81)	1.00 (0.57 to 1.78)	0.01 (–1.68 to 1.59)
MET + GLP-T		1.54 (0.63 to 3.61)	1.52 (0.64 to 3.40)	1.38 (–1.25 to 5.75)
MET + GLP-L		1.21 (0.47 to 3.08)	1.20 (0.48 to 2.94)	0.55 (–1.80 to 4.56)
MET + GLP-H		2.24 (1.26 to 3.90)	2.17 (1.25 to 3.68)	3.17 (0.93 to 5.80)
MET + TZD-T		0.80 (0.41 to 1.54)	0.81 (0.42 to 1.52)	–0.52 (–2.21 to 1.15)
MET + TZD-L		1.35 (0.55 to 3.21)	1.34 (0.56 to 3.05)	0.90 (–1.54 to 4.82)
MET + TZD-H		1.12 (0.63 to 1.97)	1.11 (0.64 to 1.93)	0.30 (–1.40 to 1.93)
MET + AGI-T		2.78 (1.16 to 6.79)	2.64 (1.15 to 6.02)	4.48 (0.49 to 11.68)
MET + AGI-L		1.34 (0.18 to 13.65)	1.33 (0.18 to 10.27)	0.88 (–2.68 to 24.10)
MET + AGI-H		0.19 (0.00 to 6.27)	0.19 (0.00 to 5.50)	–2.05 (–3.85 to 12.03)
MET + INS-BA-T		0.24 (0.06 to 0.83)	0.24 (0.06 to 0.84)	–2.02 (–3.61 to –0.37)
MET + INS-BI-T		0.66 (0.18 to 2.34)	0.66 (0.19 to 2.27)	–0.91 (–2.89 to 3.14)
MET + SGL-L	MET + DPP-H	1.17 (0.74 to 1.85)	1.16 (0.74 to 1.82)	0.40 (–0.70 to 1.83)
MET + SGL-H		1.14 (0.75 to 1.75)	1.14 (0.75 to 1.72)	0.33 (–0.67 to 1.61)
MET + GLP-T		1.73 (0.80 to 3.74)	1.70 (0.80 to 3.51)	1.69 (–0.51 to 6.04)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLP-L		1.37 (0.58 to 3.22)	1.36 (0.59 to 3.07)	0.86 (–1.07 to 4.83)
MET + GLP-H		2.53 (1.71 to 3.77)	2.44 (1.68 to 3.55)	3.49 (1.72 to 5.95)
MET + TZD-T		0.91 (0.53 to 1.55)	0.91 (0.54 to 1.53)	–0.22 (–1.22 to 1.25)
MET + TZD-L		1.53 (0.69 to 3.33)	1.51 (0.69 to 3.16)	1.23 (–0.80 to 5.08)
MET + TZD-H		1.26 (0.83 to 1.93)	1.25 (0.84 to 1.89)	0.61 (–0.43 to 2.01)
MET + AGI-T		3.15 (1.42 to 7.08)	2.99 (1.41 to 6.24)	4.82 (1.07 to 11.93)
MET + AGI-L		1.52 (0.21 to 14.86)	1.50 (0.21 to 11.21)	1.20 (–1.97 to 24.54)
MET + AGI-H		0.21 (0.00 to 6.95)	0.22 (0.00 to 6.05)	–1.85 (–2.84 to 12.32)
MET + INS-BA-T		0.27 (0.07 to 0.87)	0.28 (0.07 to 0.88)	–1.73 (–2.54 to –0.29)
MET + INS-BI-T		0.75 (0.22 to 2.48)	0.75 (0.23 to 2.39)	–0.60 (–2.02 to 3.35)
MET + SGL-H	MET + SGL-L	0.98 (0.64 to 1.46)	0.98 (0.65 to 1.45)	–0.07 (–1.28 to 1.03)
MET + GLP-T		1.48 (0.61 to 3.52)	1.46 (0.62 to 3.32)	1.29 (–1.33 to 5.72)
MET + GLP-L		1.17 (0.46 to 2.97)	1.17 (0.47 to 2.84)	0.47 (–1.87 to 4.48)
MET + GLP-H		2.16 (1.24 to 3.80)	2.09 (1.23 to 3.59)	3.08 (0.85 to 5.76)
MET + TZD-T		0.77 (0.41 to 1.51)	0.78 (0.42 to 1.50)	–0.62 (–2.21 to 1.11)
MET + TZD-L		1.31 (0.54 to 3.15)	1.29 (0.55 to 2.99)	0.82 (–1.58 to 4.82)
MET + TZD-H		1.08 (0.62 to 1.91)	1.07 (0.63 to 1.87)	0.21 (–1.44 to 1.91)
MET + AGI-T		2.69 (1.13 to 6.46)	2.56 (1.13 to 5.73)	4.40 (0.44 to 11.49)
MET + AGI-L		1.30 (0.17 to 12.73)	1.29 (0.18 to 9.59)	0.81 (–2.74 to 23.97)
MET + AGI-H		0.18 (0.00 to 5.96)	0.18 (0.00 to 5.23)	–2.14 (–3.87 to 11.90)
MET + INS-BA-T		0.23 (0.06 to 0.80)	0.24 (0.06 to 0.81)	–2.11 (–3.66 to –0.45)
MET + INS-BI-T		0.63 (0.18 to 2.28)	0.64 (0.18 to 2.21)	–1.00 (–2.93 to 3.04)
MET + GLP-T	MET + SGL-H	1.52 (0.64 to 3.56)	1.50 (0.65 to 3.36)	1.36 (–1.15 to 5.81)
MET + GLP-L		1.20 (0.48 to 3.02)	1.19 (0.49 to 2.88)	0.52 (–1.67 to 4.58)
MET + GLP-H		2.23 (1.30 to 3.78)	2.15 (1.29 to 3.58)	3.16 (1.01 to 5.81)
MET + TZD-T		0.80 (0.43 to 1.48)	0.80 (0.44 to 1.46)	–0.54 (–2.01 to 1.08)
MET + TZD-L		1.34 (0.57 to 3.17)	1.32 (0.57 to 3.01)	0.89 (–1.42 to 4.86)
MET + TZD-H		1.11 (0.66 to 1.91)	1.11 (0.66 to 1.87)	0.29 (–1.23 to 1.91)
MET + AGI-T		2.76 (1.19 to 6.50)	2.63 (1.18 to 5.76)	4.46 (0.60 to 11.62)
MET + AGI-L		1.35 (0.17 to 13.15)	1.34 (0.18 to 9.91)	0.90 (–2.62 to 24.08)
MET + AGI-H		0.19 (0.00 to 6.18)	0.19 (0.00 to 5.42)	–2.08 (–3.66 to 12.02)
MET + INS-BA-T		0.24 (0.06 to 0.80)	0.24 (0.06 to 0.80)	–2.03 (–3.42 to –0.47)
MET + INS-BI-T		0.65 (0.18 to 2.29)	0.66 (0.19 to 2.22)	–0.93 (–2.74 to 3.11)
MET + GLP-L	MET + GLP-T	0.79 (0.25 to 2.44)	0.80 (0.27 to 2.35)	–0.80 (–5.53 to 3.57)
MET + GLP-H		1.46 (0.63 to 3.39)	1.43 (0.65 to 3.23)	1.76 (–2.82 to 5.10)
MET + TZD-T		0.52 (0.21 to 1.31)	0.53 (0.22 to 1.30)	–1.89 (–6.29 to 0.68)
MET + TZD-L		0.88 (0.30 to 2.63)	0.88 (0.31 to 2.52)	–0.46 (–5.25 to 3.93)
MET + TZD-H		0.73 (0.31 to 1.73)	0.74 (0.33 to 1.70)	–1.08 (–5.55 to 1.51)
MET + AGI-T		1.82 (0.62 to 5.45)	1.76 (0.64 to 4.92)	3.05 (–2.60 to 10.38)
MET + AGI-L		0.89 (0.10 to 9.68)	0.89 (0.11 to 7.46)	–0.42 (–5.93 to 22.66)
MET + AGI-H		0.12 (0.00 to 4.41)	0.13 (0.00 to 3.91)	–3.23 (–7.71 to 10.63)
MET + INS-BA-T		0.16 (0.04 to 0.54)	0.16 (0.04 to 0.55)	–3.38 (–7.63 to –1.10)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BI-T		0.43 (0.11 to 1.70)	0.44 (0.11 to 1.67)	–2.21 (–6.63 to 1.98)
MET + GLP-H	MET + GLP-L	1.85 (0.84 to 4.11)	1.80 (0.85 to 3.92)	2.57 (–1.00 to 5.17)
MET + TZD-T		0.67 (0.25 to 1.75)	0.67 (0.26 to 1.73)	–1.07 (–5.10 to 1.26)
MET + TZD-L		1.10 (0.37 to 3.43)	1.10 (0.38 to 3.28)	0.32 (–3.88 to 4.57)
MET + TZD-H		0.92 (0.38 to 2.25)	0.92 (0.40 to 2.20)	–0.25 (–4.21 to 1.98)
MET + AGI-T		2.30 (0.74 to 7.17)	2.20 (0.76 to 6.42)	3.87 (–1.50 to 11.10)
MET + AGI-L		1.11 (0.13 to 11.98)	1.11 (0.13 to 9.20)	0.32 (–4.77 to 23.36)
MET + AGI-H		0.15 (0.00 to 5.18)	0.16 (0.00 to 4.58)	–2.40 (–6.45 to 11.05)
MET + INS-BA-T		0.20 (0.04 to 0.81)	0.20 (0.04 to 0.82)	–2.54 (–6.54 to –0.35)
MET + INS-BI-T		0.54 (0.13 to 2.18)	0.55 (0.14 to 2.12)	–1.39 (–5.45 to 2.61)
MET + TZD-T	MET + GLP-H	0.36 (0.19 to 0.67)	0.37 (0.20 to 0.68)	–3.68 (–6.30 to –1.49)
MET + TZD-L		0.60 (0.26 to 1.38)	0.62 (0.27 to 1.36)	–2.23 (–5.41 to 1.86)
MET + TZD-H		0.50 (0.31 to 0.81)	0.51 (0.33 to 0.82)	–2.86 (–5.36 to –0.84)
MET + AGI-T		1.24 (0.54 to 2.93)	1.22 (0.56 to 2.67)	1.31 (–3.17 to 8.62)
MET + AGI-L		0.60 (0.08 to 6.08)	0.62 (0.08 to 4.74)	–2.22 (–6.57 to 20.98)
MET + AGI-H		0.08 (0.00 to 2.71)	0.09 (0.00 to 2.46)	–5.07 (–7.92 to 8.66)
MET + INS-BA-T		0.11 (0.03 to 0.35)	0.11 (0.03 to 0.37)	–5.17 (–7.77 to –3.08)
MET + INS-BI-T		0.29 (0.09 to 0.95)	0.31 (0.09 to 0.96)	–3.99 (–6.71 to –0.24)
MET + TZD-L	MET + TZD-T	1.68 (0.66 to 4.25)	1.65 (0.67 to 4.03)	1.42 (–0.99 to 5.40)
MET + TZD-H		1.39 (0.74 to 2.64)	1.38 (0.75 to 2.58)	0.82 (–0.85 to 2.43)
MET + AGI-T		3.48 (1.36 to 8.84)	3.30 (1.35 to 7.85)	5.01 (1.00 to 12.15)
MET + AGI-L		1.68 (0.21 to 17.72)	1.65 (0.22 to 13.31)	1.40 (–2.14 to 24.71)
MET + AGI-H		0.23 (0.00 to 7.87)	0.24 (0.00 to 6.85)	–1.53 (–3.31 to 12.38)
MET + INS-BA-T		0.30 (0.07 to 1.06)	0.30 (0.08 to 1.06)	–1.48 (–3.11 to 0.11)
MET + INS-BI-T		0.82 (0.22 to 2.97)	0.82 (0.23 to 2.87)	–0.38 (–2.35 to 3.58)
MET + TZD-H	MET + TZD-L	0.83 (0.38 to 1.83)	0.83 (0.40 to 1.80)	–0.61 (–4.28 to 1.57)
MET + AGI-T		2.07 (0.69 to 6.27)	1.99 (0.71 to 5.65)	3.52 (–1.80 to 10.89)
MET + AGI-L		1.00 (0.12 to 10.75)	1.00 (0.13 to 8.25)	–0.01 (–5.13 to 23.23)
MET + AGI-H		0.14 (0.00 to 4.94)	0.14 (0.00 to 4.35)	–2.76 (–6.84 to 10.97)
MET + INS-BA-T		0.18 (0.04 to 0.72)	0.18 (0.04 to 0.72)	–2.91 (–6.86 to –0.61)
MET + INS-BI-T		0.48 (0.12 to 2.10)	0.49 (0.13 to 2.04)	–1.76 (–5.87 to 2.57)
MET + AGI-T	MET + TZD-H	2.49 (1.06 to 5.92)	2.38 (1.06 to 5.26)	4.17 (0.21 to 11.33)
MET + AGI-L		1.20 (0.17 to 12.44)	1.19 (0.17 to 9.32)	0.58 (–2.87 to 23.92)
MET + AGI-H		0.17 (0.00 to 5.49)	0.17 (0.00 to 4.82)	–2.35 (–4.06 to 11.71)
MET + INS-BA-T		0.22 (0.05 to 0.73)	0.22 (0.06 to 0.73)	–2.31 (–3.86 to –0.71)
MET + INS-BI-T		0.59 (0.17 to 2.05)	0.60 (0.17 to 1.99)	–1.21 (–3.13 to 2.75)
MET + AGI-L	MET + AGI-T	0.49 (0.06 to 5.33)	0.51 (0.06 to 4.18)	–3.28 (–11.39 to 19.61)
MET + AGI-H		0.07 (0.00 to 2.52)	0.07 (0.00 to 2.29)	–6.16 (–13.45 to 7.88)
MET + INS-BA-T		0.09 (0.02 to 0.34)	0.09 (0.02 to 0.35)	–6.49 (–13.48 to –2.62)
MET + INS-BI-T		0.24 (0.06 to 0.99)	0.25 (0.06 to 0.99)	–5.25 (–12.45 to –0.03)
MET + AGI-H	MET + AGI-L	0.13 (0.00 to 6.76)	0.14 (0.00 to 6.05)	–2.58 (-25.15 to 9.40)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + INS-BA-T		0.18 (0.01 to 1.84)	0.18 (0.02 to 1.83)	–2.88 (-26.20 to 0.54)
MET + INS-BI-T		0.48 (0.04 to 5.22)	0.49 (0.05 to 5.05)	–1.72 (-24.83 to 3.37)
MET + INS-BA-T	MET + AGI-H	1.29 (0.03 to 291.80)	1.29 (0.03 to 289.30)	0.13 (–13.97 to 1.72)
MET + INS-BI-T		3.53 (0.09 to 865.20)	3.47 (0.10 to 837.40)	1.04 (–12.60 to 5.13)
MET + INS-BI-T	MET + INS-BA-T	2.71 (0.79 to 11.84)	2.67 (0.79 to 11.38)	1.06 (–0.26 to 4.79)
Random-effects model	Residual deviance	249.1 vs. 259 data points		
	Deviance information criteria	1,232.17		

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Weight

Table 35: Weight: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL-T	MET	2.14 (1.70 to 2.56)
MET + SUL-L		0.12 (–1.88 to 2.12)
MET + SUL-H		1.75 (0.86 to 2.63)
MET + DPP-L		0.27 (–0.25 to 0.79)
MET + DPP-H		0.17 (–0.16 to 0.49)
MET + MEG-T		3.28 (1.34 to 5.22)
MET + MEG-L		0.18 (–1.19 to 1.54)
MET + MEG-H		0.65 (–0.38 to 1.69)
MET + SGL-L		–1.84 (–2.35 to –1.34)
MET + SGL-H		–2.25 (–2.72 to –1.79)
MET + GLP-T		–0.51 (–1.73 to 0.70)
MET + GLP-L		–0.69 (–1.41 to 0.03)
MET + GLP-H		–1.61 (–2.07 to –1.16)
MET + AGI-T		0.10 (–1.01 to 1.20)
MET + AGI-L		0.67 (–1.76 to 3.11)
MET + TZD-T		2.83 (1.98 to 3.68)
MET + TZD-L		1.60 (0.44 to 2.76)
MET + TZD-H		2.83 (2.28 to 3.38)
MET + INS-BA-T		2.98 (2.10 to 3.87)
MET + INS-BI-T		3.43 (2.33 to 4.55)
MET + SUL-L	MET + SUL-T	–2.01 (–4.03 to 0.01)
MET + SUL-H		–0.39 (–1.32 to 0.53)
MET + DPP-L		–1.87 (–2.47 to –1.26)
MET + DPP-H		–1.97 (–2.34 to –1.59)
MET + MEG-T		1.14 (–0.84 to 3.14)
MET + MEG-L		–1.96 (–3.38 to –0.52)
MET + MEG-H		–1.49 (–2.60 to –0.37)

Treatment	Reference	MD (95% CrI)
MET + SGL-L		–3.98 (–4.58 to –3.38)
MET + SGL-H		–4.38 (–4.93 to –3.83)
MET + GLP-T		–2.65 (–3.88 to –1.43)
MET + GLP-L		–2.83 (–3.63 to –2.03)
MET + GLP-H		–3.75 (–4.30 to –3.20)
MET + AGI-T		–2.03 (–3.23 to –0.85)
MET + AGI-L		–1.47 (–3.91 to 0.98)
MET + TZD-T		0.70 (–0.08 to 1.47)
MET + TZD-L		–0.53 (–1.74 to 0.67)
MET + TZD-H		0.69 (0.07 to 1.31)
MET + INS-BA-T		0.84 (–0.04 to 1.74)
MET + INS-BI-T		1.29 (0.17 to 2.43)
MET + SUL-H	MET + SUL-L	1.62 (–0.54 to 3.78)
MET + DPP-L		0.15 (–1.89 to 2.18)
MET + DPP-H		0.05 (–1.96 to 2.05)
MET + MEG-T		3.15 (0.38 to 5.93)
MET + MEG-L		0.05 (–2.38 to 2.45)
MET + MEG-H		0.53 (–1.72 to 2.78)
MET + SGL-L		–1.97 (–4.02 to 0.09)
MET + SGL-H		–2.37 (–4.42 to –0.33)
MET + GLP-T		–0.63 (–2.97 to 1.68)
MET + GLP-L		–0.81 (–2.93 to 1.31)
MET + GLP-H		–1.73 (–3.77 to 0.31)
MET + AGI-T		–0.02 (–2.31 to 2.26)
MET + AGI-L		0.55 (–2.58 to 3.67)
MET + TZD-T		2.71 (0.56 to 4.86)
MET + TZD-L		1.48 (–0.19 to 3.15)
MET + TZD-H		2.70 (0.68 to 4.71)
MET + INS-BA-T		2.86 (0.68 to 5.03)
MET + INS-BI-T		3.31 (1.03 to 5.57)
MET + DPP-L	MET + SUL-H	–1.47 (–2.47 to –0.48)
MET + DPP-H		–1.58 (–2.45 to –0.71)
MET + MEG-T		1.53 (–0.60 to 3.67)
MET + MEG-L		–1.57 (–3.20 to 0.06)
MET + MEG-H		–1.09 (–2.45 to 0.27)
MET + SGL-L		–3.59 (–4.58 to –2.60)
MET + SGL-H		–3.99 (–4.97 to –3.02)
MET + GLP-T		–2.26 (–3.74 to –0.77)
MET + GLP-L		–2.44 (–3.51 to –1.36)
MET + GLP-H		–3.36 (–4.24 to –2.48)
MET + AGI-T		–1.64 (–3.05 to –0.24)
MET + AGI-L		–1.08 (–3.58 to 1.42)

Treatment	Reference	MD (95% CrI)
MET + TZD-T		1.09 (–0.10 to 2.26)
MET + TZD-L		–0.14 (–1.57 to 1.28)
MET + TZD-H		1.08 (0.12 to 2.05)
MET + INS-BA-T		1.23 (0.06 to 2.41)
MET + INS-BI-T		1.68 (0.35 to 3.03)
MET + DPP-H	MET + DPP-L	–0.10 (–0.63 to 0.43)
MET + MEG-T		3.01 (1.00 to 5.02)
MET + MEG-L		–0.10 (–1.55 to 1.37)
MET + MEG-H		0.38 (–0.77 to 1.54)
MET + SGL-L		–2.12 (–2.82 to –1.41)
MET + SGL-H		–2.52 (–3.19 to –1.85)
MET + GLP-T		–0.78 (–2.09 to 0.51)
MET + GLP-L		–0.96 (–1.83 to –0.09)
MET + GLP-H		–1.88 (–2.54 to –1.23)
MET + AGI-T		–0.17 (–1.39 to 1.05)
MET + AGI-L		0.40 (–2.07 to 2.86)
MET + TZD-T		2.56 (1.62 to 3.51)
MET + TZD-L		1.33 (0.12 to 2.54)
MET + TZD-H		2.55 (1.86 to 3.26)
MET + INS-BA-T		2.71 (1.73 to 3.70)
MET + INS-BI-T		3.16 (1.97 to 4.36)
MET + MEG-T	MET + DPP-H	3.11 (1.15 to 5.09)
MET + MEG-L		0.01 (–1.39 to 1.41)
MET + MEG-H		0.48 (–0.60 to 1.57)
MET + SGL-L		–2.02 (–2.56 to –1.47)
MET + SGL-H		–2.42 (–2.92 to –1.92)
MET + GLP-T		–0.68 (–1.90 to 0.52)
MET + GLP-L		–0.86 (–1.60 to –0.12)
MET + GLP-H		–1.78 (–2.25 to –1.32)
MET + AGI-T		–0.07 (–1.22 to 1.08)
MET + AGI-L		0.50 (–1.91 to 2.92)
MET + TZD-T		2.66 (1.85 to 3.47)
MET + TZD-L		1.43 (0.27 to 2.60)
MET + TZD-H		2.66 (2.11 to 3.21)
MET + INS-BA-T		2.81 (1.96 to 3.68)
MET + INS-BI-T		3.26 (2.17 to 4.37)
MET + MEG-L	MET + MEG-T	–3.10 (–5.47 to –0.72)
MET + MEG-H		–2.63 (–4.82 to –0.43)
MET + SGL-L		–5.12 (–7.13 to –3.12)
MET + SGL-H		–5.53 (–7.53 to –3.53)
MET + GLP-T		–3.79 (–6.11 to –1.51)
MET + GLP-L		–3.97 (–6.06 to –1.89)

Treatment	Reference	MD (95% CrI)
MET + GLP-H		–4.89 (–6.89 to –2.90)
MET + AGI-T		–3.17 (–5.42 to –0.95)
MET + AGI-L		–2.61 (–5.71 to 0.49)
MET + TZD-T		–0.44 (–2.57 to 1.67)
MET + TZD-L		–1.67 (–3.94 to 0.58)
MET + TZD-H		–0.45 (–2.47 to 1.56)
MET + INS-BA-T		–0.30 (–2.43 to 1.84)
MET + INS-BI-T		0.15 (–2.09 to 2.39)
MET + MEG-H	MET + MEG-L	0.48 (–0.88 to 1.83)
MET + SGL-L		–2.02 (–3.48 to –0.57)
MET + SGL-H		–2.42 (–3.87 to –0.99)
MET + GLP-T		–0.69 (–2.53 to 1.14)
MET + GLP-L		–0.87 (–2.40 to 0.68)
MET + GLP-H		–1.79 (–3.23 to –0.35)
MET + AGI-T		–0.07 (–1.83 to 1.67)
MET + AGI-L		0.49 (–2.28 to 3.29)
MET + TZD-T		2.66 (1.05 to 4.26)
MET + TZD-L		1.43 (–0.36 to 3.22)
MET + TZD-H		2.65 (1.18 to 4.12)
MET + INS-BA-T		2.80 (1.19 to 4.43)
MET + INS-BI-T		3.25 (1.50 to 5.01)
MET + SGL-L	MET + MEG-H	–2.50 (–3.64 to –1.35)
MET + SGL-H		–2.90 (–4.03 to –1.77)
MET + GLP-T		–1.16 (–2.77 to 0.43)
MET + GLP-L		–1.34 (–2.60 to –0.08)
MET + GLP-H		–2.26 (–3.39 to –1.13)
MET + AGI-T		–0.55 (–2.06 to 0.95)
MET + AGI-L		0.02 (–2.61 to 2.66)
MET + TZD-T		2.18 (0.85 to 3.52)
MET + TZD-L		0.95 (–0.59 to 2.51)
MET + TZD-H		2.17 (1.00 to 3.35)
MET + INS-BA-T		2.33 (0.97 to 3.69)
MET + INS-BI-T		2.78 (1.27 to 4.29)
MET + SGL-H	MET + SGL-L	–0.40 (–0.90 to 0.09)
MET + GLP-T		1.33 (0.03 to 2.63)
MET + GLP-L		1.15 (0.28 to 2.02)
MET + GLP-H		0.23 (–0.42 to 0.89)
MET + AGI-T		1.95 (0.74 to 3.16)
MET + AGI-L		2.52 (0.05 to 4.99)
MET + TZD-T		4.68 (3.72 to 5.63)
MET + TZD-L		3.45 (2.19 to 4.70)
MET + TZD-H		4.67 (3.95 to 5.39)

Treatment	Reference	MD (95% CrI)
MET + INS-BA-T		4.82 (3.84 to 5.82)
MET + INS-BI-T		5.27 (4.08 to 6.48)
MET + GLP-T	MET + SGL-H	1.74 (0.45 to 3.02)
MET + GLP-L		1.56 (0.71 to 2.40)
MET + GLP-H		0.64 (0.01 to 1.25)
MET + AGI-T		2.35 (1.15 to 3.54)
MET + AGI-L		2.92 (0.46 to 5.38)
MET + TZD-T		5.08 (4.16 to 6.00)
MET + TZD-L		3.85 (2.62 to 5.09)
MET + TZD-H		5.07 (4.39 to 5.76)
MET + INS-BA-T		5.23 (4.27 to 6.20)
MET + INS-BI-T		5.68 (4.51 to 6.86)
MET + GLP-L	MET + GLP-T	–0.18 (–1.57 to 1.23)
MET + GLP-H		–1.10 (–2.37 to 0.17)
MET + AGI-T		0.61 (–1.02 to 2.25)
MET + AGI-L		1.18 (–1.50 to 3.91)
MET + TZD-T		3.35 (1.92 to 4.77)
MET + TZD-L		2.12 (0.47 to 3.78)
MET + TZD-H		3.34 (2.03 to 4.65)
MET + INS-BA-T		3.49 (2.09 to 4.93)
MET + INS-BI-T		3.94 (2.36 to 5.54)
MET + GLP-H	MET + GLP-L	–0.92 (–1.63 to –0.21)
MET + AGI-T		0.80 (–0.53 to 2.11)
MET + AGI-L		1.36 (–1.15 to 3.90)
MET + TZD-T		3.53 (2.44 to 4.61)
MET + TZD-L		2.30 (0.94 to 3.64)
MET + TZD-H		3.52 (2.65 to 4.39)
MET + INS-BA-T		3.67 (2.60 to 4.76)
MET + INS-BI-T		4.12 (2.87 to 5.39)
MET + AGI-T	MET + GLP-H	1.71 (0.52 to 2.91)
MET + AGI-L		2.28 (–0.17 to 4.73)
MET + TZD-T		4.45 (3.54 to 5.36)
MET + TZD-L		3.22 (1.99 to 4.44)
MET + TZD-H		4.44 (3.81 to 5.07)
MET + INS-BA-T		4.59 (3.74 to 5.46)
MET + INS-BI-T		5.04 (3.99 to 6.11)
MET + AGI-L	MET + AGI-T	0.57 (–2.10 to 3.23)
MET + TZD-T		2.73 (1.34 to 4.13)
MET + TZD-L		1.50 (–0.11 to 3.11)
MET + TZD-H		2.72 (1.49 to 3.97)
MET + INS-BA-T		2.88 (1.47 to 4.30)

Treatment	Reference	MD (95% CrI)
MET + INS-BI-T		3.33 (1.78 to 4.90)
MET + TZD-T	MET + AGI-L	2.16 (–0.37 to 4.71)
MET + TZD-L		0.93 (–1.74 to 3.60)
MET + TZD-H		2.15 (–0.32 to 4.62)
MET + INS-BA-T		2.31 (–0.26 to 4.88)
MET + INS-BI-T		2.76 (0.12 to 5.43)
MET + TZD-L	MET + TZD-T	–1.23 (–2.64 to 0.18)
MET + TZD-H		–0.01 (–0.96 to 0.96)
MET + INS-BA-T		0.14 (–1.00 to 1.31)
MET + INS-BI-T		0.59 (–0.74 to 1.95)
MET + TZD-H	MET + TZD-L	1.22 (0.03 to 2.41)
MET + INS-BA-T		1.37 (–0.04 to 2.81)
MET + INS-BI-T		1.82 (0.25 to 3.41)
MET + INS-BA-T	MET + TZD-H	0.15 (–0.82 to 1.15)
MET + INS-BI-T		0.60 (–0.58 to 1.81)
MET + INS-BI-T	MET + INS-BA-T	0.45 (–0.52 to 1.42)
Random-effects model	Residual deviance	227.2 vs. 250 data points
	Deviance information criteria	523.569

AGI = alpha-glucosidase inhibitors; CrI = credible interval; DPP = dipeptidyl peptidase-4 inhibitor; GLP = glucagon-like peptide-1 agonist; -H = high-dose; INS-BA = basal insulin; INS-BI = biphasic insulin; -L = low-dose; MEG = meglitinide; MD = mean difference; MET = metformin; SGL = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; -T = titrated; TZD = thiazolidinedione; vs. = versus.

Appendix 11: Detailed Network Meta-Analysis Results for the Individual Drug-Level Analysis

Legend

Table 36: Treatment Legend for Individual-Drug Network Meta-Analyses

Treatment	Abbreviation	Drug Class
Acarbose	ACA	Alpha-glucosidase inhibitor
Acetoheximide	ACE	Sulfonylurea
Albiglutide	ALB	GLP-1 receptor agonist
Alogliptin	ALO	DPP-4 inhibitor
Alogliptin/metformin fixed dose combination	AMC	DPP-4 inhibitor
Canagliflozin	CAN	SGLT-2 inhibitor
Chlorpropamide	CHL	Sulfonylurea
Chlorpropamide	CHO	Sulfonylurea
Dapagliflozin fixed dose combination	DAC	SGLT-2 inhibitor
Dapagliflozin	DAP	SGLT-2 inhibitor
Insulin degludec/insulin aspart mix	DSP	Insulin
Dulaglutide	DUL	GLP-1 receptor agonist
Empagliflozin fixed dose combination	EMC	SGLT-2 inhibitor
Empagliflozin	EMP	SGLT-2 inhibitor
Exenatide	EXE	GLP-1 receptor agonist
Gemigliptin	GEM	DPP-4 inhibitor
Glicazide/glicazide MR	GLC	Sulfonylurea
Glipizide	GLI	Sulfonylurea
Gliclazide	GLL	Sulfonylurea
Glimepiride	GLM	Sulfonylurea
Gliquidone	GLQ	Sulfonylurea
Glyburide (also known as or same as glibenclamide)	GLY	Sulfonylurea
Insulin aspart/aspart protamine]mixture	IAM	Insulin
Insulin aspart	IAS	Insulin
Insulin detemir	IDE	Insulin
Insulin glargine	IGA	Insulin
Insulin glargine biosimilars	IGB	Insulin
Insulin glulisine	IGL	Insulin
Insulin lispro	ILI	Insulin
Insulin lispro/lispro protamine mixture	ILM	Insulin
Insulin degludec	IND	Insulin
Insulin pork (nph/hypurin nph)	INM	Insulin
Insulin pork	INP	Insulin
Long-acting glicazide (aka modified release)	LGL	Sulfonylurea

Treatment	Abbreviation	Drug Class
Linagliptin	LIN	DPP-4 inhibitor
Liraglutide	LIR	GLP-1 receptor agonist
Lixisenatide	LIX	GLP-1 receptor agonist
Linagliptin/metformin fixed dose combination	LMC	DPP-4 inhibitor
Metformin	MET	Biguanide
Miglitol	MIG	Alpha-glucosidase inhibitor
Mitiglinide	MIT	Meglitintide
Nateglinide	NAT	Meglitintide
NPH (neutral protamine Hagedorn) insulin	NIN	Insulin
NPH insulin regular/insulin mixture	NIR	Insulin
NPH insulin regular/insulin mixture	NIRH	Insulin
NPH insulin regular/insulin mixture	NIRN	Insulin
NPH insulin regular/insulin mixture	NIRO	Insulin
Omarigliptin	OMA	DPP-4 inhibitor
Pioglitazone	PIO	Thiazolidinedione
Placebo	PLA	Not applicable
Pioglitazone/metformin fixed dose combination	PMC	Thiazolidinedione
Repaglinide	REP	Meglitintide
Regular insulin	RIN	Insulin
Rosiglitazone	ROS	Thiazolidinedione
Saxagliptin/metformin fixed dose combination	SAC	DPP-4 inhibitor
Saxagliptin	SAX	DPP-4 inhibitor
Septagliptin	SEP	DPP-4 inhibitor
Sitagliptin	SIT	DPP-4 inhibitor
Sitagliptin/metformin fixed dose combination	SMC	DPP-4 inhibitor
Tenegliptan	TEN	DPP-4 inhibitor
Trelagliptin/metformin fixed dose combination	TMC	DPP-4 inhibitor
Tolbutamide	TOL	Sulfonylurea
Tolzamide	TOZ	Sulfonylurea
Trelagliptin	TRE	DPP-4 inhibitor
Vildagliptin	VIL	DPP-4 inhibitor
Vildagliptin/metformin fixed dose combination	VMC	DPP-4 inhibitor
Voglibose	VOG	Alpha-glucosidase inhibitor
Sitagliptin XR/metformin fixed dose combination	XSM	DPP-4 inhibitor

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; MR = modified release; SGLT-2 = sodium-glucose cotransporter-2; XR = extended release.

Fractures (People)

Table 37: Fractures (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	1.40 (0.17 to 14.02)	1.40 (0.17 to 12.79)	0.37 (–1.08 to 8.97)
MET + SAX		3.03 (0.48 to 26.79)	2.97 (0.48 to 22.85)	1.87 (–0.61 to 14.70)
MET + DAP		1.11 (0.31 to 3.76)	1.11 (0.32 to 3.69)	0.10 (–0.95 to 1.88)
MET + EMP		1.56 (0.16 to 17.51)	1.55 (0.16 to 15.52)	0.51 (–1.08 to 11.20)
MET + PIO		0.94 (0.21 to 4.32)	0.94 (0.21 to 4.21)	–0.05 (–1.01 to 2.78)
MET + SAX	MET + GLM	2.18 (0.60 to 9.24)	2.13 (0.61 to 8.69)	1.24 (–1.80 to 9.67)
MET + DAP		0.77 (0.06 to 8.92)	0.77 (0.07 to 8.76)	–0.29 (–8.97 to 2.02)
MET + EMP		1.12 (0.44 to 2.86)	1.12 (0.45 to 2.78)	0.10 (–1.87 to 4.60)
MET + PIO		0.65 (0.04 to 10.11)	0.65 (0.05 to 9.86)	–0.40 (–8.93 to 2.79)
MET + DAP	MET + SAX	0.35 (0.03 to 3.38)	0.36 (0.04 to 3.33)	–1.77 (–14.64 to 1.47)
MET + EMP		0.51 (0.09 to 2.45)	0.52 (0.10 to 2.34)	–1.05 (–9.67 to 4.17)
MET + PIO		0.30 (0.02 to 3.48)	0.31 (0.03 to 3.40)	–1.83 (–14.69 to 1.93)
MET + EMP	MET + DAP	1.44 (0.11 to 19.90)	1.43 (0.11 to 17.75)	0.42 (–1.98 to 11.02)
MET + PIO		0.85 (0.13 to 6.51)	0.86 (0.13 to 6.33)	–0.14 (–2.10 to 2.96)
MET + PIO	MET + EMP	0.58 (0.04 to 10.20)	0.59 (0.04 to 9.98)	–0.52 (–11.09 to 2.69)
Random-effects model	Residual deviance	11.94 vs. 14 data points		
	Deviance information criteria	65.125		

CrI = credible interval; DAP = dapagliflozin; EMP = empagliflozin; GLM = glimepiride; MET = metformin; OR = odds ratio; PIO = pioglitazone; RD = risk difference; RR = relative risk; SAX = saxagliptin; vs. = versus.

Heart Failure

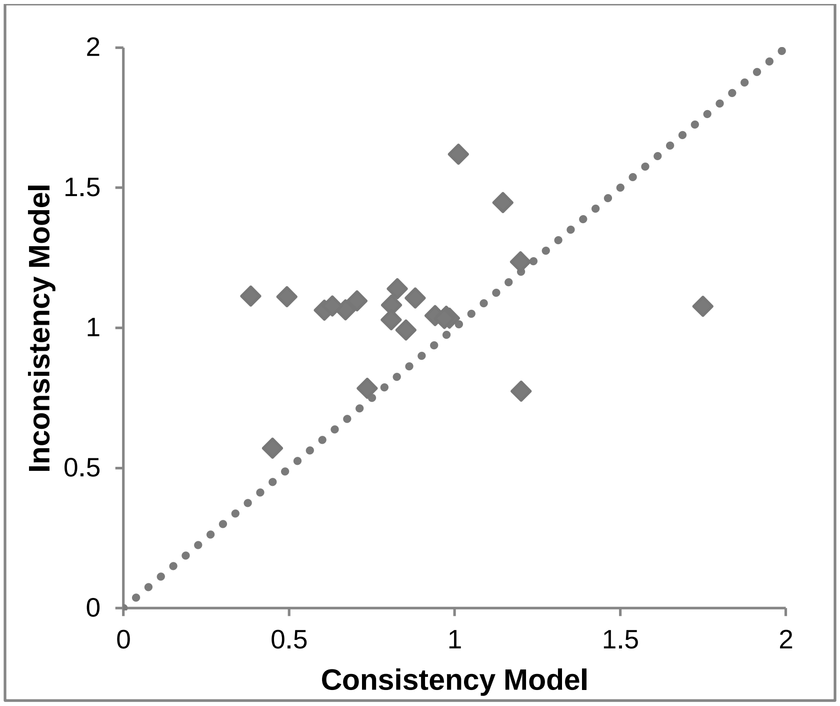
Table 38: Heart Failure: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLC	MET	1.65 (0.23 to 9.83)	1.64 (0.24 to 9.22)	0.52 (–0.89 to 6.50)
MET + GLM		1.29 (0.29 to 7.00)	1.28 (0.29 to 6.75)	0.23 (–0.93 to 3.68)
MET + GLI		0.48 (0.02 to 14.38)	0.49 (0.02 to 12.83)	–0.37 (–1.36 to 10.46)
MET + SAX		0.20 (0.02 to 1.94)	0.21 (0.02 to 1.92)	–0.61 (–1.49 to 0.64)
MET + ALO		0.43 (0.07 to 2.32)	0.43 (0.07 to 2.30)	–0.45 (–1.37 to 0.78)
MET + LIN		1.51 (0.15 to 16.46)	1.50 (0.15 to 14.87)	0.40 (–1.03 to 9.92)
MET + SIT		1.02 (0.09 to 11.46)	1.02 (0.09 to 10.84)	0.01 (–1.24 to 5.68)
MET + VIL		0.91 (0.08 to 10.77)	0.92 (0.08 to 10.14)	–0.07 (–1.22 to 6.39)
MET + PIO		3.61 (1.53 to 10.13)	3.53 (1.52 to 9.67)	2.10 (0.52 to 5.71)
MET + GLM	MET + GLC	0.79 (0.08 to 8.28)	0.79 (0.08 to 8.08)	–0.24 (–6.33 to 3.19)
MET + GLI		0.31 (0.01 to 11.97)	0.31 (0.01 to 10.89)	–0.67 (–6.84 to 9.55)
MET + SAX		0.13 (0.01 to 2.07)	0.13 (0.01 to 2.06)	–1.10 (–7.21 to 0.52)
MET + ALO		0.26 (0.02 to 3.06)	0.27 (0.02 to 3.04)	–0.94 (–7.01 to 0.70)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIN		0.94 (0.06 to 18.64)	0.94 (0.06 to 16.97)	–0.07 (–6.09 to 9.43)
MET + SIT		0.63 (0.03 to 11.22)	0.64 (0.04 to 10.63)	–0.40 (–6.55 to 5.07)
MET + VIL		0.57 (0.03 to 9.68)	0.58 (0.03 to 9.32)	–0.44 (–6.47 to 5.56)
MET + PIO		2.23 (0.45 to 13.13)	2.19 (0.47 to 12.69)	1.44 (–3.38 to 4.58)
MET + GLI	MET + GLM	0.36 (0.02 to 12.00)	0.37 (0.02 to 10.87)	–0.50 (–3.35 to 9.80)
MET + SAX		0.17 (0.01 to 0.96)	0.17 (0.01 to 0.96)	–0.82 (–3.79 to –0.02)
MET + ALO		0.32 (0.03 to 3.13)	0.32 (0.03 to 3.09)	–0.67 (–4.14 to 0.87)
MET + LIN		1.15 (0.19 to 7.68)	1.14 (0.19 to 7.02)	0.13 (–1.76 to 8.39)
MET + SIT		0.78 (0.07 to 7.67)	0.78 (0.07 to 7.36)	–0.19 (–3.03 to 4.82)
MET + VIL		0.72 (0.09 to 4.76)	0.72 (0.09 to 4.58)	–0.22 (–2.50 to 4.88)
MET + PIO		2.85 (0.51 to 14.92)	2.79 (0.52 to 14.32)	1.79 (–1.85 to 5.64)
MET + SAX	MET + GLI	0.43 (0.02 to 5.43)	0.43 (0.02 to 5.41)	–0.17 (–10.60 to 0.45)
MET + ALO		0.92 (0.02 to 32.32)	0.92 (0.02 to 32.14)	–0.02 (–11.05 to 1.24)
MET + LIN		3.24 (0.07 to 119.10)	3.19 (0.08 to 112.00)	0.59 (–9.29 to 9.94)
MET + SIT		2.18 (0.04 to 97.68)	2.16 (0.04 to 94.97)	0.31 (–10.10 to 5.66)
MET + VIL		1.96 (0.04 to 76.34)	1.95 (0.04 to 73.89)	0.23 (–9.84 to 6.03)
MET + PIO		7.73 (0.23 to 195.40)	7.51 (0.26 to 187.50)	2.27 (–8.28 to 6.13)
MET + ALO	MET + SAX	2.02 (0.12 to 39.29)	2.01 (0.12 to 38.92)	0.15 (–1.12 to 1.37)
MET + LIN		7.18 (0.59 to 151.20)	7.06 (0.59 to 140.70)	0.98 (–0.21 to 10.44)
MET + SIT		4.97 (0.24 to 109.10)	4.92 (0.24 to 105.30)	0.60 (–0.61 to 5.99)
MET + VIL		4.41 (0.31 to 96.31)	4.37 (0.31 to 93.63)	0.52 (–0.50 to 6.70)
MET + PIO		17.88 (1.70 to 218.50)	17.36 (1.68 to 210.20)	2.74 (0.70 to 6.45)
MET + LIN	MET + ALO	3.55 (0.21 to 60.20)	3.51 (0.21 to 55.06)	0.82 (–0.87 to 10.44)
MET + SIT		2.46 (0.14 to 47.02)	2.44 (0.14 to 44.20)	0.46 (–1.09 to 6.03)
MET + VIL		2.15 (0.09 to 45.45)	2.14 (0.10 to 42.27)	0.35 (–1.08 to 6.86)
MET + PIO		8.50 (1.59 to 57.53)	8.25 (1.58 to 54.69)	2.54 (0.59 to 6.24)
MET + SIT	MET + LIN	0.66 (0.04 to 12.26)	0.66 (0.04 to 11.90)	–0.32 (–9.31 to 4.58)
MET + VIL		0.59 (0.04 to 8.83)	0.59 (0.05 to 8.48)	–0.37 (–8.76 to 4.90)
MET + PIO		2.44 (0.22 to 29.44)	2.39 (0.23 to 28.08)	1.56 (–7.73 to 5.49)
MET + VIL	MET + SIT	0.94 (0.04 to 17.69)	0.94 (0.04 to 16.70)	–0.04 (–5.14 to 5.71)
MET + PIO		3.59 (0.32 to 41.88)	3.51 (0.33 to 39.90)	2.01 (–3.94 to 5.97)
MET + PIO	MET + VIL	4.07 (0.35 to 48.72)	3.97 (0.36 to 46.68)	2.01 (–4.07 to 5.87)
Random-effects model	Residual deviance	19.04 vs. 22 data points		
	Deviance information criteria	91.48		

ALO = alogliptin; CrI = credible interval; GLC = glicazide; GLI = glipizide; GLM = glimepiride; LIN = linagliptin; MET = metformin; OR = odds ratio; PIO = pioglitazone; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 22: Consistency Plot for Heart Failure (Individual-Drug Case Analysis)



Nocturnal Hypoglycemia

Table 39: Nocturnal Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + DUL	MET + SIT	1.49 (0.45 to 5.43)	1.47 (0.46 to 4.88)	1.37 (–1.87 to 10.04)
MET + IAS		1.96 (0.30 to 11.53)	1.91 (0.31 to 8.98)	2.66 (–2.31 to 21.25)
MET + IGA		5.90 (1.72 to 20.57)	5.14 (1.68 to 14.05)	12.34 (2.16 to 32.42)
MET + DSP		12.97 (1.66 to 118.00)	9.53 (1.63 to 29.45)	24.98 (2.00 to 74.22)
MET + IAS	MET + DUL	1.32 (0.13 to 11.32)	1.30 (0.15 to 8.92)	1.24 (–8.68 to 19.80)
MET + IGA		3.93 (0.66 to 23.15)	3.47 (0.69 to 16.17)	10.76 (–3.01 to 30.41)
MET + DSP		8.59 (0.74 to 112.80)	6.28 (0.77 to 31.96)	23.25 (–1.88 to 72.12)
MET + IGA	MET + IAS	3.00 (0.88 to 11.82)	2.67 (0.91 to 9.88)	8.93 (–1.27 to 21.39)
MET + DSP		6.52 (0.85 to 64.10)	4.71 (0.88 to 25.05)	21.05 (–1.07 to 65.79)
MET + DSP	MET + IGA	2.12 (0.45 to 13.68)	1.77 (0.50 to 4.87)	11.79 (–7.89 to 53.18)
Random-effects model	Residual deviance	8.187 vs. 8 data points		
	Deviance information criteria	49.407		

CrI = credible interval; DSP = insulin degludec/insulin aspart mix; DUL = dulaglutide; IAS = insulin aspart; IGA = insulin glargine; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SIT = sitagliptin; vs. = versus.

Nonsevere Hypoglycemia

Table 40: Nonservere Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLC	MET	7.48 (1.97 to 32.64)	6.65 (1.93 to 20.67)	10.69 (1.75 to 36.20)
MET + GLM		5.58 (3.42 to 9.50)	5.13 (3.26 to 8.27)	7.82 (4.44 to 13.06)
MET + GLY		12.78 (4.30 to 38.85)	10.42 (4.03 to 23.28)	17.88 (5.91 to 40.33)
MET + GLI		10.49 (4.81 to 23.46)	8.87 (4.47 to 16.80)	14.96 (6.66 to 28.52)
MET + NAT		6.11 (2.03 to 20.30)	5.57 (1.99 to 15.01)	8.66 (1.89 to 26.11)
MET + SAX		0.78 (0.46 to 1.38)	0.78 (0.47 to 1.37)	–0.41 (–1.12 to 0.65)
MET + ALO		0.43 (0.12 to 1.43)	0.44 (0.13 to 1.42)	–1.06 (–1.83 to 0.77)
MET + LIN		0.58 (0.23 to 1.32)	0.59 (0.24 to 1.31)	–0.77 (–1.56 to 0.55)
MET + SIT		0.94 (0.59 to 1.59)	0.94 (0.59 to 1.57)	–0.11 (–0.86 to 0.98)
MET + VIL		0.90 (0.31 to 2.79)	0.91 (0.31 to 2.71)	–0.18 (–1.42 to 3.00)
MET + CAN		1.36 (0.61 to 3.03)	1.35 (0.61 to 2.92)	0.65 (–0.78 to 3.48)
MET + DAP		0.72 (0.29 to 1.75)	0.73 (0.29 to 1.72)	–0.51 (–1.45 to 1.30)
MET + EMP		0.84 (0.39 to 1.95)	0.84 (0.40 to 1.92)	–0.30 (–1.23 to 1.67)
MET + LIR		0.56 (0.24 to 1.42)	0.56 (0.24 to 1.41)	–0.82 (–1.59 to 0.74)
MET + EXE		1.42 (0.59 to 3.37)	1.41 (0.59 to 3.23)	0.78 (–0.80 to 4.12)
MET + DUL		0.92 (0.32 to 2.89)	0.92 (0.33 to 2.79)	–0.14 (–1.36 to 3.26)
MET + LIX		0.82 (0.39 to 1.72)	0.82 (0.40 to 1.70)	–0.33 (–1.21 to 1.28)
MET + ROS		1.33 (0.50 to 3.54)	1.33 (0.51 to 3.38)	0.61 (–0.99 to 4.32)
MET + PIO		0.40 (0.17 to 0.85)	0.40 (0.17 to 0.85)	–1.12 (–1.72 to –0.27)
MET + IND		3.54 (0.75 to 16.14)	3.38 (0.76 to 12.61)	4.48 (–0.46 to 21.64)
MET + IAS		13.76 (4.58 to 41.68)	11.06 (4.27 to 24.07)	19.12 (6.34 to 42.12)
MET + IGA		4.98 (2.12 to 11.20)	4.63 (2.07 to 9.45)	6.85 (2.07 to 15.54)
MET + DSP		10.49 (2.37 to 44.36)	8.87 (2.31 to 24.80)	14.94 (2.52 to 43.71)
MET + GLM	MET + GLC	0.75 (0.16 to 3.16)	0.78 (0.23 to 2.92)	–2.75 (-28.37 to 7.78)
MET + GLY		1.73 (0.34 to 7.65)	1.57 (0.42 to 5.66)	6.72 (–18.20 to 28.56)
MET + GLI		1.41 (0.27 to 6.58)	1.34 (0.36 to 5.30)	4.10 (-22.06 to 20.36)
MET + NAT		0.83 (0.28 to 2.32)	0.85 (0.35 to 2.13)	–1.71 (–19.42 to 8.70)
MET + SAX		0.10 (0.02 to 0.45)	0.12 (0.03 to 0.46)	–11.05 (-36.52 to –1.99)
MET + ALO		0.06 (0.01 to 0.34)	0.07 (0.01 to 0.35)	–11.61 (-37.02 to –2.53)
MET + LIN		0.08 (0.01 to 0.37)	0.09 (0.02 to 0.38)	–11.39 (-37.04 to –2.36)
MET + SIT		0.13 (0.03 to 0.52)	0.14 (0.04 to 0.53)	–10.73 (-36.27 to –1.75)
MET + VIL		0.12 (0.02 to 0.71)	0.14 (0.03 to 0.72)	–10.69 (-36.19 to –1.21)
MET + CAN		0.18 (0.03 to 0.83)	0.20 (0.05 to 0.84)	–9.87 (-35.45 to –0.67)
MET + DAP		0.10 (0.02 to 0.48)	0.11 (0.03 to 0.49)	–11.10 (-36.60 to –2.01)
MET + EMP		0.11 (0.02 to 0.55)	0.13 (0.03 to 0.56)	–10.89 (-36.50 to –1.68)
MET + LIR		0.07 (0.01 to 0.37)	0.08 (0.02 to 0.38)	–11.43 (-36.85 to –2.38)
MET + EXE		0.19 (0.04 to 0.89)	0.21 (0.05 to 0.89)	–9.73 (-35.26 to –0.44)
MET + DUL		0.12 (0.02 to 0.70)	0.14 (0.03 to 0.71)	–10.60 (-35.94 to –1.21)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX		0.11 (0.02 to 0.50)	0.13 (0.03 to 0.51)	–10.94 (-36.44 to –1.87)
MET + ROS		0.18 (0.04 to 0.68)	0.20 (0.06 to 0.70)	–9.86 (-34.81 to –1.28)
MET + PIO		0.05 (0.01 to 0.24)	0.06 (0.01 to 0.25)	–11.75 (-37.30 to –2.79)
MET + IND		0.48 (0.06 to 3.42)	0.52 (0.08 to 2.96)	–5.62 (-31.08 to 12.31)
MET + IAS		1.87 (0.33 to 8.82)	1.67 (0.42 to 6.27)	8.03 (–18.23 to 31.21)
MET + IGA		0.67 (0.13 to 2.94)	0.70 (0.18 to 2.70)	–3.63 (-29.22 to 8.25)
MET + DSP		1.40 (0.19 to 9.39)	1.33 (0.24 to 6.32)	3.88 (-23.13 to 33.15)
MET + GLY	MET + GLM	2.29 (0.69 to 7.43)	2.03 (0.72 to 4.90)	10.00 (–3.32 to 32.51)
MET + GLI		1.89 (0.80 to 4.37)	1.73 (0.82 to 3.43)	7.05 (–2.15 to 20.55)
MET + NAT		1.10 (0.32 to 3.96)	1.09 (0.34 to 3.17)	0.82 (–8.01 to 18.48)
MET + SAX		0.14 (0.08 to 0.26)	0.15 (0.09 to 0.27)	–8.20 (–13.27 to –4.83)
MET + ALO		0.08 (0.02 to 0.27)	0.09 (0.02 to 0.28)	–8.78 (–14.11 to –5.08)
MET + LIN		0.11 (0.04 to 0.21)	0.12 (0.05 to 0.23)	–8.52 (–13.51 to –5.34)
MET + SIT		0.17 (0.09 to 0.30)	0.18 (0.11 to 0.32)	–7.89 (–13.05 to –4.50)
MET + VIL		0.16 (0.05 to 0.53)	0.18 (0.06 to 0.55)	–7.83 (–13.34 to –3.35)
MET + CAN		0.24 (0.10 to 0.60)	0.26 (0.11 to 0.62)	–7.04 (–12.50 to –2.80)
MET + DAP		0.13 (0.04 to 0.35)	0.14 (0.05 to 0.37)	–8.25 (–13.71 to –4.38)
MET + EMP		0.15 (0.07 to 0.33)	0.16 (0.08 to 0.35)	–8.02 (–12.87 to –4.68)
MET + LIR		0.10 (0.04 to 0.24)	0.11 (0.05 to 0.26)	–8.57 (–13.57 to –5.19)
MET + EXE		0.25 (0.10 to 0.65)	0.27 (0.11 to 0.67)	–6.92 (–12.38 to –2.54)
MET + DUL		0.17 (0.06 to 0.50)	0.18 (0.06 to 0.53)	–7.77 (–12.90 to –3.74)
MET + LIX		0.15 (0.06 to 0.34)	0.16 (0.07 to 0.36)	–8.08 (–13.39 to –4.38)
MET + ROS		0.24 (0.08 to 0.70)	0.26 (0.09 to 0.71)	–7.06 (–12.77 to –2.14)
MET + PIO		0.07 (0.03 to 0.17)	0.08 (0.03 to 0.18)	–8.90 (–14.14 to –5.51)
MET + IND		0.64 (0.13 to 2.98)	0.66 (0.14 to 2.54)	–3.19 (–10.67 to 13.76)
MET + IAS		2.49 (0.75 to 7.73)	2.17 (0.77 to 4.97)	11.22 (–2.68 to 34.03)
MET + IGA		0.90 (0.34 to 2.14)	0.91 (0.37 to 1.96)	–0.88 (–8.00 to 7.87)
MET + DSP		1.90 (0.40 to 8.02)	1.74 (0.43 to 4.97)	7.11 (–6.44 to 35.48)
MET + GLI	MET + GLY	0.83 (0.22 to 3.06)	0.86 (0.31 to 2.56)	–2.78 (-26.27 to 15.08)
MET + NAT		0.48 (0.11 to 2.19)	0.54 (0.16 to 1.92)	–8.68 (-31.02 to 10.65)
MET + SAX		0.06 (0.02 to 0.20)	0.08 (0.03 to 0.22)	–18.27 (-40.69 to –6.19)
MET + ALO		0.03 (0.01 to 0.16)	0.04 (0.01 to 0.18)	–18.80 (-41.23 to –6.76)
MET + LIN		0.05 (0.01 to 0.17)	0.06 (0.02 to 0.19)	–18.56 (-41.06 to –6.51)
MET + SIT		0.07 (0.02 to 0.23)	0.09 (0.04 to 0.25)	–17.95 (-40.23 to –6.01)
MET + VIL		0.07 (0.02 to 0.33)	0.09 (0.02 to 0.36)	–17.79 (-40.34 to –5.49)
MET + CAN		0.11 (0.03 to 0.39)	0.13 (0.04 to 0.41)	–17.05 (-39.46 to –4.90)
MET + DAP		0.06 (0.01 to 0.23)	0.07 (0.02 to 0.25)	–18.30 (-40.84 to –6.23)
MET + EMP		0.07 (0.02 to 0.26)	0.08 (0.03 to 0.28)	–18.08 (-40.52 to –5.85)
MET + LIR		0.04 (0.01 to 0.18)	0.05 (0.02 to 0.19)	–18.63 (-40.96 to –6.56)
MET + EXE		0.11 (0.03 to 0.39)	0.14 (0.05 to 0.42)	–16.90 (-39.00 to –5.02)
MET + DUL		0.07 (0.02 to 0.34)	0.09 (0.03 to 0.37)	–17.80 (-39.96 to –5.43)
MET + LIX		0.06 (0.02 to 0.23)	0.08 (0.03 to 0.25)	–18.08 (-40.53 to –6.11)

CADTH

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ROS		0.11 (0.05 to 0.22)	0.13 (0.06 to 0.25)	–17.11 (-37.44 to –6.37)
MET + PIO		0.03 (0.01 to 0.11)	0.04 (0.01 to 0.12)	–18.96 (-41.45 to –6.97)
MET + IND		0.28 (0.05 to 1.54)	0.33 (0.07 to 1.43)	–12.58 (-34.62 to 5.50)
MET + IAS		1.09 (0.41 to 2.80)	1.07 (0.50 to 2.24)	1.24 (–14.92 to 17.66)
MET + IGA		0.39 (0.12 to 1.19)	0.44 (0.18 to 1.17)	–10.69 (-31.55 to 1.69)
MET + DSP		0.81 (0.16 to 4.33)	0.85 (0.21 to 3.05)	–2.88 (-26.40 to 26.41)
MET + NAT	MET + GLI	0.58 (0.15 to 2.48)	0.63 (0.19 to 2.10)	–6.03 (-21.46 to 13.00)
MET + SAX		0.07 (0.03 to 0.16)	0.09 (0.05 to 0.18)	–15.36 (-28.67 to –7.18)
MET + ALO		0.04 (0.01 to 0.11)	0.05 (0.02 to 0.13)	–15.94 (-28.83 to –8.02)
MET + LIN		0.06 (0.02 to 0.16)	0.07 (0.02 to 0.18)	–15.67 (-29.32 to –7.36)
MET + SIT		0.09 (0.04 to 0.19)	0.11 (0.06 to 0.21)	–15.04 (-28.27 to –6.92)
MET + VIL		0.09 (0.02 to 0.31)	0.10 (0.03 to 0.34)	–14.94 (-28.63 to –6.30)
MET + CAN		0.13 (0.04 to 0.36)	0.15 (0.06 to 0.39)	–14.15 (-27.67 to –5.64)
MET + DAP		0.07 (0.02 to 0.22)	0.08 (0.03 to 0.24)	–15.41 (-29.07 to –6.95)
MET + EMP		0.08 (0.03 to 0.24)	0.10 (0.04 to 0.27)	–15.18 (-28.73 to –6.69)
MET + LIR		0.05 (0.02 to 0.16)	0.06 (0.02 to 0.18)	–15.73 (-29.14 to –7.35)
MET + EXE		0.13 (0.04 to 0.40)	0.16 (0.06 to 0.44)	–14.00 (-27.55 to –5.44)
MET + DUL		0.09 (0.03 to 0.32)	0.10 (0.03 to 0.35)	–14.91 (-28.33 to –6.23)
MET + LIX		0.08 (0.03 to 0.22)	0.09 (0.04 to 0.25)	–15.21 (-28.71 to –6.81)
MET + ROS		0.13 (0.04 to 0.43)	0.15 (0.05 to 0.46)	–14.15 (-27.80 to –5.23)
MET + PIO		0.04 (0.01 to 0.11)	0.05 (0.02 to 0.12)	–16.06 (-29.69 to –7.74)
MET + IND		0.34 (0.06 to 1.72)	0.38 (0.08 to 1.57)	–9.94 (-24.44 to 7.38)
MET + IAS		1.31 (0.36 to 4.80)	1.24 (0.42 to 3.33)	3.99 (–14.19 to 27.81)
MET + IGA		0.47 (0.16 to 1.33)	0.52 (0.20 to 1.28)	–7.89 (-21.69 to 3.04)
MET + DSP		1.00 (0.20 to 4.81)	1.00 (0.24 to 3.24)	0.05 (–18.14 to 28.98)
MET + SAX	MET + NAT	0.13 (0.03 to 0.44)	0.14 (0.05 to 0.45)	–9.04 (-26.49 to –2.12)
MET + ALO		0.07 (0.01 to 0.35)	0.08 (0.02 to 0.36)	–9.59 (-26.99 to –2.63)
MET + LIN		0.09 (0.02 to 0.38)	0.11 (0.03 to 0.39)	–9.40 (-26.88 to –2.43)
MET + SIT		0.15 (0.04 to 0.51)	0.17 (0.06 to 0.52)	–8.73 (-26.20 to –1.83)
MET + VIL		0.15 (0.03 to 0.73)	0.16 (0.04 to 0.74)	–8.65 (-26.29 to –1.17)
MET + CAN		0.22 (0.05 to 0.85)	0.24 (0.07 to 0.86)	–7.89 (-25.43 to –0.62)
MET + DAP		0.12 (0.03 to 0.48)	0.13 (0.03 to 0.49)	–9.09 (-26.50 to –2.10)
MET + EMP		0.14 (0.03 to 0.56)	0.15 (0.04 to 0.57)	–8.86 (-26.21 to –1.72)
MET + LIR		0.09 (0.02 to 0.38)	0.10 (0.03 to 0.39)	–9.42 (-26.88 to –2.46)
MET + EXE		0.23 (0.05 to 0.92)	0.25 (0.07 to 0.92)	–7.74 (-25.38 to –0.36)
MET + DUL		0.15 (0.03 to 0.73)	0.17 (0.04 to 0.74)	–8.61 (-26.03 to –1.16)
MET + LIX		0.13 (0.03 to 0.50)	0.15 (0.04 to 0.51)	–8.93 (-26.49 to –1.95)
MET + ROS		0.22 (0.05 to 0.82)	0.24 (0.07 to 0.83)	–7.86 (-24.95 to –0.79)
MET + PIO		0.06 (0.01 to 0.24)	0.07 (0.02 to 0.25)	–9.74 (-27.24 to –2.92)
MET + IND		0.58 (0.08 to 3.60)	0.61 (0.10 to 3.09)	–3.85 (-21.90 to 13.53)
MET + IAS		2.26 (0.46 to 9.79)	1.98 (0.52 to 6.74)	9.88 (–10.71 to 33.41)
MET + IGA		0.81 (0.19 to 3.06)	0.83 (0.24 to 2.77)	–1.74 (–19.63 to 8.90)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + DSP		1.71 (0.27 to 10.02)	1.58 (0.31 to 6.55)	5.84 (–14.95 to 34.88)
MET + ALO	MET + SAX	0.55 (0.15 to 1.80)	0.56 (0.16 to 1.78)	–0.63 (–1.73 to 1.04)
MET + LIN		0.75 (0.26 to 1.82)	0.75 (0.27 to 1.80)	–0.36 (–1.56 to 0.97)
MET + SIT		1.21 (0.66 to 2.19)	1.20 (0.67 to 2.16)	0.30 (–0.72 to 1.33)
MET + VIL		1.16 (0.35 to 3.74)	1.16 (0.36 to 3.61)	0.23 (–1.30 to 3.33)
MET + CAN		1.73 (0.68 to 4.30)	1.72 (0.69 to 4.13)	1.04 (–0.63 to 3.85)
MET + DAP		0.92 (0.33 to 2.49)	0.92 (0.34 to 2.44)	–0.12 (–1.39 to 1.76)
MET + EMP		1.08 (0.43 to 2.71)	1.08 (0.44 to 2.66)	0.11 (–1.18 to 2.04)
MET + LIR		0.71 (0.29 to 1.91)	0.71 (0.29 to 1.89)	–0.41 (–1.51 to 1.11)
MET + EXE		1.82 (0.67 to 4.74)	1.80 (0.67 to 4.54)	1.17 (–0.64 to 4.53)
MET + DUL		1.18 (0.39 to 3.77)	1.18 (0.39 to 3.65)	0.26 (–1.17 to 3.58)
MET + LIX		1.06 (0.43 to 2.54)	1.06 (0.43 to 2.49)	0.08 (–1.20 to 1.78)
MET + ROS		1.71 (0.57 to 5.01)	1.69 (0.58 to 4.80)	1.00 (–0.84 to 4.71)
MET + PIO		0.51 (0.19 to 1.25)	0.52 (0.19 to 1.25)	–0.70 (–1.83 to 0.29)
MET + IND		4.53 (0.88 to 21.19)	4.30 (0.88 to 16.72)	4.87 (–0.21 to 21.97)
MET + IAS		17.71 (5.34 to 56.84)	14.10 (4.94 to 34.08)	19.50 (6.65 to 42.48)
MET + IGA		6.39 (2.37 to 15.56)	5.91 (2.31 to 13.27)	7.24 (2.36 to 15.89)
MET + DSP		13.54 (2.80 to 57.77)	11.37 (2.71 to 33.59)	15.33 (2.83 to 44.07)
MET + LIN	MET + ALO	1.37 (0.31 to 5.72)	1.36 (0.31 to 5.63)	0.28 (–1.61 to 1.70)
MET + SIT		2.19 (0.67 to 7.77)	2.16 (0.68 to 7.64)	0.93 (–0.78 to 2.08)
MET + VIL		2.13 (0.43 to 10.49)	2.11 (0.43 to 10.16)	0.86 (–1.21 to 3.98)
MET + CAN		3.16 (0.77 to 13.33)	3.10 (0.77 to 12.83)	1.66 (–0.48 to 4.54)
MET + DAP		1.66 (0.38 to 7.57)	1.65 (0.38 to 7.42)	0.51 (–1.40 to 2.47)
MET + EMP		1.95 (0.48 to 8.81)	1.94 (0.49 to 8.58)	0.74 (–1.17 to 2.76)
MET + LIR		1.29 (0.32 to 5.90)	1.28 (0.33 to 5.82)	0.22 (–1.51 to 1.80)
MET + EXE		3.27 (0.79 to 14.49)	3.21 (0.79 to 13.89)	1.76 (–0.40 to 5.19)
MET + DUL		2.15 (0.47 to 11.14)	2.13 (0.48 to 10.73)	0.87 (–1.06 to 4.22)
MET + LIX		1.90 (0.48 to 8.11)	1.89 (0.49 to 7.95)	0.70 (–1.16 to 2.46)
MET + ROS		3.09 (0.68 to 14.79)	3.04 (0.69 to 14.21)	1.61 (–0.62 to 5.34)
MET + PIO		0.92 (0.21 to 3.78)	0.92 (0.21 to 3.75)	–0.06 (–1.89 to 0.96)
MET + IND		8.22 (1.23 to 56.51)	7.70 (1.23 to 46.10)	5.47 (0.32 to 22.56)
MET + IAS		31.72 (6.63 to 163.60)	24.95 (5.88 to 107.50)	20.06 (7.13 to 43.06)
MET + IGA		11.52 (2.79 to 48.89)	10.54 (2.69 to 42.64)	7.82 (2.82 to 16.51)
MET + DSP		24.28 (3.81 to 155.60)	19.98 (3.61 to 98.18)	15.92 (3.41 to 44.75)
MET + SIT	MET + LIN	1.61 (0.67 to 4.47)	1.60 (0.68 to 4.40)	0.66 (–0.70 to 1.90)
MET + VIL		1.56 (0.41 to 6.57)	1.55 (0.42 to 6.37)	0.59 (–1.14 to 3.81)
MET + CAN		2.32 (0.77 to 7.88)	2.28 (0.78 to 7.56)	1.39 (–0.43 to 4.34)
MET + DAP		1.24 (0.37 to 4.37)	1.23 (0.37 to 4.28)	0.25 (–1.29 to 2.21)
MET + EMP		1.42 (0.53 to 4.57)	1.41 (0.54 to 4.48)	0.45 (–0.92 to 2.44)
MET + LIR		0.95 (0.33 to 3.32)	0.95 (0.34 to 3.27)	–0.06 (–1.37 to 1.53)
MET + EXE		2.43 (0.78 to 8.44)	2.39 (0.78 to 8.09)	1.50 (–0.41 to 4.96)
MET + DUL		1.58 (0.46 to 6.64)	1.56 (0.46 to 6.39)	0.60 (–1.01 to 4.06)

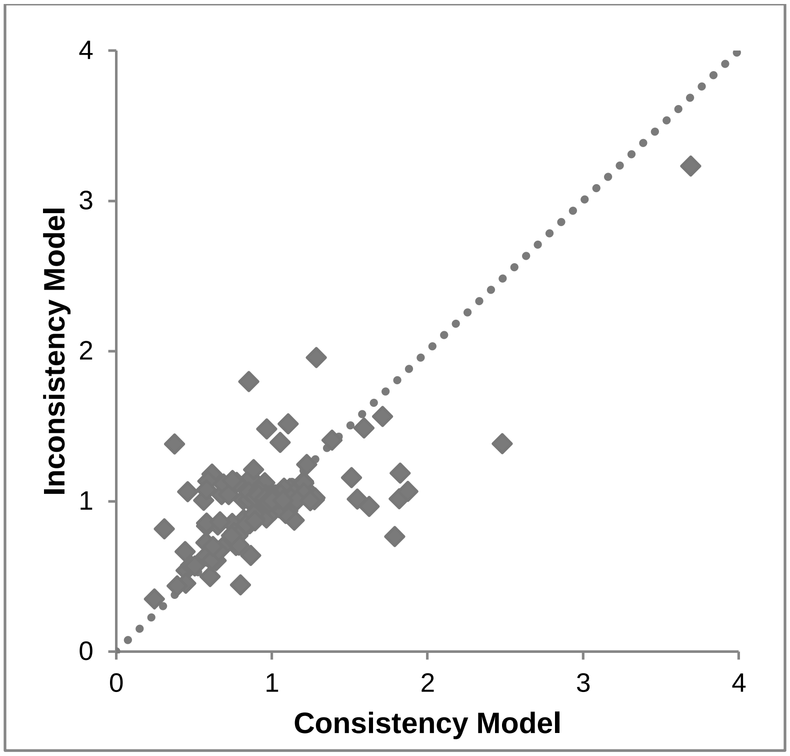
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX		1.41 (0.48 to 4.66)	1.40 (0.49 to 4.57)	0.43 (–1.08 to 2.23)
MET + ROS		2.29 (0.66 to 8.50)	2.26 (0.66 to 8.11)	1.37 (–0.64 to 5.11)
MET + PIO		0.68 (0.23 to 2.11)	0.69 (0.23 to 2.10)	–0.34 (–1.67 to 0.68)
MET + IND		6.07 (1.10 to 36.42)	5.72 (1.09 to 28.72)	5.22 (0.14 to 22.41)
MET + IAS		23.65 (6.36 to 96.90)	18.62 (5.78 to 60.75)	19.82 (7.03 to 42.93)
MET + IGA		8.56 (2.75 to 28.50)	7.87 (2.66 to 24.48)	7.57 (2.65 to 16.39)
MET + DSP		18.24 (3.52 to 96.56)	15.12 (3.38 to 57.40)	15.67 (3.19 to 44.58)
MET + VIL	MET + SIT	0.96 (0.32 to 2.92)	0.96 (0.32 to 2.83)	–0.07 (–1.54 to 2.97)
MET + CAN		1.43 (0.64 to 3.10)	1.42 (0.65 to 2.99)	0.74 (–0.75 to 3.39)
MET + DAP		0.76 (0.26 to 2.08)	0.76 (0.27 to 2.05)	–0.41 (–1.79 to 1.52)
MET + EMP		0.90 (0.37 to 2.18)	0.90 (0.37 to 2.14)	–0.18 (–1.50 to 1.76)
MET + LIR		0.59 (0.26 to 1.38)	0.59 (0.27 to 1.37)	–0.70 (–1.69 to 0.63)
MET + EXE		1.51 (0.62 to 3.45)	1.49 (0.63 to 3.32)	0.87 (–0.76 to 4.02)
MET + DUL		0.99 (0.35 to 2.75)	0.99 (0.36 to 2.66)	–0.03 (–1.34 to 3.06)
MET + LIX		0.87 (0.38 to 1.93)	0.87 (0.39 to 1.91)	–0.22 (–1.45 to 1.39)
MET + ROS		1.42 (0.50 to 3.97)	1.41 (0.50 to 3.80)	0.72 (–1.13 to 4.43)
MET + PIO		0.42 (0.16 to 0.97)	0.43 (0.16 to 0.97)	–1.00 (–2.14 to –0.05)
MET + IND		3.77 (0.82 to 16.37)	3.58 (0.82 to 12.88)	4.58 (–0.34 to 21.61)
MET + IAS		14.65 (4.76 to 42.99)	11.70 (4.43 to 25.74)	19.20 (6.48 to 41.94)
MET + IGA		5.30 (2.32 to 11.08)	4.92 (2.26 to 9.47)	6.96 (2.30 to 15.32)
MET + DSP		11.17 (2.56 to 44.40)	9.42 (2.48 to 25.54)	15.01 (2.68 to 43.69)
MET + CAN	MET + VIL	1.49 (0.40 to 5.38)	1.48 (0.41 to 5.20)	0.78 (–2.50 to 3.78)
MET + DAP		0.79 (0.19 to 3.21)	0.79 (0.19 to 3.15)	–0.34 (–3.59 to 1.81)
MET + EMP		0.92 (0.25 to 3.55)	0.92 (0.25 to 3.48)	–0.12 (–3.29 to 2.09)
MET + LIR		0.61 (0.16 to 2.39)	0.62 (0.17 to 2.36)	–0.63 (–3.72 to 1.15)
MET + EXE		1.55 (0.40 to 6.09)	1.54 (0.41 to 5.86)	0.89 (–2.48 to 4.43)
MET + DUL		1.02 (0.23 to 4.54)	1.02 (0.24 to 4.38)	0.03 (–3.16 to 3.46)
MET + LIX		0.90 (0.25 to 3.28)	0.90 (0.26 to 3.22)	–0.16 (–3.30 to 1.82)
MET + ROS		1.46 (0.33 to 6.61)	1.45 (0.34 to 6.31)	0.72 (–2.78 to 4.79)
MET + PIO		0.43 (0.11 to 1.51)	0.44 (0.12 to 1.51)	–0.93 (–4.04 to 0.40)
MET + IND		3.85 (0.60 to 24.94)	3.65 (0.61 to 20.09)	4.50 (–1.16 to 21.64)
MET + IAS		15.00 (3.39 to 72.74)	11.94 (3.11 to 45.80)	19.07 (6.04 to 42.19)
MET + IGA		5.45 (1.45 to 20.75)	5.04 (1.42 to 17.99)	6.86 (1.41 to 15.69)
MET + DSP		11.43 (1.91 to 68.53)	9.54 (1.85 to 41.43)	14.92 (2.27 to 43.66)
MET + DAP	MET + CAN	0.53 (0.16 to 1.77)	0.53 (0.16 to 1.75)	–1.15 (–4.11 to 1.13)
MET + EMP		0.62 (0.20 to 1.97)	0.63 (0.21 to 1.94)	–0.91 (–3.86 to 1.44)
MET + LIR		0.41 (0.14 to 1.29)	0.42 (0.14 to 1.29)	–1.43 (–4.24 to 0.44)
MET + EXE		1.05 (0.34 to 3.16)	1.04 (0.34 to 3.06)	0.11 (–3.00 to 3.58)
MET + DUL		0.68 (0.20 to 2.49)	0.69 (0.20 to 2.42)	–0.74 (–3.67 to 2.66)
MET + LIX		0.60 (0.21 to 1.78)	0.61 (0.22 to 1.76)	–0.97 (–3.84 to 1.14)
MET + ROS		0.98 (0.29 to 3.42)	0.98 (0.30 to 3.29)	–0.04 (–3.16 to 3.92)
MET + PIO		0.29 (0.09 to 0.86)	0.30 (0.10 to 0.86)	–1.75 (–4.61 to –0.19)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + IND		2.60 (0.49 to 13.86)	2.49 (0.50 to 11.02)	3.75 (–1.81 to 20.77)
MET + IAS		10.14 (2.77 to 37.63)	8.15 (2.59 to 23.61)	18.29 (5.41 to 41.30)
MET + IGA		3.68 (1.26 to 10.50)	3.43 (1.25 to 9.13)	6.10 (0.91 to 14.70)
MET + DSP		7.72 (1.56 to 38.41)	6.52 (1.53 to 22.97)	14.09 (1.61 to 42.84)
MET + EMP	MET + DAP	1.17 (0.36 to 4.11)	1.16 (0.37 to 4.03)	0.22 (–1.79 to 2.34)
MET + LIR		0.77 (0.23 to 2.84)	0.77 (0.24 to 2.80)	–0.30 (–2.20 to 1.42)
MET + EXE		1.98 (0.57 to 6.86)	1.95 (0.58 to 6.57)	1.25 (–1.09 to 4.79)
MET + DUL		1.28 (0.33 to 5.51)	1.28 (0.33 to 5.33)	0.36 (–1.77 to 3.86)
MET + LIX		1.14 (0.36 to 3.78)	1.14 (0.37 to 3.70)	0.18 (–1.83 to 2.06)
MET + ROS		1.85 (0.50 to 6.87)	1.83 (0.51 to 6.59)	1.10 (–1.29 to 4.83)
MET + PIO		0.55 (0.17 to 1.78)	0.55 (0.17 to 1.77)	–0.59 (–2.46 to 0.57)
MET + IND		4.93 (0.86 to 28.38)	4.66 (0.86 to 22.69)	4.93 (–0.26 to 22.17)
MET + IAS		19.24 (4.70 to 79.44)	15.20 (4.30 to 50.26)	19.52 (6.58 to 42.62)
MET + IGA		6.99 (2.07 to 22.90)	6.45 (2.02 to 19.77)	7.32 (2.24 to 16.01)
MET + DSP		14.72 (2.67 to 78.94)	12.30 (2.57 to 47.32)	15.33 (2.79 to 44.24)
MET + LIR	MET + EMP	0.66 (0.23 to 2.07)	0.66 (0.23 to 2.05)	–0.52 (–2.41 to 1.09)
MET + EXE		1.68 (0.52 to 5.21)	1.66 (0.53 to 5.01)	1.03 (–1.34 to 4.46)
MET + DUL		1.09 (0.31 to 4.13)	1.09 (0.31 to 4.01)	0.14 (–1.96 to 3.51)
MET + LIX		0.98 (0.32 to 2.80)	0.98 (0.33 to 2.75)	–0.03 (–2.12 to 1.76)
MET + ROS		1.59 (0.44 to 5.40)	1.57 (0.44 to 5.17)	0.88 (–1.63 to 4.62)
MET + PIO		0.47 (0.15 to 1.35)	0.48 (0.15 to 1.35)	–0.81 (–2.77 to 0.33)
MET + IND		4.23 (0.72 to 22.31)	4.01 (0.72 to 17.81)	4.72 (–0.63 to 21.78)
MET + IAS		16.52 (4.11 to 61.61)	13.08 (3.76 to 37.82)	19.30 (6.35 to 42.37)
MET + IGA		5.94 (1.84 to 17.35)	5.48 (1.80 to 14.98)	7.09 (1.94 to 15.73)
MET + DSP		12.54 (2.29 to 61.34)	10.48 (2.22 to 36.45)	15.14 (2.57 to 43.92)
MET + EXE	MET + LIR	2.56 (0.76 to 7.79)	2.52 (0.76 to 7.44)	1.56 (–0.45 to 4.86)
MET + DUL		1.67 (0.66 to 4.12)	1.66 (0.66 to 4.01)	0.66 (–0.49 to 3.42)
MET + LIX		1.48 (0.47 to 4.32)	1.47 (0.48 to 4.24)	0.48 (–1.16 to 2.17)
MET + ROS		2.40 (0.65 to 8.46)	2.36 (0.65 to 8.09)	1.40 (–0.71 to 5.12)
MET + PIO		0.71 (0.21 to 2.23)	0.71 (0.22 to 2.21)	–0.29 (–1.85 to 0.74)
MET + IND		6.40 (1.10 to 33.03)	6.03 (1.10 to 26.30)	5.28 (0.15 to 22.32)
MET + IAS		25.07 (6.20 to 89.25)	19.72 (5.60 to 57.71)	19.88 (6.96 to 42.83)
MET + IGA		9.00 (2.72 to 25.83)	8.25 (2.62 to 22.42)	7.63 (2.66 to 16.14)
MET + DSP		19.01 (3.46 to 91.31)	15.76 (3.31 to 54.78)	15.70 (3.21 to 44.42)
MET + DUL	MET + EXE	0.65 (0.18 to 2.57)	0.66 (0.19 to 2.51)	–0.86 (–4.25 to 2.63)
MET + LIX		0.58 (0.24 to 1.40)	0.59 (0.25 to 1.39)	–1.06 (–4.07 to 0.61)
MET + ROS		0.95 (0.28 to 3.15)	0.95 (0.29 to 3.05)	–0.12 (–3.71 to 3.62)
MET + PIO		0.28 (0.09 to 0.82)	0.29 (0.09 to 0.82)	–1.86 (–5.25 to –0.24)
MET + IND		2.49 (0.57 to 10.85)	2.39 (0.58 to 8.90)	3.61 (–1.41 to 19.94)
MET + IAS		9.75 (3.07 to 30.93)	7.82 (2.81 to 20.07)	18.13 (5.78 to 40.50)
MET + IGA		3.52 (1.62 to 7.44)	3.28 (1.58 to 6.69)	5.97 (1.88 to 13.22)
MET + DSP		7.42 (1.78 to 30.56)	6.26 (1.73 to 18.93)	13.98 (2.09 to 42.03)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX	MET + DUL	0.89 (0.24 to 3.13)	0.89 (0.25 to 3.08)	–0.19 (–3.58 to 1.76)
MET + ROS		1.45 (0.33 to 5.67)	1.44 (0.34 to 5.46)	0.73 (–2.88 to 4.47)
MET + PIO		0.43 (0.11 to 1.54)	0.43 (0.11 to 1.54)	–0.96 (–4.37 to 0.43)
MET + IND		3.87 (0.60 to 22.09)	3.67 (0.61 to 18.10)	4.50 (–1.26 to 21.39)
MET + IAS		15.10 (3.29 to 62.66)	11.92 (3.01 to 41.04)	19.05 (5.91 to 41.69)
MET + IGA		5.38 (1.42 to 18.35)	4.97 (1.39 to 16.12)	6.82 (1.39 to 15.29)
MET + DSP		11.34 (1.90 to 61.49)	9.48 (1.84 to 38.17)	14.84 (2.22 to 43.37)
MET + ROS	MET + LIX	1.63 (0.50 to 5.46)	1.61 (0.50 to 5.22)	0.92 (–1.28 to 4.70)
MET + PIO		0.49 (0.16 to 1.33)	0.49 (0.16 to 1.33)	–0.77 (–2.46 to 0.31)
MET + IND		4.31 (0.86 to 21.33)	4.08 (0.86 to 16.91)	4.75 (–0.26 to 21.76)
MET + IAS		16.79 (4.88 to 57.73)	13.35 (4.48 to 35.67)	19.38 (6.62 to 42.17)
MET + IGA		6.10 (2.27 to 15.69)	5.63 (2.21 to 13.64)	7.12 (2.41 to 15.60)
MET + DSP		12.86 (2.74 to 59.03)	10.72 (2.63 to 34.60)	15.18 (2.85 to 43.96)
MET + PIO	MET + ROS	0.30 (0.08 to 1.00)	0.30 (0.09 to 1.00)	–1.71 (–5.44 to 0.00)
MET + IND		2.62 (0.49 to 14.87)	2.51 (0.50 to 12.03)	3.69 (–1.96 to 20.72)
MET + IAS		10.29 (3.47 to 31.27)	8.21 (3.12 to 20.99)	18.24 (6.12 to 40.05)
MET + IGA		3.69 (1.21 to 11.41)	3.45 (1.20 to 10.03)	6.01 (0.84 to 14.61)
MET + DSP		7.74 (1.56 to 40.77)	6.54 (1.53 to 25.05)	14.01 (1.72 to 42.85)
MET + IND	MET + PIO	8.98 (1.68 to 49.38)	8.45 (1.66 to 39.34)	5.58 (0.60 to 22.65)
MET + IAS		34.69 (9.61 to 137.20)	27.28 (8.63 to 86.03)	20.21 (7.42 to 43.19)
MET + IGA		12.43 (4.24 to 39.09)	11.39 (4.07 to 33.55)	7.94 (3.15 to 16.64)
MET + DSP		26.22 (5.43 to 137.00)	21.77 (5.18 to 80.81)	16.03 (3.67 to 44.94)
MET + IAS	MET + IND	3.93 (0.77 to 19.46)	3.25 (0.81 to 14.00)	13.66 (–3.27 to 35.47)
MET + IGA		1.41 (0.38 to 4.95)	1.37 (0.44 to 4.62)	2.19 (–11.59 to 8.99)
MET + DSP		2.99 (0.50 to 16.99)	2.59 (0.55 to 11.77)	9.65 (–7.04 to 36.58)
MET + IGA	MET + IAS	0.36 (0.13 to 0.93)	0.42 (0.20 to 0.94)	–11.91 (-31.84 to –0.57)
MET + DSP		0.76 (0.16 to 3.50)	0.80 (0.22 to 2.55)	–3.76 (-26.62 to 22.95)
MET + DSP	MET + IGA	2.10 (0.65 to 7.12)	1.91 (0.67 to 4.70)	7.79 (–2.89 to 33.11)
Random-effects model	Residual deviance	130.2 vs. 134 data points		
	Deviance information criteria	701.125		

ALO = alogliptin; CrI = credible interval; CAN = canagliflozin; DAP = dapagliflozin; DUL = dulaglutide; DSP = insulin degludec/insulin aspart mix; EMP = empagliflozin; EXE = exenatide; GLC = glicazide; GLI = glipizide; GLM = glimepiride; GLY = glyburide; IAS = insulin aspart; IGA = insulin glargine; IND = insulin degludec; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MET = metformin; NAT = nateglinide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 23: Consistency Plot for Nonsevere Hypoglycemia (Individual-Drug Case Analysis)



Serious Adverse Events

Table 41: Serious Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLC	MET	1.61 (0.75 to 3.94)	1.58 (0.76 to 3.66)	1.57 (–0.67 to 7.15)
MET + GLM		0.85 (0.60 to 1.25)	0.85 (0.61 to 1.25)	–0.40 (–1.18 to 0.62)
MET + GLI		1.14 (0.75 to 1.75)	1.13 (0.75 to 1.72)	0.35 (–0.72 to 1.84)
MET + GLL		1.00 (0.50 to 2.05)	1.00 (0.51 to 2.00)	0.00 (–1.39 to 2.62)
MET + NAT		7.19 (1.32 to 50.71)	6.16 (1.31 to 21.74)	13.96 (0.83 to 55.77)
MET + SAX		1.18 (0.80 to 1.73)	1.17 (0.80 to 1.70)	0.47 (–0.59 to 1.77)
MET + ALO		1.36 (0.82 to 2.29)	1.34 (0.82 to 2.22)	0.92 (–0.51 to 3.16)
MET + LIN		0.78 (0.50 to 1.42)	0.79 (0.50 to 1.41)	–0.57 (–1.47 to 1.04)
MET + SIT		0.94 (0.66 to 1.32)	0.94 (0.67 to 1.31)	–0.17 (–0.98 to 0.78)
MET + VIL		0.74 (0.50 to 1.13)	0.74 (0.51 to 1.12)	–0.69 (–1.46 to 0.31)
MET + CAN		1.41 (0.69 to 3.24)	1.39 (0.70 to 3.07)	1.07 (–0.88 to 5.25)
MET + DAP		0.92 (0.56 to 1.55)	0.92 (0.56 to 1.53)	–0.21 (–1.24 to 1.37)
MET + EMP		1.06 (0.69 to 1.65)	1.06 (0.69 to 1.62)	0.17 (–0.88 to 1.61)
MET + LIR		1.51 (0.80 to 2.86)	1.49 (0.81 to 2.73)	1.32 (–0.55 to 4.50)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + EXE		0.81 (0.38 to 1.74)	0.82 (0.39 to 1.71)	–0.49 (–1.74 to 1.85)
MET + DUL		1.18 (0.61 to 2.41)	1.18 (0.62 to 2.32)	0.48 (–1.07 to 3.44)
MET + LIX		0.98 (0.61 to 1.62)	0.98 (0.62 to 1.60)	–0.04 (–1.08 to 1.55)
MET + ROS		0.90 (0.40 to 2.06)	0.90 (0.41 to 2.00)	–0.27 (–1.72 to 2.61)
MET + PIO		1.19 (0.87 to 1.77)	1.19 (0.87 to 1.74)	0.51 (–0.36 to 1.92)
MET + IAS		1.23 (0.23 to 6.97)	1.23 (0.23 to 6.05)	0.60 (–2.15 to 13.15)
MET + IGA		1.55 (0.61 to 3.82)	1.52 (0.61 to 3.56)	1.42 (–1.08 to 6.86)
MET + GLM	MET + GLC	0.53 (0.22 to 1.21)	0.54 (0.23 to 1.20)	–1.96 (–7.43 to 0.43)
MET + GLI		0.70 (0.27 to 1.66)	0.71 (0.29 to 1.63)	–1.22 (–6.73 to 1.42)
MET + GLL		0.62 (0.21 to 1.65)	0.63 (0.22 to 1.62)	–1.55 (–7.13 to 1.63)
MET + NAT		4.47 (0.97 to 25.66)	3.83 (0.97 to 12.62)	12.07 (–0.11 to 51.57)
MET + SAX		0.73 (0.29 to 1.70)	0.73 (0.31 to 1.67)	–1.13 (–6.66 to 1.49)
MET + ALO		0.84 (0.31 to 2.09)	0.84 (0.33 to 2.03)	–0.65 (–6.28 to 2.43)
MET + LIN		0.49 (0.19 to 1.23)	0.50 (0.21 to 1.23)	–2.11 (–7.53 to 0.52)
MET + SIT		0.58 (0.23 to 1.31)	0.59 (0.25 to 1.30)	–1.75 (–7.31 to 0.65)
MET + VIL		0.46 (0.18 to 1.04)	0.47 (0.20 to 1.04)	–2.26 (–7.75 to 0.08)
MET + CAN		0.88 (0.29 to 2.59)	0.89 (0.31 to 2.49)	–0.46 (–6.09 to 3.98)
MET + DAP		0.57 (0.21 to 1.43)	0.58 (0.22 to 1.42)	–1.77 (–7.42 to 0.98)
MET + EMP		0.66 (0.25 to 1.59)	0.67 (0.27 to 1.57)	–1.41 (–6.96 to 1.28)
MET + LIR		0.93 (0.32 to 2.50)	0.93 (0.34 to 2.41)	–0.29 (–5.95 to 3.63)
MET + EXE		0.51 (0.17 to 1.41)	0.52 (0.18 to 1.40)	–1.99 (–7.45 to 1.00)
MET + DUL		0.74 (0.24 to 1.95)	0.75 (0.25 to 1.90)	–1.05 (–6.86 to 2.33)
MET + LIX		0.61 (0.23 to 1.52)	0.62 (0.24 to 1.50)	–1.60 (–7.25 to 1.15)
MET + ROS		0.55 (0.17 to 1.67)	0.56 (0.18 to 1.64)	–1.80 (–7.62 to 1.76)
MET + PIO		0.74 (0.35 to 1.51)	0.75 (0.37 to 1.49)	–1.05 (–6.06 to 1.11)
MET + IAS		0.76 (0.12 to 5.05)	0.77 (0.13 to 4.45)	–0.92 (–6.93 to 11.42)
MET + IGA		0.94 (0.28 to 3.15)	0.94 (0.30 to 2.97)	–0.25 (–5.94 to 5.68)
MET + GLI	MET + GLM	1.33 (0.81 to 2.12)	1.32 (0.82 to 2.08)	0.74 (–0.51 to 2.23)
MET + GLL		1.18 (0.60 to 2.26)	1.17 (0.60 to 2.19)	0.39 (–1.01 to 2.78)
MET + NAT		8.44 (1.48 to 60.82)	7.19 (1.47 to 26.35)	14.28 (1.12 to 56.14)
MET + SAX		1.39 (0.91 to 2.06)	1.38 (0.91 to 2.02)	0.86 (–0.24 to 2.05)
MET + ALO		1.59 (0.87 to 2.80)	1.57 (0.88 to 2.70)	1.30 (–0.34 to 3.52)
MET + LIN		0.92 (0.65 to 1.45)	0.92 (0.66 to 1.44)	–0.17 (–0.88 to 1.01)
MET + SIT		1.09 (0.70 to 1.64)	1.09 (0.71 to 1.62)	0.21 (–0.86 to 1.23)
MET + VIL		0.87 (0.61 to 1.19)	0.88 (0.62 to 1.19)	–0.29 (–1.06 to 0.41)
MET + CAN		1.66 (0.75 to 3.93)	1.64 (0.75 to 3.71)	1.46 (–0.68 to 5.65)
MET + DAP		1.08 (0.59 to 1.97)	1.07 (0.59 to 1.94)	0.17 (–1.16 to 1.89)
MET + EMP		1.26 (0.83 to 1.79)	1.25 (0.83 to 1.76)	0.57 (–0.45 to 1.72)
MET + LIR		1.77 (0.90 to 3.45)	1.74 (0.90 to 3.29)	1.71 (–0.25 to 4.80)
MET + EXE		0.95 (0.44 to 2.12)	0.95 (0.45 to 2.07)	–0.11 (–1.50 to 2.28)
MET + DUL		1.40 (0.66 to 2.88)	1.38 (0.67 to 2.78)	0.87 (–0.88 to 3.80)
MET + LIX		1.16 (0.64 to 2.03)	1.15 (0.65 to 1.99)	0.36 (–1.01 to 2.01)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ROS		1.05 (0.45 to 2.56)	1.05 (0.46 to 2.47)	0.12 (–1.50 to 3.06)
MET + PIO		1.41 (0.92 to 2.14)	1.40 (0.93 to 2.09)	0.91 (–0.21 to 2.26)
MET + IAS		1.46 (0.26 to 7.92)	1.44 (0.27 to 6.84)	1.02 (–1.90 to 13.42)
MET + IGA		1.82 (0.66 to 4.51)	1.79 (0.67 to 4.19)	1.82 (–0.86 to 7.12)
MET + GLL	MET + GLI	0.88 (0.40 to 1.93)	0.88 (0.41 to 1.88)	–0.36 (–2.26 to 2.35)
MET + NAT		6.31 (1.11 to 44.33)	5.41 (1.10 to 19.96)	13.56 (0.32 to 55.26)
MET + SAX		1.03 (0.70 to 1.58)	1.03 (0.71 to 1.55)	0.10 (–1.16 to 1.36)
MET + ALO		1.20 (0.79 to 1.78)	1.19 (0.80 to 1.74)	0.57 (–0.69 to 2.24)
MET + LIN		0.69 (0.40 to 1.33)	0.70 (0.41 to 1.32)	–0.90 (–2.45 to 0.80)
MET + SIT		0.82 (0.55 to 1.21)	0.83 (0.56 to 1.20)	–0.52 (–1.81 to 0.48)
MET + VIL		0.66 (0.38 to 1.11)	0.66 (0.39 to 1.11)	–1.02 (–2.55 to 0.26)
MET + CAN		1.25 (0.56 to 2.95)	1.24 (0.57 to 2.81)	0.71 (–1.64 to 4.88)
MET + DAP		0.81 (0.42 to 1.57)	0.82 (0.43 to 1.55)	–0.55 (–2.35 to 1.34)
MET + EMP		0.94 (0.53 to 1.65)	0.94 (0.54 to 1.63)	–0.19 (–1.91 to 1.51)
MET + LIR		1.33 (0.66 to 2.63)	1.32 (0.67 to 2.53)	0.97 (–1.24 to 4.07)
MET + EXE		0.72 (0.31 to 1.64)	0.72 (0.32 to 1.61)	–0.84 (–2.63 to 1.62)
MET + DUL		1.04 (0.51 to 2.18)	1.04 (0.52 to 2.12)	0.12 (–1.80 to 3.02)
MET + LIX		0.87 (0.48 to 1.60)	0.87 (0.49 to 1.58)	–0.39 (–2.08 to 1.42)
MET + ROS		0.79 (0.34 to 1.95)	0.79 (0.35 to 1.90)	–0.62 (–2.57 to 2.38)
MET + PIO		1.06 (0.65 to 1.79)	1.06 (0.66 to 1.76)	0.17 (–1.39 to 1.83)
MET + IAS		1.07 (0.20 to 6.12)	1.07 (0.21 to 5.35)	0.21 (–2.76 to 12.69)
MET + IGA		1.35 (0.53 to 3.51)	1.34 (0.54 to 3.28)	1.03 (–1.60 to 6.39)
MET + NAT	MET + GLL	7.24 (1.18 to 58.41)	6.15 (1.17 to 26.15)	13.80 (0.56 to 55.62)
MET + SAX		1.18 (0.56 to 2.49)	1.17 (0.57 to 2.43)	0.46 (–2.14 to 2.25)
MET + ALO		1.36 (0.58 to 3.12)	1.35 (0.59 to 3.02)	0.91 (–1.96 to 3.47)
MET + LIN		0.78 (0.38 to 1.78)	0.79 (0.40 to 1.76)	–0.56 (–2.99 to 1.28)
MET + SIT		0.93 (0.44 to 1.94)	0.94 (0.46 to 1.91)	–0.17 (–2.79 to 1.38)
MET + VIL		0.74 (0.41 to 1.30)	0.75 (0.43 to 1.30)	–0.67 (–2.89 to 0.47)
MET + CAN		1.42 (0.52 to 4.07)	1.40 (0.53 to 3.86)	1.06 (–2.13 to 5.40)
MET + DAP		0.92 (0.39 to 2.16)	0.92 (0.40 to 2.12)	–0.22 (–2.93 to 1.89)
MET + EMP		1.07 (0.49 to 2.23)	1.06 (0.51 to 2.19)	0.17 (–2.43 to 1.97)
MET + LIR		1.52 (0.60 to 3.65)	1.50 (0.61 to 3.50)	1.32 (–1.79 to 4.59)
MET + EXE		0.82 (0.30 to 2.21)	0.82 (0.31 to 2.16)	–0.48 (–3.23 to 2.13)
MET + DUL		1.19 (0.46 to 3.00)	1.19 (0.47 to 2.89)	0.50 (–2.49 to 3.62)
MET + LIX		0.99 (0.42 to 2.27)	0.99 (0.43 to 2.23)	–0.03 (–2.79 to 2.03)
MET + ROS		0.89 (0.31 to 2.66)	0.90 (0.32 to 2.59)	–0.27 (–3.20 to 2.90)
MET + PIO		1.20 (0.59 to 2.52)	1.20 (0.60 to 2.46)	0.52 (–2.00 to 2.33)
MET + IAS		1.24 (0.21 to 7.47)	1.23 (0.22 to 6.49)	0.59 (–3.07 to 13.06)
MET + IGA		1.55 (0.49 to 4.53)	1.52 (0.50 to 4.25)	1.38 (–2.12 to 6.72)
MET + SAX	MET + NAT	0.16 (0.02 to 0.90)	0.19 (0.05 to 0.91)	–13.46 (–55.33 to –0.33)
MET + ALO		0.19 (0.03 to 1.13)	0.22 (0.06 to 1.12)	–12.93 (–54.66 to 0.45)
MET + LIN		0.11 (0.01 to 0.65)	0.13 (0.03 to 0.66)	–14.46 (–56.20 to –1.24)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SIT		0.13 (0.02 to 0.71)	0.15 (0.04 to 0.71)	–14.08 (–55.92 to –1.03)
MET + VIL		0.10 (0.01 to 0.57)	0.12 (0.03 to 0.58)	–14.56 (–56.41 to –1.48)
MET + CAN		0.20 (0.03 to 1.33)	0.23 (0.05 to 1.31)	–12.64 (–54.07 to 1.17)
MET + DAP		0.13 (0.02 to 0.77)	0.15 (0.04 to 0.78)	–14.13 (–56.16 to –0.80)
MET + EMP		0.15 (0.02 to 0.88)	0.17 (0.05 to 0.88)	–13.73 (–55.45 to –0.43)
MET + LIR		0.21 (0.03 to 1.24)	0.24 (0.06 to 1.23)	–12.45 (–54.12 to 0.89)
MET + EXE		0.11 (0.01 to 0.67)	0.13 (0.03 to 0.68)	–14.33 (–55.70 to –1.14)
MET + DUL		0.17 (0.02 to 0.99)	0.20 (0.04 to 0.99)	–13.28 (–55.16 to –0.02)
MET + LIX		0.14 (0.02 to 0.80)	0.16 (0.04 to 0.80)	–13.89 (–55.63 to –0.70)
MET + ROS		0.12 (0.02 to 0.82)	0.14 (0.03 to 0.83)	–14.14 (–55.75 to –0.66)
MET + PIO		0.17 (0.02 to 0.88)	0.19 (0.06 to 0.88)	–13.36 (–55.03 to –0.43)
MET + IAS		0.17 (0.01 to 1.80)	0.20 (0.03 to 1.71)	–12.51 (–53.50 to 4.09)
MET + IGA		0.21 (0.03 to 1.46)	0.24 (0.06 to 1.43)	–12.25 (–53.92 to 1.78)
MET + ALO	MET + SAX	1.15 (0.67 to 1.93)	1.15 (0.68 to 1.88)	0.45 (–1.21 to 2.53)
MET + LIN		0.67 (0.41 to 1.20)	0.67 (0.42 to 1.19)	–1.02 (–2.32 to 0.53)
MET + SIT		0.80 (0.51 to 1.20)	0.80 (0.52 to 1.20)	–0.62 (–1.98 to 0.50)
MET + VIL		0.63 (0.39 to 1.01)	0.64 (0.40 to 1.01)	–1.15 (–2.45 to 0.02)
MET + CAN		1.20 (0.54 to 2.87)	1.19 (0.55 to 2.73)	0.60 (–1.71 to 4.80)
MET + DAP		0.78 (0.42 to 1.46)	0.78 (0.43 to 1.45)	–0.68 (–2.29 to 1.18)
MET + EMP		0.90 (0.53 to 1.51)	0.90 (0.54 to 1.49)	–0.30 (–1.81 to 1.31)
MET + LIR		1.29 (0.65 to 2.51)	1.28 (0.66 to 2.40)	0.86 (–1.33 to 3.98)
MET + EXE		0.69 (0.30 to 1.56)	0.70 (0.31 to 1.54)	–0.94 (–2.71 to 1.51)
MET + DUL		1.00 (0.49 to 2.10)	1.00 (0.49 to 2.03)	0.01 (–1.–1.91 to 2.99)
MET + LIX		0.84 (0.46 to 1.53)	0.84 (0.47 to 1.51)	–0.50 (–2.12 to 1.33)
MET + ROS		0.76 (0.33 to 1.85)	0.77 (0.34 to 1.81)	–0.73 (–2.58 to 2.26)
MET + PIO		1.02 (0.64 to 1.66)	1.02 (0.65 to 1.64)	0.05 (–1.–1.43 to 1.65)
MET + IAS		1.04 (0.19 to 5.89)	1.04 (0.20 to 5.13)	0.13 (–2.90 to 12.64)
MET + IGA		1.31 (0.49 to 3.34)	1.30 (0.50 to 3.12)	0.95 (–1.–1.81 to 6.34)
MET + LIN	MET + ALO	0.58 (0.31 to 1.23)	0.59 (0.32 to 1.22)	–1.–1.47 (–3.76 to 0.59)
MET + SIT		0.69 (0.41 to 1.14)	0.70 (0.42 to 1.13)	–1.09 (–3.23 to 0.33)
MET + VIL		0.55 (0.30 to 1.00)	0.56 (0.31 to 1.00)	–1.60 (–3.86 to 0.00)
MET + CAN		1.04 (0.43 to 2.70)	1.04 (0.44 to 2.57)	0.15 (–2.84 to 4.54)
MET + DAP		0.68 (0.33 to 1.40)	0.69 (0.34 to 1.38)	–1.11 (–3.61 to 1.02)
MET + EMP		0.79 (0.41 to 1.50)	0.79 (0.42 to 1.48)	–0.74 (–3.12 to 1.22)
MET + LIR		1.12 (0.51 to 2.36)	1.11 (0.53 to 2.27)	0.41 (–2.42 to 3.68)
MET + EXE		0.59 (0.25 to 1.48)	0.60 (0.26 to 1.46)	–1.41 (–3.86 to 1.31)
MET + DUL		0.87 (0.40 to 1.91)	0.88 (0.41 to 1.86)	–0.43 (–2.99 to 2.56)
MET + LIX		0.73 (0.37 to 1.43)	0.73 (0.38 to 1.42)	–0.96 (–3.34 to 1.10)
MET + ROS		0.66 (0.27 to 1.66)	0.67 (0.28 to 1.63)	–1.15 (–3.86 to 1.87)
MET + PIO		0.89 (0.50 to 1.60)	0.89 (0.52 to 1.57)	–0.40 (–2.65 to 1.48)
MET + IAS		0.90 (0.17 to 5.22)	0.91 (0.17 to 4.56)	–0.33 (–3.71 to 12.14)
MET + IGA		1.12 (0.42 to 3.09)	1.11 (0.44 to 2.91)	0.40 (–2.63 to 5.92)

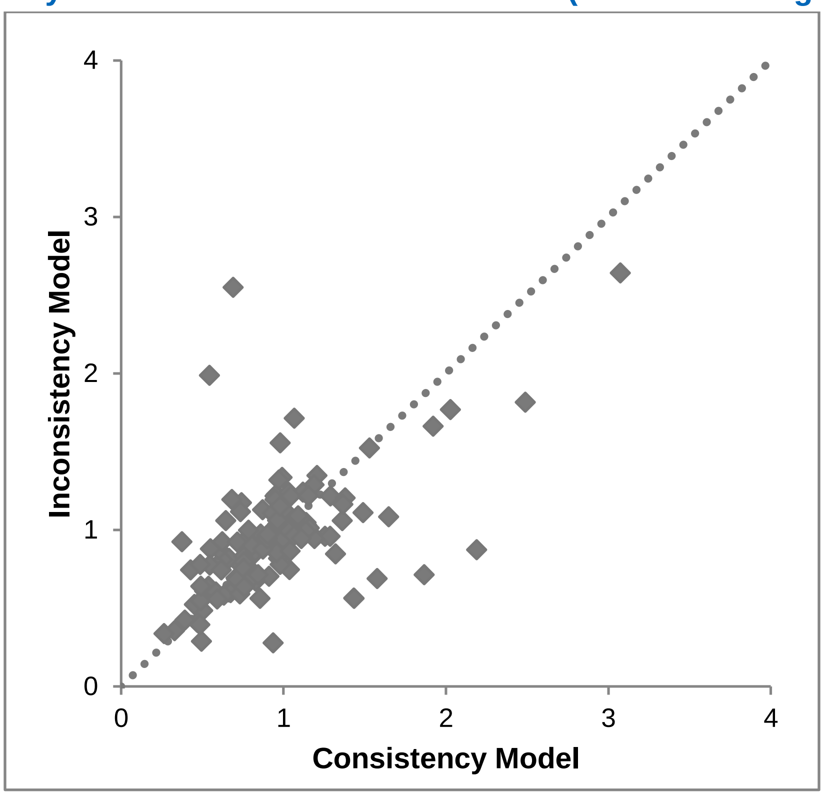
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SIT	MET + LIN	1.19 (0.63 to 1.96)	1.19 (0.64 to 1.93)	0.39 (–1.23 to 1.49)
MET + VIL		0.95 (0.52 to 1.47)	0.95 (0.53 to 1.45)	–0.10 (–1.57 to 0.77)
MET + CAN		1.81 (0.72 to 4.62)	1.78 (0.73 to 4.35)	1.63 (–0.83 to 5.87)
MET + DAP		1.17 (0.54 to 2.31)	1.16 (0.55 to 2.26)	0.35 (–1.48 to 2.13)
MET + EMP		1.36 (0.71 to 2.22)	1.35 (0.71 to 2.17)	0.74 (–0.90 to 2.08)
MET + LIR		1.91 (0.88 to 3.95)	1.87 (0.88 to 3.76)	1.85 (–0.34 to 4.94)
MET + EXE		1.02 (0.43 to 2.42)	1.02 (0.44 to 2.35)	0.04 (–1.74 to 2.50)
MET + DUL		1.51 (0.63 to 3.23)	1.49 (0.64 to 3.11)	1.04 (–1.10 to 3.97)
MET + LIX		1.25 (0.61 to 2.33)	1.24 (0.62 to 2.28)	0.52 (–1.25 to 2.21)
MET + ROS		1.13 (0.43 to 2.91)	1.12 (0.44 to 2.81)	0.26 (–1.77 to 3.26)
MET + PIO		1.52 (0.85 to 2.56)	1.51 (0.86 to 2.50)	1.07 (–0.46 to 2.50)
MET + IAS		1.55 (0.26 to 8.67)	1.54 (0.27 to 7.53)	1.14 (–2.01 to 13.66)
MET + IGA		1.96 (0.65 to 5.17)	1.92 (0.66 to 4.80)	1.96 (–0.95 to 7.37)
MET + VIL	MET + SIT	0.79 (0.50 to 1.30)	0.80 (0.50 to 1.29)	–0.51 (–1.57 to 0.60)
MET + CAN		1.53 (0.73 to 3.31)	1.51 (0.73 to 3.13)	1.26 (–0.75 to 5.23)
MET + DAP		0.99 (0.53 to 1.85)	0.99 (0.54 to 1.81)	–0.03 (–1.43 to 1.75)
MET + EMP		1.14 (0.69 to 1.89)	1.13 (0.70 to 1.85)	0.33 (–0.92 to 1.87)
MET + LIR		1.62 (0.89 to 2.95)	1.59 (0.89 to 2.81)	1.48 (–0.30 to 4.49)
MET + EXE		0.87 (0.40 to 1.88)	0.88 (0.41 to 1.84)	–0.31 (–1.69 to 2.00)
MET + DUL		1.27 (0.66 to 2.46)	1.27 (0.67 to 2.37)	0.67 (–0.89 to 3.41)
MET + LIX		1.06 (0.62 to 1.82)	1.05 (0.63 to 1.79)	0.13 (–1.12 to 1.76)
MET + ROS		0.96 (0.43 to 2.29)	0.96 (0.44 to 2.23)	–0.10 (–1.64 to 2.82)
MET + PIO		1.29 (0.84 to 2.06)	1.28 (0.84 to 2.01)	0.69 (–0.48 to 2.21)
MET + IAS		1.32 (0.25 to 6.95)	1.30 (0.26 to 6.00)	0.77 (–2.00 to 13.10)
MET + IGA		1.65 (0.68 to 3.89)	1.63 (0.69 to 3.63)	1.58 (–0.79 to 6.78)
MET + CAN	MET + VIL	1.92 (0.84 to 4.58)	1.88 (0.85 to 4.32)	1.77 (–0.38 to 5.94)
MET + DAP		1.24 (0.66 to 2.35)	1.23 (0.66 to 2.30)	0.46 (–0.87 to 2.18)
MET + EMP		1.44 (0.88 to 2.30)	1.43 (0.88 to 2.25)	0.85 (–0.30 to 2.21)
MET + LIR		2.05 (1.00 to 4.10)	2.00 (1.00 to 3.90)	2.01 (–0.01 to 5.11)
MET + EXE		1.10 (0.49 to 2.49)	1.10 (0.49 to 2.43)	0.20 (–1.24 to 2.56)
MET + DUL		1.61 (0.75 to 3.43)	1.59 (0.75 to 3.28)	1.17 (–0.61 to 4.12)
MET + LIX		1.33 (0.72 to 2.47)	1.32 (0.72 to 2.42)	0.64 (–0.71 to 2.36)
MET + ROS		1.20 (0.51 to 3.04)	1.20 (0.52 to 2.94)	0.39 (–1.19 to 3.35)
MET + PIO		1.63 (1.04 to 2.54)	1.61 (1.03 to 2.48)	1.21 (0.08 to 2.54)
MET + IAS		1.68 (0.30 to 9.30)	1.65 (0.30 to 7.97)	1.29 (–1.60 to 13.72)
MET + IGA		2.11 (0.76 to 5.26)	2.06 (0.77 to 4.88)	2.12 (–0.54 to 7.44)
MET + DAP	MET + CAN	0.65 (0.25 to 1.62)	0.66 (0.27 to 1.60)	–1.27 (–5.54 to 1.32)
MET + EMP		0.75 (0.31 to 1.74)	0.76 (0.32 to 1.71)	–0.91 (–5.13 to 1.54)
MET + LIR		1.07 (0.39 to 2.61)	1.07 (0.40 to 2.51)	0.26 (–4.24 to 3.85)
MET + EXE		0.57 (0.20 to 1.55)	0.58 (0.21 to 1.53)	–1.56 (–5.59 to 1.27)
MET + DUL		0.84 (0.30 to 2.15)	0.85 (0.31 to 2.10)	–0.56 (–4.88 to 2.81)
MET + LIX		0.69 (0.28 to 1.61)	0.70 (0.30 to 1.59)	–1.11 (–5.24 to 1.32)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ROS		0.63 (0.21 to 1.92)	0.64 (0.22 to 1.88)	–1.32 (–5.72 to 2.09)
MET + PIO		0.85 (0.37 to 1.90)	0.86 (0.39 to 1.87)	–0.54 (–4.63 to 1.85)
MET + IAS		0.85 (0.15 to 5.14)	0.85 (0.15 to 4.55)	–0.52 (–5.06 to 11.69)
MET + IGA		1.07 (0.35 to 3.34)	1.07 (0.36 to 3.15)	0.25 (–4.11 to 6.03)
MET + EMP	MET + DAP	1.16 (0.59 to 2.22)	1.15 (0.59 to 2.17)	0.37 (–1.49 to 2.12)
MET + LIR		1.65 (0.70 to 3.70)	1.62 (0.70 to 3.53)	1.52 (–1.06 to 4.84)
MET + EXE		0.88 (0.34 to 2.18)	0.89 (0.35 to 2.14)	–0.28 (–2.32 to 2.24)
MET + DUL		1.29 (0.56 to 3.14)	1.28 (0.57 to 3.01)	0.69 (–1.53 to 3.87)
MET + LIX		1.07 (0.54 to 2.19)	1.06 (0.55 to 2.14)	0.16 (–1.66 to 2.07)
MET + ROS		0.97 (0.38 to 2.66)	0.97 (0.39 to 2.58)	–0.07 (–2.16 to 3.04)
MET + PIO		1.31 (0.71 to 2.43)	1.30 (0.72 to 2.37)	0.72 (–1.08 to 2.43)
MET + IAS		1.34 (0.22 to 8.36)	1.32 (0.23 to 7.20)	0.80 (–2.52 to 13.53)
MET + IGA		1.69 (0.58 to 4.68)	1.66 (0.58 to 4.35)	1.62 (–1.36 to 7.12)
MET + LIR	MET + EMP	1.41 (0.70 to 2.97)	1.39 (0.70 to 2.84)	1.12 (–1.08 to 4.39)
MET + EXE		0.76 (0.33 to 1.83)	0.76 (0.34 to 1.79)	–0.68 (–2.46 to 1.91)
MET + DUL		1.12 (0.53 to 2.46)	1.11 (0.54 to 2.38)	0.32 (–1.71 to 3.34)
MET + LIX		0.92 (0.49 to 1.77)	0.92 (0.50 to 1.74)	–0.22 (–1.97 to 1.68)
MET + ROS		0.84 (0.34 to 2.16)	0.85 (0.35 to 2.10)	–0.43 (–2.49 to 2.61)
MET + PIO		1.13 (0.68 to 1.94)	1.12 (0.69 to 1.91)	0.35 (–1.24 to 1.98)
MET + IAS		1.17 (0.20 to 6.53)	1.17 (0.21 to 5.67)	0.48 (–2.73 to 12.92)
MET + IGA		1.47 (0.53 to 3.77)	1.45 (0.54 to 3.52)	1.26 (–1.61 to 6.58)
MET + EXE	MET + LIR	0.54 (0.21 to 1.40)	0.55 (0.22 to 1.38)	–1.77 (–4.97 to 1.06)
MET + DUL		0.79 (0.38 to 1.60)	0.80 (0.39 to 1.57)	–0.79 (–3.74 to 1.80)
MET + LIX		0.64 (0.35 to 1.28)	0.65 (0.36 to 1.27)	–1.37 (–4.24 to 0.73)
MET + ROS		0.60 (0.22 to 1.50)	0.61 (0.23 to 1.48)	–1.50 (–4.99 to 1.50)
MET + PIO		0.79 (0.39 to 1.63)	0.80 (0.41 to 1.61)	–0.80 (–4.07 to 1.50)
MET + IAS		0.81 (0.13 to 4.84)	0.82 (0.14 to 4.29)	–0.69 (–5.04 to 11.64)
MET + IGA		1.02 (0.34 to 3.00)	1.02 (0.36 to 2.83)	0.07 (–3.75 to 5.69)
MET + DUL	MET + EXE	1.46 (0.55 to 3.95)	1.45 (0.56 to 3.81)	0.96 (–1.75 to 4.08)
MET + LIX		1.21 (0.56 to 2.55)	1.21 (0.57 to 2.50)	0.45 (–1.75 to 2.03)
MET + ROS		1.11 (0.36 to 3.47)	1.11 (0.36 to 3.36)	0.23 (–2.55 to 3.33)
MET + PIO		1.47 (0.70 to 3.22)	1.46 (0.71 to 3.14)	0.99 (–1.24 to 2.70)
MET + IAS		1.52 (0.27 to 8.55)	1.50 (0.27 to 7.54)	1.07 (–2.36 to 13.27)
MET + IGA		1.89 (0.64 to 5.61)	1.85 (0.64 to 5.26)	1.82 (–1.10 to 7.27)
MET + LIX	MET + DUL	0.82 (0.39 to 1.83)	0.83 (0.40 to 1.80)	–0.55 (–3.44 to 1.57)
MET + ROS		0.76 (0.28 to 2.06)	0.76 (0.29 to 2.02)	–0.72 (–3.79 to 2.26)
MET + PIO		1.01 (0.48 to 2.18)	1.01 (0.50 to 2.13)	0.03 (–2.95 to 2.14)
MET + IAS		1.03 (0.17 to 6.23)	1.03 (0.18 to 5.49)	0.10 (–3.89 to 12.49)
MET + IGA		1.29 (0.43 to 3.82)	1.28 (0.44 to 3.58)	0.86 (–2.71 to 6.37)
MET + ROS	MET + LIX	0.92 (0.37 to 2.33)	0.92 (0.37 to 2.27)	–0.21 (–2.31 to 2.74)
MET + PIO		1.21 (0.69 to 2.21)	1.21 (0.70 to 2.16)	0.55 (–1.20 to 2.23)
MET + IAS		1.25 (0.22 to 7.13)	1.24 (0.23 to 6.23)	0.63 (–2.53 to 13.09)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + IGA		1.56 (0.56 to 4.25)	1.54 (0.56 to 3.96)	1.42 (–1.43 to 6.95)
MET + PIO	MET + ROS	1.35 (0.56 to 3.26)	1.34 (0.57 to 3.17)	0.80 (–2.19 to 2.80)
MET + IAS		1.36 (0.21 to 9.35)	1.35 (0.22 to 8.11)	0.80 (–3.16 to 13.29)
MET + IGA		1.74 (0.48 to 5.83)	1.70 (0.50 to 5.44)	1.64 (–2.27 to 7.27)
MET + IAS	MET + PIO	1.03 (0.18 to 5.97)	1.03 (0.19 to 5.18)	0.08 (–3.03 to 12.63)
MET + IGA		1.27 (0.47 to 3.36)	1.26 (0.48 to 3.15)	0.85 (–1.96 to 6.35)
MET + IGA	MET + IAS	1.26 (0.29 to 5.18)	1.25 (0.33 to 4.99)	0.73 (–9.20 to 4.72)
Random-effects model	Residual deviance	122.8 vs. 130 data points		
	Deviance information criteria	685.156		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLC = glicazide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; IAS = insulin aspart; IGA = insulin glargine; LIX = lixisenatide; LIN = linagliptin; LIR = liraglutide; MET = metformin; NAT = nateglinide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 24: Consistency Plot for Serious Adverse Events (Individual-Drug Case Analysis)



Severe Hypoglycemia

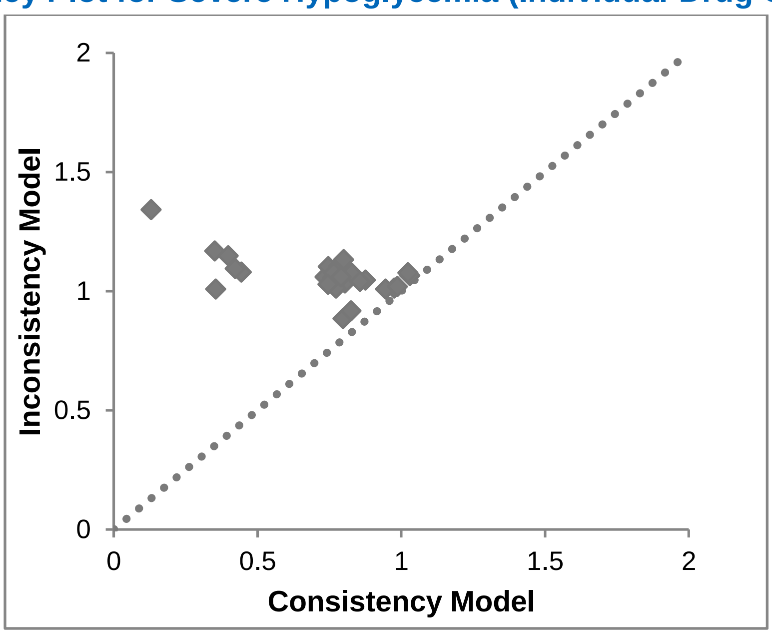
Table 42: Severe Hypoglycemia : Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	3.18 (0.69 to 24.16)	3.11 (0.69 to 21.14)	1.95 (–0.41 to 12.88)
MET + GLY		1.34 (0.15 to 13.11)	1.33 (0.15 to 12.25)	0.29 (–1.37 to 7.48)
MET + GLI		4.90 (0.65 to 53.64)	4.70 (0.65 to 38.24)	3.49 (–0.39 to 29.42)
MET + SAX		0.46 (0.03 to 6.67)	0.46 (0.03 to 6.41)	–0.44 (–1.70 to 4.38)
MET + LIN		0.23 (0.01 to 2.72)	0.24 (0.01 to 2.68)	–0.64 (–1.96 to 1.24)
MET + SIT		0.54 (0.11 to 3.72)	0.54 (0.11 to 3.65)	–0.39 (–1.63 to 1.84)
MET + CAN		0.19 (0.01 to 1.69)	0.19 (0.01 to 1.68)	–0.69 (–1.95 to 0.49)
MET + LIR		0.45 (0.05 to 4.91)	0.45 (0.05 to 4.78)	–0.45 (–1.77 to 2.71)
MET + LIX		0.38 (0.02 to 6.66)	0.39 (0.02 to 6.37)	–0.48 (–1.84 to 4.73)
MET + IGA		1.38 (0.11 to 21.85)	1.38 (0.11 to 18.69)	0.31 (–1.39 to 15.47)
MET + GLY	MET + GLM	0.40 (0.02 to 6.11)	0.41 (0.02 to 5.74)	–1.56 (–13.01 to 6.22)
MET + GLI		1.45 (0.20 to 12.23)	1.43 (0.22 to 9.69)	1.16 (–6.15 to 23.69)
MET + SAX		0.14 (0.01 to 1.63)	0.14 (0.01 to 1.60)	–2.30 (–12.03 to 1.51)
MET + LIN		0.07 (0.01 to 0.44)	0.07 (0.01 to 0.45)	–2.65 (–12.63 to –0.57)
MET + SIT		0.17 (0.04 to 0.60)	0.17 (0.04 to 0.61)	–2.37 (–11.95 to –0.39)
MET + CAN		0.06 (0.00 to 0.68)	0.06 (0.00 to 0.68)	–2.71 (–13.51 to –0.32)
MET + LIR		0.14 (0.02 to 0.82)	0.14 (0.02 to 0.82)	–2.38 (–11.99 to –0.23)
MET + LIX		0.11 (0.01 to 2.14)	0.11 (0.01 to 2.07)	–2.33 (–12.56 to 2.27)
MET + IGA		0.41 (0.04 to 6.13)	0.42 (0.04 to 5.43)	–1.34 (–10.45 to 11.72)
MET + GLI	MET + GLY	3.83 (0.17 to 87.65)	3.66 (0.18 to 67.29)	2.96 (–5.35 to 29.11)
MET + SAX		0.35 (0.01 to 10.64)	0.35 (0.01 to 10.14)	–0.65 (–7.92 to 4.22)
MET + LIN		0.16 (0.01 to 5.13)	0.17 (0.01 to 5.05)	–0.94 (–8.12 to 1.32)
MET + SIT		0.41 (0.02 to 7.72)	0.41 (0.03 to 7.56)	–0.66 (–8.02 to 1.96)
MET + CAN		0.13 (0.00 to 3.46)	0.14 (0.00 to 3.42)	–1.01 (–8.25 to 0.69)
MET + LIR		0.33 (0.02 to 8.68)	0.33 (0.02 to 8.50)	–0.73 (–7.98 to 2.70)
MET + LIX		0.28 (0.01 to 10.45)	0.28 (0.01 to 9.98)	–0.73 (–7.91 to 4.59)
MET + IGA		1.04 (0.03 to 36.44)	1.04 (0.03 to 31.33)	0.03 (–7.36 to 15.49)
MET + SAX	MET + GLI	0.10 (0.01 to 0.71)	0.10 (0.01 to 0.72)	–3.80 (–27.14 to –0.27)
MET + LIN		0.05 (0.00 to 0.67)	0.05 (0.00 to 0.68)	–4.16 (–29.74 to –0.24)
MET + SIT		0.11 (0.02 to 0.42)	0.12 (0.03 to 0.42)	–3.93 (–28.39 to –0.38)
MET + CAN		0.04 (0.00 to 0.54)	0.04 (0.00 to 0.55)	–4.24 (–30.09 to –0.32)
MET + LIR		0.09 (0.01 to 0.96)	0.10 (0.01 to 0.96)	–3.87 (–28.84 to –0.04)
MET + LIX		0.08 (0.00 to 1.23)	0.08 (0.00 to 1.22)	–3.79 (–27.99 to 0.42)
MET + IGA		0.28 (0.02 to 4.27)	0.30 (0.03 to 3.88)	–2.46 (–25.53 to 7.51)
MET + LIN	MET + SAX	0.47 (0.02 to 13.34)	0.47 (0.02 to 13.18)	–0.17 (–4.79 to 1.42)
MET + SIT		1.20 (0.16 to 11.00)	1.20 (0.16 to 10.95)	0.06 (–3.92 to 1.28)
MET + CAN		0.41 (0.01 to 10.31)	0.41 (0.01 to 10.21)	–0.21 (–5.07 to 0.89)
MET + LIR		0.96 (0.06 to 17.89)	0.96 (0.06 to 17.64)	–0.01 (–4.49 to 2.55)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX		0.83 (0.03 to 20.35)	0.83 (0.03 to 19.87)	–0.05 (–3.98 to 4.63)
MET + IGA		3.08 (0.15 to 83.30)	3.03 (0.16 to 76.94)	0.68 (–2.83 to 15.27)
MET + SIT	MET + LIN	2.42 (0.22 to 36.19)	2.41 (0.22 to 35.75)	0.23 (–1.31 to 2.21)
MET + CAN		0.78 (0.02 to 32.26)	0.78 (0.02 to 31.95)	–0.04 (–1.95 to 1.18)
MET + LIR		1.97 (0.12 to 42.45)	1.96 (0.12 to 41.73)	0.15 (–1.39 to 2.98)
MET + LIX		1.71 (0.05 to 71.85)	1.70 (0.05 to 67.63)	0.10 (–1.65 to 5.35)
MET + IGA		6.58 (0.25 to 167.80)	6.44 (0.25 to 153.00)	0.93 (–0.77 to 15.85)
MET + CAN	MET + SIT	0.37 (0.01 to 3.36)	0.37 (0.01 to 3.33)	–0.27 (–2.44 to 0.72)
MET + LIR		0.81 (0.11 to 5.48)	0.81 (0.12 to 5.38)	–0.07 (–1.47 to 2.30)
MET + LIX		0.69 (0.05 to 9.10)	0.69 (0.05 to 8.63)	–0.11 (–1.65 to 4.68)
MET + IGA		2.48 (0.34 to 23.78)	2.45 (0.34 to 20.54)	0.67 (–0.57 to 15.16)
MET + LIR	MET + CAN	2.26 (0.19 to 72.41)	2.25 (0.19 to 70.60)	0.19 (–0.83 to 3.40)
MET + LIX		1.90 (0.07 to 101.00)	1.89 (0.07 to 93.99)	0.13 (–0.91 to 5.54)
MET + IGA		7.43 (0.37 to 321.60)	7.26 (0.38 to 285.70)	1.01 (–0.46 to 16.29)
MET + LIX	MET + LIR	0.85 (0.03 to 18.72)	0.85 (0.03 to 17.83)	–0.04 (–2.84 to 5.01)
MET + IGA		3.00 (0.20 to 61.00)	2.97 (0.20 to 53.45)	0.69 (–1.58 to 15.53)
MET + IGA	MET + LIX	3.84 (0.14 to 133.80)	3.77 (0.15 to 120.10)	0.69 (–3.55 to 15.49)
Random-effects model	Residual deviance	18.96 vs. 26 data points		
	Deviance information criteria	102.777		

CAN = canagliflozin; CrI = credible interval; GLI = glipizide; GLM = glimepiride; GLY = glyburide; IGA = insulin glargine; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; vs. = versus.

Figure 25: Consistency Plot for Severe Hypoglycemia (Individual-Drug Case Analysis)



Urogenital Adverse Events (People)

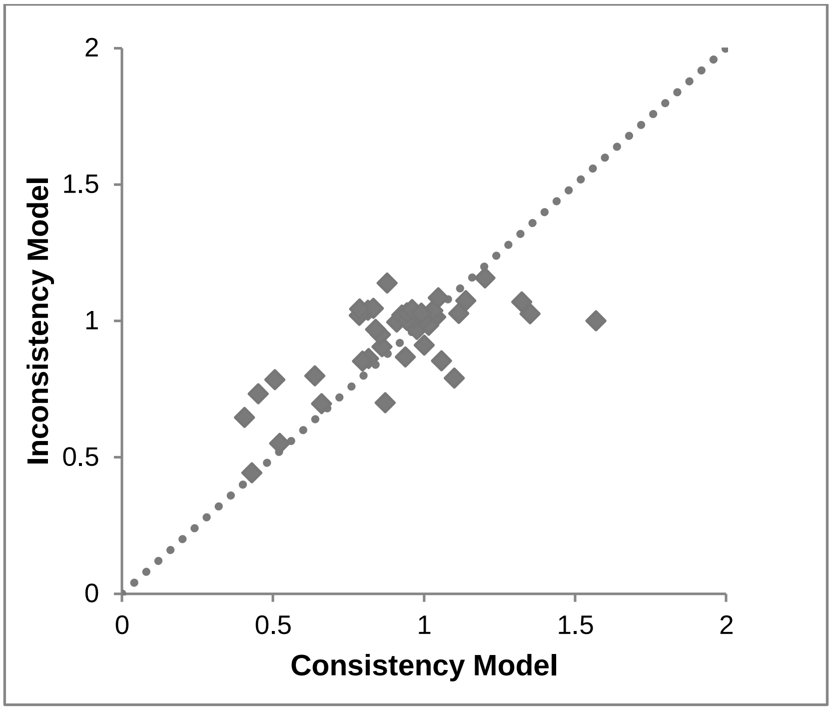
Table 43: Urogenital Adverse Events (People): Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	1.10 (0.73 to 1.65)	1.09 (0.74 to 1.61)	0.33 (–1.05 to 1.99)
MET + GLI		0.60 (0.28 to 1.26)	0.61 (0.29 to 1.25)	–1.39 (–2.81 to 0.84)
MET + SAX		1.13 (0.75 to 1.74)	1.12 (0.75 to 1.70)	0.43 (–0.99 to 2.29)
MET + LIN		1.02 (0.57 to 1.74)	1.02 (0.58 to 1.70)	0.06 (–1.67 to 2.31)
MET + SIT		1.10 (0.73 to 1.67)	1.10 (0.74 to 1.64)	0.35 (–1.05 to 2.07)
MET + DAP		2.15 (0.86 to 5.94)	2.06 (0.86 to 5.09)	3.82 (–0.53 to 13.93)
MET + EMP		1.00 (0.63 to 1.55)	1.00 (0.64 to 1.53)	0.00 (–1.41 to 1.74)
MET + EXE		1.27 (0.43 to 3.77)	1.26 (0.44 to 3.44)	0.91 (–2.13 to 8.52)
MET + DUL		0.93 (0.37 to 2.22)	0.93 (0.38 to 2.12)	–0.24 (–2.40 to 3.82)
MET + PIO		0.73 (0.22 to 2.27)	0.73 (0.23 to 2.18)	–0.95 (–3.01 to 4.09)
MET + IGA		0.78 (0.07 to 7.53)	0.79 (0.07 to 6.11)	–0.76 (–3.64 to 18.04)
MET + GLI	MET + GLM	0.55 (0.25 to 1.19)	0.56 (0.25 to 1.18)	–1.69 (–3.62 to 0.62)
MET + SAX		1.03 (0.64 to 1.69)	1.03 (0.65 to 1.65)	0.11 (–1.73 to 2.10)
MET + LIN		0.93 (0.57 to 1.48)	0.93 (0.58 to 1.46)	–0.27 (–1.87 to 1.66)
MET + SIT		1.01 (0.63 to 1.60)	1.01 (0.64 to 1.57)	0.04 (–1.80 to 1.85)
MET + DAP		1.95 (0.73 to 5.73)	1.88 (0.74 to 4.95)	3.45 (–1.19 to 13.73)
MET + EMP		0.92 (0.61 to 1.34)	0.92 (0.62 to 1.33)	–0.31 (–1.77 to 1.16)
MET + EXE		1.18 (0.38 to 3.57)	1.17 (0.39 to 3.27)	0.65 (–2.72 to 8.29)
MET + DUL		0.85 (0.33 to 2.11)	0.85 (0.34 to 2.03)	–0.58 (–3.08 to 3.62)
MET + PIO		0.67 (0.20 to 2.10)	0.67 (0.21 to 2.01)	–1.25 (–3.68 to 3.76)
MET + IGA		0.71 (0.07 to 6.89)	0.72 (0.07 to 5.67)	–1.08 (–4.17 to 17.69)
MET + SAX	MET + GLI	1.88 (0.86 to 4.20)	1.84 (0.87 to 4.05)	1.81 (–0.54 to 3.84)
MET + LIN		1.69 (0.69 to 4.14)	1.66 (0.70 to 3.99)	1.42 (–1.19 to 3.94)
MET + SIT		1.83 (1.00 to 3.44)	1.79 (1.00 to 3.35)	1.71 (0.01 to 3.14)
MET + DAP		3.56 (1.12 to 12.47)	3.37 (1.12 to 10.69)	5.14 (0.40 to 15.31)
MET + EMP		1.66 (0.72 to 3.78)	1.64 (0.73 to 3.66)	1.38 (–1.06 to 3.44)
MET + EXE		2.13 (0.69 to 6.88)	2.07 (0.70 to 6.25)	2.29 (–0.93 to 9.66)
MET + DUL		1.54 (0.54 to 4.44)	1.53 (0.55 to 4.23)	1.11 (–1.51 to 5.17)
MET + PIO		1.19 (0.34 to 4.10)	1.19 (0.35 to 3.90)	0.39 (–2.12 to 5.26)
MET + IGA		1.31 (0.12 to 12.51)	1.30 (0.12 to 10.13)	0.63 (–2.77 to 19.13)
MET + LIN	MET + SAX	0.90 (0.47 to 1.70)	0.90 (0.48 to 1.67)	–0.39 (–2.70 to 2.18)
MET + SIT		0.98 (0.60 to 1.56)	0.98 (0.62 to 1.53)	–0.09 (–1.99 to 1.76)
MET + DAP		1.92 (0.68 to 5.62)	1.85 (0.69 to 4.84)	3.40 (–1.50 to 13.74)
MET + EMP		0.89 (0.50 to 1.52)	0.89 (0.51 to 1.50)	–0.44 (–2.59 to 1.61)
MET + EXE		1.13 (0.38 to 3.44)	1.12 (0.39 to 3.17)	0.50 (–2.86 to 8.00)
MET + DUL		0.82 (0.32 to 2.08)	0.83 (0.33 to 2.01)	–0.69 (–3.30 to 3.59)
MET + PIO		0.64 (0.19 to 2.08)	0.65 (0.20 to 2.00)	–1.37 (–3.89 to 3.67)
MET + IGA		0.70 (0.06 to 6.65)	0.70 (0.06 to 5.46)	–1.15 (–4.42 to 17.51)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SIT	MET + LIN	1.09 (0.58 to 2.08)	1.08 (0.59 to 2.02)	0.31 (–2.23 to 2.56)
MET + DAP		2.11 (0.73 to 6.65)	2.02 (0.74 to 5.73)	3.71 (–1.19 to 14.07)
MET + EMP		0.99 (0.54 to 1.78)	0.99 (0.55 to 1.75)	–0.04 (–2.36 to 1.94)
MET + EXE		1.27 (0.38 to 4.12)	1.26 (0.40 to 3.77)	0.91 (–2.90 to 8.60)
MET + DUL		0.91 (0.33 to 2.54)	0.92 (0.34 to 2.43)	–0.30 (–3.26 to 4.10)
MET + PIO		0.72 (0.20 to 2.49)	0.73 (0.21 to 2.39)	–0.97 (–3.96 to 4.17)
MET + IGA		0.76 (0.07 to 8.02)	0.77 (0.07 to 6.56)	–0.81 (–4.36 to 18.03)
MET + DAP	MET + SIT	1.96 (0.72 to 5.74)	1.89 (0.73 to 4.94)	3.47 (–1.26 to 13.75)
MET + EMP		0.91 (0.53 to 1.56)	0.91 (0.54 to 1.54)	–0.34 (–2.34 to 1.70)
MET + EXE		1.16 (0.43 to 3.13)	1.15 (0.44 to 2.89)	0.59 (–2.27 to 7.74)
MET + DUL		0.84 (0.36 to 1.95)	0.84 (0.37 to 1.89)	–0.60 (–2.84 to 3.33)
MET + PIO		0.66 (0.21 to 1.87)	0.67 (0.22 to 1.81)	–1.28 (–3.43 to 3.29)
MET + IGA		0.71 (0.07 to 6.24)	0.71 (0.07 to 5.13)	–1.10 (–4.18 to 17.22)
MET + EMP	MET + DAP	0.47 (0.16 to 1.30)	0.48 (0.18 to 1.28)	–3.80 (–14.14 to 0.96)
MET + EXE		0.59 (0.14 to 2.40)	0.61 (0.16 to 2.25)	–2.78 (–13.20 to 5.52)
MET + DUL		0.43 (0.11 to 1.50)	0.45 (0.13 to 1.47)	–3.97 (–14.45 to 1.87)
MET + PIO		0.33 (0.07 to 1.46)	0.35 (0.08 to 1.43)	–4.62 (–14.92 to 1.75)
MET + IGA		0.36 (0.02 to 3.92)	0.38 (0.03 to 3.32)	–4.13 (–14.73 to 14.17)
MET + EXE	MET + EMP	1.28 (0.41 to 4.11)	1.27 (0.42 to 3.76)	0.94 (–2.44 to 8.63)
MET + DUL		0.93 (0.35 to 2.39)	0.93 (0.36 to 2.29)	–0.25 (–2.91 to 3.95)
MET + PIO		0.73 (0.21 to 2.34)	0.74 (0.22 to 2.24)	–0.92 (–3.53 to 4.07)
MET + IGA		0.78 (0.07 to 7.89)	0.78 (0.08 to 6.47)	–0.77 (–3.95 to 18.02)
MET + DUL	MET + EXE	0.73 (0.19 to 2.78)	0.74 (0.21 to 2.68)	–1.16 (–8.86 to 3.80)
MET + PIO		0.57 (0.19 to 1.63)	0.58 (0.20 to 1.60)	–1.79 (–7.74 to 1.79)
MET + IGA		0.62 (0.06 to 4.28)	0.63 (0.07 to 3.67)	–1.38 (–7.42 to 13.74)
MET + PIO	MET + DUL	0.79 (0.19 to 3.21)	0.79 (0.20 to 3.08)	–0.64 (–5.13 to 4.52)
MET + IGA		0.82 (0.07 to 8.75)	0.83 (0.07 to 7.24)	–0.54 (–5.35 to 17.93)
MET + IGA	MET + PIO	1.09 (0.09 to 10.42)	1.09 (0.10 to 8.42)	0.21 (–4.59 to 17.56)

CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLI = glipizide; GLM = glimepiride; IGA = insulin glargine; LIN = linagliptin; MET = metformin; OR = odds ratio; PIO = pioglitazone; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin.

Figure 26: Consistency Plot for Urogenital Adverse Events (People) (Individual-Drug Case Analysis)



Withdrawals Due to Adverse Events (WAE)

Table 44: Withdrawals Due to Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLC	MET	1.16 (0.46 to 3.02)	1.15 (0.46 to 2.87)	0.41 (–1.52 to 4.88)
MET + GLM		0.82 (0.55 to 1.25)	0.82 (0.55 to 1.25)	–0.48 (–1.31 to 0.62)
MET + GLY		2.39 (0.62 to 9.66)	2.30 (0.62 to 7.91)	3.51 (–1.04 to 18.13)
MET + GLI		0.82 (0.38 to 1.67)	0.82 (0.39 to 1.65)	–0.49 (–1.73 to 1.67)
MET + GLL		0.51 (0.17 to 1.61)	0.52 (0.17 to 1.59)	–1.30 (–2.37 to 1.52)
MET + MIT		0.39 (0.01 to 5.57)	0.39 (0.01 to 4.98)	–1.63 (–2.91 to 10.45)
MET + NAT		0.93 (0.25 to 3.34)	0.94 (0.26 to 3.15)	–0.17 (–2.04 to 5.65)
MET + SAX		1.15 (0.67 to 1.97)	1.15 (0.67 to 1.92)	0.39 (–0.94 to 2.38)
MET + ALO		0.83 (0.36 to 1.94)	0.83 (0.36 to 1.89)	–0.46 (–1.81 to 2.32)
MET + LIN		0.69 (0.35 to 1.47)	0.69 (0.35 to 1.45)	–0.83 (–1.86 to 1.17)
MET + SIT		0.89 (0.60 to 1.36)	0.89 (0.60 to 1.35)	–0.30 (–1.15 to 0.87)
MET + VIL		0.76 (0.44 to 1.36)	0.76 (0.45 to 1.35)	–0.64 (–1.60 to 0.90)
MET + CAN		1.31 (0.62 to 2.98)	1.30 (0.62 to 2.84)	0.81 (–1.07 to 4.67)
MET + DAP		0.61 (0.28 to 1.39)	0.61 (0.28 to 1.38)	–1.04 (–2.05 to 1.00)
MET + EMP		1.11 (0.55 to 2.27)	1.10 (0.56 to 2.20)	0.28 (–1.24 to 3.12)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIR		2.54 (1.25 to 5.34)	2.44 (1.24 to 4.81)	3.90 (0.68 to 9.97)
MET + EXE		2.12 (1.06 to 4.30)	2.06 (1.05 to 3.96)	2.87 (0.15 to 7.71)
MET + DUL		1.28 (0.61 to 2.80)	1.27 (0.62 to 2.68)	0.74 (–1.05 to 4.41)
MET + ALB		1.55 (0.65 to 3.82)	1.52 (0.65 to 3.56)	1.42 (–0.96 to 6.72)
MET + LIX		1.89 (0.99 to 3.67)	1.85 (0.99 to 3.44)	2.28 (–0.04 to 6.36)
MET + ROS		1.82 (0.82 to 4.48)	1.78 (0.82 to 4.10)	2.11 (–0.50 to 7.89)
MET + PIO		1.35 (0.78 to 2.45)	1.34 (0.78 to 2.36)	0.92 (–0.62 to 3.50)
MET + IGA		0.33 (0.06 to 1.42)	0.34 (0.06 to 1.41)	–1.77 (–2.76 to 1.07)
MET + GLM	MET + GLC	0.71 (0.27 to 1.86)	0.72 (0.28 to 1.84)	–0.87 (–5.27 to 1.19)
MET + GLY		2.05 (0.45 to 9.93)	1.98 (0.47 to 8.38)	2.92 (–2.74 to 17.31)
MET + GLI		0.70 (0.22 to 2.15)	0.71 (0.23 to 2.11)	–0.88 (–5.34 to 1.83)
MET + GLL		0.44 (0.11 to 1.81)	0.45 (0.12 to 1.78)	–1.64 (–6.09 to 1.45)
MET + MIT		0.34 (0.01 to 5.74)	0.35 (0.01 to 5.13)	–1.79 (–6.65 to 9.96)
MET + NAT		0.81 (0.18 to 3.42)	0.81 (0.19 to 3.24)	–0.54 (–5.10 to 5.05)
MET + SAX		0.99 (0.34 to 2.82)	0.99 (0.36 to 2.75)	–0.02 (–4.53 to 2.69)
MET + ALO		0.72 (0.21 to 2.41)	0.72 (0.22 to 2.35)	–0.83 (–5.29 to 2.35)
MET + LIN		0.60 (0.19 to 1.92)	0.60 (0.20 to 1.89)	–1.20 (–5.67 to 1.42)
MET + SIT		0.77 (0.29 to 2.03)	0.77 (0.30 to 2.00)	–0.69 (–5.08 to 1.41)
MET + VIL		0.65 (0.24 to 1.84)	0.66 (0.25 to 1.82)	–1.03 (–5.43 to 1.24)
MET + CAN		1.14 (0.36 to 3.73)	1.14 (0.38 to 3.57)	0.40 (–4.12 to 4.54)
MET + DAP		0.53 (0.15 to 1.86)	0.54 (0.16 to 1.84)	–1.41 (–5.97 to 1.34)
MET + EMP		0.96 (0.30 to 3.04)	0.96 (0.32 to 2.94)	–0.12 (–4.67 to 3.20)
MET + LIR		2.20 (0.69 to 6.93)	2.12 (0.71 to 6.31)	3.36 (–1.91 to 9.63)
MET + EXE		1.84 (0.59 to 5.46)	1.79 (0.61 to 5.08)	2.37 (–2.56 to 7.34)
MET + DUL		1.11 (0.34 to 3.65)	1.11 (0.35 to 3.50)	0.32 (–4.41 to 4.37)
MET + ALB		1.35 (0.38 to 4.62)	1.34 (0.39 to 4.33)	1.00 (–3.90 to 6.50)
MET + LIX		1.63 (0.53 to 4.93)	1.60 (0.55 to 4.63)	1.82 (–3.00 to 6.28)
MET + ROS		1.58 (0.55 to 4.79)	1.55 (0.57 to 4.47)	1.61 (–2.67 to 7.15)
MET + PIO		1.17 (0.49 to 2.78)	1.16 (0.51 to 2.70)	0.49 (–3.34 to 2.87)
MET + IGA		0.28 (0.04 to 1.52)	0.29 (0.04 to 1.50)	–2.08 (–6.47 to 1.01)
MET + GLY	MET + GLM	2.90 (0.71 to 12.36)	2.79 (0.71 to 10.11)	3.97 (–0.73 to 18.61)
MET + GLI		0.99 (0.44 to 2.12)	1.00 (0.45 to 2.07)	–0.01 (–1.48 to 2.11)
MET + GLL		0.62 (0.21 to 1.95)	0.63 (0.21 to 1.91)	–0.81 (–2.14 to 1.88)
MET + MIT		0.47 (0.02 to 7.07)	0.48 (0.02 to 6.29)	–1.12 (–2.76 to 10.88)
MET + NAT		1.14 (0.29 to 4.28)	1.14 (0.30 to 4.01)	0.29 (–1.86 to 6.17)
MET + SAX		1.40 (0.76 to 2.56)	1.39 (0.76 to 2.49)	0.86 (–0.65 to 2.83)
MET + ALO		1.01 (0.42 to 2.47)	1.01 (0.42 to 2.40)	0.03 (–1.56 to 2.75)
MET + LIN		0.84 (0.44 to 1.71)	0.84 (0.45 to 1.68)	–0.35 (–1.43 to 1.43)
MET + SIT		1.08 (0.68 to 1.75)	1.08 (0.69 to 1.72)	0.18 (–0.89 to 1.30)
MET + VIL		0.92 (0.53 to 1.67)	0.92 (0.54 to 1.64)	–0.17 (–1.26 to 1.26)
MET + CAN		1.60 (0.69 to 3.86)	1.58 (0.70 to 3.67)	1.28 (–0.81 to 5.14)
MET + DAP		0.74 (0.30 to 1.86)	0.74 (0.31 to 1.83)	–0.56 (–1.99 to 1.57)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + EMP		1.35 (0.68 to 2.75)	1.34 (0.68 to 2.65)	0.74 (–0.79 to 3.43)
MET + LIR		3.09 (1.53 to 6.50)	2.95 (1.51 to 5.86)	4.34 (1.24 to 10.19)
MET + EXE		2.60 (1.23 to 5.38)	2.50 (1.23 to 4.96)	3.33 (0.56 to 8.08)
MET + DUL		1.57 (0.71 to 3.55)	1.55 (0.71 to 3.38)	1.21 (–0.74 to 4.82)
MET + ALB		1.90 (0.80 to 4.57)	1.86 (0.80 to 4.25)	1.90 (–0.48 to 7.02)
MET + LIX		2.31 (1.10 to 4.80)	2.24 (1.10 to 4.49)	2.76 (0.25 to 6.84)
MET + ROS		2.22 (0.92 to 5.78)	2.16 (0.92 to 5.31)	2.56 (–0.21 to 8.39)
MET + PIO		1.65 (0.94 to 2.97)	1.63 (0.94 to 2.86)	1.39 (–0.16 to 3.76)
MET + IGA		0.40 (0.07 to 1.75)	0.41 (0.07 to 1.73)	–1.28 (–2.58 to 1.51)
MET + GLI	MET + GLY	0.34 (0.07 to 1.58)	0.35 (0.08 to 1.56)	–3.95 (–18.65 to 1.10)
MET + GLL		0.21 (0.04 to 1.24)	0.22 (0.04 to 1.23)	–4.66 (–19.14 to 0.51)
MET + MIT		0.16 (0.00 to 3.42)	0.17 (0.01 to 3.13)	–4.54 (–19.23 to 7.58)
MET + NAT		0.39 (0.06 to 2.43)	0.41 (0.07 to 2.35)	–3.46 (–18.22 to 3.65)
MET + SAX		0.48 (0.11 to 2.11)	0.50 (0.13 to 2.07)	–3.07 (–17.79 to 1.93)
MET + ALO		0.35 (0.07 to 1.75)	0.36 (0.08 to 1.72)	–3.89 (–18.40 to 1.48)
MET + LIN		0.29 (0.06 to 1.41)	0.30 (0.08 to 1.40)	–4.26 (–18.87 to 0.75)
MET + SIT		0.37 (0.09 to 1.56)	0.39 (0.11 to 1.55)	–3.77 (–18.40 to 0.96)
MET + VIL		0.32 (0.07 to 1.39)	0.33 (0.09 to 1.38)	–4.10 (–18.69 to 0.71)
MET + CAN		0.55 (0.11 to 2.68)	0.57 (0.14 to 2.60)	–2.55 (–17.31 to 3.45)
MET + DAP		0.25 (0.05 to 1.27)	0.27 (0.06 to 1.26)	–4.49 (–19.07 to 0.53)
MET + EMP		0.46 (0.10 to 2.14)	0.48 (0.12 to 2.09)	–3.15 (–17.82 to 2.26)
MET + LIR		1.06 (0.23 to 5.05)	1.06 (0.27 to 4.69)	0.33 (–14.32 to 8.03)
MET + EXE		0.89 (0.19 to 4.07)	0.89 (0.22 to 3.83)	–0.63 (–15.45 to 6.12)
MET + DUL		0.54 (0.11 to 2.56)	0.56 (0.13 to 2.47)	–2.67 (–17.32 to 3.16)
MET + ALB		0.65 (0.13 to 3.27)	0.67 (0.15 to 3.12)	–2.00 (–16.90 to 5.02)
MET + LIX		0.79 (0.17 to 3.58)	0.80 (0.20 to 3.41)	–1.19 (–15.90 to 5.06)
MET + ROS		0.77 (0.25 to 2.31)	0.78 (0.29 to 2.24)	–1.32 (–13.31 to 3.10)
MET + PIO		0.57 (0.13 to 2.37)	0.59 (0.16 to 2.31)	–2.53 (–17.16 to 2.57)
MET + IGA		0.13 (0.02 to 1.05)	0.14 (0.02 to 1.05)	–5.12 (–19.88 to 0.11)
MET + GLL	MET + GLI	0.63 (0.17 to 2.40)	0.63 (0.18 to 2.36)	–0.78 (–3.08 to 2.13)
MET + MIT		0.47 (0.01 to 7.80)	0.48 (0.01 to 6.97)	–1.05 (–3.61 to 11.06)
MET + NAT		1.15 (0.27 to 4.98)	1.14 (0.27 to 4.67)	0.30 (–2.48 to 6.23)
MET + SAX		1.41 (0.66 to 3.11)	1.40 (0.67 to 3.03)	0.87 (–1.26 to 2.83)
MET + ALO		1.01 (0.50 to 2.22)	1.01 (0.51 to 2.18)	0.02 (–1.54 to 2.19)
MET + LIN		0.84 (0.33 to 2.46)	0.85 (0.34 to 2.41)	–0.33 (–2.53 to 1.94)
MET + SIT		1.09 (0.55 to 2.34)	1.09 (0.56 to 2.30)	0.19 (–1.74 to 1.59)
MET + VIL		0.93 (0.40 to 2.35)	0.93 (0.40 to 2.31)	–0.16 (–2.35 to 1.70)
MET + CAN		1.61 (0.60 to 4.73)	1.59 (0.61 to 4.52)	1.28 (–1.40 to 5.26)
MET + DAP		0.74 (0.26 to 2.31)	0.75 (0.26 to 2.27)	–0.55 (–2.87 to 1.78)
MET + EMP		1.36 (0.52 to 3.78)	1.35 (0.53 to 3.64)	0.76 (–1.73 to 3.80)
MET + LIR		3.11 (1.22 to 8.51)	2.97 (1.21 to 7.71)	4.32 (0.67 to 10.40)
MET + EXE		2.60 (1.01 to 7.04)	2.51 (1.01 to 6.53)	3.30 (0.02 to 8.20)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + DUL		1.58 (0.60 to 4.54)	1.56 (0.61 to 4.33)	1.20 (–1.39 to 4.98)
MET + ALB		1.91 (0.65 to 5.91)	1.87 (0.65 to 5.54)	1.87 (–1.15 to 7.18)
MET + LIX		2.31 (0.91 to 6.11)	2.24 (0.92 to 5.73)	2.72 (–0.29 to 6.94)
MET + ROS		2.24 (0.77 to 7.19)	2.18 (0.78 to 6.60)	2.56 (–0.77 to 8.46)
MET + PIO		1.66 (0.73 to 4.07)	1.64 (0.73 to 3.91)	1.39 (–0.99 to 4.07)
MET + IGA		0.41 (0.06 to 2.00)	0.41 (0.07 to 1.97)	–1.22 (–3.48 to 1.63)
MET + MIT	MET + GLL	0.76 (0.02 to 14.22)	0.77 (0.02 to 12.62)	–0.29 (–3.25 to 11.70)
MET + NAT		1.83 (0.32 to 9.80)	1.81 (0.33 to 9.23)	1.06 (–2.16 to 6.94)
MET + SAX		2.24 (0.64 to 7.58)	2.20 (0.65 to 7.34)	1.64 (–1.29 to 3.85)
MET + ALO		1.62 (0.41 to 6.30)	1.60 (0.42 to 6.11)	0.80 (–2.10 to 3.66)
MET + LIN		1.35 (0.38 to 4.96)	1.35 (0.39 to 4.85)	0.47 (–2.28 to 2.56)
MET + SIT		1.74 (0.55 to 5.46)	1.72 (0.56 to 5.35)	0.99 (–1.76 to 2.43)
MET + VIL		1.49 (0.57 to 3.94)	1.48 (0.58 to 3.87)	0.63 (–1.59 to 1.90)
MET + CAN		2.57 (0.68 to 10.10)	2.52 (0.69 to 9.54)	2.04 (–1.06 to 5.96)
MET + DAP		1.18 (0.30 to 4.75)	1.18 (0.31 to 4.64)	0.24 (–2.58 to 2.45)
MET + EMP		2.17 (0.60 to 7.77)	2.13 (0.61 to 7.47)	1.53 (–1.35 to 4.46)
MET + LIR		4.99 (1.35 to 18.14)	4.72 (1.33 to 16.47)	5.06 (1.09 to 11.11)
MET + EXE		4.17 (1.13 to 14.86)	3.98 (1.12 to 13.77)	4.06 (0.39 to 8.97)
MET + DUL		2.53 (0.66 to 9.35)	2.47 (0.67 to 8.92)	1.99 (–1.17 to 5.68)
MET + ALB		3.06 (0.74 to 12.03)	2.97 (0.75 to 11.24)	2.65 (–0.81 to 7.90)
MET + LIX		3.72 (1.00 to 13.15)	3.58 (1.00 to 12.25)	3.50 (0.01 to 7.72)
MET + ROS		3.61 (0.91 to 14.34)	3.47 (0.92 to 13.25)	3.30 (–0.28 to 9.11)
MET + PIO		2.66 (0.82 to 8.51)	2.60 (0.83 to 8.15)	2.15 (–0.64 to 4.73)
MET + IGA		0.64 (0.09 to 3.93)	0.65 (0.09 to 3.84)	–0.45 (–3.26 to 2.37)
MET + NAT	MET + MIT	2.44 (0.12 to 84.11)	2.39 (0.13 to 80.05)	1.22 (–10.64 to 6.97)
MET + SAX		2.96 (0.20 to 93.50)	2.90 (0.22 to 90.62)	1.90 (–10.16 to 4.34)
MET + ALO		2.14 (0.13 to 73.52)	2.11 (0.15 to 71.26)	1.06 (–10.85 to 4.17)
MET + LIN		1.78 (0.12 to 56.02)	1.76 (0.13 to 54.55)	0.75 (–11.16 to 3.07)
MET + SIT		2.29 (0.16 to 71.57)	2.27 (0.17 to 69.62)	1.30 (–10.74 to 2.99)
MET + VIL		1.96 (0.13 to 61.06)	1.94 (0.14 to 59.56)	0.94 (–11.09 to 2.93)
MET + CAN		3.42 (0.22 to 111.70)	3.33 (0.24 to 106.70)	2.22 (–9.58 to 6.35)
MET + DAP		1.56 (0.10 to 51.44)	1.55 (0.11 to 50.36)	0.54 (–11.44 to 2.87)
MET + EMP		2.86 (0.18 to 89.29)	2.80 (0.20 to 86.34)	1.75 (–10.21 to 4.92)
MET + LIR		6.57 (0.43 to 203.80)	6.18 (0.46 to 189.40)	5.06 (–6.55 to 11.46)
MET + EXE		5.51 (0.35 to 178.80)	5.23 (0.38 to 166.80)	4.13 (–7.74 to 9.34)
MET + DUL		3.35 (0.21 to 105.60)	3.26 (0.23 to 100.40)	2.17 (–9.57 to 6.08)
MET + ALB		4.03 (0.24 to 128.60)	3.89 (0.27 to 122.40)	2.75 (–9.03 to 8.22)
MET + LIX		4.93 (0.32 to 160.30)	4.72 (0.35 to 151.60)	3.62 (–8.16 to 8.07)
MET + ROS		4.78 (0.29 to 151.50)	4.58 (0.31 to 141.00)	3.41 (–8.51 to 9.41)
MET + PIO		3.48 (0.23 to 107.90)	3.38 (0.26 to 103.30)	2.36 (–9.54 to 5.36)
MET + IGA		0.82 (0.04 to 36.26)	0.82 (0.04 to 35.49)	–0.16 (–11.92 to 2.87)
MET + SAX	MET + NAT	1.23 (0.31 to 5.04)	1.22 (0.33 to 4.88)	0.54 (–5.38 to 3.34)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ALO		0.89 (0.20 to 4.14)	0.89 (0.21 to 4.03)	–0.26 (–6.16 to 3.00)
MET + LIN		0.74 (0.18 to 3.35)	0.75 (0.19 to 3.29)	–0.61 (–6.49 to 2.10)
MET + SIT		0.95 (0.26 to 3.79)	0.96 (0.27 to 3.71)	–0.11 (–5.93 to 2.08)
MET + VIL		0.81 (0.21 to 3.42)	0.82 (0.22 to 3.35)	–0.44 (–6.31 to 1.94)
MET + CAN		1.42 (0.33 to 6.49)	1.40 (0.35 to 6.20)	0.96 (–4.93 to 5.24)
MET + DAP		0.65 (0.15 to 3.07)	0.66 (0.16 to 3.02)	–0.82 (–6.70 to 1.91)
MET + EMP		1.18 (0.28 to 5.27)	1.18 (0.30 to 5.09)	0.44 (–5.45 to 3.88)
MET + LIR		2.74 (0.64 to 12.11)	2.62 (0.66 to 11.10)	3.89 (–2.50 to 10.26)
MET + EXE		2.28 (0.55 to 9.75)	2.20 (0.58 to 9.09)	2.91 (–3.15 to 8.11)
MET + DUL		1.38 (0.32 to 6.36)	1.37 (0.34 to 6.07)	0.89 (–5.03 to 5.05)
MET + ALB		1.66 (0.36 to 8.18)	1.63 (0.38 to 7.66)	1.51 (–4.57 to 7.19)
MET + LIX		2.02 (0.49 to 8.69)	1.97 (0.51 to 8.15)	2.36 (–3.76 to 7.01)
MET + ROS		1.97 (0.45 to 9.10)	1.92 (0.47 to 8.49)	2.19 (–4.01 to 8.20)
MET + PIO		1.46 (0.38 to 5.87)	1.44 (0.40 to 5.67)	1.07 (–4.82 to 4.21)
MET + IGA		0.35 (0.04 to 2.41)	0.36 (0.04 to 2.38)	–1.50 (–7.35 to 1.64)
MET + ALO	MET + SAX	0.72 (0.29 to 1.84)	0.73 (0.30 to 1.81)	–0.83 (–3.02 to 2.03)
MET + LIN		0.60 (0.26 to 1.49)	0.61 (0.27 to 1.48)	–1.19 (–3.31 to 1.11)
MET + SIT		0.77 (0.43 to 1.42)	0.78 (0.45 to 1.41)	–0.68 (–2.63 to 0.86)
MET + VIL		0.66 (0.32 to 1.43)	0.67 (0.33 to 1.42)	–1.02 (–3.14 to 0.92)
MET + CAN		1.15 (0.46 to 2.95)	1.14 (0.48 to 2.82)	0.43 (–2.26 to 4.41)
MET + DAP		0.53 (0.20 to 1.43)	0.54 (0.21 to 1.41)	–1.40 (–3.59 to 0.96)
MET + EMP		0.97 (0.41 to 2.32)	0.97 (0.42 to 2.25)	–0.10 (–2.54 to 2.95)
MET + LIR		2.21 (0.95 to 5.27)	2.13 (0.95 to 4.79)	3.47 (–0.19 to 9.57)
MET + EXE		1.85 (0.79 to 4.35)	1.80 (0.80 to 4.05)	2.44 (–0.83 to 7.45)
MET + DUL		1.12 (0.46 to 2.80)	1.12 (0.47 to 2.68)	0.35 (–2.25 to 4.11)
MET + ALB		1.35 (0.50 to 3.74)	1.34 (0.52 to 3.50)	1.03 (–1.98 to 6.35)
MET + LIX		1.65 (0.72 to 3.75)	1.62 (0.73 to 3.53)	1.89 (–1.12 to 6.14)
MET + ROS		1.59 (0.62 to 4.47)	1.56 (0.63 to 4.13)	1.69 (–1.55 to 7.63)
MET + PIO		1.18 (0.57 to 2.50)	1.17 (0.58 to 2.43)	0.52 (–1.86 to 3.28)
MET + IGA		0.29 (0.05 to 1.33)	0.29 (0.05 to 1.31)	–2.09 (–4.21 to 0.80)
MET + LIN	MET + ALO	0.83 (0.29 to 2.50)	0.84 (0.30 to 2.45)	–0.36 (–3.15 to 1.91)
MET + SIT		1.07 (0.46 to 2.51)	1.07 (0.48 to 2.47)	0.15 (–2.50 to 1.72)
MET + VIL		0.91 (0.35 to 2.45)	0.91 (0.36 to 2.41)	–0.20 (–2.93 to 1.72)
MET + CAN		1.58 (0.53 to 5.00)	1.56 (0.54 to 4.75)	1.22 (–1.94 to 5.22)
MET + DAP		0.73 (0.23 to 2.37)	0.74 (0.24 to 2.33)	–0.57 (–3.45 to 1.79)
MET + EMP		1.33 (0.46 to 3.98)	1.32 (0.47 to 3.84)	0.71 (–2.27 to 3.81)
MET + LIR		3.07 (1.07 to 9.08)	2.92 (1.06 to 8.23)	4.24 (0.25 to 10.34)
MET + EXE		2.56 (0.89 to 7.37)	2.47 (0.90 to 6.83)	3.25 (–0.41 to 8.18)
MET + DUL		1.56 (0.52 to 4.74)	1.54 (0.53 to 4.51)	1.17 (–1.94 to 4.96)
MET + ALB		1.88 (0.57 to 6.12)	1.84 (0.58 to 5.72)	1.84 (–1.62 to 7.19)
MET + LIX		2.28 (0.80 to 6.48)	2.21 (0.80 to 6.07)	2.68 (–0.83 to 6.93)
MET + ROS		2.20 (0.69 to 7.43)	2.14 (0.70 to 6.83)	2.49 (–1.24 to 8.46)

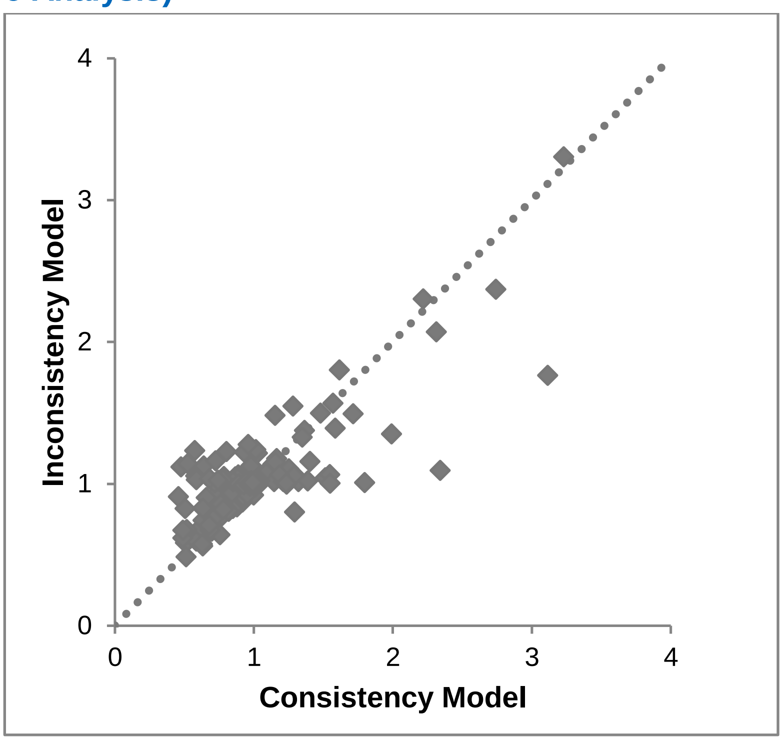
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + PIO		1.64 (0.65 to 4.23)	1.61 (0.66 to 4.07)	1.34 (–1.49 to 4.00)
MET + IGA		0.40 (0.06 to 2.03)	0.40 (0.06 to 2.00)	–1.26 (–4.08 to 1.63)
MET + SIT	MET + LIN	1.30 (0.59 to 2.74)	1.29 (0.59 to 2.69)	0.53 (–1.46 to 1.89)
MET + VIL		1.10 (0.47 to 2.54)	1.10 (0.48 to 2.50)	0.17 (–1.80 to 1.80)
MET + CAN		1.89 (0.68 to 5.39)	1.86 (0.69 to 5.11)	1.59 (–0.97 to 5.51)
MET + DAP		0.88 (0.29 to 2.59)	0.88 (0.30 to 2.54)	–0.22 (–2.35 to 1.97)
MET + EMP		1.61 (0.61 to 3.98)	1.59 (0.62 to 3.84)	1.08 (–1.21 to 3.95)
MET + LIR		3.67 (1.36 to 9.60)	3.49 (1.34 to 8.72)	4.63 (1.00 to 10.64)
MET + EXE		3.07 (1.14 to 7.86)	2.95 (1.13 to 7.26)	3.62 (0.39 to 8.46)
MET + DUL		1.87 (0.64 to 5.14)	1.84 (0.65 to 4.90)	1.54 (–1.07 to 5.28)
MET + ALB		2.25 (0.75 to 6.52)	2.20 (0.75 to 6.09)	2.22 (–0.69 to 7.40)
MET + LIX		2.76 (1.02 to 6.89)	2.67 (1.02 to 6.45)	3.08 (0.07 to 7.22)
MET + ROS		2.65 (0.87 to 7.89)	2.57 (0.87 to 7.24)	2.89 (–0.39 to 8.65)
MET + PIO		1.97 (0.81 to 4.55)	1.93 (0.82 to 4.37)	1.70 (–0.59 to 4.30)
MET + IGA		0.48 (0.08 to 2.28)	0.48 (0.08 to 2.24)	–0.92 (–2.97 to 1.87)
MET + VIL	MET + SIT	0.85 (0.45 to 1.61)	0.85 (0.46 to 1.59)	–0.35 (–1.64 to 1.22)
MET + CAN		1.47 (0.68 to 3.38)	1.46 (0.68 to 3.22)	1.09 (–0.89 to 4.88)
MET + DAP		0.68 (0.28 to 1.69)	0.69 (0.28 to 1.67)	–0.74 (–2.20 to 1.39)
MET + EMP		1.25 (0.58 to 2.66)	1.24 (0.59 to 2.57)	0.57 (–1.20 to 3.37)
MET + LIR		2.85 (1.44 to 5.77)	2.73 (1.42 to 5.20)	4.16 (1.08 to 9.97)
MET + EXE		2.39 (1.13 to 4.85)	2.31 (1.13 to 4.48)	3.15 (0.35 to 7.84)
MET + DUL		1.45 (0.68 to 3.05)	1.43 (0.69 to 2.91)	1.03 (–0.85 to 4.48)
MET + ALB		1.75 (0.72 to 4.18)	1.72 (0.73 to 3.90)	1.71 (–0.72 to 6.85)
MET + LIX		2.13 (1.03 to 4.26)	2.08 (1.03 to 3.99)	2.58 (0.08 to 6.59)
MET + ROS		2.05 (0.85 to 5.19)	2.00 (0.85 to 4.78)	2.38 (–0.42 to 8.15)
MET + PIO		1.52 (0.83 to 2.82)	1.50 (0.83 to 2.72)	1.21 (–0.48 to 3.69)
MET + IGA		0.37 (0.07 to 1.55)	0.38 (0.07 to 1.53)	–1.45 (–2.77 to 1.22)
MET + CAN	MET + VIL	1.73 (0.69 to 4.49)	1.71 (0.69 to 4.24)	1.45 (–0.88 to 5.30)
MET + DAP		0.80 (0.30 to 2.17)	0.81 (0.31 to 2.13)	–0.39 (–2.14 to 1.77)
MET + EMP		1.46 (0.62 to 3.39)	1.45 (0.62 to 3.27)	0.90 (–1.07 to 3.72)
MET + LIR		3.35 (1.41 to 7.96)	3.19 (1.40 to 7.18)	4.49 (1.05 to 10.46)
MET + EXE		2.80 (1.18 to 6.49)	2.70 (1.17 to 5.98)	3.47 (0.48 to 8.31)
MET + DUL		1.71 (0.68 to 4.20)	1.68 (0.68 to 3.99)	1.37 (–0.91 to 5.02)
MET + ALB		2.06 (0.75 to 5.45)	2.02 (0.76 to 5.07)	2.06 (–0.67 to 7.27)
MET + LIX		2.50 (1.06 to 5.68)	2.42 (1.06 to 5.31)	2.90 (0.17 to 7.05)
MET + ROS		2.42 (0.91 to 6.52)	2.35 (0.91 to 5.98)	2.72 (–0.26 to 8.50)
MET + PIO		1.79 (0.91 to 3.48)	1.76 (0.91 to 3.35)	1.54 (–0.24 to 3.94)
MET + IGA		0.44 (0.07 to 1.99)	0.44 (0.08 to 1.96)	–1.10 (–2.76 to 1.68)
MET + DAP	MET + CAN	0.46 (0.15 to 1.40)	0.47 (0.16 to 1.39)	–1.82 (–5.72 to 0.83)
MET + EMP		0.84 (0.29 to 2.33)	0.85 (0.31 to 2.27)	–0.52 (–4.62 to 2.79)
MET + LIR		1.93 (0.68 to 5.36)	1.87 (0.70 to 4.90)	3.00 (–1.83 to 9.15)
MET + EXE		1.62 (0.57 to 4.31)	1.58 (0.58 to 4.02)	2.01 (–2.63 to 7.10)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + DUL		0.98 (0.34 to 2.75)	0.98 (0.36 to 2.65)	–0.06 (–4.17 to 3.82)
MET + ALB		1.18 (0.36 to 3.70)	1.17 (0.38 to 3.48)	0.59 (–3.83 to 6.08)
MET + LIX		1.44 (0.52 to 3.80)	1.42 (0.53 to 3.58)	1.44 (–2.99 to 5.87)
MET + ROS		1.39 (0.44 to 4.43)	1.37 (0.46 to 4.12)	1.24 (–3.42 to 7.38)
MET + PIO		1.03 (0.40 to 2.56)	1.03 (0.42 to 2.48)	0.10 (–3.93 to 3.17)
MET + IGA		0.25 (0.04 to 1.23)	0.26 (0.04 to 1.22)	–2.48 (–6.35 to 0.55)
MET + EMP	MET + DAP	1.83 (0.62 to 5.39)	1.80 (0.63 to 5.17)	1.29 (–1.17 to 4.32)
MET + LIR		4.16 (1.43 to 12.62)	3.95 (1.40 to 11.35)	4.85 (1.15 to 10.99)
MET + EXE		3.51 (1.19 to 9.99)	3.37 (1.18 to 9.22)	3.85 (0.52 to 8.76)
MET + DUL		2.13 (0.70 to 6.38)	2.08 (0.71 to 6.07)	1.76 (–0.87 to 5.49)
MET + ALB		2.55 (0.77 to 8.46)	2.49 (0.78 to 7.84)	2.41 (–0.64 to 7.76)
MET + LIX		3.13 (1.11 to 8.60)	3.02 (1.10 to 8.03)	3.29 (0.29 to 7.47)
MET + ROS		3.01 (0.94 to 9.89)	2.91 (0.94 to 9.07)	3.09 (–0.17 to 8.94)
MET + PIO		2.22 (0.83 to 6.07)	2.18 (0.83 to 5.80)	1.92 (–0.54 to 4.73)
MET + IGA		0.55 (0.08 to 2.93)	0.55 (0.08 to 2.86)	–0.70 (–2.89 to 2.18)
MET + LIR	MET + EMP	2.29 (0.89 to 5.97)	2.20 (0.89 to 5.44)	3.53 (–0.48 to 9.65)
MET + EXE		1.92 (0.72 to 4.91)	1.87 (0.73 to 4.56)	2.54 (–1.32 to 7.47)
MET + DUL		1.16 (0.43 to 3.21)	1.15 (0.44 to 3.08)	0.45 (–2.75 to 4.34)
MET + ALB		1.40 (0.47 to 4.15)	1.39 (0.48 to 3.91)	1.12 (–2.48 to 6.39)
MET + LIX		1.71 (0.65 to 4.33)	1.67 (0.66 to 4.08)	1.98 (–1.64 to 6.28)
MET + ROS		1.65 (0.57 to 5.04)	1.62 (0.58 to 4.65)	1.79 (–2.04 to 7.81)
MET + PIO		1.22 (0.51 to 2.88)	1.21 (0.53 to 2.79)	0.62 (–2.43 to 3.44)
MET + IGA		0.30 (0.05 to 1.50)	0.30 (0.05 to 1.49)	–1.98 (–4.90 to 1.07)
MET + EXE	MET + LIR	0.84 (0.32 to 2.08)	0.85 (0.34 to 1.99)	–0.99 (–7.44 to 4.44)
MET + DUL		0.51 (0.23 to 1.10)	0.52 (0.25 to 1.10)	–3.04 (–8.32 to 0.45)
MET + ALB		0.61 (0.21 to 1.77)	0.63 (0.22 to 1.70)	–2.35 (–8.61 to 3.30)
MET + LIX		0.75 (0.29 to 1.85)	0.76 (0.31 to 1.78)	–1.54 (–7.87 to 3.42)
MET + ROS		0.72 (0.25 to 2.14)	0.74 (0.27 to 2.04)	–1.69 (–8.24 to 4.62)
MET + PIO		0.53 (0.23 to 1.24)	0.55 (0.25 to 1.23)	–2.93 (–8.94 to 0.90)
MET + IGA		0.13 (0.02 to 0.62)	0.14 (0.02 to 0.64)	–5.50 (–11.57 to –1.61)
MET + DUL	MET + EXE	0.60 (0.23 to 1.66)	0.62 (0.24 to 1.62)	–2.08 (–7.03 to 2.32)
MET + ALB		0.73 (0.25 to 2.19)	0.74 (0.27 to 2.09)	–1.39 (–6.60 to 4.28)
MET + LIX		0.89 (0.44 to 1.83)	0.90 (0.46 to 1.77)	–0.56 (–4.69 to 3.09)
MET + ROS		0.86 (0.30 to 2.58)	0.87 (0.32 to 2.44)	–0.71 (–6.23 to 5.60)
MET + PIO		0.64 (0.29 to 1.41)	0.65 (0.31 to 1.39)	–1.91 (–6.56 to 1.37)
MET + IGA		0.16 (0.03 to 0.65)	0.17 (0.03 to 0.66)	–4.47 (–9.15 to –1.40)
MET + ALB	MET + DUL	1.21 (0.39 to 3.69)	1.20 (0.41 to 3.46)	0.65 (–3.43 to 6.09)
MET + LIX		1.47 (0.55 to 3.81)	1.45 (0.56 to 3.61)	1.51 (–2.71 to 5.86)
MET + ROS		1.42 (0.48 to 4.47)	1.40 (0.49 to 4.15)	1.33 (–3.08 to 7.30)
MET + PIO		1.06 (0.42 to 2.64)	1.05 (0.43 to 2.56)	0.18 (–3.69 to 3.23)
MET + IGA		0.26 (0.04 to 1.26)	0.26 (0.04 to 1.25)	–2.42 (–6.15 to 0.63)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX	MET + ALB	1.23 (0.41 to 3.51)	1.21 (0.43 to 3.31)	0.86 (–4.83 to 5.47)
MET + ROS		1.18 (0.36 to 4.02)	1.17 (0.38 to 3.75)	0.68 (–5.21 to 6.90)
MET + PIO		0.87 (0.32 to 2.38)	0.88 (0.34 to 2.31)	–0.51 (–5.76 to 2.80)
MET + IGA		0.21 (0.03 to 1.11)	0.22 (0.03 to 1.10)	–3.08 (–8.34 to 0.27)
MET + ROS	MET + LIX	0.97 (0.34 to 2.84)	0.97 (0.36 to 2.67)	–0.15 (–5.07 to 5.98)
MET + PIO		0.72 (0.32 to 1.63)	0.73 (0.34 to 1.59)	–1.34 (–5.56 to 1.93)
MET + IGA		0.17 (0.03 to 0.80)	0.18 (0.03 to 0.81)	–3.92 (–8.05 to –0.72)
MET + PIO	MET + ROS	0.74 (0.27 to 1.86)	0.75 (0.29 to 1.81)	–1.16 (–7.00 to 2.28)
MET + IGA		0.18 (0.03 to 0.95)	0.19 (0.03 to 0.95)	–3.77 (–9.60 to –0.16)
MET + IGA	MET + PIO	0.24 (0.04 to 1.10)	0.25 (0.04 to 1.09)	–2.61 (–5.24 to 0.29)
Random–effects model	Residual deviance	149.5 vs. 148 data points		
	Deviance information criteria	780.747		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; IGA = insulin glargine; GLC = glicazide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; GLY = glyburide; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MET = metformin; MIT = mitiglinide; NAT = nateglinide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 27: Consistency Plot for Withdrawals Due to Adverse Events (Individual-Drug Case Analysis)



CADTH

Bladder Cancer

Table 45: Bladder Cancer: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	0.89 (0.01 to 523.20)	0.89 (0.01 to 482.80)	–0.01 (–0.63 to 9.39)
MET + GLI		0.56 (0.00 to 2,400.00)	0.56 (0.00 to 1,025.00)	–0.02 (–0.62 to 45.71)
MET + SAX		3.10 (0.02 to 3,999.00)	3.08 (0.02 to 1,712.00)	0.20 (–0.49 to 63.54)
MET + ALO		2.33 (0.00 to 13,720.00)	2.32 (0.00 to 1,815.00)	0.12 (–0.53 to 88.91)
MET + SIT		1.18 (0.00 to 646.40)	1.18 (0.00 to 571.20)	0.01 (–0.65 to 14.04)
MET + DAP		1.03 (0.03 to 29.27)	1.03 (0.03 to 28.93)	0.00 (–0.55 to 1.14)
MET + GLI	MET + GLM	0.69 (0.00 to 154.20)	0.70 (0.00 to 96.61)	0.00 (–3.83 to 34.79)
MET + SAX		3.41 (0.12 to 205.00)	3.31 (0.12 to 136.60)	0.15 (–1.22 to 52.47)
MET + ALO		2.95 (0.01 to 2804.00)	2.84 (0.01 to 764.60)	0.08 (–2.95 to 84.49)
MET + SIT		1.03 (0.00 to 442.70)	1.03 (0.00 to 417.90)	0.00 (–6.57 to 10.40)
MET + DAP		1.06 (0.00 to 338.60)	1.06 (0.00 to 335.10)	0.00 (–9.43 to 1.26)
MET + SAX	MET + GLI	4.60 (0.14 to 699.30)	4.31 (0.19 to 661.90)	0.13 (–8.39 to 29.44)
MET + ALO		3.67 (0.16 to 509.40)	3.25 (0.16 to 366.40)	0.09 (–2.19 to 59.81)
MET + SIT		1.40 (0.00 to 4,509.00)	1.39 (0.00 to 3,948.00)	0.00 (–37.02 to 9.69)
MET + DAP		2.05 (0.00 to 2,034.00)	2.05 (0.00 to 2,029.00)	0.02 (–45.55 to 1.21)
MET + ALO	MET + SAX	0.82 (0.00 to 321.60)	0.84 (0.00 to 158.40)	0.00 (–22.91 to 60.34)
MET + SIT		0.25 (0.00 to 343.60)	0.26 (0.00 to 316.40)	–0.12 (–56.41 to 8.33)
MET + DAP		0.31 (0.00 to 166.60)	0.31 (0.00 to 165.30)	–0.20 (–63.58 to 1.10)
MET + SIT	MET + ALO	0.32 (0.00 to 823.70)	0.33 (0.00 to 763.90)	–0.06 (–85.45 to 9.07)
MET + DAP		0.41 (0.00 to 642.10)	0.41 (0.00 to 638.60)	–0.10 (–88.91 to 1.08)
MET + DAP	MET + SIT	0.90 (0.00 to 1,224.00)	0.90 (0.00 to 1,215.00)	–0.01 (–14.10 to 1.26)
Random-effects model	Residual deviance	5.709 vs. 13 data points		
	Deviance information criteria	41.432		

ALO = alogliptin; CrI = credible interval; DAP = dapagliflozin; GLI = glipizide; GLM = glimepiride; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; vs. = versus.

Body Mass Index (BMI)

Table 46: Body Mass Index Reference Case : Mean Difference for All Treatment Comparisons — Random-Effects Model

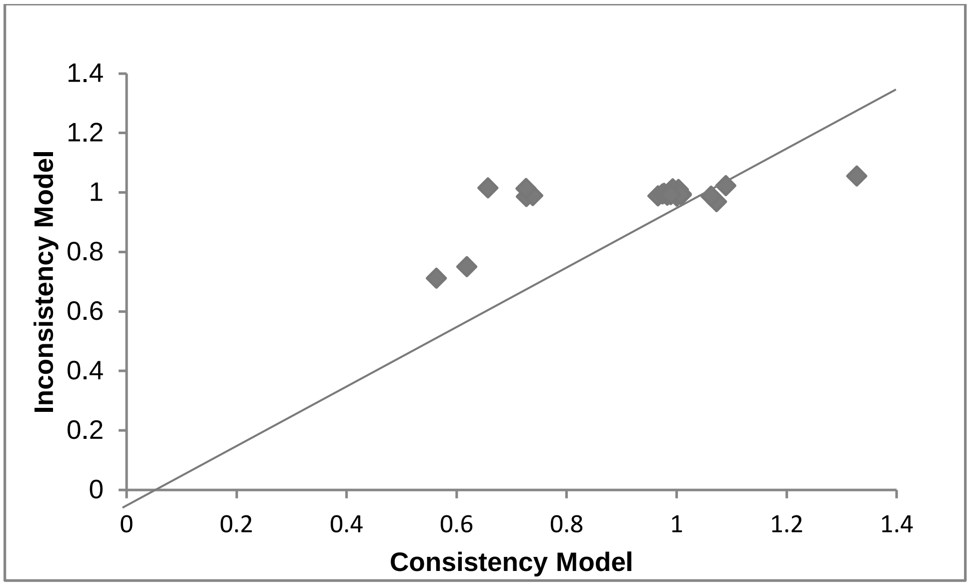
Treatment	Reference	MD (95% CrI)
MET + GLM	MET	0.45 (–0.30 to 1.37)
MET + SAX		–0.03 (–1.15 to 1.09)
MET + SIT		–0.17 (–1.28 to 0.82)
MET + VIL		–0.49 (–1.43 to 0.29)
MET + EXE		–1.28 (–2.16 to –0.31)
MET + ROS		2.90 (1.41 to 4.25)
MET + PIO		0.59 (–0.41 to 1.70)

CADTH

Treatment	Reference	MD (95% CrI)
MET + IGA		2.44 (–0.74 to 5.69)
MET + SAX	MET + GLM	–0.48 (–1.95 to 0.82)
MET + SIT		–0.62 (–2.11 to 0.58)
MET + VIL		–0.94 (–2.30 to 0.10)
MET + EXE		–1.73 (–2.69 to –0.83)
MET + ROS		2.46 (0.72 to 3.92)
MET + PIO		0.14 (–0.77 to 1.03)
MET + IGA		1.99 (–1.20 to 5.22)
MET + SIT	MET + SAX	–0.14 (–1.74 to 1.32)
MET + VIL		–0.46 (–1.95 to 0.87)
MET + EXE		–1.25 (–2.65 to 0.26)
MET + ROS		2.93 (1.07 to 4.61)
MET + PIO		0.62 (–0.84 to 2.23)
MET + IGA		2.47 (–0.86 to 5.93)
MET + VIL	MET + SIT	–0.32 (–1.55 to 0.87)
MET + EXE		–1.11 (–2.41 to 0.40)
MET + ROS		3.08 (1.29 to 4.78)
MET + PIO		0.76 (–0.60 to 2.36)
MET + IGA		2.61 (–0.65 to 6.08)
MET + EXE	MET + VIL	–0.79 (–1.93 to 0.61)
MET + ROS		3.39 (1.73 to 5.02)
MET + PIO		1.08 (–0.14 to 2.58)
MET + IGA		2.93 (–0.35 to 6.34)
MET + ROS	MET + EXE	4.18 (2.38 to 5.74)
MET + PIO		1.87 (0.68 to 3.10)
MET + IGA		3.72 (0.65 to 6.83)
MET + PIO	MET + ROS	–2.32 (–3.92 to –0.45)
MET + IGA		–0.46 (–3.91 to 3.11)
MET + IGA	MET + PIO	1.85 (–1.41 to 5.16)
Random-effects model	Residual deviance	26.45 vs. 28 data points
	Deviance information criteria	38.532

CrI = credible interval; EXE = exenatide; GLM = glimepiride; IGA = insulin glargine; MD = mean difference; MET = metformin; PIO = pioglitazone; ROS = rosiglitazone; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 28: Consistency Plot for Body Mass Index (Individual-Drug Case Analysis)



Cardiovascular Death

Table 47: Cardiovascular Mortality : Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	2.99 (0.11 to 1305.00)	2.97 (0.11 to 323.40)	0.49 (–0.28 to 75.26)
MET + GLY		0.16 (0.00 to 140.00)	0.16 (0.00 to 103.60)	–0.18 (–0.44 to 25.36)
MET + GLI		2.38 (0.35 to 41.30)	2.37 (0.35 to 38.07)	0.35 (–0.20 to 7.71)
MET + SAX		0.95 (0.23 to 4.26)	0.95 (0.23 to 4.23)	–0.01 (–0.29 to 0.68)
MET + ALO		0.90 (0.08 to 20.18)	0.90 (0.08 to 19.41)	–0.03 (–0.33 to 3.91)
MET + LIN		3.26 (0.06 to 1875.00)	3.24 (0.06 to 348.20)	0.56 (–0.30 to 80.79)
MET + SIT		0.60 (0.15 to 2.81)	0.60 (0.15 to 2.80)	–0.10 (–0.33 to 0.35)
MET + VIL		1.04 (0.08 to 9.90)	1.04 (0.08 to 9.69)	0.01 (–0.33 to 1.95)
MET + CAN		1.03 (0.00 to 101.40)	1.03 (0.00 to 81.56)	0.01 (–0.38 to 18.81)
MET + DAP		0.90 (0.11 to 9.58)	0.90 (0.11 to 9.39)	–0.03 (–0.34 to 1.54)
MET + EMP		0.97 (0.04 to 23.10)	0.97 (0.04 to 22.03)	–0.01 (–0.36 to 4.88)
MET + LIR		0.15 (0.01 to 2.31)	0.15 (0.01 to 2.31)	–0.20 (–0.43 to 0.33)
MET + EXE		1.28 (0.04 to 29.75)	1.28 (0.04 to 27.64)	0.07 (–0.34 to 6.38)
MET + DUL		1.11 (0.05 to 31.54)	1.11 (0.05 to 29.69)	0.03 (–0.34 to 6.44)
MET + LIX		0.78 (0.02 to 68.04)	0.78 (0.02 to 56.73)	–0.05 (–0.39 to 13.83)
MET + ROS		0.90 (0.00 to 190.10)	0.90 (0.00 to 133.40)	–0.02 (–0.41 to 25.95)
MET + PIO		1.51 (0.15 to 29.50)	1.51 (0.15 to 27.53)	0.13 (–0.30 to 6.31)
MET + GLY	MET + GLM	0.03 (0.00 to 139.60)	0.03 (0.00 to 76.30)	–0.54 (–75.01 to 23.57)
MET + GLI		0.83 (0.00 to 38.34)	0.83 (0.01 to 36.98)	–0.09 (–69.78 to 4.33)
MET + SAX		0.30 (0.00 to 10.29)	0.31 (0.00 to 10.28)	–0.49 (–75.09 to 0.52)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ALO		0.26 (0.00 to 20.61)	0.27 (0.00 to 20.26)	–0.42 (–73.60 to 2.23)
MET + LIN		1.01 (0.11 to 9.40)	1.01 (0.12 to 8.38)	0.00 (–15.73 to 20.64)
MET + SIT		0.19 (0.00 to 4.46)	0.20 (0.00 to 4.44)	–0.58 (–75.11 to 0.16)
MET + VIL		0.37 (0.00 to 18.53)	0.38 (0.00 to 18.33)	–0.40 (–75.16 to 1.29)
MET + CAN		0.24 (0.00 to 145.20)	0.26 (0.00 to 130.40)	–0.36 (–70.27 to 14.62)
MET + DAP		0.29 (0.00 to 15.63)	0.29 (0.00 to 15.48)	–0.46 (–75.21 to 1.06)
MET + EMP		0.28 (0.00 to 69.64)	0.29 (0.00 to 65.60)	–0.41 (–75.16 to 4.09)
MET + LIR		0.04 (0.00 to 2.24)	0.04 (0.00 to 2.24)	–0.70 (–75.29 to 0.08)
MET + EXE		0.44 (0.00 to 40.11)	0.45 (0.00 to 38.87)	–0.27 (–72.44 to 4.20)
MET + DUL		0.30 (0.00 to 39.11)	0.30 (0.00 to 37.67)	–0.37 (–73.88 to 4.91)
MET + LIX		0.24 (0.00 to 26.33)	0.24 (0.00 to 23.82)	–0.41 (–75.07 to 11.58)
MET + ROS		0.16 (0.00 to 178.60)	0.17 (0.00 to 113.70)	–0.36 (–74.87 to 24.95)
MET + PIO		0.49 (0.00 to 26.86)	0.49 (0.00 to 26.39)	–0.30 (–70.46 to 2.69)
MET + GLI	MET + GLY	20.47 (0.02 to 218,800.00)	20.16 (0.02 to 213,100.00)	0.44 (–24.85 to 7.79)
MET + SAX		6.85 (0.00 to 93,640.00)	6.82 (0.01 to 93,450.00)	0.15 (–25.36 to 0.87)
MET + ALO		7.06 (0.00 to 96,700.00)	7.01 (0.01 to 96,240.00)	0.12 (–25.08 to 4.02)
MET + LIN		35.19 (0.01 to 588,700.00)	32.03 (0.01 to 332,800.00)	0.54 (–23.18 to 80.37)
MET + SIT		3.89 (0.00 to 50,010.00)	3.88 (0.00 to 49,930.00)	0.08 (–25.45 to 0.49)
MET + VIL		6.94 (0.00 to 109,400.00)	6.91 (0.01 to 108,100.00)	0.17 (–25.24 to 2.00)
MET + CAN		7.04 (0.00 to 96,340.00)	6.96 (0.00 to 88,980.00)	0.10 (–24.49 to 18.55)
MET + DAP		6.08 (0.00 to 82,520.00)	6.06 (0.00 to 82,290.00)	0.13 (–25.42 to 1.60)
MET + EMP		5.72 (0.01 to 131,000.00)	5.69 (0.01 to 125,900.00)	0.10 (–24.09 to 4.91)
MET + LIR		0.90 (0.00 to 9,650.00)	0.90 (0.00 to 9,645.00)	0.00 (–25.49 to 0.48)
MET + EXE		8.94 (0.00 to 197,700.00)	8.89 (0.01 to 191,200.00)	0.18 (–25.06 to 6.29)
MET + DUL		8.09 (0.01 to 155,600.00)	8.00 (0.01 to 155,000.00)	0.15 (–24.84 to 6.18)
MET + LIX		4.22 (0.01 to 98,450.00)	4.20 (0.01 to 89,600.00)	0.07 (–24.87 to 13.58)
MET + ROS		3.86 (0.16 to 1,194.00)	3.76 (0.18 to 1,182.00)	0.04 (–9.73 to 8.96)
MET + PIO		9.45 (0.01 to 119,200.00)	9.40 (0.01 to 118,200.00)	0.24 (–24.94 to 6.28)
MET + SAX	MET + GLI	0.38 (0.03 to 3.07)	0.38 (0.03 to 3.06)	–0.36 (–7.57 to 0.33)
MET + ALO		0.37 (0.05 to 2.03)	0.38 (0.05 to 2.02)	–0.33 (–5.09 to 0.53)
MET + LIN		1.26 (0.02 to 368.20)	1.25 (0.02 to 110.40)	0.11 (–4.36 to 76.78)
MET + SIT		0.23 (0.03 to 1.62)	0.23 (0.03 to 1.61)	–0.46 (–7.57 to 0.10)
MET + VIL		0.41 (0.02 to 7.92)	0.41 (0.02 to 7.83)	–0.32 (–7.61 to 1.55)
MET + CAN		0.42 (0.00 to 67.55)	0.43 (0.00 to 56.16)	–0.25 (–7.62 to 18.34)
MET + DAP		0.36 (0.01 to 5.39)	0.36 (0.01 to 5.34)	–0.35 (–7.57 to 1.10)
MET + EMP		0.38 (0.01 to 19.55)	0.38 (0.01 to 18.25)	–0.29 (–7.77 to 4.58)
MET + LIR		0.06 (0.00 to 1.74)	0.06 (0.00 to 1.74)	–0.55 (–7.90 to 0.12)
MET + EXE		0.49 (0.01 to 18.13)	0.49 (0.01 to 17.01)	–0.25 (–6.10 to 4.66)
MET + DUL		0.40 (0.01 to 16.88)	0.40 (0.01 to 15.62)	–0.28 (–6.46 to 4.88)
MET + LIX		0.30 (0.01 to 34.33)	0.30 (0.01 to 27.92)	–0.32 (–7.23 to 13.48)
MET + ROS		0.26 (0.00 to 88.60)	0.26 (0.00 to 69.31)	–0.31 (–7.48 to 25.58)
MET + PIO		0.61 (0.03 to 12.01)	0.61 (0.03 to 11.72)	–0.20 (–5.93 to 3.39)

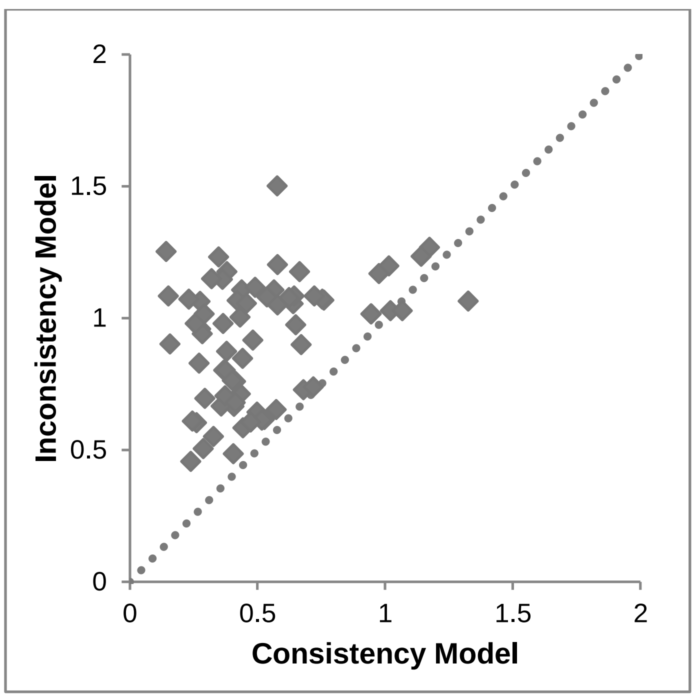
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ALO	MET + SAX	0.94 (0.08 to 17.86)	0.94 (0.08 to 17.30)	–0.01 (–0.61 to 3.75)
MET + LIN		3.65 (0.05 to 2,014.00)	3.62 (0.05 to 345.20)	0.57 (–0.57 to 80.74)
MET + SIT		0.65 (0.11 to 3.66)	0.65 (0.11 to 3.64)	–0.08 (–0.70 to 0.33)
MET + VIL		1.09 (0.08 to 13.83)	1.09 (0.08 to 13.59)	0.02 (–0.74 to 1.94)
MET + CAN		1.05 (0.00 to 136.70)	1.05 (0.00 to 113.20)	0.01 (–0.80 to 18.81)
MET + DAP		0.96 (0.08 to 8.42)	0.96 (0.08 to 8.32)	–0.01 (–0.71 to 1.47)
MET + EMP		1.01 (0.03 to 37.19)	1.01 (0.03 to 35.55)	0.00 (–0.77 to 4.95)
MET + LIR		0.16 (0.01 to 2.96)	0.16 (0.01 to 2.95)	–0.18 (–0.89 to 0.34)
MET + EXE		1.35 (0.03 to 36.34)	1.35 (0.03 to 33.99)	0.07 (–0.72 to 6.40)
MET + DUL		1.09 (0.04 to 35.80)	1.09 (0.04 to 33.80)	0.02 (–0.62 to 6.34)
MET + LIX		0.75 (0.03 to 89.69)	0.75 (0.03 to 73.10)	–0.05 (–0.69 to 13.77)
MET + ROS		0.77 (0.00 to 309.10)	0.77 (0.00 to 186.20)	–0.05 (–0.77 to 25.96)
MET + PIO		1.64 (0.12 to 32.22)	1.63 (0.12 to 30.45)	0.13 (–0.63 to 6.25)
MET + LIN	MET + ALO	4.36 (0.04 to 945.60)	4.32 (0.04 to 303.60)	0.47 (–2.24 to 79.68)
MET + SIT		0.62 (0.05 to 8.82)	0.63 (0.05 to 8.80)	–0.08 (–3.77 to 0.31)
MET + VIL		1.11 (0.04 to 34.25)	1.11 (0.04 to 33.65)	0.02 (–3.79 to 1.94)
MET + CAN		1.06 (0.00 to 226.30)	1.06 (0.00 to 188.60)	0.01 (–3.80 to 18.52)
MET + DAP		0.98 (0.02 to 23.04)	0.98 (0.02 to 22.78)	0.00 (–3.93 to 1.48)
MET + EMP		1.05 (0.01 to 69.31)	1.05 (0.01 to 65.87)	0.01 (–3.91 to 4.87)
MET + LIR		0.15 (0.00 to 5.97)	0.15 (0.00 to 5.96)	–0.18 (–4.08 to 0.36)
MET + EXE		1.34 (0.02 to 70.78)	1.33 (0.02 to 67.51)	0.06 (–3.05 to 5.52)
MET + DUL		1.02 (0.03 to 64.91)	1.02 (0.03 to 61.83)	0.00 (–3.04 to 5.39)
MET + LIX		0.81 (0.02 to 114.80)	0.81 (0.02 to 93.43)	–0.02 (–3.25 to 13.74)
MET + ROS		0.73 (0.00 to 292.60)	0.73 (0.00 to 195.10)	–0.04 (–3.78 to 25.91)
MET + PIO		1.63 (0.06 to 56.63)	1.63 (0.07 to 54.89)	0.11 (–2.69 to 4.88)
MET + SIT	MET + LIN	0.18 (0.00 to 8.41)	0.18 (0.00 to 8.40)	–0.66 (–80.65 to 0.21)
MET + VIL		0.37 (0.00 to 29.35)	0.37 (0.00 to 29.12)	–0.40 (–80.79 to 1.26)
MET + CAN		0.23 (0.00 to 195.40)	0.25 (0.00 to 170.20)	–0.41 (–76.51 to 14.44)
MET + DAP		0.29 (0.00 to 25.66)	0.29 (0.00 to 25.52)	–0.51 (–80.68 to 0.94)
MET + EMP		0.26 (0.00 to 111.80)	0.26 (0.00 to 106.70)	–0.44 (–80.49 to 4.08)
MET + LIR		0.04 (0.00 to 4.84)	0.04 (0.00 to 4.83)	–0.76 (–80.96 to 0.13)
MET + EXE		0.41 (0.00 to 67.44)	0.41 (0.00 to 64.67)	–0.34 (–77.67 to 4.08)
MET + DUL		0.30 (0.00 to 60.43)	0.30 (0.00 to 55.35)	–0.42 (–79.82 to 4.61)
MET + LIX		0.25 (0.00 to 42.85)	0.25 (0.00 to 39.76)	–0.40 (–80.12 to 10.71)
MET + ROS		0.17 (0.00 to 139.50)	0.17 (0.00 to 102.40)	–0.35 (–79.83 to 23.54)
MET + PIO		0.41 (0.00 to 46.85)	0.41 (0.00 to 46.17)	–0.37 (–76.31 to 2.82)
MET + VIL	MET + SIT	1.70 (0.13 to 27.91)	1.70 (0.13 to 27.49)	0.09 (–0.41 to 2.05)
MET + CAN		1.68 (0.01 to 229.00)	1.68 (0.01 to 190.70)	0.10 (–0.46 to 18.89)
MET + DAP		1.57 (0.13 to 16.98)	1.57 (0.13 to 16.78)	0.07 (–0.41 to 1.58)
MET + EMP		1.63 (0.04 to 58.26)	1.63 (0.04 to 55.76)	0.08 (–0.48 to 5.03)
MET + LIR		0.25 (0.01 to 3.50)	0.25 (0.01 to 3.48)	–0.09 (–0.51 to 0.34)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + EXE		2.06 (0.06 to 53.35)	2.05 (0.06 to 50.32)	0.14 (–0.38 to 6.40)
MET + DUL		1.77 (0.08 to 47.69)	1.77 (0.08 to 44.69)	0.11 (–0.32 to 6.34)
MET + LIX		1.33 (0.03 to 76.15)	1.33 (0.03 to 64.44)	0.04 (–0.38 to 13.72)
MET + ROS		1.24 (0.00 to 447.10)	1.23 (0.00 to 346.90)	0.04 (–0.45 to 26.04)
MET + PIO		2.72 (0.20 to 39.30)	2.71 (0.21 to 36.45)	0.22 (–0.30 to 6.25)
MET + CAN	MET + VIL	0.93 (0.00 to 120.00)	0.93 (0.00 to 100.60)	–0.01 (–1.71 to 18.51)
MET + DAP		0.87 (0.04 to 18.58)	0.87 (0.04 to 18.35)	–0.03 (–1.97 to 1.49)
MET + EMP		0.85 (0.02 to 52.42)	0.85 (0.02 to 50.36)	–0.03 (–1.88 to 4.88)
MET + LIR		0.14 (0.00 to 4.77)	0.14 (0.00 to 4.76)	–0.20 (–2.14 to 0.29)
MET + EXE		1.11 (0.02 to 56.42)	1.11 (0.02 to 53.61)	0.02 (–1.71 to 6.20)
MET + DUL		1.02 (0.02 to 69.26)	1.02 (0.02 to 64.02)	0.00 (–1.93 to 6.28)
MET + LIX		0.71 (0.01 to 112.80)	0.71 (0.01 to 94.70)	–0.05 (–1.93 to 13.69)
MET + ROS		0.71 (0.00 to 444.10)	0.71 (0.00 to 289.60)	–0.06 (–1.83 to 25.60)
MET + PIO		1.48 (0.09 to 39.51)	1.48 (0.09 to 37.47)	0.10 (–1.46 to 5.93)
MET + DAP	MET + CAN	0.84 (0.01 to 442.80)	0.84 (0.01 to 441.70)	–0.03 (–18.63 to 1.32)
MET + EMP		0.95 (0.01 to 643.10)	0.95 (0.01 to 627.00)	0.00 (–18.36 to 4.30)
MET + LIR		0.16 (0.00 to 79.16)	0.16 (0.00 to 79.05)	–0.18 (–18.89 to 0.29)
MET + EXE		1.22 (0.01 to 1,004.00)	1.22 (0.01 to 917.00)	0.03 (–18.54 to 6.35)
MET + DUL		1.00 (0.00 to 1,359.00)	1.00 (0.00 to 1,323.00)	0.00 (–18.54 to 6.31)
MET + LIX		0.85 (0.00 to 1,384.00)	0.85 (0.00 to 1,129.00)	–0.02 (–18.47 to 12.70)
MET + ROS		0.72 (0.00 to 1,039.00)	0.72 (0.00 to 785.50)	–0.02 (–17.36 to 22.78)
MET + PIO		1.55 (0.01 to 1,109.00)	1.55 (0.01 to 1,033.00)	0.07 (–18.58 to 5.69)
MET + EMP	MET + DAP	1.06 (0.03 to 63.42)	1.06 (0.03 to 60.68)	0.01 (–1.38 to 4.91)
MET + LIR		0.17 (0.00 to 4.72)	0.17 (0.00 to 4.71)	–0.17 (–1.71 to 0.35)
MET + EXE		1.36 (0.02 to 93.87)	1.36 (0.02 to 87.18)	0.06 (–1.38 to 6.40)
MET + DUL		1.28 (0.02 to 82.11)	1.28 (0.02 to 73.26)	0.05 (–1.55 to 6.52)
MET + LIX		0.88 (0.02 to 91.87)	0.88 (0.02 to 77.46)	–0.02 (–1.58 to 13.86)
MET + ROS		0.78 (0.00 to 202.30)	0.78 (0.00 to 154.80)	–0.03 (–1.31 to 25.76)
MET + PIO		1.62 (0.09 to 61.48)	1.62 (0.10 to 58.48)	0.12 (–1.33 to 6.27)
MET + LIR	MET + EMP	0.16 (0.00 to 8.71)	0.16 (0.00 to 8.69)	–0.17 (–5.12 to 0.38)
MET + EXE		1.23 (0.01 to 110.80)	1.23 (0.01 to 104.80)	0.04 (–4.73 to 6.39)
MET + DUL		1.17 (0.01 to 111.90)	1.17 (0.01 to 100.70)	0.03 (–4.81 to 6.40)
MET + LIX		0.76 (0.01 to 169.50)	0.76 (0.01 to 137.80)	–0.03 (–4.67 to 13.53)
MET + ROS		0.84 (0.00 to 186.40)	0.84 (0.00 to 123.30)	–0.02 (–4.55 to 25.70)
MET + PIO		1.42 (0.03 to 127.00)	1.42 (0.03 to 121.70)	0.08 (–4.71 to 6.39)
MET + EXE	MET + LIR	8.63 (0.13 to 538.70)	8.57 (0.13 to 505.60)	0.25 (–0.30 to 6.53)
MET + DUL		6.97 (0.24 to 312.00)	6.94 (0.24 to 300.70)	0.21 (–0.18 to 6.54)
MET + LIX		5.48 (0.10 to 777.30)	5.46 (0.10 to 627.90)	0.13 (–0.33 to 14.02)
MET + ROS		5.25 (0.00 to 2,162.00)	5.23 (0.00 to 1,214.00)	0.15 (–0.45 to 26.09)
MET + PIO		10.72 (0.31 to 602.00)	10.64 (0.31 to 562.30)	0.32 (–0.23 to 6.34)
MET + DUL	MET + EXE	0.85 (0.01 to 75.29)	0.85 (0.01 to 69.73)	–0.03 (–5.44 to 5.80)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX		0.67 (0.00 to 107.70)	0.67 (0.00 to 86.89)	–0.06 (–6.33 to 13.03)
MET + ROS		0.51 (0.00 to 183.60)	0.51 (0.00 to 112.00)	–0.08 (–6.25 to 25.51)
MET + PIO		1.15 (0.05 to 62.03)	1.14 (0.06 to 60.59)	0.03 (–4.55 to 3.82)
MET + LIX	MET + DUL	0.70 (0.01 to 109.80)	0.70 (0.01 to 88.66)	–0.04 (–6.17 to 13.49)
MET + ROS		0.65 (0.00 to 277.50)	0.65 (0.00 to 240.10)	–0.05 (–5.72 to 24.79)
MET + PIO		1.53 (0.03 to 82.54)	1.53 (0.03 to 78.33)	0.10 (–5.60 to 5.44)
MET + ROS	MET + LIX	1.12 (0.00 to 247.50)	1.12 (0.00 to 136.10)	0.01 (–13.65 to 25.26)
MET + PIO		2.14 (0.02 to 123.20)	2.13 (0.02 to 118.00)	0.15 (–12.43 to 5.75)
MET + PIO	MET + ROS	1.98 (0.01 to 2,038.00)	1.98 (0.01 to 1,995.00)	0.13 (–25.77 to 6.13)
Random-effects model	Residual deviance	36.73 vs. 71 data points		
	Deviance information criteria	216.532		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; GLY = glyburide; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MET = metformin; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 29: Consistency Plot for Cardiovascular Mortality (Individual-Drug Case Analysis)



CADTH

Diastolic Blood Pressure (Diastolic BP)

Table 48: Diastolic Blood Pressure: Mean Difference for All Treatment Comparisons — Random-Effects Model

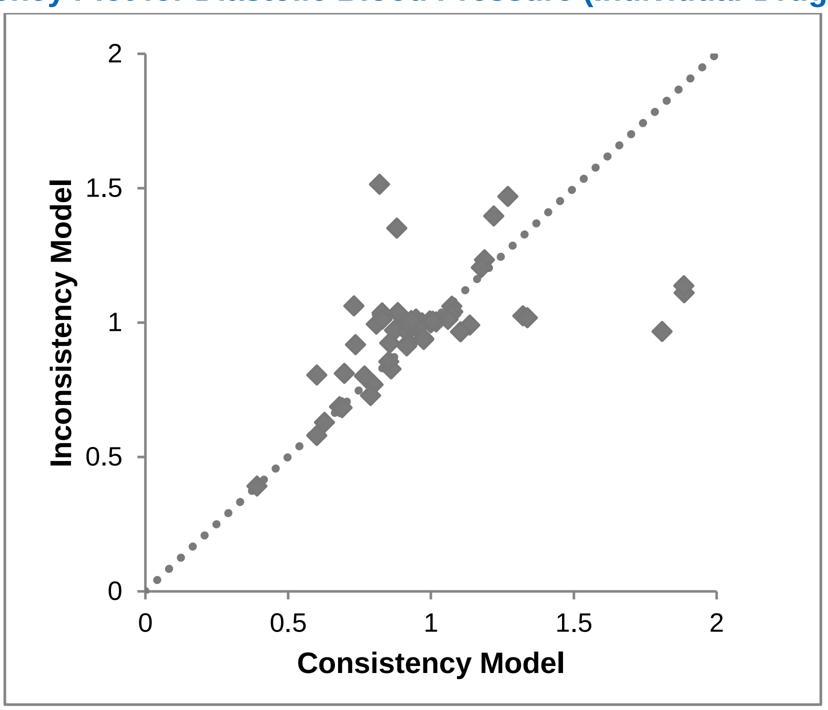
Treatment	Reference	MD (95% CrI)
MET + GLM	MET	–0.29 (–1.49 to 0.84)
MET + GLY		–1.47 (–5.96 to 3.43)
MET + SIT		–0.93 (–1.77 to –0.02)
MET + VIL		–1.72 (–3.87 to 0.40)
MET + CAN		–2.13 (–3.25 to –1.00)
MET + DAP		–1.61 (–3.31 to 0.05)
MET + EMP		–2.50 (–3.65 to –1.33)
MET + EXE		–1.74 (–3.00 to –0.44)
MET + LIR		–0.39 (–1.92 to 1.19)
MET + DUL		–0.45 (–1.92 to 1.02)
MET + LIX		–2.17 (–4.21 to –0.08)
MET + ROS		–2.49 (–7.30 to 2.69)
MET + PIO		–1.80 (–3.32 to –0.40)
MET + GLY	MET + GLM	–1.17 (–5.74 to 3.93)
MET + SIT		–0.64 (–1.83 to 0.65)
MET + VIL		–1.43 (–3.84 to 1.02)
MET + CAN		–1.84 (–3.34 to –0.27)
MET + DAP		–1.32 (–3.34 to 0.71)
MET + EMP		–2.20 (–3.37 to –0.92)
MET + EXE		–1.44 (–2.97 to 0.13)
MET + LIR		–0.09 (–1.86 to 1.76)
MET + DUL		–0.15 (–1.88 to 1.63)
MET + LIX		–1.87 (–4.08 to 0.41)
MET + ROS		–2.20 (–7.07 to 3.20)
MET + PIO		–1.51 (–2.81 to –0.28)
MET + SIT	MET + GLY	0.54 (–4.31 to 4.98)
MET + VIL		–0.26 (–5.73 to 4.80)
MET + CAN		–0.66 (–5.64 to 3.90)
MET + DAP		–0.15 (–5.39 to 4.65)
MET + EMP		–1.03 (–6.12 to 3.56)
MET + EXE		–0.27 (–5.35 to 4.40)
MET + LIR		1.08 (–3.96 to 5.73)
MET + DUL		1.02 (–4.01 to 5.65)
MET + LIX		–0.70 (–6.02 to 4.19)
MET + ROS		–1.02 (–2.80 to 0.78)
MET + PIO		–0.34 (–5.53 to 4.32)
MET + VIL	MET + SIT	–0.79 (–3.12 to 1.50)
MET + CAN		–1.20 (–2.40 to –0.02)

Treatment	Reference	MD (95% CrI)
MET + DAP		–0.68 (–2.65 to 1.18)
MET + EMP		–1.57 (–2.93 to –0.23)
MET + EXE		–0.81 (–2.12 to 0.51)
MET + LIR		0.54 (–0.86 to 1.93)
MET + DUL		0.48 (–0.88 to 1.81)
MET + LIX		–1.24 (–3.29 to 0.78)
MET + ROS		–1.56 (–6.35 to 3.55)
MET + PIO		–0.87 (–2.38 to 0.50)
MET + CAN	MET + VIL	–0.41 (–2.83 to 2.01)
MET + DAP		0.11 (–2.67 to 2.80)
MET + EMP		–0.77 (–3.19 to 1.66)
MET + EXE		–0.01 (–2.47 to 2.45)
MET + LIR		1.34 (–1.30 to 3.98)
MET + DUL		1.28 (–1.33 to 3.84)
MET + LIX		–0.44 (–3.41 to 2.56)
MET + ROS		–0.77 (–6.15 to 4.90)
MET + PIO		–0.08 (–2.71 to 2.43)
MET + DAP	MET + CAN	0.52 (–1.55 to 2.51)
MET + EMP		–0.37 (–1.90 to 1.21)
MET + EXE		0.39 (–1.22 to 2.03)
MET + LIR		1.74 (–0.05 to 3.52)
MET + DUL		1.68 (–0.06 to 3.42)
MET + LIX		–0.03 (–2.29 to 2.21)
MET + ROS		–0.36 (–5.24 to 4.89)
MET + PIO		0.33 (–1.47 to 2.01)
MET + EMP	MET + DAP	–0.89 (–2.88 to 1.19)
MET + EXE		–0.13 (–2.20 to 2.04)
MET + LIR		1.22 (–1.00 to 3.61)
MET + DUL		1.16 (–0.98 to 3.44)
MET + LIX		–0.55 (–3.25 to 2.15)
MET + ROS		–0.88 (–5.98 to 4.58)
MET + PIO		–0.19 (–2.40 to 2.01)
MET + EXE	MET + EMP	0.76 (–0.90 to 2.38)
MET + LIR		2.11 (0.23 to 3.98)
MET + DUL		2.05 (0.21 to 3.87)
MET + LIX		0.33 (–1.98 to 2.67)
MET + ROS		0.01 (–4.94 to 5.41)
MET + PIO		0.70 (–1.01 to 2.24)
MET + LIR	MET + EXE	1.35 (–0.40 to 3.09)
MET + DUL		1.29 (–0.48 to 3.05)
MET + LIX		–0.43 (–2.32 to 1.46)
MET + ROS		–0.75 (–5.76 to 4.60)

Treatment	Reference	MD (95% CrI)
MET + PIO		–0.06 (–1.75 to 1.48)
MET + DUL	MET + LIR	–0.06 (–1.47 to 1.35)
MET + LIX		–1.78 (–3.84 to 0.22)
MET + ROS		–2.10 (–7.11 to 3.17)
MET + PIO		–1.41 (–3.42 to 0.46)
MET + LIX	MET + DUL	–1.72 (–3.94 to 0.52)
MET + ROS		–2.04 (–7.02 to 3.23)
MET + PIO		–1.35 (–3.32 to 0.45)
MET + ROS	MET + LIX	–0.32 (–5.53 to 5.28)
MET + PIO		0.36 (–2.04 to 2.64)
MET + PIO	MET + ROS	0.69 (–4.75 to 5.65)
Random-effects model	Residual deviance	53.29 vs. 55 data points
	Deviance information criteria	154.046

CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLM = glimepiride; GLY = glyburide; LIR = liraglutide; LIX = lixisenatide; MD = mean difference; MET = metformin; PIO = pioglitazone; ROS = rosiglitazone; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 30: Consistency Plot for Diastolic Blood Pressure (Individual-Drug Case Analysis)



Fatal Stoke

Table 49: Fatal Stroke: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	5.47 (0.12 to 2,730.00)	5.41 (0.12 to 411.00)	0.88 (–0.25 to 83.71)
MET + GLI		2.20 (0.10 to 96.82)	2.20 (0.10 to 80.84)	0.24 (–0.29 to 15.74)
MET + VIL		0.87 (0.09 to 8.59)	0.87 (0.09 to 8.48)	–0.02 (–0.32 to 1.31)
MET + SAX		0.80 (0.10 to 5.76)	0.80 (0.10 to 5.73)	–0.04 (–0.31 to 0.78)
MET + ALO		0.36 (0.00 to 103.20)	0.36 (0.00 to 88.13)	–0.11 (–0.39 to 14.58)
MET + SIT		0.91 (0.12 to 7.02)	0.91 (0.12 to 6.97)	–0.02 (–0.31 to 0.90)
MET + CAN		0.70 (0.00 to 219.00)	0.70 (0.00 to 157.90)	–0.06 (–0.37 to 26.99)
MET + DAP		0.65 (0.04 to 9.67)	0.65 (0.04 to 9.53)	–0.06 (–0.34 to 1.50)
MET + EMP		0.97 (0.04 to 48.59)	0.97 (0.04 to 45.27)	–0.01 (–0.34 to 6.66)
MET + LIR		4.34 (0.01 to 3336.00)	4.31 (0.01 to 480.10)	0.69 (–0.31 to 86.32)
MET + EXE		0.79 (0.01 to 19.47)	0.79 (0.01 to 18.73)	–0.04 (–0.34 to 3.34)
MET + DUL		3.40 (0.13 to 329.50)	3.38 (0.13 to 207.70)	0.49 (–0.26 to 36.69)
MET + LIX		0.70 (0.02 to 35.21)	0.70 (0.02 to 33.44)	–0.05 (–0.35 to 5.31)
MET + PIO		0.76 (0.04 to 14.64)	0.76 (0.04 to 14.28)	–0.04 (–0.35 to 2.49)
MET + GLI	MET + GLM	0.43 (0.00 to 59.54)	0.43 (0.00 to 53.57)	–0.37 (–81.82 to 11.88)
MET + VIL		0.16 (0.00 to 14.65)	0.16 (0.00 to 14.54)	–0.84 (–83.60 to 0.91)
MET + SAX		0.15 (0.00 to 9.46)	0.15 (0.00 to 9.41)	–0.86 (–83.60 to 0.44)
MET + ALO		0.05 (0.00 to 68.32)	0.05 (0.00 to 59.65)	–0.73 (–83.33 to 12.96)
MET + SIT		0.19 (0.00 to 4.58)	0.19 (0.00 to 4.57)	–0.82 (–83.54 to 0.27)
MET + CAN		0.12 (0.00 to 105.10)	0.13 (0.00 to 76.31)	–0.60 (–82.67 to 21.74)
MET + DAP		0.11 (0.00 to 12.79)	0.11 (0.00 to 12.71)	–0.86 (–83.61 to 1.00)
MET + EMP		0.17 (0.00 to 42.65)	0.17 (0.00 to 40.04)	–0.71 (–83.27 to 5.43)
MET + LIR		0.76 (0.00 to 1,481.00)	0.78 (0.00 to 390.20)	–0.07 (–77.17 to 83.17)
MET + EXE		0.13 (0.00 to 20.38)	0.13 (0.00 to 20.01)	–0.78 (–83.03 to 2.12)
MET + DUL		0.59 (0.00 to 171.40)	0.60 (0.00 to 122.50)	–0.23 (–78.38 to 33.50)
MET + LIX		0.13 (0.00 to 19.33)	0.14 (0.00 to 18.57)	–0.75 (–83.48 to 3.26)
MET + PIO		0.13 (0.00 to 15.68)	0.13 (0.00 to 15.52)	–0.81 (–83.67 to 1.61)
MET + VIL	MET + GLI	0.39 (0.00 to 19.07)	0.39 (0.01 to 18.91)	–0.21 (–15.76 to 1.14)
MET + SAX		0.38 (0.01 to 4.94)	0.38 (0.01 to 4.93)	–0.24 (–15.56 to 0.31)
MET + ALO		0.14 (0.00 to 83.63)	0.14 (0.00 to 74.12)	–0.22 (–15.52 to 13.66)
MET + SIT		0.42 (0.01 to 8.13)	0.42 (0.01 to 8.10)	–0.22 (–15.59 to 0.53)
MET + CAN		0.29 (0.00 to 176.90)	0.29 (0.00 to 117.30)	–0.17 (–14.79 to 26.14)
MET + DAP		0.28 (0.00 to 14.84)	0.28 (0.00 to 14.66)	–0.26 (–15.56 to 1.20)
MET + EMP		0.48 (0.00 to 57.19)	0.48 (0.00 to 53.59)	–0.15 (–15.54 to 6.15)
MET + LIR		2.05 (0.00 to 3,657.00)	2.02 (0.00 to 694.60)	0.28 (–11.73 to 85.20)
MET + EXE		0.33 (0.00 to 19.72)	0.33 (0.00 to 19.31)	–0.20 (–15.30 to 2.49)
MET + DUL		1.51 (0.01 to 268.90)	1.50 (0.02 to 202.80)	0.14 (–14.11 to 35.44)
MET + LIX		0.32 (0.00 to 32.18)	0.32 (0.00 to 30.38)	–0.20 (–15.36 to 4.74)

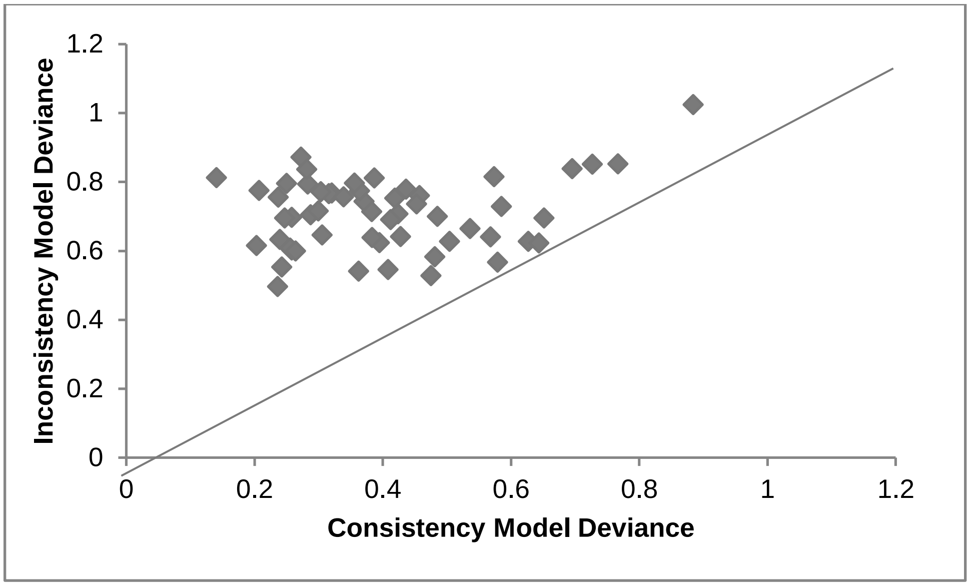
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + PIO		0.33 (0.00 to 19.14)	0.34 (0.00 to 18.79)	–0.21 (–15.65 to 2.11)
MET + SAX	MET + VIL	0.90 (0.04 to 17.40)	0.90 (0.04 to 17.31)	–0.01 (–1.36 to 0.84)
MET + ALO		0.40 (0.00 to 141.10)	0.41 (0.00 to 118.10)	–0.05 (–1.34 to 14.48)
MET + SIT		1.03 (0.05 to 18.97)	1.03 (0.05 to 18.82)	0.00 (–1.34 to 0.93)
MET + CAN		0.82 (0.00 to 316.00)	0.82 (0.00 to 238.80)	–0.02 (–1.31 to 26.90)
MET + DAP		0.70 (0.02 to 26.27)	0.71 (0.02 to 25.81)	–0.04 (–1.39 to 1.53)
MET + EMP		1.11 (0.02 to 89.66)	1.11 (0.02 to 84.23)	0.01 (–1.34 to 6.64)
MET + LIR		4.85 (0.01 to 6,188.00)	4.79 (0.01 to 1,047.00)	0.62 (–1.01 to 86.29)
MET + EXE		0.89 (0.01 to 40.35)	0.89 (0.01 to 39.10)	–0.01 (–1.30 to 3.32)
MET + DUL		4.23 (0.07 to 741.60)	4.20 (0.07 to 422.20)	0.47 (–1.09 to 36.70)
MET + LIX		0.82 (0.01 to 68.67)	0.82 (0.01 to 65.22)	–0.02 (–1.35 to 5.24)
MET + PIO		0.84 (0.03 to 23.44)	0.84 (0.03 to 22.93)	–0.02 (–1.17 to 2.42)
MET + ALO	MET + SAX	0.42 (0.00 to 171.90)	0.42 (0.00 to 147.70)	–0.06 (–0.87 to 14.60)
MET + SIT		1.15 (0.10 to 13.26)	1.15 (0.10 to 13.16)	0.02 (–0.74 to 0.86)
MET + CAN		0.88 (0.00 to 413.90)	0.88 (0.00 to 269.40)	–0.01 (–0.80 to 26.98)
MET + DAP		0.79 (0.04 to 15.80)	0.79 (0.04 to 15.57)	–0.03 (–0.76 to 1.47)
MET + EMP		1.30 (0.03 to 96.43)	1.30 (0.03 to 89.71)	0.04 (–0.82 to 6.62)
MET + LIR		5.95 (0.01 to 6373.00)	5.88 (0.01 to 913.70)	0.69 (–0.62 to 86.33)
MET + EXE		0.99 (0.01 to 35.97)	0.99 (0.01 to 34.99)	0.00 (–0.81 to 3.33)
MET + DUL		4.40 (0.11 to 533.10)	4.36 (0.11 to 356.90)	0.50 (–0.53 to 36.65)
MET + LIX		0.90 (0.02 to 56.65)	0.90 (0.02 to 53.14)	–0.01 (–0.77 to 5.25)
MET + PIO		0.95 (0.04 to 29.07)	0.95 (0.04 to 28.50)	–0.01 (–0.82 to 2.51)
MET + SIT	MET + ALO	2.63 (0.01 to 24,420.00)	2.62 (0.01 to 24,320.00)	0.07 (–14.50 to 0.94)
MET + CAN		2.15 (0.00 to 126,700.00)	2.14 (0.00 to 80,010.00)	0.03 (–12.81 to 24.95)
MET + DAP		1.88 (0.00 to 18,190.00)	1.87 (0.00 to 18,140.00)	0.03 (–14.61 to 1.57)
MET + EMP		3.10 (0.01 to 45,410.00)	3.08 (0.01 to 43,350.00)	0.07 (–14.18 to 6.26)
MET + LIR		15.29 (0.00 to 87,9100.00)	14.09 (0.01 to 372,900.00)	0.53 (–11.74 to 85.76)
MET + EXE		2.12 (0.00 to 31,840.00)	2.12 (0.00 to 31,260.00)	0.04 (–14.33 to 3.17)
MET + DUL		11.80 (0.02 to 116,300.00)	11.44 (0.02 to 106,600.00)	0.43 (–13.12 to 35.72)
MET + LIX		2.29 (0.00 to 35,820.00)	2.29 (0.00 to 34,890.00)	0.03 (–14.14 to 5.06)
MET + PIO		1.90 (0.01 to 17760.00)	1.90 (0.01 to 17550.00)	0.03 (–13.75 to 1.77)
MET + CAN	MET + SIT	0.80 (0.00 to 358.90)	0.80 (0.00 to 224.80)	–0.03 (–0.90 to 26.98)
MET + DAP		0.70 (0.02 to 18.57)	0.70 (0.02 to 18.38)	–0.04 (–0.96 to 1.53)
MET + EMP		1.06 (0.03 to 80.09)	1.06 (0.03 to 75.85)	0.01 (–0.89 to 6.60)
MET + LIR		5.21 (0.01 to 3,910.00)	5.15 (0.01 to 628.80)	0.66 (–0.62 to 86.20)
MET + EXE		0.84 (0.01 to 29.85)	0.84 (0.01 to 28.90)	–0.02 (–0.85 to 3.28)
MET + DUL		3.65 (0.15 to 306.20)	3.62 (0.15 to 200.50)	0.46 (–0.43 to 36.22)
MET + LIX		0.78 (0.02 to 39.81)	0.78 (0.02 to 37.43)	–0.02 (–0.83 to 5.21)
MET + PIO		0.81 (0.03 to 25.00)	0.82 (0.03 to 24.40)	–0.02 (–0.90 to 2.45)
MET + DAP	MET + CAN	0.93 (0.00 to 528.30)	0.93 (0.00 to 524.30)	–0.01 (–26.98 to 1.46)
MET + EMP		1.47 (0.00 to 981.00)	1.47 (0.00 to 944.50)	0.03 (–26.61 to 6.31)
MET + LIR		6.55 (0.00 to 39,360.00)	6.18 (0.00 to 12,160.00)	0.49 (–21.31 to 84.25)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + EXE		1.01 (0.00 to 1,181.00)	1.01 (0.00 to 1,161.00)	0.00 (–26.85 to 3.11)
MET + DUL		4.85 (0.01 to 9,122.00)	4.77 (0.01 to 6,527.00)	0.33 (–25.02 to 35.46)
MET + LIX		1.02 (0.00 to 802.90)	1.02 (0.00 to 755.10)	0.00 (–26.82 to 4.67)
MET + PIO		1.14 (0.00 to 785.40)	1.14 (0.00 to 772.30)	0.01 (–27.00 to 2.38)
MET + EMP	MET + DAP	1.47 (0.02 to 182.90)	1.47 (0.02 to 171.90)	0.04 (–1.45 to 6.68)
MET + LIR		7.63 (0.01 to 8,121.00)	7.49 (0.01 to 1684.00)	0.71 (–1.03 to 86.27)
MET + EXE		1.19 (0.01 to 96.14)	1.18 (0.01 to 93.36)	0.02 (–1.54 to 3.33)
MET + DUL		5.48 (0.08 to 864.70)	5.43 (0.08 to 604.50)	0.50 (–1.16 to 36.65)
MET + LIX		1.11 (0.01 to 116.30)	1.11 (0.01 to 110.60)	0.01 (–1.43 to 5.21)
MET + PIO		1.19 (0.02 to 81.00)	1.19 (0.02 to 79.19)	0.02 (–1.56 to 2.52)
MET + LIR	MET + EMP	4.30 (0.00 to 8,632.00)	4.22 (0.00 to 1739.00)	0.51 (–5.43 to 86.08)
MET + EXE		0.74 (0.00 to 75.21)	0.74 (0.00 to 73.36)	–0.03 (–6.61 to 3.29)
MET + DUL		3.36 (0.02 to 1,262.00)	3.33 (0.02 to 761.70)	0.35 (–5.66 to 36.45)
MET + LIX		0.76 (0.00 to 88.27)	0.76 (0.00 to 81.86)	–0.03 (–6.53 to 5.10)
MET + PIO		0.70 (0.01 to 70.18)	0.70 (0.01 to 68.99)	–0.04 (–6.65 to 2.45)
MET + EXE	MET + LIR	0.16 (0.00 to 167.40)	0.16 (0.00 to 163.40)	–0.61 (–85.76 to 2.33)
MET + DUL		0.81 (0.00 to 113.90)	0.83 (0.01 to 110.00)	–0.06 (–73.60 to 10.30)
MET + LIX		0.14 (0.00 to 131.90)	0.15 (0.00 to 126.80)	–0.61 (–85.27 to 3.47)
MET + PIO		0.17 (0.00 to 90.78)	0.17 (0.00 to 89.98)	–0.63 (–86.18 to 1.77)
MET + DUL	MET + EXE	4.65 (0.04 to 2,235.00)	4.60 (0.05 to 1539.00)	0.44 (–2.59 to 36.45)
MET + LIX		1.01 (0.01 to 157.50)	1.01 (0.01 to 147.30)	0.00 (–3.13 to 5.09)
MET + PIO		0.97 (0.02 to 83.92)	0.97 (0.02 to 82.63)	0.00 (–3.09 to 2.23)
MET + LIX	MET + DUL	0.20 (0.00 to 26.10)	0.20 (0.00 to 24.90)	–0.43 (–36.45 to 4.43)
MET + PIO		0.20 (0.00 to 19.97)	0.20 (0.00 to 19.63)	–0.46 (–36.47 to 1.93)
MET + PIO	MET + LIX	1.06 (0.01 to 117.10)	1.06 (0.01 to 114.50)	0.00 (–5.26 to 2.42)
Random-effects model	Residual deviance	22.29 vs. 55 data points		
	Deviance information criteria	154.4		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLI = glipizide; GLM = glimepiride; LIR = liraglutide; LIX = lixisenatide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

CADTH

Figure 31: Consistency Plot for Fatal Stroke (Individual-Drug Case Analysis)



Glycated Hemoglobin (A1C)

Table 50: A1C: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + GLC	MET	–0.57 (–0.92 to –0.21)
MET + GLM		–0.75 (–0.90 to –0.61)
MET + GLY		–0.97 (–1.35 to –0.60)
MET + GLI		–0.48 (–0.76 to –0.20)
MET + GLL		–0.94 (–1.36 to –0.53)
MET + REP		–1.08 (–1.84 to –0.29)
MET + MIT		–0.30 (–0.77 to 0.17)
MET + NAT		–0.46 (–0.84 to –0.07)
MET + SAX		–0.40 (–0.57 to –0.24)
MET + ALO		–0.63 (–0.92 to –0.34)
MET + LIN		–0.60 (–0.91 to –0.29)
MET + SIT		–0.58 (–0.71 to –0.46)
MET + VIL		–0.70 (–0.90 to –0.51)
MET + GEM		–0.58 (–1.05 to –0.10)
MET + CAN		–0.67 (–0.93 to –0.41)
MET + DAP		–0.60 (–0.87 to –0.33)
MET + EMP		–0.78 (–1.11 to –0.46)
MET + LIR		–0.96 (–1.21 to –0.70)
MET + EXE		–0.85 (–1.08 to –0.63)
MET + DUL		–1.13 (–1.45 to –0.82)
MET + LIX		–0.56 (–0.86 to –0.26)

Treatment	Reference	MD (95% CrI)
MET + ALB		–0.86 (–1.28 to –0.43)
MET + ACA		–0.47 (–1.17 to 0.24)
MET + ROS		–0.97 (–1.20 to –0.75)
MET + PIO		–0.68 (–0.86 to –0.51)
MET + IAS		–1.11 (–1.61 to –0.61)
MET + IGA		–0.87 (–1.17 to –0.55)
MET + IND		–0.72 (–3.00 to 1.61)
MET + DSP		–1.02 (–3.46 to 1.51)
MET + GLM	MET + GLC	–0.19 (–0.55 to 0.18)
MET + GLY		–0.41 (–0.89 to 0.08)
MET + GLI		0.09 (–0.36 to 0.53)
MET + GLL		–0.38 (–0.91 to 0.15)
MET + REP		–0.51 (–1.36 to 0.35)
MET + MIT		0.27 (–0.32 to 0.86)
MET + NAT		0.11 (–0.27 to 0.48)
MET + SAX		0.16 (–0.22 to 0.55)
MET + ALO		–0.06 (–0.52 to 0.39)
MET + LIN		–0.03 (–0.50 to 0.44)
MET + SIT		–0.02 (–0.38 to 0.35)
MET + VIL		–0.14 (–0.52 to 0.25)
MET + GEM		–0.01 (–0.59 to 0.58)
MET + CAN		–0.10 (–0.54 to 0.33)
MET + DAP		–0.03 (–0.48 to 0.41)
MET + EMP		–0.22 (–0.69 to 0.26)
MET + LIR		–0.39 (–0.82 to 0.04)
MET + EXE		–0.29 (–0.69 to 0.12)
MET + DUL		–0.57 (–1.04 to –0.09)
MET + LIX		0.01 (–0.44 to 0.46)
MET + ALB		–0.29 (–0.83 to 0.25)
MET + ACA		0.10 (–0.67 to 0.87)
MET + ROS		–0.41 (–0.79 to –0.02)
MET + PIO		–0.11 (–0.46 to 0.23)
MET + IAS		–0.54 (–1.14 to 0.05)
MET + IGA		–0.30 (–0.75 to 0.16)
MET + IND		–0.15 (–2.46 to 2.22)
MET + DSP		–0.45 (–2.93 to 2.12)
MET + GLY	MET + GLM	–0.22 (–0.61 to 0.17)
MET + GLI		0.27 (–0.03 to 0.58)
MET + GLL		–0.19 (–0.60 to 0.22)
MET + REP		–0.32 (–1.10 to 0.47)
MET + MIT		0.46 (–0.04 to 0.95)
MET + NAT		0.30 (–0.10 to 0.70)

Treatment	Reference	MD (95% CrI)
MET + SAX		0.35 (0.15 to 0.56)
MET + ALO		0.12 (–0.20 to 0.45)
MET + LIN		0.16 (–0.16 to 0.47)
MET + SIT		0.17 (0.01 to 0.33)
MET + VIL		0.05 (–0.15 to 0.25)
MET + GEM		0.18 (–0.31 to 0.67)
MET + CAN		0.09 (–0.21 to 0.38)
MET + DAP		0.15 (–0.16 to 0.46)
MET + EMP		–0.03 (–0.35 to 0.30)
MET + LIR		–0.20 (–0.47 to 0.07)
MET + EXE		–0.10 (–0.34 to 0.14)
MET + DUL		–0.38 (–0.72 to –0.04)
MET + LIX		0.20 (–0.11 to 0.51)
MET + ALB		–0.11 (–0.53 to 0.32)
MET + ACA		0.28 (–0.42 to 1.00)
MET + ROS		–0.22 (–0.47 to 0.03)
MET + PIO		0.07 (–0.11 to 0.25)
MET + IAS		–0.35 (–0.87 to 0.15)
MET + IGA		–0.11 (–0.43 to 0.22)
MET + IND		0.03 (–2.25 to 2.36)
MET + DSP		–0.27 (–2.71 to 2.27)
MET + GLI	MET + GLY	0.49 (0.03 to 0.95)
MET + GLL		0.03 (–0.52 to 0.57)
MET + REP		–0.10 (–0.96 to 0.76)
MET + MIT		0.68 (0.07 to 1.28)
MET + NAT		0.52 (0.00 to 1.03)
MET + SAX		0.57 (0.16 to 0.97)
MET + ALO		0.34 (–0.13 to 0.81)
MET + LIN		0.38 (–0.11 to 0.85)
MET + SIT		0.39 (0.01 to 0.77)
MET + VIL		0.27 (–0.14 to 0.68)
MET + GEM		0.40 (–0.20 to 0.99)
MET + CAN		0.31 (–0.15 to 0.76)
MET + DAP		0.37 (–0.09 to 0.84)
MET + EMP		0.19 (–0.30 to 0.68)
MET + LIR		0.02 (–0.42 to 0.45)
MET + EXE		0.12 (–0.30 to 0.53)
MET + DUL		–0.16 (–0.64 to 0.32)
MET + LIX		0.42 (–0.05 to 0.87)
MET + ALB		0.11 (–0.44 to 0.67)
MET + ACA		0.50 (–0.10 to 1.11)
MET + ROS		0.00 (–0.31 to 0.32)

Treatment	Reference	MD (95% CrI)
MET + PIO		0.29 (–0.11 to 0.69)
MET + IAS		–0.13 (–0.59 to 0.32)
MET + IGA		0.11 (–0.33 to 0.54)
MET + IND		0.25 (–2.06 to 2.59)
MET + DSP		–0.05 (–2.51 to 2.50)
MET + GLL	MET + GLI	–0.46 (–0.96 to 0.02)
MET + REP		–0.59 (–1.42 to 0.23)
MET + MIT		0.19 (–0.37 to 0.73)
MET + NAT		0.02 (–0.45 to 0.50)
MET + SAX		0.08 (–0.21 to 0.36)
MET + ALO		–0.15 (–0.47 to 0.17)
MET + LIN		–0.12 (–0.54 to 0.30)
MET + SIT		–0.10 (–0.39 to 0.18)
MET + VIL		–0.22 (–0.55 to 0.10)
MET + GEM		–0.10 (–0.64 to 0.44)
MET + CAN		–0.19 (–0.57 to 0.19)
MET + DAP		–0.12 (–0.51 to 0.27)
MET + EMP		–0.30 (–0.72 to 0.12)
MET + LIR		–0.48 (–0.84 to –0.11)
MET + EXE		–0.37 (–0.72 to –0.02)
MET + DUL		–0.65 (–1.06 to –0.24)
MET + LIX		–0.08 (–0.47 to 0.32)
MET + ALB		–0.38 (–0.88 to 0.13)
MET + ACA		0.01 (–0.74 to 0.77)
MET + ROS		–0.49 (–0.84 to –0.14)
MET + PIO		–0.20 (–0.52 to 0.12)
MET + IAS		–0.63 (–1.20 to –0.06)
MET + IGA		–0.38 (–0.79 to 0.02)
MET + IND		–0.24 (–2.53 to 2.10)
MET + DSP		–0.54 (–2.98 to 2.01)
MET + REP	MET + GLL	–0.13 (–1.00 to 0.75)
MET + MIT		0.65 (0.02 to 1.28)
MET + NAT		0.49 (–0.06 to 1.04)
MET + SAX		0.54 (0.10 to 0.98)
MET + ALO		0.31 (–0.18 to 0.81)
MET + LIN		0.35 (–0.15 to 0.85)
MET + SIT		0.36 (–0.05 to 0.77)
MET + VIL		0.24 (–0.12 to 0.60)
MET + GEM		0.37 (–0.24 to 0.99)
MET + CAN		0.28 (–0.20 to 0.75)
MET + DAP		0.34 (–0.15 to 0.83)
MET + EMP		0.16 (–0.35 to 0.68)

Treatment	Reference	MD (95% CrI)
MET + LIR		–0.01 (–0.49 to 0.46)
MET + EXE		0.09 (–0.37 to 0.54)
MET + DUL		–0.19 (–0.70 to 0.32)
MET + LIX		0.39 (–0.10 to 0.89)
MET + ALB		0.08 (–0.50 to 0.67)
MET + ACA		0.47 (–0.34 to 1.28)
MET + ROS		–0.03 (–0.49 to 0.43)
MET + PIO		0.26 (–0.16 to 0.68)
MET + IAS		–0.16 (–0.81 to 0.47)
MET + IGA		0.08 (–0.42 to 0.58)
MET + IND		0.22 (–2.10 to 2.59)
MET + DSP		–0.08 (–2.56 to 2.50)
MET + MIT	MET + REP	0.78 (–0.13 to 1.69)
MET + NAT		0.62 (–0.24 to 1.48)
MET + SAX		0.67 (–0.13 to 1.45)
MET + ALO		0.44 (–0.39 to 1.27)
MET + LIN		0.48 (–0.36 to 1.31)
MET + SIT		0.49 (–0.30 to 1.27)
MET + VIL		0.37 (–0.43 to 1.16)
MET + GEM		0.50 (–0.41 to 1.40)
MET + CAN		0.41 (–0.42 to 1.21)
MET + DAP		0.47 (–0.35 to 1.29)
MET + EMP		0.29 (–0.55 to 1.12)
MET + LIR		0.12 (–0.70 to 0.93)
MET + EXE		0.22 (–0.58 to 1.02)
MET + DUL		–0.06 (–0.90 to 0.78)
MET + LIX		0.52 (–0.30 to 1.34)
MET + ALB		0.21 (–0.68 to 1.08)
MET + ACA		0.61 (–0.45 to 1.66)
MET + ROS		0.10 (–0.71 to 0.90)
MET + PIO		0.39 (–0.41 to 1.19)
MET + IAS		–0.03 (–0.97 to 0.89)
MET + IGA		0.21 (–0.63 to 1.04)
MET + IND		0.35 (–2.04 to 2.82)
MET + DSP		0.05 (–2.53 to 2.71)
MET + NAT	MET + MIT	–0.16 (–0.76 to 0.45)
MET + SAX		–0.11 (–0.61 to 0.40)
MET + ALO		–0.33 (–0.89 to 0.22)
MET + LIN		–0.30 (–0.87 to 0.27)
MET + SIT		–0.29 (–0.77 to 0.20)
MET + VIL		–0.41 (–0.92 to 0.11)
MET + GEM		–0.28 (–0.96 to 0.40)

Treatment	Reference	MD (95% CrI)
MET + CAN		–0.37 (–0.91 to 0.16)
MET + DAP		–0.30 (–0.85 to 0.24)
MET + EMP		–0.49 (–1.06 to 0.10)
MET + LIR		–0.66 (–1.20 to –0.12)
MET + EXE		–0.56 (–1.08 to –0.03)
MET + DUL		–0.84 (–1.41 to –0.27)
MET + LIX		–0.26 (–0.82 to 0.30)
MET + ALB		–0.56 (–1.20 to 0.08)
MET + ACA		–0.17 (–1.02 to 0.68)
MET + ROS		–0.68 (–1.20 to –0.15)
MET + PIO		–0.38 (–0.89 to 0.12)
MET + IAS		–0.81 (–1.49 to –0.12)
MET + IGA		–0.57 (–1.13 to –0.01)
MET + IND		–0.42 (–2.74 to 1.94)
MET + DSP		–0.72 (–3.23 to 1.84)
MET + SAX	MET + NAT	0.05 (–0.36 to 0.46)
MET + ALO		–0.17 (–0.65 to 0.30)
MET + LIN		–0.14 (–0.63 to 0.35)
MET + SIT		–0.13 (–0.53 to 0.27)
MET + VIL		–0.24 (–0.67 to 0.17)
MET + GEM		–0.12 (–0.73 to 0.48)
MET + CAN		–0.21 (–0.67 to 0.25)
MET + DAP		–0.14 (–0.61 to 0.33)
MET + EMP		–0.33 (–0.83 to 0.17)
MET + LIR		–0.50 (–0.95 to –0.05)
MET + EXE		–0.39 (–0.84 to 0.04)
MET + DUL		–0.67 (–1.17 to –0.19)
MET + LIX		–0.10 (–0.58 to 0.38)
MET + ALB		–0.40 (–0.97 to 0.16)
MET + ACA		–0.01 (–0.80 to 0.78)
MET + ROS		–0.52 (–0.94 to –0.08)
MET + PIO		–0.22 (–0.62 to 0.17)
MET + IAS		–0.65 (–1.27 to –0.04)
MET + IGA		–0.41 (–0.89 to 0.07)
MET + IND		–0.26 (–2.58 to 2.10)
MET + DSP		–0.56 (–3.03 to 2.00)
MET + ALO	MET + SAX	–0.23 (–0.55 to 0.09)
MET + LIN		–0.19 (–0.55 to 0.15)
MET + SIT		–0.18 (–0.37 to 0.01)
MET + VIL		–0.30 (–0.54 to –0.06)
MET + GEM		–0.17 (–0.67 to 0.32)
MET + CAN		–0.27 (–0.58 to 0.04)

Treatment	Reference	MD (95% CrI)
MET + DAP		–0.20 (–0.52 to 0.12)
MET + EMP		–0.38 (–0.74 to –0.02)
MET + LIR		–0.55 (–0.85 to –0.26)
MET + EXE		–0.45 (–0.72 to –0.18)
MET + DUL		–0.73 (–1.08 to –0.38)
MET + LIX		–0.15 (–0.49 to 0.18)
MET + ALB		–0.46 (–0.90 to 0.00)
MET + ACA		–0.07 (–0.78 to 0.66)
MET + ROS		–0.57 (–0.84 to –0.29)
MET + PIO		–0.28 (–0.51 to –0.05)
MET + IAS		–0.70 (–1.23 to –0.18)
MET + IGA		–0.46 (–0.81 to –0.11)
MET + IND		–0.32 (–2.60 to 2.03)
MET + DSP		–0.62 (–3.07 to 1.91)
MET + LIN	MET + ALO	0.03 (–0.40 to 0.46)
MET + SIT		0.05 (–0.26 to 0.35)
MET + VIL		–0.07 (–0.42 to 0.27)
MET + GEM		0.05 (–0.50 to 0.61)
MET + CAN		–0.04 (–0.43 to 0.35)
MET + DAP		0.03 (–0.37 to 0.43)
MET + EMP		–0.15 (–0.59 to 0.28)
MET + LIR		–0.33 (–0.71 to 0.05)
MET + EXE		–0.22 (–0.59 to 0.14)
MET + DUL		–0.50 (–0.93 to –0.07)
MET + LIX		0.07 (–0.34 to 0.48)
MET + ALB		–0.23 (–0.74 to 0.28)
MET + ACA		0.16 (–0.60 to 0.92)
MET + ROS		–0.34 (–0.71 to 0.02)
MET + PIO		–0.05 (–0.39 to 0.28)
MET + IAS		–0.48 (–1.05 to 0.10)
MET + IGA		–0.24 (–0.66 to 0.18)
MET + IND		–0.09 (–2.39 to 2.28)
MET + DSP		–0.39 (–2.85 to 2.14)
MET + SIT	MET + LIN	0.01 (–0.31 to 0.34)
MET + VIL		–0.10 (–0.46 to 0.25)
MET + GEM		0.02 (–0.54 to 0.58)
MET + CAN		–0.07 (–0.48 to 0.33)
MET + DAP		0.00 (–0.42 to 0.42)
MET + EMP		–0.19 (–0.62 to 0.25)
MET + LIR		–0.36 (–0.75 to 0.04)
MET + EXE		–0.25 (–0.63 to 0.12)
MET + DUL		–0.53 (–0.98 to –0.09)

Treatment	Reference	MD (95% CrI)
MET + LIX		0.04 (–0.39 to 0.47)
MET + ALB		–0.26 (–0.78 to 0.26)
MET + ACA		0.13 (–0.63 to 0.90)
MET + ROS		–0.38 (–0.76 to 0.01)
MET + PIO		–0.08 (–0.43 to 0.26)
MET + IAS		–0.51 (–1.10 to 0.08)
MET + IGA		–0.27 (–0.70 to 0.17)
MET + IND		–0.12 (–2.41 to 2.22)
MET + DSP		–0.42 (–2.88 to 2.13)
MET + VIL	MET + SIT	–0.12 (–0.31 to 0.08)
MET + GEM		0.01 (–0.45 to 0.47)
MET + CAN		–0.08 (–0.36 to 0.19)
MET + DAP		–0.02 (–0.31 to 0.28)
MET + EMP		–0.20 (–0.54 to 0.14)
MET + LIR		–0.37 (–0.62 to –0.12)
MET + EXE		–0.27 (–0.50 to –0.04)
MET + DUL		–0.55 (–0.87 to –0.23)
MET + LIX		0.03 (–0.26 to 0.32)
MET + ALB		–0.28 (–0.70 to 0.15)
MET + ACA		0.12 (–0.59 to 0.82)
MET + ROS		–0.39 (–0.63 to –0.15)
MET + PIO		–0.10 (–0.28 to 0.09)
MET + IAS		–0.52 (–1.03 to –0.02)
MET + IGA		–0.28 (–0.59 to 0.02)
MET + IND		–0.14 (–2.41 to 2.19)
MET + DSP		–0.44 (–2.88 to 2.09)
MET + GEM	MET + VIL	0.13 (–0.37 to 0.63)
MET + CAN		0.03 (–0.28 to 0.35)
MET + DAP		0.10 (–0.23 to 0.43)
MET + EMP		–0.08 (–0.45 to 0.28)
MET + LIR		–0.26 (–0.56 to 0.05)
MET + EXE		–0.15 (–0.43 to 0.13)
MET + DUL		–0.43 (–0.79 to –0.07)
MET + LIX		0.14 (–0.19 to 0.49)
MET + ALB		–0.16 (–0.61 to 0.29)
MET + ACA		0.23 (–0.50 to 0.96)
MET + ROS		–0.27 (–0.56 to 0.02)
MET + PIO		0.02 (–0.20 to 0.24)
MET + IAS		–0.41 (–0.94 to 0.12)
MET + IGA		–0.16 (–0.51 to 0.19)
MET + IND		–0.02 (–2.31 to 2.32)
MET + DSP		–0.32 (–2.77 to 2.22)

CADTH

Treatment	Reference	MD (95% CrI)
MET + CAN	MET + GEM	–0.09 (–0.62 to 0.44)
MET + DAP		–0.02 (–0.57 to 0.52)
MET + EMP		–0.21 (–0.78 to 0.36)
MET + LIR		–0.38 (–0.91 to 0.14)
MET + EXE		–0.28 (–0.79 to 0.23)
MET + DUL		–0.56 (–1.12 to 0.00)
MET + LIX		0.02 (–0.52 to 0.56)
MET + ALB		–0.28 (–0.91 to 0.34)
MET + ACA		0.11 (–0.73 to 0.96)
MET + ROS		–0.40 (–0.92 to 0.12)
MET + PIO		–0.10 (–0.60 to 0.39)
MET + IAS		–0.53 (–1.22 to 0.15)
MET + IGA		–0.29 (–0.84 to 0.26)
MET + IND		–0.14 (–2.46 to 2.23)
MET + DSP		–0.44 (–2.94 to 2.13)
MET + DAP	MET + CAN	0.07 (–0.31 to 0.44)
MET + EMP		–0.12 (–0.53 to 0.30)
MET + LIR		–0.29 (–0.64 to 0.07)
MET + EXE		–0.18 (–0.52 to 0.15)
MET + DUL		–0.46 (–0.87 to –0.06)
MET + LIX		0.11 (–0.27 to 0.50)
MET + ALB		–0.19 (–0.68 to 0.30)
MET + ACA		0.20 (–0.54 to 0.95)
MET + ROS		–0.30 (–0.65 to 0.04)
MET + PIO		–0.01 (–0.32 to 0.30)
MET + IAS		–0.44 (–1.01 to 0.13)
MET + IGA		–0.20 (–0.59 to 0.20)
MET + IND		–0.05 (–2.35 to 2.29)
MET + DSP		–0.35 (–2.80 to 2.20)
MET + EMP	MET + DAP	–0.18 (–0.61 to 0.24)
MET + LIR		–0.36 (–0.73 to 0.01)
MET + EXE		–0.25 (–0.61 to 0.11)
MET + DUL		–0.53 (–0.95 to –0.12)
MET + LIX		0.04 (–0.36 to 0.45)
MET + ALB		–0.26 (–0.76 to 0.24)
MET + ACA		0.13 (–0.62 to 0.89)
MET + ROS		–0.37 (–0.73 to –0.02)
MET + PIO		–0.08 (–0.41 to 0.24)
MET + IAS		–0.51 (–1.08 to 0.06)
MET + IGA		–0.27 (–0.68 to 0.15)
MET + IND		–0.12 (–2.42 to 2.22)
MET + DSP		–0.42 (–2.89 to 2.12)

Treatment	Reference	MD (95% CrI)
MET + LIR	MET + EMP	–0.17 (–0.58 to 0.23)
MET + EXE		–0.07 (–0.45 to 0.32)
MET + DUL		–0.35 (–0.80 to 0.10)
MET + LIX		0.23 (–0.21 to 0.66)
MET + ALB		–0.08 (–0.60 to 0.45)
MET + ACA		0.31 (–0.45 to 1.09)
MET + ROS		–0.19 (–0.58 to 0.21)
MET + PIO		0.10 (–0.25 to 0.46)
MET + IAS		–0.32 (–0.92 to 0.27)
MET + IGA		–0.08 (–0.52 to 0.37)
MET + IND		0.06 (–2.23 to 2.40)
MET + DSP		–0.24 (–2.70 to 2.32)
MET + EXE	MET + LIR	0.11 (–0.21 to 0.42)
MET + DUL		–0.17 (–0.50 to 0.15)
MET + LIX		0.40 (0.09 to 0.72)
MET + ALB		0.10 (–0.39 to 0.58)
MET + ACA		0.49 (–0.25 to 1.24)
MET + ROS		–0.02 (–0.34 to 0.32)
MET + PIO		0.28 (–0.01 to 0.57)
MET + IAS		–0.15 (–0.70 to 0.40)
MET + IGA		0.09 (–0.29 to 0.47)
MET + IND		0.24 (–2.05 to 2.57)
MET + DSP		–0.06 (–2.51 to 2.47)
MET + DUL	MET + EXE	–0.28 (–0.66 to 0.10)
MET + LIX		0.29 (–0.01 to 0.60)
MET + ALB		–0.01 (–0.48 to 0.47)
MET + ACA		0.38 (–0.34 to 1.13)
MET + ROS		–0.12 (–0.43 to 0.19)
MET + PIO		0.17 (–0.08 to 0.43)
MET + IAS		–0.26 (–0.77 to 0.26)
MET + IGA		–0.01 (–0.31 to 0.29)
MET + IND		0.13 (–2.15 to 2.47)
MET + DSP		–0.17 (–2.61 to 2.36)
MET + LIX	MET + DUL	0.57 (0.18 to 0.98)
MET + ALB		0.27 (–0.25 to 0.79)
MET + ACA		0.66 (–0.11 to 1.43)
MET + ROS		0.16 (–0.22 to 0.54)
MET + PIO		0.45 (0.10 to 0.80)
MET + IAS		0.02 (–0.57 to 0.61)
MET + IGA		0.27 (–0.16 to 0.70)
MET + IND		0.41 (–1.89 to 2.75)
MET + DSP		0.11 (–2.35 to 2.67)

Treatment	Reference	MD (95% CrI)
MET + ALB	MET + LIX	–0.30 (–0.81 to 0.20)
MET + ACA		0.09 (–0.67 to 0.84)
MET + ROS		–0.42 (–0.78 to –0.05)
MET + PIO		–0.12 (–0.46 to 0.20)
MET + IAS		–0.55 (–1.11 to 0.02)
MET + IGA		–0.31 (–0.70 to 0.09)
MET + IND		–0.16 (–2.45 to 2.15)
MET + DSP		–0.46 (–2.90 to 2.09)
MET + ACA	MET + ALB	0.39 (–0.43 to 1.22)
MET + ROS		–0.11 (–0.59 to 0.36)
MET + PIO		0.18 (–0.27 to 0.62)
MET + IAS		–0.25 (–0.90 to 0.40)
MET + IGA		–0.01 (–0.52 to 0.50)
MET + IND		0.14 (–2.17 to 2.50)
MET + DSP		–0.16 (–2.63 to 2.42)
MET + ROS	MET + ACA	–0.50 (–1.19 to 0.17)
MET + PIO		–0.21 (–0.94 to 0.50)
MET + IAS		–0.64 (–1.39 to 0.12)
MET + IGA		–0.40 (–1.14 to 0.35)
MET + IND		–0.25 (–2.61 to 2.17)
MET + DSP		–0.55 (–3.09 to 2.11)
MET + PIO	MET + ROS	0.29 (0.02 to 0.56)
MET + IAS		–0.14 (–0.63 to 0.36)
MET + IGA		0.11 (–0.25 to 0.47)
MET + IND		0.25 (–2.04 to 2.59)
MET + DSP		–0.05 (–2.50 to 2.50)
MET + IAS	MET + PIO	–0.43 (–0.95 to 0.09)
MET + IGA		–0.19 (–0.52 to 0.16)
MET + IND		–0.04 (–2.32 to 2.29)
MET + DSP		–0.34 (–2.78 to 2.20)
MET + IGA	MET + IAS	0.24 (–0.25 to 0.74)
MET + IND		0.39 (–1.92 to 2.74)
MET + DSP		0.09 (–2.40 to 2.63)
MET + IND	MET + IGA	0.15 (–2.11 to 2.48)
MET + DSP		–0.15 (–2.57 to 2.35)
MET + DSP	MET + IND	–0.30 (–3.63 to 3.04)
Random-effects model	Residual deviance	179.5 vs. 189 data points
	Deviance information criteria	–189.683

ACA = acarbose; ALB = albiglutide; ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DSP = insulin deludec/insulin aspart mix; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; IAS = insulin aspart; IGA = insulin glargine; IND = insulin degludec; GEM = gemigliptin; GLC = glicazide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; GLY = glyburide; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MD = mean difference; MET = metformin; MIT = mitiglinide; NAT = nateglinide; PIO = pioglitazone; REP = repaglinide; ROS = rosiglitazone; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

HDL Cholesterol

Table 51: High-Density Lipoprotein Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + GLC	MET	–0.07 (–0.14 to 0.00)
MET + GLM		–0.02 (–0.06 to 0.01)
MET + GLL		–0.09 (–0.26 to 0.08)
MET + REP		–0.02 (–0.12 to 0.08)
MET + NAT		0.00 (–0.05 to 0.05)
MET + SAX		–0.03 (–0.15 to 0.08)
MET + ALO		0.00 (–0.06 to 0.06)
MET + LIN		0.01 (–0.06 to 0.08)
MET + SIT		0.00 (–0.03 to 0.02)
MET + VIL		–0.04 (–0.09 to 0.02)
MET + CAN		0.08 (0.04 to 0.12)
MET + DAP		0.04 (–0.04 to 0.13)
MET + EMP		0.04 (0.00 to 0.09)
MET + LIR		0.00 (–0.05 to 0.05)
MET + EXE		–0.02 (–0.06 to 0.02)
MET + DUL		–0.02 (–0.06 to 0.03)
MET + ROS		0.10 (0.05 to 0.14)
MET + PIO		0.10 (0.07 to 0.13)
MET + IGA		–0.01 (–0.08 to 0.06)
MET + GLM	MET + GLC	0.04 (–0.03 to 0.11)
MET + GLL		–0.02 (–0.20 to 0.16)
MET + REP		0.05 (–0.07 to 0.16)
MET + NAT		0.07 (–0.02 to 0.15)
MET + SAX		0.04 (–0.10 to 0.17)
MET + ALO		0.07 (–0.02 to 0.15)
MET + LIN		0.07 (–0.02 to 0.17)
MET + SIT		0.07 (0.00 to 0.14)
MET + VIL		0.03 (–0.04 to 0.11)
MET + CAN		0.15 (0.07 to 0.22)
MET + DAP		0.11 (0.01 to 0.22)
MET + EMP		0.11 (0.03 to 0.19)
MET + LIR		0.07 (–0.02 to 0.15)
MET + EXE		0.05 (–0.03 to 0.12)
MET + DUL		0.05 (–0.03 to 0.13)
MET + ROS		0.16 (0.09 to 0.25)
MET + PIO		0.17 (0.11 to 0.23)
MET + IGA		0.06 (–0.04 to 0.15)
MET + GLL	MET + GLM	–0.07 (–0.24 to 0.11)

Treatment	Reference	MD (95% Crl)
MET + REP		0.00 (–0.10 to 0.11)
MET + NAT		0.02 (–0.04 to 0.09)
MET + SAX		–0.01 (–0.13 to 0.11)
MET + ALO		0.02 (–0.04 to 0.10)
MET + LIN		0.03 (–0.03 to 0.09)
MET + SIT		0.02 (–0.02 to 0.06)
MET + VIL		–0.02 (–0.07 to 0.05)
MET + CAN		0.10 (0.05 to 0.16)
MET + DAP		0.07 (–0.02 to 0.16)
MET + EMP		0.07 (0.01 to 0.13)
MET + LIR		0.02 (–0.04 to 0.09)
MET + EXE		0.00 (–0.05 to 0.06)
MET + DUL		0.01 (–0.05 to 0.07)
MET + ROS		0.12 (0.07 to 0.18)
MET + PIO		0.13 (0.09 to 0.16)
MET + IGA		0.01 (–0.06 to 0.09)
MET + REP	MET + GLL	0.07 (–0.13 to 0.27)
MET + NAT		0.09 (–0.09 to 0.27)
MET + SAX		0.06 (–0.15 to 0.26)
MET + ALO		0.09 (–0.09 to 0.27)
MET + LIN		0.10 (–0.09 to 0.28)
MET + SIT		0.09 (–0.08 to 0.26)
MET + VIL		0.05 (–0.11 to 0.21)
MET + CAN		0.17 (0.00 to 0.34)
MET + DAP		0.13 (–0.06 to 0.33)
MET + EMP		0.13 (–0.04 to 0.31)
MET + LIR		0.09 (–0.09 to 0.26)
MET + EXE		0.07 (–0.10 to 0.24)
MET + DUL		0.07 (–0.10 to 0.25)
MET + ROS		0.19 (0.01 to 0.36)
MET + PIO		0.19 (0.02 to 0.36)
MET + IGA		0.08 (–0.11 to 0.26)
MET + NAT	MET + REP	0.02 (–0.09 to 0.13)
MET + SAX		–0.01 (–0.16 to 0.14)
MET + ALO		0.02 (–0.09 to 0.14)
MET + LIN		0.03 (–0.09 to 0.15)
MET + SIT		0.02 (–0.08 to 0.12)
MET + VIL		–0.02 (–0.13 to 0.09)
MET + CAN		0.10 (0.00 to 0.20)
MET + DAP		0.07 (–0.06 to 0.19)
MET + EMP		0.06 (–0.04 to 0.17)
MET + LIR		0.02 (–0.09 to 0.13)

Treatment	Reference	MD (95% CrI)
MET + EXE		0.00 (–0.10 to 0.11)
MET + DUL		0.00 (–0.10 to 0.11)
MET + ROS		0.12 (0.01 to 0.22)
MET + PIO		0.12 (0.02 to 0.22)
MET + IGA		0.01 (–0.11 to 0.13)
MET + SAX	MET + NAT	–0.03 (–0.16 to 0.10)
MET + ALO		0.00 (–0.08 to 0.08)
MET + LIN		0.01 (–0.08 to 0.09)
MET + SIT		0.00 (–0.06 to 0.06)
MET + VIL		–0.04 (–0.11 to 0.04)
MET + CAN		0.08 (0.01 to 0.15)
MET + DAP		0.04 (–0.05 to 0.14)
MET + EMP		0.04 (–0.03 to 0.11)
MET + LIR		0.00 (–0.08 to 0.08)
MET + EXE		–0.02 (–0.09 to 0.05)
MET + DUL		–0.02 (–0.09 to 0.06)
MET + ROS		0.10 (0.03 to 0.17)
MET + PIO		0.10 (0.04 to 0.17)
MET + IGA		–0.01 (–0.10 to 0.08)
MET + ALO	MET + SAX	0.03 (–0.10 to 0.16)
MET + LIN		0.04 (–0.09 to 0.17)
MET + SIT		0.03 (–0.09 to 0.15)
MET + VIL		–0.01 (–0.13 to 0.12)
MET + CAN		0.11 (–0.01 to 0.23)
MET + DAP		0.08 (0.00 to 0.16)
MET + EMP		0.08 (–0.05 to 0.20)
MET + LIR		0.03 (–0.09 to 0.16)
MET + EXE		0.01 (–0.11 to 0.13)
MET + DUL		0.02 (–0.11 to 0.14)
MET + ROS		0.13 (0.00 to 0.25)
MET + PIO		0.13 (0.01 to 0.25)
MET + IGA		0.02 (–0.11 to 0.15)
MET + LIN	MET + ALO	0.01 (–0.09 to 0.10)
MET + SIT		0.00 (–0.07 to 0.06)
MET + VIL		–0.04 (–0.11 to 0.04)
MET + CAN		0.08 (0.00 to 0.15)
MET + DAP		0.05 (–0.06 to 0.15)
MET + EMP		0.04 (–0.03 to 0.12)
MET + LIR		0.00 (–0.08 to 0.08)
MET + EXE		–0.02 (–0.09 to 0.05)
MET + DUL		–0.01 (–0.09 to 0.06)
MET + ROS		0.10 (0.02 to 0.17)

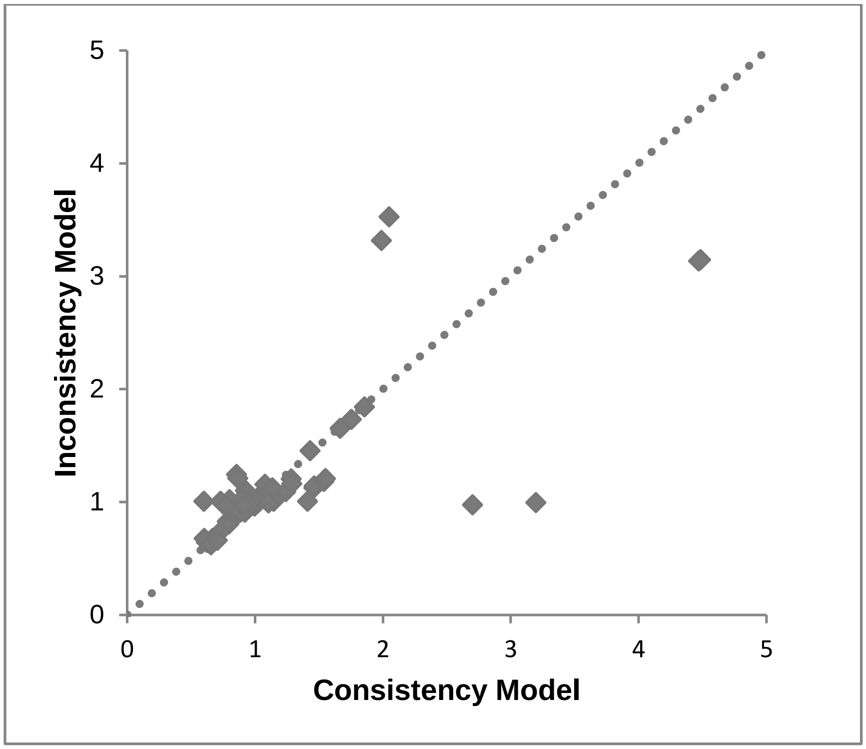
CADTH

Treatment	Reference	MD (95% CrI)
MET + PIO		0.10 (0.04 to 0.16)
MET + IGA		–0.01 (–0.11 to 0.08)
MET + SIT	MET + LIN	–0.01 (–0.08 to 0.06)
MET + VIL		–0.05 (–0.12 to 0.04)
MET + CAN		0.07 (–0.01 to 0.15)
MET + DAP		0.04 (–0.07 to 0.15)
MET + EMP		0.04 (–0.05 to 0.12)
MET + LIR		–0.01 (–0.09 to 0.08)
MET + EXE		–0.03 (–0.10 to 0.05)
MET + DUL		–0.02 (–0.11 to 0.06)
MET + ROS		0.09 (0.01 to 0.17)
MET + PIO		0.10 (0.03 to 0.17)
MET + IGA		–0.02 (–0.12 to 0.08)
MET + VIL	MET + SIT	–0.04 (–0.09 to 0.02)
MET + CAN		0.08 (0.04 to 0.12)
MET + DAP		0.05 (–0.04 to 0.13)
MET + EMP		0.05 (–0.01 to 0.10)
MET + LIR		0.00 (–0.05 to 0.05)
MET + EXE		–0.02 (–0.06 to 0.02)
MET + DUL		–0.01 (–0.06 to 0.03)
MET + ROS		0.10 (0.05 to 0.15)
MET + PIO		0.10 (0.07 to 0.14)
MET + IGA		–0.01 (–0.08 to 0.05)
MET + CAN	MET + VIL	0.12 (0.05 to 0.18)
MET + DAP		0.09 (–0.02 to 0.18)
MET + EMP		0.09 (0.01 to 0.15)
MET + LIR		0.04 (–0.04 to 0.10)
MET + EXE		0.02 (–0.05 to 0.08)
MET + DUL		0.03 (–0.05 to 0.09)
MET + ROS		0.14 (0.07 to 0.20)
MET + PIO		0.14 (0.09 to 0.18)
MET + IGA		0.03 (–0.06 to 0.11)
MET + DAP	MET + CAN	–0.03 (–0.13 to 0.06)
MET + EMP		–0.04 (–0.10 to 0.02)
MET + LIR		–0.08 (–0.14 to –0.02)
MET + EXE		–0.10 (–0.15 to –0.04)
MET + DUL		–0.09 (–0.15 to –0.04)
MET + ROS		0.02 (–0.04 to 0.08)
MET + PIO		0.02 (–0.03 to 0.07)
MET + IGA		–0.09 (–0.17 to –0.02)
MET + EMP	MET + DAP	0.00 (–0.09 to 0.09)
MET + LIR		–0.05 (–0.14 to 0.05)

Treatment	Reference	MD (95% CrI)
MET + EXE		–0.07 (–0.16 to 0.03)
MET + DUL		–0.06 (–0.15 to 0.04)
MET + ROS		0.05 (–0.04 to 0.14)
MET + PIO		0.06 (–0.03 to 0.15)
MET + IGA		–0.06 (–0.16 to 0.05)
MET + LIR	MET + EMP	–0.04 (–0.11 to 0.03)
MET + EXE		–0.06 (–0.12 to 0.00)
MET + DUL		–0.06 (–0.12 to 0.01)
MET + ROS		0.05 (–0.01 to 0.12)
MET + PIO		0.06 (0.01 to 0.11)
MET + IGA		–0.06 (–0.14 to 0.03)
MET + EXE	MET + LIR	–0.02 (–0.08 to 0.04)
MET + DUL		–0.01 (–0.06 to 0.03)
MET + ROS		0.10 (0.03 to 0.17)
MET + PIO		0.10 (0.04 to 0.16)
MET + IGA		–0.01 (–0.09 to 0.07)
MET + DUL	MET + EXE	0.01 (–0.06 to 0.06)
MET + ROS		0.12 (0.06 to 0.18)
MET + PIO		0.12 (0.08 to 0.17)
MET + IGA		0.01 (–0.07 to 0.08)
MET + ROS	MET + DUL	0.11 (0.05 to 0.18)
MET + PIO		0.12 (0.06 to 0.17)
MET + IGA		0.00 (–0.08 to 0.08)
MET + PIO	MET + ROS	0.01 (–0.05 to 0.06)
MET + IGA		–0.11 (–0.19 to –0.03)
MET + IGA	MET + PIO	–0.11 (–0.19 to –0.04)
Random-effects model	Residual deviance	89.57 vs. 76 data points
	Deviance information criteria	–315.915

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLC = glicazide; GLL = gliclazide; GLM = glimepiride; LIN = linagliptin; LIR = liraglutide; MD = mean difference; MET = metformin; NAT = nateglinide; PIO = pioglitazone; REP = repaglinide; ROS = rosiglitazone; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 32: Consistency Plot for High-Density Lipoprotein Cholesterol (Individual-Drug Case Analysis)



LDL Cholesterol

Table 52: Low-Density Lipoprotein Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + GLC	MET	–0.13 (–0.43 to 0.15)
MET + GLM		0.09 (–0.09 to 0.25)
MET + REP		0.01 (–0.37 to 0.40)
MET + NAT		0.10 (–0.26 to 0.45)
MET + SAX		0.11 (–0.32 to 0.56)
MET + ALO		0.02 (–0.23 to 0.28)
MET + LIN		0.03 (–0.28 to 0.32)
MET + SIT		–0.01 (–0.11 to 0.09)
MET + VIL		–0.28 (–0.49 to –0.07)
MET + CAN		0.17 (0.02 to 0.32)
MET + DAP		0.17 (–0.16 to 0.49)
MET + EMP		0.13 (–0.05 to 0.31)
MET + LIR		–0.12 (–0.35 to 0.10)
MET + EXE		0.08 (–0.09 to 0.24)

Treatment	Reference	MD (95% CrI)
MET + DUL		–0.23 (–0.44 to –0.02)
MET + ROS		0.35 (0.18 to 0.52)
MET + PIO		0.14 (0.00 to 0.27)
MET + IGA		–0.09 (–0.33 to 0.15)
MET + GLM	MET + GLC	0.22 (–0.09 to 0.52)
MET + REP		0.15 (–0.34 to 0.63)
MET + NAT		0.23 (–0.23 to 0.70)
MET + SAX		0.25 (–0.28 to 0.79)
MET + ALO		0.16 (–0.20 to 0.52)
MET + LIN		0.16 (–0.23 to 0.54)
MET + SIT		0.12 (–0.17 to 0.42)
MET + VIL		–0.15 (–0.48 to 0.20)
MET + CAN		0.30 (–0.02 to 0.63)
MET + DAP		0.30 (–0.13 to 0.75)
MET + EMP		0.26 (–0.08 to 0.61)
MET + LIR		0.02 (–0.34 to 0.37)
MET + EXE		0.21 (–0.11 to 0.53)
MET + DUL		–0.09 (–0.44 to 0.26)
MET + ROS		0.48 (0.15 to 0.82)
MET + PIO		0.27 (0.01 to 0.53)
MET + IGA		0.04 (–0.32 to 0.41)
MET + REP	MET + GLM	–0.07 (–0.49 to 0.36)
MET + NAT		0.01 (–0.38 to 0.42)
MET + SAX		0.03 (–0.43 to 0.51)
MET + ALO		–0.06 (–0.35 to 0.24)
MET + LIN		–0.06 (–0.30 to 0.19)
MET + SIT		–0.10 (–0.27 to 0.08)
MET + VIL		–0.37 (–0.62 to –0.11)
MET + CAN		0.08 (–0.14 to 0.31)
MET + DAP		0.08 (–0.28 to 0.46)
MET + EMP		0.04 (–0.20 to 0.30)
MET + LIR		–0.21 (–0.47 to 0.06)
MET + EXE		–0.01 (–0.23 to 0.22)
MET + DUL		–0.31 (–0.56 to –0.05)
MET + ROS		0.26 (0.03 to 0.51)
MET + PIO		0.05 (–0.11 to 0.21)
MET + IGA		–0.18 (–0.45 to 0.11)
MET + NAT	MET + REP	0.08 (–0.45 to 0.61)
MET + SAX		0.10 (–0.48 to 0.70)
MET + ALO		0.01 (–0.45 to 0.47)
MET + LIN		0.01 (–0.48 to 0.50)
MET + SIT		–0.02 (–0.42 to 0.38)

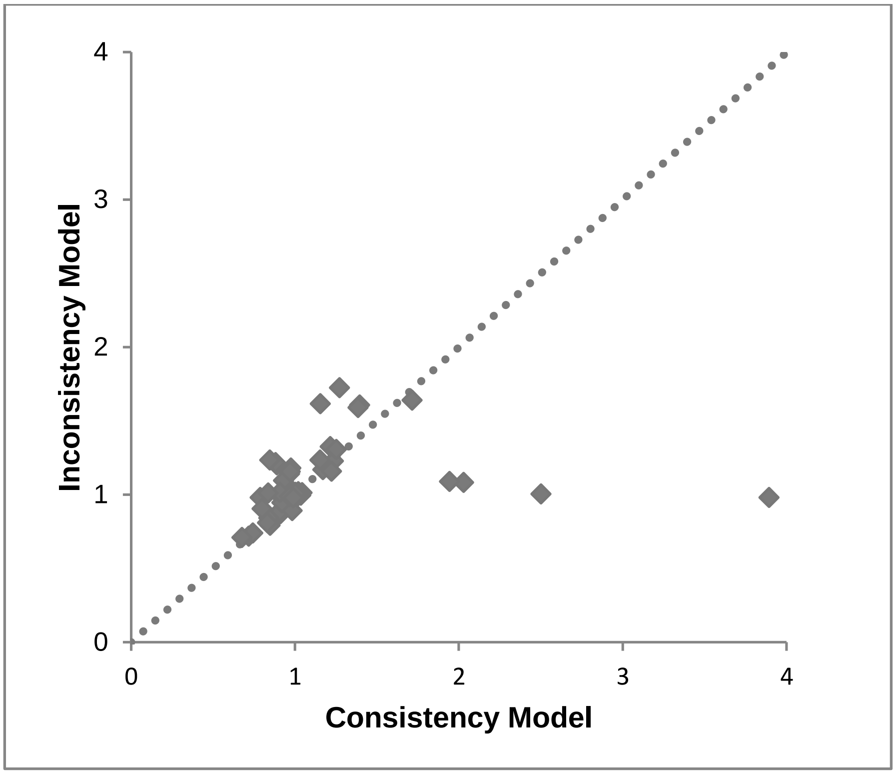
Treatment	Reference	MD (95% CrI)
MET + VIL		–0.30 (–0.74 to 0.15)
MET + CAN		0.16 (–0.26 to 0.58)
MET + DAP		0.15 (–0.35 to 0.67)
MET + EMP		0.12 (–0.31 to 0.55)
MET + LIR		–0.13 (–0.58 to 0.31)
MET + EXE		0.07 (–0.35 to 0.49)
MET + DUL		–0.24 (–0.67 to 0.20)
MET + ROS		0.33 (–0.09 to 0.76)
MET + PIO		0.12 (–0.28 to 0.53)
MET + IGA		–0.11 (–0.56 to 0.36)
MET + SAX	MET + NAT	0.02 (–0.54 to 0.59)
MET + ALO		–0.07 (–0.52 to 0.37)
MET + LIN		–0.07 (–0.54 to 0.39)
MET + SIT		–0.11 (–0.48 to 0.26)
MET + VIL		–0.38 (–0.79 to 0.03)
MET + CAN		0.07 (–0.32 to 0.46)
MET + DAP		0.07 (–0.40 to 0.55)
MET + EMP		0.03 (–0.37 to 0.43)
MET + LIR		–0.22 (–0.64 to 0.21)
MET + EXE		–0.02 (–0.42 to 0.37)
MET + DUL		–0.32 (–0.74 to 0.09)
MET + ROS		0.25 (–0.14 to 0.65)
MET + PIO		0.04 (–0.35 to 0.42)
MET + IGA		–0.19 (–0.62 to 0.24)
MET + ALO	MET + SAX	–0.09 (–0.61 to 0.42)
MET + LIN		–0.09 (–0.63 to 0.43)
MET + SIT		–0.12 (–0.59 to 0.32)
MET + VIL		–0.40 (–0.89 to 0.10)
MET + CAN		0.06 (–0.41 to 0.52)
MET + DAP		0.05 (–0.25 to 0.35)
MET + EMP		0.02 (–0.46 to 0.49)
MET + LIR		–0.23 (–0.73 to 0.25)
MET + EXE		–0.03 (–0.51 to 0.43)
MET + DUL		–0.34 (–0.83 to 0.14)
MET + ROS		0.23 (–0.24 to 0.70)
MET + PIO		0.02 (–0.45 to 0.47)
MET + IGA		–0.21 (–0.71 to 0.30)
MET + LIN	MET + ALO	0.00 (–0.38 to 0.37)
MET + SIT		–0.03 (–0.31 to 0.23)
MET + VIL		–0.31 (–0.63 to 0.01)
MET + CAN		0.15 (–0.15 to 0.44)
MET + DAP		0.14 (–0.27 to 0.56)

Treatment	Reference	MD (95% CrI)
MET + EMP		0.11 (–0.21 to 0.42)
MET + LIR		–0.14 (–0.48 to 0.19)
MET + EXE		0.05 (–0.24 to 0.35)
MET + DUL		–0.25 (–0.58 to 0.07)
MET + ROS		0.32 (0.02 to 0.63)
MET + PIO		0.11 (–0.14 to 0.36)
MET + IGA		–0.12 (–0.46 to 0.23)
MET + SIT	MET + LIN	–0.04 (–0.33 to 0.27)
MET + VIL		–0.31 (–0.65 to 0.05)
MET + CAN		0.14 (–0.18 to 0.48)
MET + DAP		0.14 (–0.30 to 0.60)
MET + EMP		0.10 (–0.24 to 0.46)
MET + LIR		–0.15 (–0.50 to 0.23)
MET + EXE		0.05 (–0.28 to 0.38)
MET + DUL		–0.25 (–0.61 to 0.10)
MET + ROS		0.32 (–0.01 to 0.67)
MET + PIO		0.11 (–0.18 to 0.40)
MET + IGA		–0.12 (–0.48 to 0.26)
MET + VIL	MET + SIT	–0.27 (–0.48 to –0.06)
MET + CAN		0.18 (0.02 to 0.34)
MET + DAP		0.18 (–0.16 to 0.52)
MET + EMP		0.14 (–0.06 to 0.35)
MET + LIR		–0.11 (–0.32 to 0.10)
MET + EXE		0.09 (–0.08 to 0.26)
MET + DUL		–0.22 (–0.41 to –0.01)
MET + ROS		0.36 (0.18 to 0.55)
MET + PIO		0.15 (0.01 to 0.29)
MET + IGA		–0.08 (–0.30 to 0.15)
MET + CAN	MET + VIL	0.45 (0.20 to 0.71)
MET + DAP		0.45 (0.06 to 0.83)
MET + EMP		0.41 (0.14 to 0.69)
MET + LIR		0.16 (–0.13 to 0.46)
MET + EXE		0.36 (0.10 to 0.61)
MET + DUL		0.06 (–0.23 to 0.34)
MET + ROS		0.63 (0.37 to 0.90)
MET + PIO		0.42 (0.20 to 0.64)
MET + IGA		0.19 (–0.12 to 0.50)
MET + DAP	MET + CAN	0.00 (–0.36 to 0.36)
MET + EMP		–0.04 (–0.28 to 0.20)
MET + LIR		–0.29 (–0.55 to –0.04)
MET + EXE		–0.09 (–0.31 to 0.12)
MET + DUL		–0.40 (–0.65 to –0.15)

Treatment	Reference	MD (95% CrI)
MET + ROS		0.18 (–0.04 to 0.41)
MET + PIO		–0.03 (–0.24 to 0.16)
MET + IGA		–0.26 (–0.53 to 0.01)
MET + EMP	MET + DAP	–0.04 (–0.41 to 0.34)
MET + LIR		–0.29 (–0.68 to 0.10)
MET + EXE		–0.09 (–0.46 to 0.27)
MET + DUL		–0.39 (–0.78 to –0.01)
MET + ROS		0.18 (–0.18 to 0.55)
MET + PIO		–0.03 (–0.39 to 0.31)
MET + IGA		–0.26 (–0.67 to 0.15)
MET + LIR	MET + EMP	–0.25 (–0.54 to 0.04)
MET + EXE		–0.05 (–0.31 to 0.19)
MET + DUL		–0.36 (–0.63 to –0.09)
MET + ROS		0.22 (–0.03 to 0.47)
MET + PIO		0.01 (–0.22 to 0.23)
MET + IGA		–0.22 (–0.52 to 0.08)
MET + EXE	MET + LIR	0.20 (–0.07 to 0.46)
MET + DUL		–0.11 (–0.32 to 0.10)
MET + ROS		0.47 (0.20 to 0.75)
MET + PIO		0.26 (0.01 to 0.50)
MET + IGA		0.03 (–0.28 to 0.34)
MET + DUL	MET + EXE	–0.31 (–0.56 to –0.05)
MET + ROS		0.27 (0.04 to 0.51)
MET + PIO		0.06 (–0.13 to 0.24)
MET + IGA		–0.17 (–0.42 to 0.09)
MET + ROS	MET + DUL	0.57 (0.32 to 0.84)
MET + PIO		0.36 (0.13 to 0.59)
MET + IGA		0.13 (–0.16 to 0.44)
MET + PIO	MET + ROS	–0.21 (–0.43 to –0.01)
MET + IGA		–0.44 (–0.73 to –0.15)
MET + IGA	MET + PIO	–0.23 (–0.48 to 0.04)
Random-effects model	Residual deviance	76.19 vs. 70 data points
	Deviance information criteria	–124.736

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLC = glicazide; GLM = glimepiride; LIN = linagliptin; LIR = liraglutide; MD = mean difference; MET = metformin; NAT = nateglinide; PIO = pioglitazone; REP = repaglinide; ROS = rosiglitazone; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 33: Consistency Plot for Low-Density Lipoprotein Cholesterol (Individual-Drug Case Analysis)



Nonfatal Myocardial Infarction (Nonfatal MI)

Table 53: Nonfatal Myocardial Infarction: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

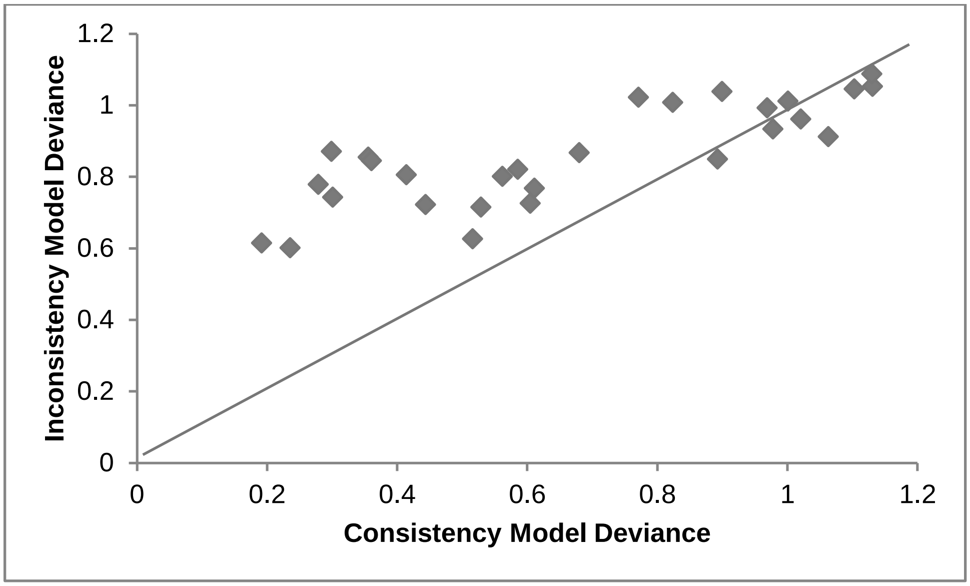
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLC	MET	0.30 (0.00 to 144.70)	0.30 (0.00 to 127.00)	–0.07 (–0.61 to 11.85)
MET + GLM		2.28 (0.14 to 121.20)	2.28 (0.14 to 113.60)	0.19 (–0.41 to 6.70)
MET + GLI		0.64 (0.01 to 17.64)	0.64 (0.01 to 17.32)	–0.04 (–0.53 to 2.05)
MET + NAT		0.03 (0.00 to 23.99)	0.03 (0.00 to 23.50)	–0.13 (–0.66 to 2.03)
MET + SAX		1.96 (0.16 to 32.40)	1.96 (0.16 to 31.59)	0.13 (–0.36 to 3.10)
MET + ALO		0.63 (0.01 to 18.06)	0.63 (0.01 to 17.70)	–0.04 (–0.53 to 2.10)
MET + LIN		1.44 (0.09 to 69.01)	1.44 (0.09 to 66.58)	0.06 (–0.47 to 3.89)
MET + SIT		0.12 (0.00 to 14.27)	0.12 (0.00 to 13.97)	–0.11 (–0.62 to 1.89)
MET + DAP		3.31 (0.13 to 131.00)	3.29 (0.13 to 116.80)	0.33 (–0.37 to 11.06)
MET + LIR		8.51 (0.21 to 1876.00)	8.37 (0.21 to 861.20)	1.26 (–0.28 to 56.08)
MET + DUL		1.46 (0.00 to 931.10)	1.46 (0.00 to 521.40)	0.06 (–0.55 to 40.66)
MET + PIO		1.16 (0.01 to 242.40)	1.16 (0.01 to 201.50)	0.02 (–0.53 to 16.58)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET + GLC	8.95 (0.01 to 12130.00)	8.87 (0.01 to 11800.00)	0.25 (–11.64 to 6.64)
MET + GLI		2.20 (0.00 to 1732.00)	2.20 (0.00 to 1719.00)	0.02 (–11.41 to 1.88)
MET + NAT		0.11 (0.00 to 2.32)	0.12 (0.00 to 2.30)	–0.03 (–9.46 to 0.11)
MET + SAX		7.41 (0.01 to 4933.00)	7.38 (0.01 to 4868.00)	0.19 (–11.60 to 3.11)
MET + ALO		2.25 (0.00 to 1779.00)	2.25 (0.00 to 1771.00)	0.02 (–11.42 to 1.92)
MET + LIN		5.67 (0.01 to 7275.00)	5.64 (0.01 to 7071.00)	0.14 (–11.75 to 3.88)
MET + SIT		0.39 (0.00 to 828.70)	0.39 (0.00 to 818.60)	–0.01 (–11.55 to 1.75)
MET + DAP		12.55 (0.01 to 12970.00)	12.39 (0.01 to 12230.00)	0.36 (–11.31 to 10.89)
MET + LIR		37.27 (0.03 to 95410.00)	35.23 (0.03 to 58600.00)	1.21 (–10.32 to 55.96)
MET + DUL		4.81 (0.00 to 35430.00)	4.76 (0.00 to 22010.00)	0.09 (–11.39 to 40.44)
MET + PIO		3.35 (0.13 to 633.00)	3.30 (0.14 to 623.70)	0.06 (–3.96 to 9.90)
MET + GLI	MET + GLM	0.26 (0.00 to 21.44)	0.26 (0.00 to 21.07)	–0.22 (–6.69 to 1.94)
MET + NAT		0.01 (0.00 to 15.97)	0.01 (0.00 to 15.64)	–0.34 (–6.77 to 1.82)
MET + SAX		0.85 (0.01 to 41.26)	0.85 (0.01 to 40.10)	–0.04 (–6.61 to 3.02)
MET + ALO		0.26 (0.00 to 21.26)	0.26 (0.00 to 20.89)	–0.22 (–6.70 to 1.97)
MET + LIN		0.62 (0.17 to 2.25)	0.63 (0.18 to 2.24)	–0.10 (–3.56 to 0.52)
MET + SIT		0.05 (0.00 to 14.70)	0.05 (0.00 to 14.39)	–0.31 (–6.75 to 1.76)
MET + DAP		1.41 (0.01 to 121.40)	1.41 (0.01 to 108.20)	0.11 (–6.47 to 10.88)
MET + LIR		3.69 (0.11 to 302.50)	3.57 (0.11 to 176.10)	0.87 (–1.84 to 53.43)
MET + DUL		0.61 (0.00 to 163.30)	0.61 (0.00 to 100.70)	–0.07 (–4.36 to 38.24)
MET + PIO		0.46 (0.00 to 167.20)	0.46 (0.00 to 136.60)	–0.14 (–6.62 to 16.26)
MET + NAT	MET + GLI	0.04 (0.00 to 64.98)	0.04 (0.00 to 62.65)	–0.07 (–2.16 to 1.95)
MET + SAX		3.01 (0.19 to 108.90)	2.99 (0.19 to 107.60)	0.14 (–1.26 to 2.74)
MET + ALO		0.98 (0.19 to 4.94)	0.98 (0.19 to 4.91)	0.00 (–0.85 to 0.96)
MET + LIN		2.36 (0.03 to 571.20)	2.36 (0.03 to 552.60)	0.10 (–2.05 to 3.92)
MET + SIT		0.22 (0.00 to 6.58)	0.22 (0.00 to 6.46)	–0.04 (–1.62 to 1.21)
MET + DAP		5.33 (0.10 to 401.80)	5.29 (0.10 to 378.40)	0.34 (–1.49 to 10.89)
MET + LIR		14.59 (0.09 to 12,480.00)	14.26 (0.09 to 6,420.00)	1.26 (–1.52 to 56.16)
MET + DUL		2.23 (0.00 to 5,636.00)	2.22 (0.00 to 3,194.00)	0.08 (–1.95 to 40.64)
MET + PIO		1.79 (0.01 to 698.70)	1.78 (0.01 to 584.90)	0.04 (–1.62 to 16.40)
MET + SAX	MET + NAT	74.49 (0.07 to 135,900.00)	74.04 (0.07 to 134,100.00)	0.28 (–1.74 to 3.23)
MET + ALO		22.87 (0.01 to 54,790.00)	22.79 (0.01 to 54,210.00)	0.07 (–1.94 to 2.22)
MET + LIN		62.74 (0.04 to 140,300.00)	62.45 (0.04 to 138,000.00)	0.21 (–1.95 to 3.96)
MET + SIT		4.02 (0.00 to 19,180.00)	4.01 (0.00 to 18,940.00)	0.01 (–2.06 to 2.02)
MET + DAP		130.50 (0.09 to 340,800.00)	128.90 (0.09 to 323,100.00)	0.48 (–1.57 to 11.05)
MET + LIR		401.30 (0.16 to 1,946,000.00)	378.50 (0.16 to 1,315,000.00)	1.40 (–1.26 to 56.11)
MET + DUL		56.19 (0.00 to 737,900.00)	55.00 (0.00 to 477,900.00)	0.19 (–1.76 to 40.66)
MET + PIO		36.71 (0.39 to 31,330.00)	35.97 (0.40 to 30,570.00)	0.14 (–0.25 to 14.30)
MET + ALO	MET + SAX	0.31 (0.01 to 6.92)	0.32 (0.01 to 6.80)	–0.14 (–2.85 to 1.47)
MET + LIN		0.74 (0.02 to 69.90)	0.74 (0.02 to 67.22)	–0.06 (–3.12 to 3.85)
MET + SIT		0.06 (0.00 to 6.12)	0.06 (0.00 to 6.01)	–0.23 (–3.11 to 1.33)
MET + DAP		1.61 (0.09 to 50.45)	1.60 (0.09 to 46.34)	0.12 (–1.87 to 10.08)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIR		4.24 (0.04 to 2005.00)	4.17 (0.04 to 925.60)	0.97 (–2.52 to 56.04)
MET + DUL		0.67 (0.00 to 873.10)	0.67 (0.00 to 478.80)	–0.06 (–2.95 to 40.52)
MET + PIO		0.53 (0.00 to 181.00)	0.54 (0.00 to 151.70)	–0.08 (–2.90 to 16.29)
MET + LIN	MET + ALO	2.37 (0.03 to 609.20)	2.36 (0.03 to 593.10)	0.10 (–2.08 to 3.92)
MET + SIT		0.22 (0.00 to 10.09)	0.22 (0.00 to 9.89)	–0.04 (–1.78 to 1.31)
MET + DAP		5.36 (0.08 to 571.20)	5.31 (0.08 to 520.80)	0.34 (–1.56 to 10.92)
MET + LIR		14.82 (0.08 to 13,980.00)	14.47 (0.08 to 7,446.00)	1.25 (–1.57 to 56.16)
MET + DUL		2.16 (0.00 to 5,843.00)	2.16 (0.00 to 3,342.00)	0.08 (–1.96 to 40.65)
MET + PIO		1.78 (0.01 to 689.50)	1.78 (0.01 to 588.30)	0.04 (–1.61 to 16.27)
MET + SIT	MET + LIN	0.07 (0.00 to 23.43)	0.07 (0.00 to 22.92)	–0.18 (–3.96 to 1.89)
MET + DAP		2.22 (0.02 to 183.90)	2.21 (0.02 to 164.30)	0.22 (–3.72 to 11.01)
MET + LIR		6.21 (0.16 to 480.10)	5.99 (0.16 to 278.00)	1.07 (–0.92 to 54.42)
MET + DUL		0.98 (0.00 to 274.40)	0.98 (0.00 to 166.70)	0.00 (–2.35 to 39.39)
MET + PIO		0.73 (0.00 to 272.90)	0.73 (0.00 to 227.10)	–0.04 (–3.85 to 16.45)
MET + DAP	MET + SIT	30.16 (0.15 to 17,610.00)	29.75 (0.16 to 16,780.00)	0.42 (–1.25 to 11.03)
MET + LIR		90.34 (0.16 to 183,800.00)	86.79 (0.16 to 112,800.00)	1.35 (–1.19 to 56.16)
MET + DUL		11.83 (0.00 to 75,370.00)	11.74 (0.00 to 46,380.00)	0.16 (–1.73 to 40.68)
MET + PIO		10.40 (0.02 to 19,760.00)	10.34 (0.02 to 16,230.00)	0.11 (–1.51 to 16.46)
MET + LIR	MET + DAP	2.74 (0.01 to 1,718.00)	2.70 (0.01 to 826.40)	0.68 (–10.26 to 55.96)
MET + DUL		0.39 (0.00 to 715.60)	0.40 (0.00 to 423.30)	–0.16 (–10.83 to 40.37)
MET + PIO		0.32 (0.00 to 156.00)	0.32 (0.00 to 128.80)	–0.22 (–10.75 to 16.13)
MET + DUL	MET + LIR	0.17 (0.00 to 5.77)	0.18 (0.00 to 4.79)	–0.70 (–32.34 to 11.90)
MET + PIO		0.11 (0.00 to 71.51)	0.11 (0.00 to 59.48)	–1.03 (–55.79 to 15.30)
MET + PIO	MET + DUL	0.83 (0.00 to 7,560.00)	0.83 (0.00 to 6,448.00)	–0.01 (–40.35 to 16.06)
Random-effects model	Residual deviance	18.76 vs. 28 data points		
	Deviance information criteria	103.709		

ALO = alogliptin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; GLC = glicazide; GLI = glipizide; GLM = glimepiride; LIN = linagliptin; LIR = liraglutide; MET = metformin; NAT = nateglinide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; vs. = versus.

Figure 34: Consistency Plot for Nonfatal Myocardial Infarction (Individual-Drug Case Analysis)



Nonfatal Stroke

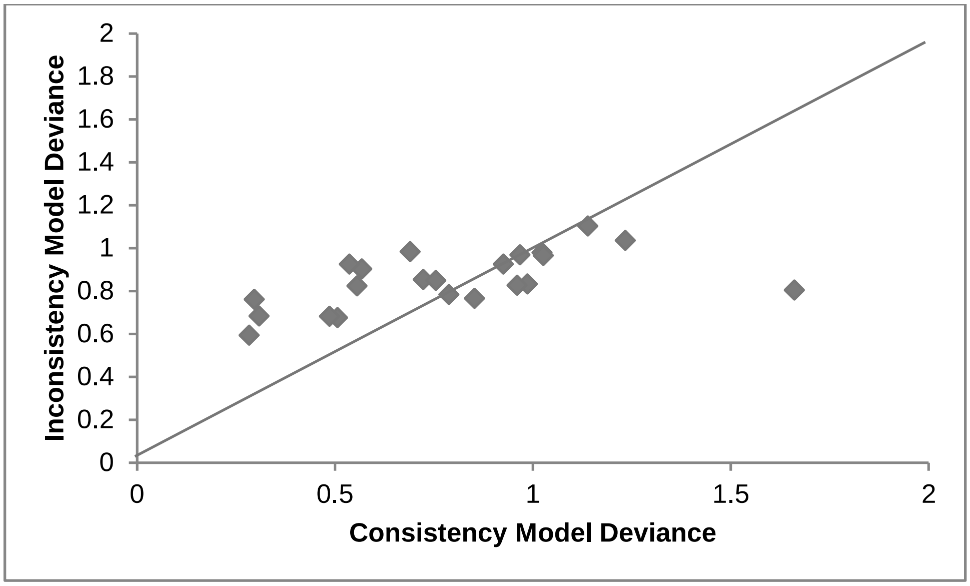
Table 54: Nonfatal Stroke: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	11.59 (0.23 to 1460.00)	11.16 (0.23 to 350.60)	2.86 (–0.35 to 78.72)
MET + GLI		0.47 (0.00 to 50.53)	0.47 (0.00 to 45.78)	–0.12 (–0.75 to 9.02)
MET + SAX		0.37 (0.00 to 156.00)	0.37 (0.00 to 106.50)	–0.13 (–0.76 to 26.75)
MET + ALO		0.27 (0.00 to 17.17)	0.27 (0.00 to 16.68)	–0.17 (–0.79 to 2.79)
MET + LIN		2.76 (0.04 to 403.20)	2.74 (0.04 to 192.70)	0.46 (–0.58 to 51.83)
MET + SIT		2.73 (0.34 to 33.04)	2.72 (0.34 to 31.27)	0.50 (–0.37 to 5.62)
MET + VIL		1.58 (0.24 to 12.89)	1.58 (0.25 to 12.71)	0.16 (–0.51 to 1.72)
MET + EXE		0.20 (0.00 to 13.74)	0.21 (0.00 to 13.39)	–0.18 (–0.80 to 2.78)
MET + PIO		1.48 (0.19 to 13.53)	1.48 (0.19 to 13.29)	0.13 (–0.55 to 1.93)
MET + GLI	MET + GLM	0.04 (0.00 to 16.12)	0.04 (0.00 to 14.81)	–2.56 (–78.47 to 6.08)
MET + SAX		0.03 (0.00 to 31.38)	0.03 (0.00 to 23.15)	–2.34 (–77.91 to 20.01)
MET + ALO		0.02 (0.00 to 6.55)	0.02 (0.00 to 6.42)	–2.87 (–78.87 to 1.45)
MET + LIN		0.24 (0.04 to 1.06)	0.28 (0.05 to 1.04)	–1.97 (–38.80 to 0.06)
MET + SIT		0.27 (0.00 to 6.66)	0.28 (0.01 to 6.58)	–2.02 (–76.44 to 1.47)
MET + VIL		0.14 (0.00 to 8.69)	0.15 (0.00 to 8.62)	–2.62 (–78.56 to 1.07)
MET + EXE		0.02 (0.00 to 2.67)	0.02 (0.00 to 2.64)	–2.86 (–78.31 to 0.53)
MET + PIO		0.14 (0.00 to 6.73)	0.14 (0.00 to 6.67)	–2.59 (–78.38 to 0.90)
MET + SAX	MET + GLI	0.87 (0.02 to 34.24)	0.87 (0.02 to 27.37)	0.00 (–4.15 to 21.14)
MET + ALO		0.57 (0.05 to 4.46)	0.58 (0.06 to 4.45)	–0.02 (–6.96 to 0.50)
MET + LIN		7.00 (0.01 to 24,700.00)	6.82 (0.01 to 16,090.00)	0.40 (–7.75 to 51.66)
MET + SIT		6.07 (0.06 to 7,344.00)	6.01 (0.06 to 7,124.00)	0.50 (–8.12 to 5.43)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + VIL		3.40 (0.03 to 4,471.00)	3.39 (0.04 to 4,446.00)	0.24 (–8.80 to 1.79)
MET + EXE		0.42 (0.00 to 1,443.00)	0.42 (0.00 to 1,420.00)	–0.03 (–9.05 to 2.65)
MET + PIO		2.93 (0.04 to 2,994.00)	2.92 (0.04 to 2,968.00)	0.19 (–8.53 to 1.84)
MET + ALO	MET + SAX	0.66 (0.01 to 41.87)	0.66 (0.01 to 41.64)	–0.01 (–25.28 to 1.26)
MET + LIN		7.60 (0.01 to 5,3010.00)	7.38 (0.01 to 3,3400.00)	0.36 (–24.31 to 51.32)
MET + SIT		7.65 (0.02 to 17,020.00)	7.55 (0.03 to 16,410.00)	0.50 (–25.66 to 5.36)
MET + VIL		4.44 (0.01 to 9,044.00)	4.42 (0.01 to 8,974.00)	0.25 (–26.48 to 1.80)
MET + EXE		0.46 (0.00 to 2,383.00)	0.47 (0.00 to 2,337.00)	–0.02 (–26.62 to 2.65)
MET + PIO		3.80 (0.01 to 7,138.00)	3.79 (0.01 to 7,081.00)	0.21 (–26.33 to 1.85)
MET + LIN	MET + ALO	11.71 (0.03 to 32,160.00)	11.39 (0.03 to 22,690.00)	0.54 (–2.26 to 51.97)
MET + SIT		10.48 (0.15 to 10,850.00)	10.36 (0.16 to 10,640.00)	0.61 (–2.20 to 5.66)
MET + VIL		5.92 (0.10 to 6,662.00)	5.89 (0.10 to 6,598.00)	0.31 (–2.62 to 1.87)
MET + EXE		0.73 (0.00 to 2,142.00)	0.73 (0.00 to 2,107.00)	–0.01 (–2.79 to 2.83)
MET + PIO		5.01 (0.12 to 4,916.00)	4.98 (0.12 to 4,868.00)	0.26 (–2.39 to 1.93)
MET + SIT	MET + LIN	1.13 (0.01 to 42.17)	1.13 (0.02 to 41.69)	0.05 (–49.43 to 3.09)
MET + VIL		0.59 (0.00 to 48.30)	0.60 (0.01 to 47.67)	–0.27 (–51.70 to 1.51)
MET + EXE		0.06 (0.00 to 14.49)	0.06 (0.00 to 14.27)	–0.54 (–51.48 to 1.58)
MET + PIO		0.58 (0.00 to 36.20)	0.58 (0.01 to 35.87)	–0.27 (–51.42 to 1.47)
MET + VIL	MET + SIT	0.57 (0.04 to 7.34)	0.57 (0.04 to 7.24)	–0.32 (–5.51 to 1.48)
MET + EXE		0.08 (0.00 to 2.94)	0.08 (0.00 to 2.88)	–0.61 (–5.24 to 1.38)
MET + PIO		0.54 (0.04 to 4.79)	0.54 (0.05 to 4.73)	–0.32 (–5.24 to 1.24)
MET + EXE	MET + VIL	0.13 (0.00 to 9.55)	0.13 (0.00 to 9.31)	–0.32 (–1.87 to 2.60)
MET + PIO		0.95 (0.11 to 7.36)	0.95 (0.11 to 7.25)	–0.02 (–1.54 to 1.69)
MET + PIO	MET + EXE	6.91 (0.12 to 11,100.00)	6.87 (0.13 to 10,990.00)	0.28 (–2.40 to 1.91)
Random-effects model	Residual deviance	17.29 vs. 22 data points		
	Deviance information criteria	86.698		

ALO = alogliptin; CrI = credible interval; EXE = exenatide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; LIN = linagliptin; MET = metformin; OR = odds ratio; PIO = pioglitazone; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 35: Consistency Plot for Nonfatal Stroke (Individual-Drug Case Analysis)



Pancreatic Cancer

Table 55: Pancreatic Cancer: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SAX	MET + GLM	3.31 (0.09 to 262.00)	3.30 (0.09 to 245.00)	0.17 (–0.17 to 7.04)
MET + LIN		0.98 (0.03 to 25.62)	0.98 (0.03 to 25.42)	0.00 (–0.21 to 1.05)
MET + SIT		2.70 (0.07 to 212.20)	2.70 (0.07 to 200.50)	0.11 (–0.19 to 5.45)
MET + LIR		10.37 (0.08 to 5771.00)	10.29 (0.08 to 1433.00)	0.65 (–0.16 to 74.48)
MET + DUL		7.34 (0.01 to 10410.00)	7.30 (0.01 to 1958.00)	0.46 (–0.19 to 86.32)
MET + LIN	MET + SAX	0.27 (0.00 to 31.66)	0.28 (0.00 to 31.44)	–0.15 (–7.04 to 0.96)
MET + SIT		0.74 (0.00 to 239.10)	0.74 (0.00 to 228.50)	–0.05 (–6.86 to 5.39)
MET + LIR		3.21 (0.00 to 3922.00)	3.14 (0.00 to 1367.00)	0.39 (–5.72 to 74.06)
MET + DUL		2.22 (0.00 to 8462.00)	2.20 (0.00 to 1668.00)	0.19 (–5.42 to 85.34)
MET + SIT	MET + LIN	3.02 (0.02 to 614.30)	3.02 (0.02 to 578.10)	0.10 (–1.00 to 5.45)
MET + LIR		11.60 (0.03 to 15490.00)	11.42 (0.03 to 4086.00)	0.60 (–0.72 to 74.11)
MET + DUL		8.46 (0.00 to 21870.00)	8.33 (0.00 to 5689.00)	0.42 (–0.72 to 86.25)
MET + LIR	MET + SIT	3.05 (0.11 to 1409.00)	3.00 (0.11 to 372.20)	0.34 (–1.39 to 72.80)
MET + DUL		2.90 (0.00 to 3010.00)	2.84 (0.00 to 640.50)	0.24 (–2.42 to 85.09)
MET + DUL	MET + LIR	0.70 (0.00 to 113.80)	0.75 (0.00 to 61.96)	–0.02 (–38.80 to 61.89)
Random-effects model	Residual deviance	4.888 vs. 10 data points		
	Deviance information criteria	36.722		

CrI = credible interval; DUL = dulaglutide; GLM = glimepiride; MET = metformin; LIN = linagliptin; LIR = liraglutide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; vs. = versus.

Systolic Blood Pressure (SBP)

Table 56: Systolic Blood Pressure: Mean Difference for All Treatment Comparisons — Random-Effects Model

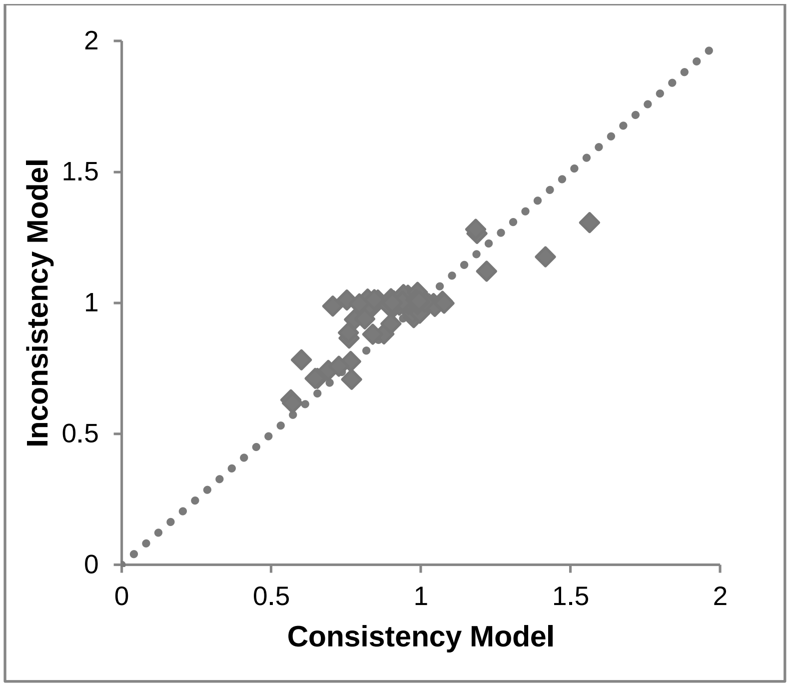
Treatment	Reference	MD (95% CrI)
MET + GLM	MET	0.54 (–1.17 to 2.16)
MET + SAX		0.95 (–1.73 to 3.60)
MET + SIT		–0.86 (–2.30 to 0.34)
MET + VIL		–3.67 (–7.81 to 0.50)
MET + CAN		–3.73 (–5.49 to –2.31)
MET + DAP		–2.72 (–4.58 to –0.83)
MET + EMP		–4.81 (–6.59 to –3.03)
MET + LIR		–1.17 (–3.89 to 1.28)
MET + EXE		–4.27 (–6.32 to –2.40)
MET + DUL		–1.54 (–3.84 to 0.55)
MET + LIX		–4.68 (–8.28 to –1.25)
MET + PIO		–3.27 (–5.22 to –1.42)
MET + IAS		1.92 (–3.32 to 6.99)
MET + IGA		1.08 (–2.81 to 4.71)
MET + IND		–1.89 (–8.06 to 3.96)
MET + SAX	MET + GLM	0.42 (–2.68 to 3.56)
MET + SIT		–1.40 (–3.30 to 0.36)
MET + VIL		–4.21 (–8.62 to 0.16)
MET + CAN		–4.27 (–6.52 to –2.23)
MET + DAP		–3.25 (–5.73 to –0.71)
MET + EMP		–5.35 (–7.15 to –3.42)
MET + LIR		–1.71 (–4.71 to 1.13)
MET + EXE		–4.81 (–7.21 to –2.43)
MET + DUL		–2.08 (–4.74 to 0.45)
MET + LIX		–5.22 (–9.02 to –1.50)
MET + PIO		–3.81 (–5.66 to –2.00)
MET + IAS		1.38 (–3.93 to 6.66)
MET + IGA		0.54 (–3.47 to 4.41)
MET + IND		–2.42 (–8.69 to 3.63)
MET + SIT	MET + SAX	–1.82 (–4.85 to 1.03)
MET + VIL		–4.62 (–9.64 to 0.26)
MET + CAN		–4.68 (–7.90 to –1.73)
MET + DAP		–3.67 (–6.21 to –1.10)
MET + EMP		–5.76 (–8.97 to –2.55)
MET + LIR		–2.13 (–5.89 to 1.46)
MET + EXE		–5.23 (–8.56 to –1.95)
MET + DUL		–2.49 (–6.03 to 0.87)
MET + LIX		–5.64 (–10.11 to –1.31)
MET + PIO		–4.22 (–7.56 to –1.00)
MET + IAS		0.96 (–4.81 to 6.65)
MET + IGA		0.12 (–4.53 to 4.61)
MET + IND		–2.84 (–9.62 to 3.56)

Treatment	Reference	MD (95% CrI)
MET + VIL	MET + SIT	–2.81 (–6.87 to 1.35)
MET + CAN		–2.87 (–4.38 to –1.44)
MET + DAP		–1.85 (–4.01 to 0.48)
MET + EMP		–3.95 (–5.92 to –1.75)
MET + LIR		–0.31 (–2.67 to 1.99)
MET + EXE		–3.41 (–5.43 to –1.20)
MET + DUL		–0.68 (–2.70 to 1.40)
MET + LIX		–3.82 (–7.39 to –0.18)
MET + PIO		–2.41 (–4.36 to –0.39)
MET + IAS		2.78 (–2.13 to 7.76)
MET + IGA		1.94 (–1.56 to 5.41)
MET + IND		–1.02 (–6.96 to 4.67)
MET + CAN	MET + VIL	–0.06 (–4.37 to 4.20)
MET + DAP		0.96 (–3.55 to 5.52)
MET + EMP		–1.14 (–5.61 to 3.31)
MET + LIR		2.50 (–2.25 to 7.17)
MET + EXE		–0.60 (–5.07 to 3.90)
MET + DUL		2.13 (–2.45 to 6.62)
MET + LIX		–1.01 (–6.43 to 4.37)
MET + PIO		0.40 (–4.13 to 4.86)
MET + IAS		5.59 (–0.80 to 12.09)
MET + IGA		4.75 (–0.69 to 10.16)
MET + IND		1.79 (–5.50 to 8.92)
MET + DAP	MET + CAN	1.02 (–1.32 to 3.59)
MET + EMP		–1.08 (–3.25 to 1.38)
MET + LIR		2.56 (–0.14 to 5.27)
MET + EXE		–0.54 (–2.81 to 1.97)
MET + DUL		2.19 (–0.18 to 4.70)
MET + LIX		–0.95 (–4.67 to 2.86)
MET + PIO		0.46 (–1.75 to 2.83)
MET + IAS		5.65 (0.45 to 10.76)
MET + IGA		4.81 (1.02 to 8.56)
MET + IND		1.84 (–4.24 to 7.72)
MET + EMP	MET + DAP	–2.10 (–4.71 to 0.46)
MET + LIR		1.54 (–1.74 to 4.59)
MET + EXE		–1.56 (–4.31 to 1.03)
MET + DUL		1.17 (–1.71 to 3.90)
MET + LIX		–1.97 (–6.01 to 1.90)
MET + PIO		–0.56 (–3.27 to 2.04)
MET + IAS		4.63 (–0.89 to 9.96)
MET + IGA		3.79 (–0.55 to 7.82)
MET + IND		0.83 (–5.65 to 6.99)
MET + LIR	MET + EMP	3.64 (0.44 to 6.59)
MET + EXE		0.54 (–2.11 to 3.06)
MET + DUL		3.27 (0.44 to 5.94)
MET + LIX		0.13 (–3.84 to 3.94)

Treatment	Reference	MD (95% CrI)
MET + PIO		1.54 (–0.83 to 3.80)
MET + IAS		6.73 (1.30 to 12.03)
MET + IGA		5.89 (1.70 to 9.83)
MET + IND		2.93 (–3.48 to 8.98)
MET + EXE	MET + LIR	–3.10 (–6.09 to 0.11)
MET + DUL		–0.37 (–2.64 to 1.97)
MET + LIX		–3.51 (–7.67 to 0.80)
MET + PIO		–2.10 (–5.05 to 0.98)
MET + IAS		3.09 (–2.31 to 8.60)
MET + IGA		2.25 (–1.90 to 6.40)
MET + IND		–0.71 (–7.20 to 5.51)
MET + DUL	MET + EXE	2.73 (–0.14 to 5.45)
MET + LIX		–0.41 (–3.33 to 2.52)
MET + PIO		1.00 (–1.39 to 3.37)
MET + IAS		6.19 (0.79 to 11.46)
MET + IGA		5.35 (1.20 to 9.32)
MET + IND		2.39 (–4.05 to 8.44)
MET + LIX	MET + DUL	–3.14 (–7.16 to 0.95)
MET + PIO		–1.73 (–4.39 to 1.04)
MET + IAS		3.46 (–1.86 to 8.81)
MET + IGA		2.62 (–1.43 to 6.63)
MET + IND		–0.34 (–6.69 to 5.75)
MET + PIO	MET + LIX	1.41 (–2.32 to 5.17)
MET + IAS		6.60 (0.46 to 12.52)
MET + IGA		5.76 (0.76 to 10.60)
MET + IND		2.80 (–4.25 to 9.38)
MET + IAS	MET + PIO	5.19 (–0.20 to 10.55)
MET + IGA		4.35 (0.28 to 8.32)
MET + IND		1.39 (–4.96 to 7.44)
MET + IGA	MET + IAS	–0.84 (–4.36 to 2.68)
MET + IND		–3.80 (–9.77 to 2.17)
MET + IND	MET + IGA	–2.96 (–7.75 to 1.67)
Random-effects model	Residual deviance	58.72 vs. 64 data points
	Deviance information criteria	215.917

CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; IAS = insulin aspart; IGA = insulin glargine; IND = insulin degludec; GLM = glimepiride; LIR = liraglutide; LIX = lixisenatide; MD = mean difference; MET = metformin; PIO = pioglitazone; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 36: Consistency Plot for Systolic Blood Pressure (Individual-Drug Case Analysis)



Transient Ischemic Attack (TIA)

Table 57: Transient Ischemic Attack: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

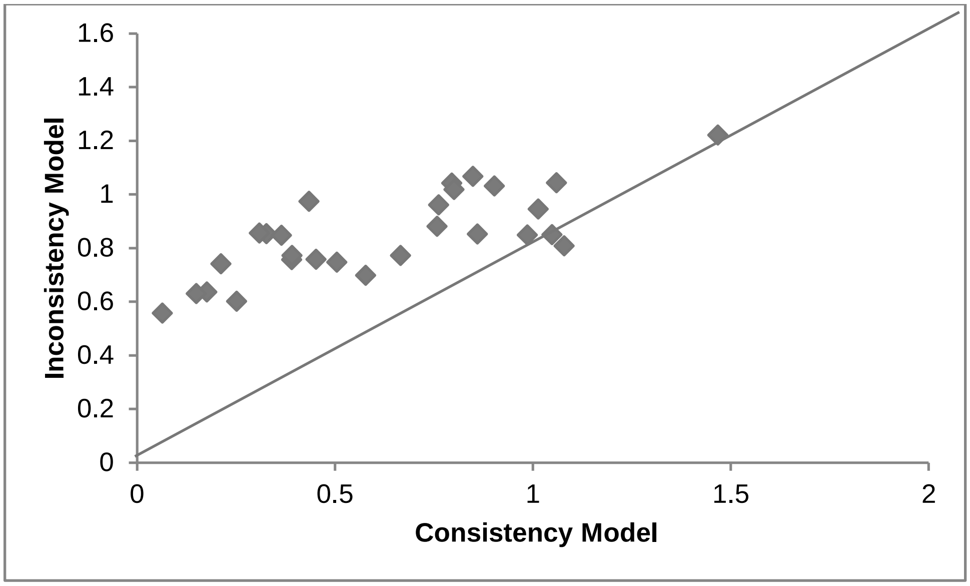
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	4.53 (0.10 to 269.00)	4.49 (0.10 to 211.80)	0.70 (–0.42 to 21.19)
MET + GLI		0.43 (0.00 to 76.47)	0.43 (0.00 to 68.09)	–0.07 (–0.59 to 9.67)
MET + MIT		4.22 (0.15 to 583.30)	4.18 (0.15 to 335.40)	0.65 (–0.33 to 37.45)
MET + SAX		1.78 (0.07 to 76.68)	1.78 (0.07 to 70.46)	0.14 (–0.46 to 8.60)
MET + ALO		3.26 (0.01 to 1,592.00)	3.25 (0.01 to 437.50)	0.42 (–0.47 to 72.77)
MET + LIN		0.60 (0.00 to 64.92)	0.60 (0.00 to 60.69)	–0.06 (–0.60 to 6.48)
MET + SIT		1.48 (0.02 to 120.20)	1.48 (0.02 to 110.90)	0.09 (–0.54 to 7.97)
MET + VIL		0.21 (0.00 to 6.19)	0.21 (0.00 to 6.12)	–0.12 (–0.58 to 0.95)
MET + CAN		0.92 (0.00 to 285.90)	0.92 (0.00 to 222.90)	–0.01 (–0.58 to 21.48)
MET + DAP		0.75 (0.08 to 5.66)	0.75 (0.08 to 5.63)	–0.04 (–0.48 to 0.72)
MET + EMP		4.55 (0.05 to 468.90)	4.51 (0.05 to 311.70)	0.69 (–0.45 to 33.52)
MET + PIO		0.80 (0.00 to 237.40)	0.80 (0.00 to 145.80)	–0.03 (–0.50 to 35.03)
MET + GLI	MET + GLM	0.11 (0.00 to 8.14)	0.11 (0.00 to 7.57)	–0.56 (–18.97 to 5.00)
MET + MIT		0.97 (0.00 to 354.50)	0.97 (0.01 to 242.50)	–0.02 (–19.73 to 36.40)
MET + SAX		0.44 (0.01 to 7.89)	0.44 (0.01 to 7.57)	–0.34 (–17.68 to 3.70)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + ALO		0.80 (0.00 to 258.90)	0.80 (0.00 to 108.70)	–0.04 (–15.48 to 66.59)
MET + LIN		0.15 (0.00 to 1.28)	0.15 (0.01 to 1.26)	–0.65 (–16.48 to 0.16)
MET + SIT		0.37 (0.00 to 20.43)	0.37 (0.00 to 19.69)	–0.39 (–19.28 to 4.51)
MET + VIL		0.04 (0.00 to 8.22)	0.05 (0.00 to 8.14)	–0.82 (–21.26 to 0.76)
MET + CAN		0.20 (0.00 to 86.07)	0.21 (0.00 to 69.72)	–0.45 (–20.24 to 19.92)
MET + DAP		0.16 (0.00 to 6.09)	0.17 (0.00 to 6.06)	–0.71 (–21.17 to 0.47)
MET + EMP		0.96 (0.09 to 10.95)	0.96 (0.10 to 9.14)	–0.01 (–7.22 to 19.12)
MET + PIO		0.18 (0.00 to 165.50)	0.19 (0.00 to 105.70)	–0.47 (–20.78 to 33.53)
MET + MIT	MET + GLI	11.62 (0.02 to 10850.00)	11.38 (0.02 to 7341.00)	0.60 (–8.66 to 37.38)
MET + SAX		3.65 (0.14 to 438.00)	3.62 (0.15 to 425.30)	0.13 (–5.58 to 5.50)
MET + ALO		6.74 (0.42 to 577.70)	6.28 (0.42 to 330.50)	0.43 (–0.20 to 63.31)
MET + LIN		1.27 (0.01 to 673.40)	1.27 (0.01 to 642.80)	0.01 (–8.33 to 5.37)
MET + SIT		3.66 (0.01 to 1,871.00)	3.63 (0.01 to 1,765.00)	0.14 (–8.45 to 6.97)
MET + VIL		0.44 (0.00 to 364.70)	0.44 (0.00 to 359.30)	–0.03 (–9.80 to 1.06)
MET + CAN		2.22 (0.00 to 3,606.00)	2.21 (0.00 to 2,968.00)	0.05 (–8.91 to 20.90)
MET + DAP		1.73 (0.01 to 382.20)	1.73 (0.01 to 380.60)	0.03 (–9.55 to 0.74)
MET + EMP		9.32 (0.07 to 4,996.00)	8.96 (0.07 to 4,021.00)	0.55 (–5.28 to 31.40)
MET + PIO		1.91 (0.00 to 6,331.00)	1.91 (0.00 to 3,471.00)	0.03 (–9.21 to 34.71)
MET + SAX	MET + MIT	0.39 (0.00 to 56.62)	0.39 (0.00 to 52.89)	–0.38 (–36.77 to 7.57)
MET + ALO		0.70 (0.00 to 1,027.00)	0.71 (0.00 to 335.30)	–0.10 (–34.91 to 70.61)
MET + LIN		0.13 (0.00 to 42.44)	0.14 (0.00 to 39.54)	–0.59 (–37.13 to 5.50)
MET + SIT		0.31 (0.00 to 74.73)	0.32 (0.00 to 70.42)	–0.44 (–37.24 to 7.47)
MET + VIL		0.04 (0.00 to 6.13)	0.04 (0.00 to 6.05)	–0.76 (–37.51 to 0.66)
MET + CAN		0.19 (0.00 to 158.90)	0.20 (0.00 to 118.50)	–0.45 (–37.04 to 20.43)
MET + DAP		0.17 (0.00 to 9.19)	0.17 (0.00 to 9.14)	–0.68 (–37.50 to 0.60)
MET + EMP		1.05 (0.00 to 299.70)	1.04 (0.00 to 218.60)	0.02 (–35.55 to 31.92)
MET + PIO		0.16 (0.00 to 152.70)	0.16 (0.00 to 92.88)	–0.46 (–36.86 to 33.51)
MET + ALO	MET + SAX	1.95 (0.01 to 336.30)	1.92 (0.01 to 135.60)	0.18 (–3.36 to 68.12)
MET + LIN		0.32 (0.00 to 24.88)	0.33 (0.00 to 23.86)	–0.14 (–6.79 to 4.34)
MET + SIT		0.89 (0.01 to 80.76)	0.89 (0.01 to 77.23)	–0.02 (–7.38 to 6.58)
MET + VIL		0.11 (0.00 to 14.45)	0.11 (0.00 to 14.31)	–0.26 (–8.69 to 0.90)
MET + CAN		0.52 (0.00 to 261.90)	0.52 (0.00 to 201.10)	–0.08 (–7.99 to 20.86)
MET + DAP		0.42 (0.01 to 8.45)	0.42 (0.01 to 8.42)	–0.16 (–8.44 to 0.47)
MET + EMP		2.41 (0.05 to 172.90)	2.38 (0.05 to 135.30)	0.34 (–4.32 to 30.80)
MET + PIO		0.44 (0.00 to 346.30)	0.44 (0.00 to 212.80)	–0.09 (–8.20 to 34.55)
MET + LIN	MET + ALO	0.16 (0.00 to 188.70)	0.17 (0.00 to 177.60)	–0.37 (–71.85 to 4.19)
MET + SIT		0.43 (0.00 to 451.00)	0.43 (0.00 to 427.90)	–0.23 (–71.50 to 5.94)
MET + VIL		0.05 (0.00 to 96.32)	0.06 (0.00 to 95.25)	–0.54 (–72.90 to 0.76)
MET + CAN		0.27 (0.00 to 741.20)	0.27 (0.00 to 636.60)	–0.24 (–71.63 to 18.79)
MET + DAP		0.23 (0.00 to 73.02)	0.23 (0.00 to 72.77)	–0.44 (–72.76 to 0.54)
MET + EMP		1.22 (0.00 to 1204.00)	1.21 (0.01 to 952.10)	0.03 (–66.51 to 25.93)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + PIO		0.22 (0.00 to 1710.00)	0.23 (0.00 to 930.50)	–0.23 (–71.65 to 32.05)
MET + SIT	MET + LIN	2.65 (0.02 to 420.00)	2.63 (0.02 to 407.90)	0.12 (–5.36 to 6.99)
MET + VIL		0.31 (0.00 to 163.40)	0.31 (0.00 to 161.60)	–0.06 (–6.56 to 1.08)
MET + CAN		1.63 (0.00 to 1148.00)	1.62 (0.00 to 937.40)	0.03 (–5.82 to 20.95)
MET + DAP		1.23 (0.01 to 162.70)	1.22 (0.01 to 161.90)	0.02 (–6.44 to 0.82)
MET + EMP		7.22 (0.28 to 377.40)	6.94 (0.29 to 337.30)	0.59 (–0.98 to 29.49)
MET + PIO		1.40 (0.00 to 3,307.00)	1.40 (0.00 to 1,905.00)	0.02 (–6.16 to 34.97)
MET + VIL	MET + SIT	0.12 (0.00 to 41.71)	0.12 (0.00 to 41.29)	–0.23 (–8.01 to 0.98)
MET + CAN		0.64 (0.00 to 161.00)	0.64 (0.00 to 136.50)	–0.05 (–5.42 to 18.78)
MET + DAP		0.49 (0.01 to 43.15)	0.49 (0.01 to 42.85)	–0.13 (–7.98 to 0.80)
MET + EMP		2.78 (0.03 to 487.80)	2.73 (0.03 to 385.40)	0.39 (–4.94 to 31.57)
MET + PIO		0.51 (0.00 to 761.90)	0.51 (0.00 to 442.30)	–0.07 (–7.68 to 34.72)
MET + CAN	MET + VIL	5.03 (0.00 to 10,470.00)	5.01 (0.00 to 8,547.00)	0.11 (–1.01 to 21.51)
MET + DAP		3.76 (0.06 to 916.30)	3.75 (0.06 to 912.50)	0.08 (–1.04 to 0.91)
MET + EMP		22.06 (0.08 to 26,750.00)	21.58 (0.08 to 20,820.00)	0.79 (–0.73 to 33.62)
MET + PIO		3.70 (0.14 to 357.40)	3.68 (0.14 to 235.20)	0.08 (–0.19 to 34.34)
MET + DAP	MET + CAN	0.74 (0.00 to 714.40)	0.74 (0.00 to 710.80)	–0.04 (–21.50 to 0.87)
MET + EMP		4.71 (0.01 to 10,060.00)	4.60 (0.01 to 8,408.00)	0.42 (–18.86 to 31.96)
MET + PIO		0.95 (0.00 to 6,736.00)	0.95 (0.00 to 4,132.00)	0.00 (–20.95 to 33.90)
MET + EMP	MET + DAP	5.99 (0.07 to 725.60)	5.92 (0.07 to 496.30)	0.70 (–0.53 to 33.49)
MET + PIO		1.06 (0.00 to 519.40)	1.06 (0.00 to 301.00)	0.01 (–0.78 to 35.18)
MET + PIO	MET + EMP	0.19 (0.00 to 233.60)	0.19 (0.00 to 146.20)	–0.43 (–32.61 to 32.25)
Random-effects model	Residual deviance	17.67 vs. 28 data points		
	Deviance information criteria	100.279		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; EMP = empagliflozin; GLI = glipizide; GLM = glimepiride; LIN = linagliptin; MET = metformin; MIT = mitiglinide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 37: Consistency Plot for Transient Ischemic Attack (Individual-Drug Case Analysis)



Total Adverse Events (Total AE)

Table 58: Total Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLC	MET	1.13 (0.64 to 1.96)	1.06 (0.77 to 1.35)	2.94 (–10.72 to 16.46)
MET + GLM		1.12 (0.92 to 1.34)	1.06 (0.96 to 1.16)	2.78 (–1.94 to 7.22)
MET + GLY		1.87 (0.90 to 3.84)	1.33 (0.94 to 1.66)	15.37 (–2.63 to 30.34)
MET + GLI		1.04 (0.75 to 1.45)	1.02 (0.85 to 1.20)	1.08 (–7.20 to 9.32)
MET + GLL		0.91 (0.61 to 1.38)	0.95 (0.75 to 1.17)	–2.26 (–11.92 to 8.07)
MET + MIT		0.93 (0.43 to 1.99)	0.96 (0.59 to 1.36)	–1.73 (–19.47 to 16.79)
MET + NAT		1.19 (0.72 to 1.98)	1.09 (0.83 to 1.36)	4.32 (–7.96 to 16.72)
MET + SAX		1.04 (0.88 to 1.23)	1.02 (0.93 to 1.11)	0.94 (–3.16 to 5.10)
MET + ALO		1.02 (0.70 to 1.46)	1.01 (0.81 to 1.20)	0.53 (–8.83 to 9.34)
MET + LIN		0.82 (0.63 to 1.08)	0.90 (0.76 to 1.04)	–4.85 (–11.28 to 1.83)
MET + SIT		0.91 (0.78 to 1.08)	0.95 (0.87 to 1.04)	–2.27 (–6.22 to 1.84)
MET + VIL		0.94 (0.76 to 1.17)	0.97 (0.85 to 1.08)	–1.63 (–6.92 to 3.88)
MET + CAN		1.19 (0.86 to 1.67)	1.09 (0.92 to 1.27)	4.33 (–3.81 to 12.69)
MET + DAP		1.04 (0.81 to 1.35)	1.02 (0.89 to 1.16)	1.01 (–5.23 to 7.53)
MET + EMP		0.94 (0.71 to 1.22)	0.97 (0.82 to 1.11)	–1.60 (–8.26 to 5.03)
MET + LIR		1.46 (1.06 to 2.04)	1.20 (1.03 to 1.38)	9.42 (1.47 to 17.35)
MET + EXE		1.41 (0.83 to 2.34)	1.18 (0.90 to 1.44)	8.61 (–4.54 to 20.50)
MET + DUL		1.36 (0.99 to 1.90)	1.16 (1.00 to 1.34)	7.70 (–0.16 to 15.80)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + LIX		1.23 (0.90 to 1.66)	1.11 (0.95 to 1.27)	5.20 (–2.51 to 12.54)
MET + ROS		1.21 (0.87 to 1.66)	1.10 (0.93 to 1.27)	4.68 (–3.33 to 12.53)
MET + PIO		1.01 (0.69 to 1.49)	1.01 (0.81 to 1.21)	0.29 (–9.13 to 9.88)
MET + IAS		2.74 (1.35 to 5.60)	1.51 (1.16 to 1.79)	23.84 (7.39 to 36.38)
MET + IGA		2.43 (1.52 to 3.84)	1.45 (1.22 to 1.66)	21.23 (10.43 to 30.40)
MET + GLM	MET + GLC	1.00 (0.56 to 1.76)	1.00 (0.77 to 1.37)	–0.11 (–14.24 to 13.77)
MET + GLY		1.67 (0.67 to 4.03)	1.25 (0.83 to 1.82)	12.32 (–9.57 to 32.19)
MET + GLI		0.93 (0.48 to 1.76)	0.96 (0.71 to 1.37)	–1.82 (–17.92 to 13.82)
MET + GLL		0.82 (0.43 to 1.56)	0.90 (0.65 to 1.28)	–5.00 (–20.52 to 10.77)
MET + MIT		0.83 (0.32 to 2.15)	0.91 (0.53 to 1.46)	–4.64 (–26.70 to 18.66)
MET + NAT		1.06 (0.50 to 2.27)	1.03 (0.71 to 1.52)	1.45 (–16.86 to 19.98)
MET + SAX		0.92 (0.52 to 1.65)	0.96 (0.74 to 1.33)	–1.95 (–15.98 to 12.17)
MET + ALO		0.91 (0.46 to 1.77)	0.95 (0.68 to 1.36)	–2.37 (–19.12 to 13.89)
MET + LIN		0.73 (0.40 to 1.37)	0.84 (0.63 to 1.20)	–7.74 (–22.39 to 7.55)
MET + SIT		0.81 (0.46 to 1.44)	0.90 (0.69 to 1.24)	–5.16 (–19.18 to 8.78)
MET + VIL		0.83 (0.49 to 1.44)	0.91 (0.72 to 1.24)	–4.53 (–17.50 to 8.81)
MET + CAN		1.06 (0.55 to 2.02)	1.03 (0.76 to 1.46)	1.52 (–14.56 to 17.23)
MET + DAP		0.93 (0.50 to 1.73)	0.96 (0.73 to 1.36)	–1.89 (–16.75 to 13.38)
MET + EMP		0.83 (0.46 to 1.53)	0.91 (0.69 to 1.28)	–4.52 (–19.20 to 10.26)
MET + LIR		1.31 (0.69 to 2.46)	1.13 (0.85 to 1.59)	6.65 (–9.17 to 22.02)
MET + EXE		1.25 (0.59 to 2.67)	1.11 (0.78 to 1.62)	5.57 (–12.81 to 23.72)
MET + DUL		1.22 (0.64 to 2.29)	1.10 (0.82 to 1.54)	5.00 (–10.94 to 20.33)
MET + LIX		1.10 (0.58 to 2.05)	1.05 (0.79 to 1.47)	2.31 (–13.21 to 17.54)
MET + ROS		1.08 (0.56 to 2.03)	1.04 (0.77 to 1.46)	1.83 (–14.00 to 17.26)
MET + PIO		0.90 (0.61 to 1.35)	0.95 (0.79 to 1.19)	–2.57 (–12.28 to 7.26)
MET + IAS		2.43 (0.98 to 6.20)	1.41 (0.99 to 2.04)	20.62 (–0.38 to 39.91)
MET + IGA		2.18 (1.05 to 4.40)	1.37 (1.02 to 1.92)	18.38 (1.13 to 34.48)
MET + GLY	MET + GLM	1.68 (0.79 to 3.48)	1.26 (0.89 to 1.59)	12.63 (–5.81 to 28.01)
MET + GLI		0.93 (0.65 to 1.35)	0.97 (0.79 to 1.16)	–1.70 (–10.67 to 7.49)
MET + GLL		0.82 (0.55 to 1.27)	0.90 (0.71 to 1.12)	–5.04 (–14.72 to 5.87)
MET + MIT		0.83 (0.38 to 1.85)	0.91 (0.56 to 1.31)	–4.60 (–22.37 to 14.99)
MET + NAT		1.06 (0.63 to 1.84)	1.03 (0.78 to 1.31)	1.42 (–11.30 to 14.97)
MET + SAX		0.93 (0.75 to 1.16)	0.96 (0.87 to 1.08)	–1.84 (–7.01 to 3.76)
MET + ALO		0.91 (0.61 to 1.35)	0.95 (0.76 to 1.16)	–2.24 (–12.16 to 7.46)
MET + LIN		0.73 (0.57 to 0.97)	0.85 (0.73 to 0.99)	–7.67 (–13.91 to –0.70)
MET + SIT		0.82 (0.67 to 1.01)	0.90 (0.81 to 1.01)	–5.06 (–9.99 to 0.36)
MET + VIL		0.84 (0.67 to 1.07)	0.91 (0.81 to 1.04)	–4.45 (–9.92 to 1.66)
MET + CAN		1.07 (0.74 to 1.56)	1.03 (0.85 to 1.23)	1.56 (–7.53 to 11.00)
MET + DAP		0.93 (0.69 to 1.29)	0.96 (0.82 to 1.14)	–1.75 (–9.25 to 6.33)
MET + EMP		0.84 (0.64 to 1.11)	0.91 (0.78 to 1.05)	–4.35 (–11.12 to 2.50)
MET + LIR		1.31 (0.93 to 1.89)	1.13 (0.96 to 1.33)	6.62 (–1.87 to 15.61)
MET + EXE		1.26 (0.74 to 2.18)	1.12 (0.85 to 1.39)	5.78 (–7.62 to 18.71)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + DUL		1.22 (0.87 to 1.77)	1.10 (0.93 to 1.30)	4.96 (–3.57 to 14.04)
MET + LIX		1.10 (0.78 to 1.56)	1.05 (0.88 to 1.23)	2.35 (–6.23 to 10.96)
MET + ROS		1.08 (0.75 to 1.55)	1.04 (0.86 to 1.23)	1.87 (–7.06 to 10.89)
MET + PIO		0.90 (0.61 to 1.38)	0.95 (0.76 to 1.17)	–2.53 (–12.23 to 7.98)
MET + IAS		2.45 (1.18 to 5.12)	1.42 (1.08 to 1.73)	21.04 (4.17 to 34.29)
MET + IGA		2.18 (1.36 to 3.52)	1.37 (1.15 to 1.61)	18.50 (7.55 to 28.31)
MET + GLI	MET + GLY	0.56 (0.25 to 1.24)	0.77 (0.58 to 1.11)	–14.11 (–31.22 to 5.22)
MET + GLL		0.49 (0.22 to 1.14)	0.72 (0.52 to 1.07)	–17.45 (–35.08 to 3.26)
MET + MIT		0.50 (0.17 to 1.40)	0.73 (0.42 to 1.16)	–16.94 (–41.07 to 8.07)
MET + NAT		0.64 (0.27 to 1.54)	0.82 (0.58 to 1.23)	–10.98 (–30.04 to 10.52)
MET + SAX		0.56 (0.27 to 1.17)	0.77 (0.61 to 1.09)	–14.33 (–29.75 to 3.85)
MET + ALO		0.55 (0.24 to 1.23)	0.77 (0.56 to 1.11)	–14.65 (–32.69 to 5.11)
MET + LIN		0.44 (0.20 to 0.96)	0.68 (0.51 to 0.98)	–20.09 (–36.47 to –0.94)
MET + SIT		0.49 (0.24 to 1.01)	0.72 (0.57 to 1.00)	–17.57 (–32.40 to 0.13)
MET + VIL		0.50 (0.24 to 1.07)	0.73 (0.57 to 1.04)	–16.98 (–32.62 to 1.76)
MET + CAN		0.63 (0.29 to 1.41)	0.82 (0.63 to 1.19)	–11.04 (–27.60 to 8.51)
MET + DAP		0.56 (0.26 to 1.20)	0.77 (0.60 to 1.10)	–14.35 (–30.59 to 4.60)
MET + EMP		0.50 (0.24 to 1.11)	0.73 (0.56 to 1.06)	–16.92 (–33.02 to 2.52)
MET + LIR		0.78 (0.36 to 1.73)	0.91 (0.69 to 1.30)	–5.91 (–22.83 to 13.51)
MET + EXE		0.76 (0.32 to 1.79)	0.89 (0.64 to 1.30)	–6.65 (–26.01 to 14.11)
MET + DUL		0.73 (0.34 to 1.63)	0.88 (0.67 to 1.26)	–7.48 (–24.16 to 12.06)
MET + LIX		0.66 (0.30 to 1.45)	0.84 (0.64 to 1.20)	–10.12 (–26.72 to 9.13)
MET + ROS		0.64 (0.32 to 1.31)	0.83 (0.66 to 1.14)	–10.65 (–25.43 to 6.64)
MET + PIO		0.54 (0.25 to 1.22)	0.76 (0.56 to 1.11)	–14.98 (–32.33 to 4.98)
MET + IAS		1.47 (0.83 to 2.57)	1.13 (0.94 to 1.42)	8.30 (–4.09 to 20.63)
MET + IGA		1.30 (0.63 to 2.60)	1.10 (0.87 to 1.48)	5.93 (–9.76 to 22.31)
MET + GLL	MET + GLI	0.87 (0.53 to 1.50)	0.93 (0.70 to 1.24)	–3.32 (–15.72 to 10.04)
MET + MIT		0.89 (0.39 to 2.03)	0.94 (0.57 to 1.39)	–2.76 (–22.30 to 17.31)
MET + NAT		1.14 (0.63 to 2.11)	1.07 (0.78 to 1.43)	3.14 (–11.35 to 18.27)
MET + SAX		0.99 (0.70 to 1.43)	1.00 (0.84 to 1.22)	–0.14 (–8.97 to 8.85)
MET + ALO		0.98 (0.71 to 1.31)	0.99 (0.83 to 1.15)	–0.50 (–8.53 to 6.64)
MET + LIN		0.79 (0.52 to 1.20)	0.88 (0.70 to 1.11)	–5.89 (–16.05 to 4.52)
MET + SIT		0.88 (0.64 to 1.20)	0.93 (0.80 to 1.11)	–3.30 (–11.16 to 4.52)
MET + VIL		0.90 (0.61 to 1.33)	0.94 (0.78 to 1.17)	–2.70 (–12.15 to 7.04)
MET + CAN		1.14 (0.72 to 1.82)	1.07 (0.85 to 1.36)	3.23 (–8.01 to 14.74)
MET + DAP		1.00 (0.65 to 1.53)	1.00 (0.81 to 1.25)	–0.02 (–10.49 to 10.52)
MET + EMP		0.90 (0.59 to 1.37)	0.94 (0.76 to 1.19)	–2.68 (–13.00 to 7.82)
MET + LIR		1.40 (0.90 to 2.19)	1.17 (0.95 to 1.46)	8.32 (–2.51 to 19.26)
MET + EXE		1.35 (0.73 to 2.48)	1.15 (0.85 to 1.51)	7.45 (–7.70 to 22.07)
MET + DUL		1.31 (0.85 to 2.04)	1.14 (0.92 to 1.42)	6.66 (–4.13 to 17.50)
MET + LIX		1.18 (0.76 to 1.82)	1.09 (0.87 to 1.36)	4.07 (–6.78 to 14.74)
MET + ROS		1.16 (0.73 to 1.84)	1.08 (0.86 to 1.36)	3.66 (–7.76 to 15.07)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + PIO		0.97 (0.58 to 1.62)	0.98 (0.75 to 1.28)	–0.74 (–13.22 to 11.89)
MET + IAS		2.63 (1.20 to 5.76)	1.47 (1.09 to 1.89)	22.65 (4.40 to 37.68)
MET + IGA		2.32 (1.35 to 4.02)	1.42 (1.14 to 1.77)	20.06 (7.37 to 32.00)
MET + MIT	MET + GLL	1.01 (0.43 to 2.40)	1.01 (0.60 to 1.54)	0.34 (–19.73 to 21.29)
MET + NAT		1.30 (0.68 to 2.50)	1.14 (0.81 to 1.59)	6.38 (–9.59 to 22.40)
MET + SAX		1.14 (0.73 to 1.76)	1.07 (0.85 to 1.38)	3.19 (–7.83 to 13.64)
MET + ALO		1.12 (0.63 to 1.89)	1.06 (0.78 to 1.42)	2.80 (–11.45 to 15.52)
MET + LIN		0.90 (0.56 to 1.46)	0.94 (0.73 to 1.25)	–2.67 (–14.46 to 9.15)
MET + SIT		1.00 (0.64 to 1.53)	1.00 (0.80 to 1.28)	–0.02 (–10.98 to 10.13)
MET + VIL		1.02 (0.72 to 1.45)	1.01 (0.85 to 1.25)	0.59 (–8.19 to 8.93)
MET + CAN		1.30 (0.77 to 2.21)	1.15 (0.88 to 1.53)	6.48 (–6.52 to 19.36)
MET + DAP		1.14 (0.70 to 1.86)	1.07 (0.83 to 1.42)	3.23 (–8.83 to 15.11)
MET + EMP		1.03 (0.62 to 1.64)	1.02 (0.78 to 1.33)	0.69 (–11.69 to 12.00)
MET + LIR		1.60 (0.95 to 2.69)	1.26 (0.97 to 1.66)	11.62 (–1.36 to 24.12)
MET + EXE		1.54 (0.80 to 2.97)	1.24 (0.89 to 1.69)	10.68 (–5.55 to 26.33)
MET + DUL		1.50 (0.88 to 2.51)	1.22 (0.94 to 1.62)	9.96 (–3.05 to 22.54)
MET + LIX		1.35 (0.81 to 2.20)	1.16 (0.90 to 1.53)	7.36 (–5.29 to 19.28)
MET + ROS		1.32 (0.78 to 2.20)	1.15 (0.88 to 1.53)	6.87 (–6.32 to 19.34)
MET + PIO		1.10 (0.67 to 1.83)	1.06 (0.81 to 1.39)	2.45 (–9.96 to 14.81)
MET + IAS		3.01 (1.31 to 6.80)	1.58 (1.13 to 2.13)	25.93 (6.66 to 41.78)
MET + IGA		2.66 (1.43 to 4.86)	1.52 (1.17 to 2.01)	23.47 (8.66 to 36.62)
MET + NAT	MET + MIT	1.28 (0.52 to 3.20)	1.13 (0.73 to 1.93)	6.04 (–16.14 to 27.62)
MET + SAX		1.12 (0.51 to 2.44)	1.06 (0.74 to 1.74)	2.74 (–16.41 to 20.74)
MET + ALO		1.09 (0.47 to 2.55)	1.05 (0.69 to 1.76)	2.20 (–18.70 to 22.05)
MET + LIN		0.89 (0.39 to 1.98)	0.93 (0.63 to 1.54)	–2.98 (–22.91 to 15.54)
MET + SIT		0.98 (0.45 to 2.13)	0.99 (0.69 to 1.62)	–0.47 (–19.54 to 17.20)
MET + VIL		1.01 (0.45 to 2.24)	1.00 (0.69 to 1.66)	0.19 (–19.47 to 18.49)
MET + CAN		1.28 (0.57 to 3.03)	1.13 (0.78 to 1.90)	6.02 (–13.83 to 26.19)
MET + DAP		1.12 (0.50 to 2.55)	1.06 (0.73 to 1.78)	2.80 (–16.78 to 21.85)
MET + EMP		1.01 (0.45 to 2.29)	1.01 (0.68 to 1.67)	0.22 (–19.65 to 19.17)
MET + LIR		1.57 (0.69 to 3.66)	1.25 (0.86 to 2.08)	11.14 (–9.05 to 30.71)
MET + EXE		1.52 (0.60 to 3.84)	1.23 (0.79 to 2.10)	10.31 (–12.47 to 31.98)
MET + DUL		1.47 (0.64 to 3.43)	1.21 (0.83 to 2.02)	9.46 (–10.70 to 29.13)
MET + LIX		1.32 (0.58 to 3.02)	1.15 (0.79 to 1.92)	6.93 (–13.13 to 26.04)
MET + ROS		1.30 (0.56 to 2.96)	1.14 (0.77 to 1.89)	6.40 (–14.05 to 25.60)
MET + PIO		1.09 (0.46 to 2.58)	1.05 (0.68 to 1.77)	2.08 (–19.08 to 22.22)
MET + IAS		2.93 (1.04 to 8.68)	1.55 (1.02 to 2.64)	25.09 (0.99 to 47.89)
MET + IGA		2.61 (1.07 to 6.30)	1.51 (1.03 to 2.50)	22.83 (1.62 to 42.56)
MET + SAX	MET + NAT	0.88 (0.50 to 1.48)	0.94 (0.73 to 1.24)	–3.29 (–16.91 to 9.56)
MET + ALO		0.86 (0.45 to 1.56)	0.93 (0.68 to 1.27)	–3.64 (–19.67 to 11.00)
MET + LIN		0.69 (0.39 to 1.22)	0.82 (0.62 to 1.12)	–9.06 (–23.16 to 4.73)
MET + SIT		0.77 (0.45 to 1.30)	0.87 (0.69 to 1.16)	–6.43 (–19.83 to 6.35)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + VIL		0.79 (0.45 to 1.36)	0.88 (0.69 to 1.19)	–5.93 (–19.53 to 7.49)
MET + CAN		1.00 (0.55 to 1.82)	1.00 (0.76 to 1.36)	0.06 (–14.66 to 14.79)
MET + DAP		0.88 (0.49 to 1.55)	0.94 (0.72 to 1.27)	–3.26 (–17.63 to 10.67)
MET + EMP		0.79 (0.44 to 1.39)	0.89 (0.68 to 1.20)	–5.86 (–20.00 to 7.97)
MET + LIR		1.23 (0.68 to 2.24)	1.10 (0.85 to 1.49)	5.17 (–9.46 to 19.72)
MET + EXE		1.19 (0.56 to 2.43)	1.08 (0.76 to 1.52)	4.26 (–13.97 to 21.43)
MET + DUL		1.15 (0.63 to 2.09)	1.07 (0.81 to 1.45)	3.50 (–11.32 to 18.07)
MET + LIX		1.04 (0.57 to 1.86)	1.02 (0.77 to 1.38)	0.89 (–13.90 to 15.20)
MET + ROS		1.02 (0.55 to 1.85)	1.01 (0.76 to 1.38)	0.36 (–14.58 to 15.18)
MET + PIO		0.85 (0.44 to 1.61)	0.92 (0.67 to 1.29)	–3.92 (–20.04 to 11.79)
MET + IAS		2.31 (0.93 to 5.51)	1.37 (0.97 to 1.91)	19.25 (–1.69 to 37.14)
MET + IGA		2.05 (1.02 to 4.00)	1.33 (1.01 to 1.80)	16.92 (0.43 to 32.24)
MET + ALO	MET + SAX	0.98 (0.65 to 1.44)	0.99 (0.79 to 1.20)	–0.42 (–10.44 to 9.06)
MET + LIN		0.79 (0.58 to 1.08)	0.88 (0.74 to 1.04)	–5.82 (–13.13 to 1.83)
MET + SIT		0.88 (0.72 to 1.08)	0.93 (0.84 to 1.04)	–3.21 (–8.23 to 1.93)
MET + VIL		0.90 (0.69 to 1.17)	0.95 (0.82 to 1.09)	–2.56 (–9.05 to 3.98)
MET + CAN		1.15 (0.80 to 1.65)	1.07 (0.89 to 1.27)	3.39 (–5.67 to 12.39)
MET + DAP		1.00 (0.75 to 1.34)	1.00 (0.86 to 1.16)	0.06 (–7.01 to 7.37)
MET + EMP		0.90 (0.66 to 1.22)	0.95 (0.80 to 1.11)	–2.49 (–10.21 to 5.03)
MET + LIR		1.41 (0.99 to 2.03)	1.18 (1.00 to 1.38)	8.46 (–0.19 to 17.24)
MET + EXE		1.36 (0.79 to 2.32)	1.16 (0.88 to 1.44)	7.65 (–5.86 to 20.25)
MET + DUL		1.31 (0.93 to 1.89)	1.14 (0.96 to 1.34)	6.76 (–1.87 to 15.67)
MET + LIX		1.18 (0.84 to 1.66)	1.09 (0.91 to 1.27)	4.20 (–4.46 to 12.52)
MET + ROS		1.16 (0.81 to 1.66)	1.08 (0.89 to 1.27)	3.75 (–5.31 to 12.49)
MET + PIO		0.97 (0.64 to 1.47)	0.99 (0.78 to 1.21)	–0.65 (–11.04 to 9.60)
MET + IAS		2.63 (1.27 to 5.47)	1.47 (1.12 to 1.79)	22.79 (5.96 to 35.89)
MET + IGA		2.34 (1.44 to 3.74)	1.42 (1.18 to 1.66)	20.31 (9.07 to 29.95)
MET + LIN	MET + ALO	0.80 (0.52 to 1.29)	0.89 (0.70 to 1.16)	–5.36 (–16.05 to 6.17)
MET + SIT		0.89 (0.63 to 1.32)	0.94 (0.79 to 1.17)	–2.77 (–11.57 to 6.73)
MET + VIL		0.92 (0.61 to 1.42)	0.96 (0.78 to 1.22)	–2.14 (–12.06 to 8.65)
MET + CAN		1.16 (0.72 to 1.93)	1.08 (0.85 to 1.40)	3.76 (–8.04 to 16.09)
MET + DAP		1.02 (0.66 to 1.63)	1.01 (0.81 to 1.31)	0.54 (–10.34 to 12.08)
MET + EMP		0.92 (0.59 to 1.46)	0.95 (0.76 to 1.23)	–2.18 (–12.91 to 9.27)
MET + LIR		1.43 (0.91 to 2.36)	1.19 (0.96 to 1.53)	8.82 (–2.45 to 20.99)
MET + EXE		1.38 (0.74 to 2.65)	1.17 (0.86 to 1.57)	8.04 (–7.45 to 23.53)
MET + DUL		1.33 (0.84 to 2.21)	1.15 (0.92 to 1.49)	7.15 (–4.23 to 19.46)
MET + LIX		1.20 (0.76 to 1.94)	1.10 (0.87 to 1.41)	4.59 (–6.73 to 16.34)
MET + ROS		1.18 (0.73 to 1.94)	1.09 (0.86 to 1.41)	4.13 (–7.70 to 16.34)
MET + PIO		0.99 (0.58 to 1.70)	1.00 (0.75 to 1.33)	–0.23 (–13.39 to 13.09)
MET + IAS		2.68 (1.21 to 6.18)	1.48 (1.09 to 1.97)	23.14 (4.68 to 39.38)
MET + IGA		2.38 (1.36 to 4.30)	1.43 (1.14 to 1.85)	20.67 (7.41 to 33.68)
MET + SIT	MET + LIN	1.11 (0.82 to 1.50)	1.06 (0.90 to 1.27)	2.64 (–4.86 to 9.86)

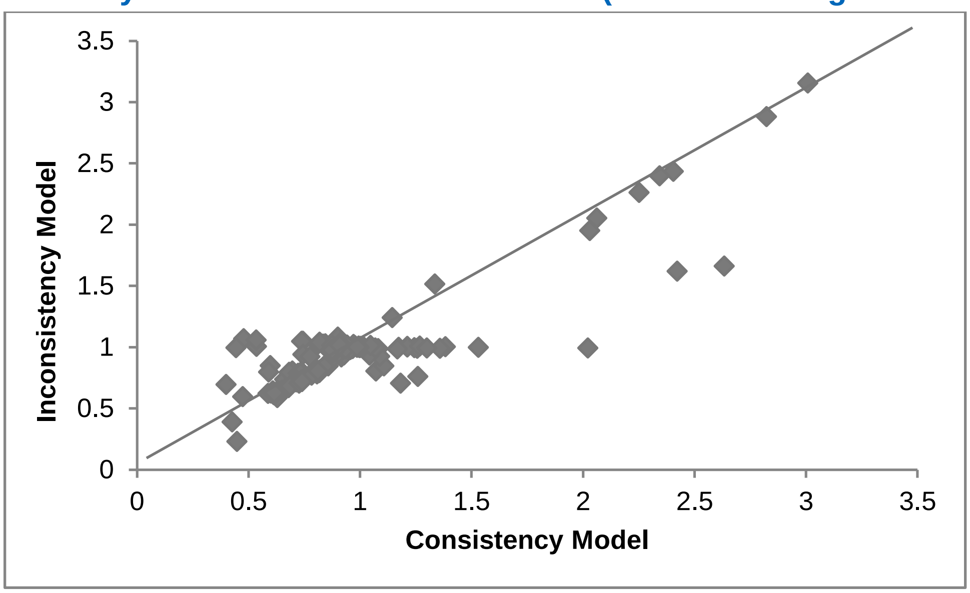
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + VIL		1.14 (0.82 to 1.58)	1.08 (0.90 to 1.30)	3.24 (–4.91 to 11.17)
MET + CAN		1.45 (0.95 to 2.22)	1.22 (0.97 to 1.52)	9.16 (–1.20 to 19.55)
MET + DAP		1.27 (0.88 to 1.85)	1.14 (0.93 to 1.41)	5.86 (–3.23 to 15.10)
MET + EMP		1.15 (0.79 to 1.63)	1.08 (0.87 to 1.32)	3.33 (–5.88 to 11.93)
MET + LIR		1.78 (1.17 to 2.70)	1.34 (1.09 to 1.65)	14.29 (3.94 to 24.21)
MET + EXE		1.72 (0.95 to 3.06)	1.32 (0.97 to 1.70)	13.38 (–1.27 to 27.03)
MET + DUL		1.66 (1.09 to 2.52)	1.30 (1.04 to 1.60)	12.59 (2.03 to 22.60)
MET + LIX		1.50 (1.00 to 2.22)	1.24 (1.00 to 1.53)	10.03 (–0.08 to 19.56)
MET + ROS		1.46 (0.97 to 2.24)	1.22 (0.98 to 1.53)	9.41 (–0.74 to 19.80)
MET + PIO		1.24 (0.77 to 1.94)	1.12 (0.86 to 1.43)	5.22 (–6.44 to 16.35)
MET + IAS		3.33 (1.52 to 7.20)	1.68 (1.23 to 2.14)	28.53 (10.44 to 42.79)
MET + IGA		2.96 (1.75 to 4.97)	1.62 (1.30 to 2.00)	26.09 (13.75 to 37.03)
MET + VIL	MET + SIT	1.03 (0.80 to 1.33)	1.02 (0.88 to 1.17)	0.67 (–5.51 to 6.98)
MET + CAN		1.30 (0.92 to 1.87)	1.15 (0.95 to 1.36)	6.60 (–2.10 to 15.43)
MET + DAP		1.14 (0.85 to 1.56)	1.07 (0.91 to 1.26)	3.27 (–4.01 to 10.98)
MET + EMP		1.03 (0.75 to 1.38)	1.02 (0.85 to 1.19)	0.68 (–6.87 to 8.05)
MET + LIR		1.60 (1.18 to 2.19)	1.26 (1.09 to 1.44)	11.69 (4.12 to 19.22)
MET + EXE		1.55 (0.90 to 2.62)	1.24 (0.95 to 1.54)	10.83 (–2.48 to 23.30)
MET + DUL		1.50 (1.10 to 2.05)	1.22 (1.05 to 1.41)	10.01 (2.32 to 17.67)
MET + LIX		1.35 (0.97 to 1.85)	1.17 (0.99 to 1.36)	7.44 (–0.67 to 15.25)
MET + ROS		1.32 (0.93 to 1.86)	1.16 (0.96 to 1.36)	6.98 (–1.89 to 15.39)
MET + PIO		1.11 (0.73 to 1.68)	1.06 (0.84 to 1.30)	2.49 (–7.52 to 12.93)
MET + IAS		3.01 (1.49 to 6.04)	1.58 (1.22 to 1.90)	26.06 (9.84 to 38.47)
MET + IGA		2.66 (1.72 to 4.08)	1.52 (1.30 to 1.75)	23.50 (13.41 to 32.11)
MET + CAN	MET + VIL	1.27 (0.86 to 1.89)	1.13 (0.92 to 1.38)	6.01 (–3.81 to 15.73)
MET + DAP		1.11 (0.80 to 1.56)	1.06 (0.88 to 1.27)	2.64 (–5.63 to 11.09)
MET + EMP		1.00 (0.71 to 1.38)	1.00 (0.83 to 1.19)	0.09 (–8.26 to 7.90)
MET + LIR		1.56 (1.06 to 2.30)	1.24 (1.03 to 1.49)	11.03 (1.44 to 20.44)
MET + EXE		1.51 (0.86 to 2.64)	1.23 (0.92 to 1.55)	10.21 (–3.81 to 23.46)
MET + DUL		1.46 (1.00 to 2.13)	1.21 (1.00 to 1.44)	9.40 (–0.04 to 18.59)
MET + LIX		1.31 (0.91 to 1.88)	1.15 (0.95 to 1.37)	6.76 (–2.45 to 15.60)
MET + ROS		1.29 (0.87 to 1.88)	1.14 (0.93 to 1.37)	6.31 (–3.34 to 15.59)
MET + PIO		1.08 (0.75 to 1.55)	1.04 (0.85 to 1.25)	1.85 (–6.91 to 10.83)
MET + IAS		2.93 (1.38 to 6.22)	1.56 (1.17 to 1.93)	25.38 (8.04 to 39.18)
MET + IGA		2.59 (1.56 to 4.23)	1.50 (1.23 to 1.80)	22.86 (10.92 to 33.05)
MET + DAP	MET + CAN	0.88 (0.57 to 1.34)	0.94 (0.76 to 1.16)	–3.30 (–13.92 to 7.21)
MET + EMP		0.79 (0.51 to 1.21)	0.88 (0.71 to 1.10)	–5.91 (–16.63 to 4.63)
MET + LIR		1.23 (0.77 to 1.94)	1.10 (0.89 to 1.36)	5.06 (–6.27 to 16.27)
MET + EXE		1.19 (0.63 to 2.16)	1.08 (0.80 to 1.40)	4.27 (–11.24 to 18.64)
MET + DUL		1.15 (0.72 to 1.81)	1.07 (0.86 to 1.32)	3.42 (–8.02 to 14.63)
MET + LIX		1.03 (0.66 to 1.60)	1.02 (0.82 to 1.26)	0.83 (–10.14 to 11.60)
MET + ROS		1.01 (0.64 to 1.59)	1.01 (0.81 to 1.25)	0.30 (–11.10 to 11.46)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + PIO		0.85 (0.51 to 1.43)	0.92 (0.71 to 1.19)	–4.13 (–16.54 to 8.86)
MET + IAS		2.30 (1.05 to 5.00)	1.38 (1.02 to 1.75)	19.37 (1.24 to 34.31)
MET + IGA		2.04 (1.18 to 3.51)	1.33 (1.07 to 1.64)	16.83 (4.07 to 28.66)
MET + EMP	MET + DAP	0.90 (0.61 to 1.30)	0.95 (0.77 to 1.15)	–2.58 (–12.00 to 6.54)
MET + LIR		1.40 (0.93 to 2.12)	1.17 (0.96 to 1.42)	8.39 (–1.91 to 18.33)
MET + EXE		1.36 (0.74 to 2.38)	1.16 (0.86 to 1.47)	7.59 (–7.34 to 20.93)
MET + DUL		1.31 (0.86 to 1.97)	1.14 (0.93 to 1.38)	6.71 (–3.69 to 16.67)
MET + LIX		1.18 (0.78 to 1.74)	1.09 (0.88 to 1.32)	4.17 (–6.05 to 13.66)
MET + ROS		1.16 (0.75 to 1.74)	1.08 (0.86 to 1.32)	3.77 (–7.10 to 13.68)
MET + PIO		0.97 (0.60 to 1.56)	0.98 (0.76 to 1.25)	–0.75 (–12.50 to 11.07)
MET + IAS		2.62 (1.24 to 5.62)	1.47 (1.10 to 1.84)	22.60 (5.25 to 36.93)
MET + IGA		2.33 (1.37 to 3.88)	1.42 (1.15 to 1.72)	20.21 (7.80 to 31.05)
MET + LIR	MET + EMP	1.56 (1.03 to 2.38)	1.24 (1.01 to 1.53)	10.97 (0.69 to 21.21)
MET + EXE		1.50 (0.85 to 2.69)	1.22 (0.91 to 1.58)	10.09 (–4.10 to 23.96)
MET + DUL		1.45 (0.98 to 2.23)	1.21 (0.99 to 1.49)	9.30 (–0.60 to 19.72)
MET + LIX		1.31 (0.88 to 1.97)	1.15 (0.93 to 1.41)	6.72 (–3.29 to 16.73)
MET + ROS		1.29 (0.85 to 1.93)	1.14 (0.92 to 1.40)	6.28 (–4.14 to 16.24)
MET + PIO		1.08 (0.69 to 1.71)	1.04 (0.81 to 1.32)	1.92 (–9.08 to 13.21)
MET + IAS		2.92 (1.35 to 6.25)	1.56 (1.16 to 1.97)	25.31 (7.51 to 39.47)
MET + IGA		2.59 (1.55 to 4.38)	1.50 (1.22 to 1.84)	22.76 (10.75 to 33.93)
MET + EXE	MET + LIR	0.97 (0.52 to 1.75)	0.99 (0.73 to 1.26)	–0.79 (–16.09 to 13.32)
MET + DUL		0.94 (0.67 to 1.29)	0.97 (0.84 to 1.12)	–1.62 (–9.63 to 6.29)
MET + LIX		0.84 (0.54 to 1.29)	0.92 (0.75 to 1.13)	–4.24 (–15.13 to 6.37)
MET + ROS		0.83 (0.52 to 1.29)	0.92 (0.74 to 1.13)	–4.74 (–16.10 to 6.25)
MET + PIO		0.69 (0.42 to 1.14)	0.84 (0.65 to 1.06)	–9.17 (–21.34 to 3.26)
MET + IAS		1.87 (0.86 to 4.11)	1.25 (0.94 to 1.57)	14.24 (–3.69 to 29.19)
MET + IGA		1.66 (0.96 to 2.83)	1.21 (0.99 to 1.47)	11.79 (–0.85 to 23.44)
MET + DUL	MET + EXE	0.96 (0.54 to 1.79)	0.98 (0.77 to 1.33)	–0.88 (–14.96 to 14.36)
MET + LIX		0.88 (0.57 to 1.32)	0.94 (0.79 to 1.16)	–3.30 (–13.42 to 6.92)
MET + ROS		0.86 (0.47 to 1.57)	0.93 (0.72 to 1.25)	–3.86 (–18.26 to 11.15)
MET + PIO		0.72 (0.38 to 1.37)	0.85 (0.63 to 1.18)	–8.23 (–23.62 to 7.84)
MET + IAS		1.93 (0.83 to 4.68)	1.27 (0.93 to 1.74)	15.03 (–4.32 to 33.21)
MET + IGA		1.72 (0.89 to 3.43)	1.23 (0.96 to 1.65)	12.60 (–2.77 to 28.43)
MET + LIX	MET + DUL	0.90 (0.58 to 1.38)	0.95 (0.78 to 1.17)	–2.62 (–13.27 to 8.04)
MET + ROS		0.88 (0.56 to 1.37)	0.94 (0.76 to 1.16)	–3.10 (–14.19 to 7.78)
MET + PIO		0.74 (0.45 to 1.23)	0.86 (0.67 to 1.10)	–7.52 (–19.63 to 5.05)
MET + IAS		2.01 (0.93 to 4.31)	1.29 (0.97 to 1.62)	15.97 (–1.69 to 30.64)
MET + IGA		1.78 (1.03 to 3.03)	1.24 (1.01 to 1.52)	13.40 (0.81 to 25.05)
MET + ROS	MET + LIX	0.98 (0.63 to 1.51)	0.99 (0.80 to 1.22)	–0.40 (–11.59 to 10.25)
MET + PIO		0.82 (0.50 to 1.33)	0.91 (0.70 to 1.15)	–4.84 (–16.83 to 7.09)
MET + IAS		2.22 (1.05 to 4.86)	1.35 (1.02 to 1.71)	18.48 (1.11 to 33.37)
MET + IGA		1.97 (1.16 to 3.38)	1.31 (1.07 to 1.60)	15.98 (3.68 to 27.70)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + PIO	MET + ROS	0.83 (0.52 to 1.38)	0.91 (0.71 to 1.18)	–4.50 (–16.32 to 8.08)
MET + IAS		2.27 (1.10 to 4.71)	1.37 (1.05 to 1.70)	18.98 (2.40 to 32.84)
MET + IGA		2.02 (1.19 to 3.39)	1.32 (1.08 to 1.62)	16.61 (4.18 to 27.92)
MET + IAS	MET + PIO	2.69 (1.20 to 6.21)	1.49 (1.09 to 2.00)	23.16 (4.48 to 39.74)
MET + IGA		2.41 (1.31 to 4.32)	1.44 (1.12 to 1.87)	20.98 (6.61 to 33.85)
MET + IGA	MET + IAS	0.89 (0.45 to 1.68)	0.97 (0.81 to 1.21)	–2.37 (–15.19 to 11.84)
Random-effects model	Residual deviance	120.5 vs. 121 data points		
	Deviance information criteria	855.301		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLC = glicazide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; GLY = glyburide; IAS = insulin aspart; IGA = insulin glargine; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MET = metformin; MIT = mitiglinide; NAT = nateglinide; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 38: Consistency Plot for Total Adverse Events (Individual-Drug Case Analysis)



Total Cholesterol

Table 59: Total Cholesterol: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + GLM	MET	0.00 (–0.16 to 0.15)
MET + REP		0.00 (–0.41 to 0.40)
MET + NAT		0.00 (–0.35 to 0.35)
MET + ALO		–0.05 (–0.32 to 0.21)

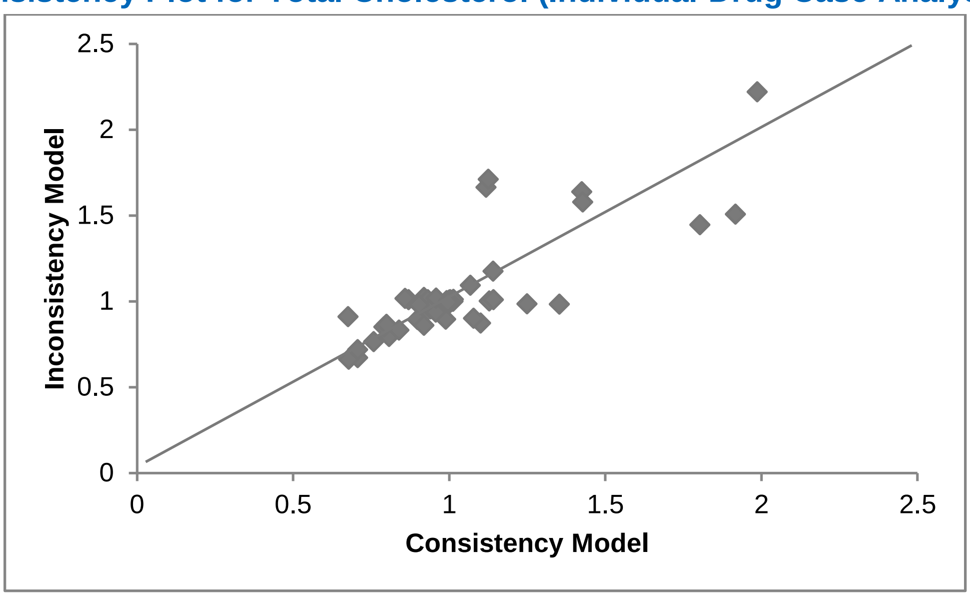
Treatment	Reference	MD (95% CrI)
MET + LIN		0.00 (–0.29 to 0.28)
MET + SIT		–0.04 (–0.14 to 0.06)
MET + CAN		0.27 (–0.14 to 0.69)
MET + EMP		0.15 (–0.04 to 0.33)
MET + LIR		–0.17 (–0.45 to 0.11)
MET + EXE		–0.01 (–0.20 to 0.15)
MET + DUL		–0.33 (–0.58 to –0.07)
MET + ROS		0.46 (0.29 to 0.65)
MET + PIO		0.15 (0.00 to 0.30)
MET + IGA		–0.17 (–0.42 to 0.11)
MET + REP	MET + GLM	0.00 (–0.44 to 0.44)
MET + NAT		0.00 (–0.38 to 0.38)
MET + ALO		–0.05 (–0.33 to 0.23)
MET + LIN		0.00 (–0.23 to 0.24)
MET + SIT		–0.04 (–0.20 to 0.13)
MET + CAN		0.27 (–0.16 to 0.71)
MET + EMP		0.14 (–0.09 to 0.39)
MET + LIR		–0.17 (–0.47 to 0.14)
MET + EXE		–0.01 (–0.23 to 0.19)
MET + DUL		–0.33 (–0.61 to –0.03)
MET + ROS		0.46 (0.24 to 0.70)
MET + PIO		0.15 (0.01 to 0.31)
MET + IGA		–0.17 (–0.45 to 0.15)
MET + NAT	MET + REP	0.00 (–0.53 to 0.53)
MET + ALO		–0.05 (–0.54 to 0.44)
MET + LIN		0.01 (–0.49 to 0.50)
MET + SIT		–0.04 (–0.46 to 0.38)
MET + CAN		0.27 (–0.31 to 0.86)
MET + EMP		0.15 (–0.30 to 0.59)
MET + LIR		–0.17 (–0.66 to 0.32)
MET + EXE		–0.01 (–0.46 to 0.43)
MET + DUL		–0.32 (–0.80 to 0.16)
MET + ROS		0.47 (0.02 to 0.91)
MET + PIO		0.15 (–0.28 to 0.59)
MET + IGA		–0.17 (–0.65 to 0.32)
MET + ALO	MET + NAT	–0.05 (–0.49 to 0.38)
MET + LIN		0.00 (–0.44 to 0.45)
MET + SIT		–0.04 (–0.40 to 0.33)
MET + CAN		0.27 (–0.27 to 0.82)
MET + EMP		0.15 (–0.25 to 0.54)
MET + LIR		–0.17 (–0.61 to 0.28)
MET + EXE		–0.01 (–0.40 to 0.37)

Treatment	Reference	MD (95% CrI)
MET + DUL		–0.32 (–0.75 to 0.11)
MET + ROS		0.47 (0.08 to 0.86)
MET + PIO		0.15 (–0.22 to 0.53)
MET + IGA		–0.17 (–0.60 to 0.28)
MET + LIN	MET + ALO	0.05 (–0.31 to 0.41)
MET + SIT		0.01 (–0.26 to 0.29)
MET + CAN		0.32 (–0.16 to 0.81)
MET + EMP		0.20 (–0.12 to 0.52)
MET + LIR		–0.12 (–0.50 to 0.26)
MET + EXE		0.04 (–0.27 to 0.33)
MET + DUL		–0.27 (–0.64 to 0.09)
MET + ROS		0.52 (0.20 to 0.84)
MET + PIO		0.20 (–0.05 to 0.46)
MET + IGA		–0.12 (–0.47 to 0.27)
MET + SIT	MET + LIN	–0.04 (–0.32 to 0.25)
MET + CAN		0.27 (–0.22 to 0.77)
MET + EMP		0.14 (–0.19 to 0.49)
MET + LIR		–0.17 (–0.55 to 0.22)
MET + EXE		–0.01 (–0.33 to 0.29)
MET + DUL		–0.33 (–0.69 to 0.05)
MET + ROS		0.46 (0.14 to 0.80)
MET + PIO		0.15 (–0.12 to 0.44)
MET + IGA		–0.17 (–0.53 to 0.23)
MET + CAN	MET + SIT	0.31 (–0.09 to 0.72)
MET + EMP		0.19 (–0.03 to 0.40)
MET + LIR		–0.13 (–0.39 to 0.13)
MET + EXE		0.03 (–0.17 to 0.20)
MET + DUL		–0.28 (–0.54 to –0.03)
MET + ROS		0.51 (0.31 to 0.70)
MET + PIO		0.19 (0.04 to 0.35)
MET + IGA		–0.13 (–0.37 to 0.14)
MET + EMP	MET + CAN	–0.13 (–0.58 to 0.33)
MET + LIR		–0.44 (–0.92 to 0.04)
MET + EXE		–0.28 (–0.73 to 0.16)
MET + DUL		–0.60 (–1.08 to –0.12)
MET + ROS		0.19 (–0.25 to 0.64)
MET + PIO		–0.12 (–0.55 to 0.31)
MET + IGA		–0.44 (–0.91 to 0.04)
MET + LIR	MET + EMP	–0.32 (–0.65 to 0.02)
MET + EXE		–0.15 (–0.42 to 0.08)
MET + DUL		–0.47 (–0.78 to –0.16)
MET + ROS		0.32 (0.06 to 0.58)

Treatment	Reference	MD (95% CrI)
MET + PIO		0.01 (–0.23 to 0.24)
MET + IGA		–0.31 (–0.63 to 0.03)
MET + EXE	MET + LIR	0.16 (–0.17 to 0.47)
MET + DUL		–0.15 (–0.52 to 0.21)
MET + ROS		0.64 (0.31 to 0.96)
MET + PIO		0.32 (0.02 to 0.63)
MET + IGA		0.00 (–0.34 to 0.38)
MET + DUL	MET + EXE	–0.32 (–0.61 to 0.00)
MET + ROS		0.47 (0.24 to 0.73)
MET + PIO		0.16 (–0.02 to 0.37)
MET + IGA		–0.16 (–0.44 to 0.17)
MET + ROS	MET + DUL	0.79 (0.48 to 1.10)
MET + PIO		0.48 (0.19 to 0.76)
MET + IGA		0.16 (–0.19 to 0.52)
MET + PIO	MET + ROS	–0.31 (–0.54 to –0.09)
MET + IGA		–0.63 (–0.94 to –0.31)
MET + IGA	MET + PIO	–0.32 (–0.60 to –0.02)
Random-effects model	Residual deviance	54.93 vs. 53 data points
	Deviance information criteria	–89.591

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLM = glimepiride; IGA = insulin glargine; LIN = linagliptin; LIR = liraglutide; MD = mean difference; MET = metformin; NAT = nateglinide; PIO = pioglitazone; REP = repaglinide; ROS = rosiglitazone; SIT = sitagliptin; vs. = versus.

Figure 39: Consistency Plot for Total Cholesterol (Individual-Drug Case Analysis)



Unstable Angina

Table 60: Unstable Angina: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

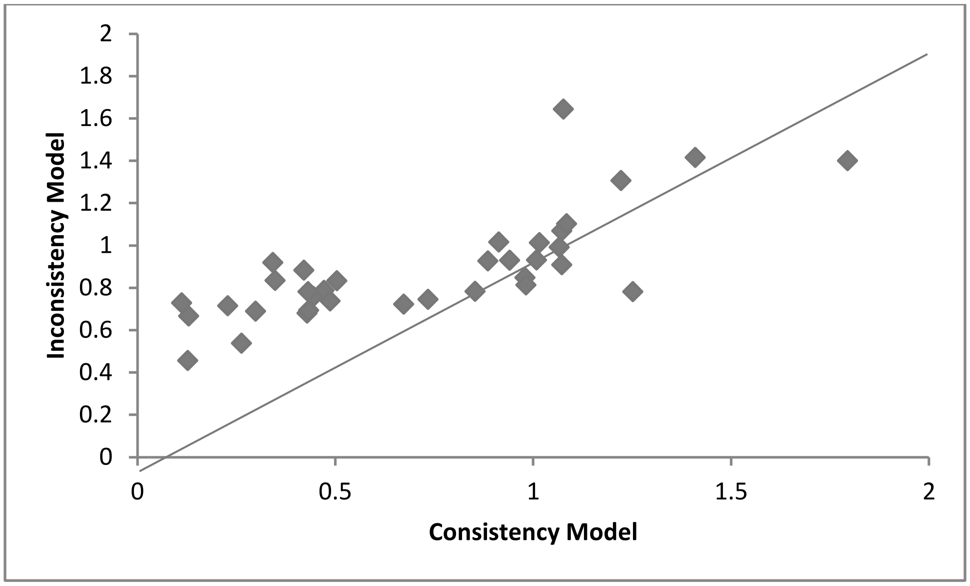
Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLM	MET	0.12 (0.00 to 2.72)	0.12 (0.00 to 2.71)	–0.26 (–0.72 to 0.43)
MET + GLI		0.75 (0.04 to 15.88)	0.75 (0.04 to 15.35)	–0.07 (–0.59 to 3.73)
MET + SAX		0.19 (0.00 to 5.62)	0.19 (0.00 to 5.54)	–0.23 (–0.70 to 1.21)
MET + ALO		0.61 (0.04 to 10.16)	0.61 (0.04 to 9.93)	–0.11 (–0.60 to 2.11)
MET + LIN		0.11 (0.00 to 10.66)	0.11 (0.00 to 10.36)	–0.24 (–0.71 to 2.73)
MET + SIT		1.71 (0.42 to 8.86)	1.70 (0.42 to 8.75)	0.22 (–0.34 to 1.46)
MET + VIL		0.21 (0.00 to 6.38)	0.21 (0.00 to 6.29)	–0.21 (–0.68 to 1.51)
MET + CAN		0.31 (0.00 to 10.69)	0.31 (0.00 to 10.43)	–0.19 (–0.69 to 2.40)
MET + DAP		0.94 (0.03 to 25.75)	0.94 (0.03 to 23.97)	–0.02 (–0.57 to 6.40)
MET + EMP		0.12 (0.00 to 4.35)	0.12 (0.00 to 4.32)	–0.25 (–0.72 to 0.86)
MET + EXE		0.40 (0.00 to 51.72)	0.40 (0.00 to 45.74)	–0.15 (–0.70 to 11.18)
MET + ROS		0.22 (0.00 to 13.87)	0.22 (0.00 to 13.47)	–0.21 (–0.67 to 3.14)
MET + PIO		3.40 (0.18 to 109.90)	3.37 (0.18 to 90.96)	0.76 (–0.45 to 17.53)
MET + IGA		12.22 (0.43 to 1198.00)	11.74 (0.43 to 272.20)	3.37 (–0.24 to 78.82)
MET + GLI	MET + GLM	6.96 (0.20 to 377.30)	6.92 (0.20 to 370.10)	0.17 (–0.34 to 3.87)
MET + SAX		1.57 (0.09 to 51.98)	1.57 (0.09 to 51.53)	0.01 (–0.42 to 1.27)
MET + ALO		5.57 (0.15 to 307.50)	5.55 (0.15 to 305.20)	0.13 (–0.44 to 2.26)
MET + LIN		0.96 (0.03 to 34.67)	0.96 (0.03 to 33.61)	0.00 (–0.38 to 2.70)
MET + SIT		13.54 (0.63 to 1,186.00)	13.46 (0.63 to 1,176.00)	0.48 (–0.21 to 1.65)
MET + VIL		1.58 (0.00 to 467.10)	1.58 (0.00 to 459.20)	0.01 (–0.65 to 1.80)
MET + CAN		2.25 (0.00 to 834.10)	2.24 (0.00 to 811.60)	0.04 (–0.60 to 2.66)
MET + DAP		7.93 (0.08 to 1,346.00)	7.89 (0.08 to 1,283.00)	0.23 (–0.46 to 6.66)
MET + EMP		1.02 (0.19 to 5.60)	1.02 (0.19 to 5.55)	0.00 (–0.25 to 0.67)
MET + EXE		3.32 (0.00 to 1,614.00)	3.31 (0.00 to 1,469.00)	0.06 (–0.55 to 11.38)
MET + ROS		1.68 (0.00 to 667.70)	1.68 (0.00 to 630.50)	0.01 (–0.62 to 3.44)
MET + PIO		30.13 (0.50 to 4,977.00)	29.54 (0.50 to 4,214.00)	1.01 (–0.17 to 17.65)
MET + IGA		114.10 (1.13 to 43,210.00)	104.40 (1.12 to 16,870.00)	3.61 (0.02 to 78.95)
MET + SAX	MET + GLI	0.26 (0.01 to 3.16)	0.26 (0.01 to 3.12)	–0.13 (–3.31 to 0.50)
MET + ALO		0.82 (0.15 to 3.95)	0.82 (0.15 to 3.94)	–0.02 (–2.48 to 0.64)
MET + LIN		0.14 (0.00 to 17.77)	0.14 (0.00 to 17.19)	–0.14 (–3.65 to 2.40)
MET + SIT		2.28 (0.09 to 63.70)	2.27 (0.09 to 62.90)	0.27 (–3.53 to 1.54)
MET + VIL		0.25 (0.00 to 25.95)	0.25 (0.00 to 25.56)	–0.13 (–3.92 to 1.51)
MET + CAN		0.35 (0.00 to 46.58)	0.35 (0.00 to 45.36)	–0.10 (–3.87 to 2.45)
MET + DAP		1.17 (0.01 to 108.60)	1.16 (0.01 to 102.30)	0.03 (–3.65 to 6.31)
MET + EMP		0.15 (0.00 to 6.69)	0.15 (0.00 to 6.64)	–0.16 (–3.80 to 0.66)
MET + EXE		0.47 (0.00 to 143.00)	0.47 (0.00 to 127.60)	–0.06 (–3.60 to 10.79)
MET + ROS		0.25 (0.00 to 44.30)	0.25 (0.00 to 42.47)	–0.11 (–3.87 to 3.14)
MET + PIO		4.53 (0.10 to 335.90)	4.46 (0.10 to 281.90)	0.71 (–2.78 to 17.04)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + IGA		16.17 (0.19 to 3,592.00)	15.11 (0.19 to 1,224.00)	3.19 (–1.81 to 78.56)
MET + ALO	MET + SAX	3.25 (0.17 to 110.90)	3.24 (0.18 to 110.20)	0.09 (–0.89 to 1.95)
MET + LIN		0.60 (0.01 to 51.06)	0.60 (0.01 to 49.46)	–0.01 (–1.18 to 2.72)
MET + SIT		9.27 (0.26 to 603.70)	9.21 (0.26 to 599.30)	0.45 (–1.02 to 1.65)
MET + VIL		0.96 (0.00 to 239.60)	0.96 (0.00 to 235.70)	0.00 (–1.44 to 1.75)
MET + CAN		1.45 (0.00 to 328.20)	1.45 (0.00 to 322.10)	0.02 (–1.40 to 2.60)
MET + DAP		4.98 (0.04 to 763.10)	4.96 (0.04 to 718.40)	0.18 (–1.15 to 6.57)
MET + EMP		0.64 (0.01 to 16.83)	0.64 (0.01 to 16.73)	–0.01 (–1.22 to 0.80)
MET + EXE		1.94 (0.00 to 887.40)	1.94 (0.00 to 800.60)	0.04 (–1.17 to 11.27)
MET + ROS		0.91 (0.00 to 412.00)	0.91 (0.00 to 395.90)	0.00 (–1.36 to 3.36)
MET + PIO		18.78 (0.29 to 2,403.00)	18.39 (0.29 to 2,006.00)	0.95 (–0.63 to 17.54)
MET + IGA		70.06 (0.56 to 23,460.00)	64.30 (0.57 to 8,273.00)	3.52 (–0.22 to 78.91)
MET + LIN	MET + ALO	0.17 (0.00 to 21.95)	0.17 (0.00 to 21.14)	–0.11 (–2.15 to 2.61)
MET + SIT		2.82 (0.14 to 63.96)	2.81 (0.15 to 63.33)	0.32 (–1.95 to 1.59)
MET + VIL		0.32 (0.00 to 25.98)	0.32 (0.00 to 25.51)	–0.10 (–2.25 to 1.56)
MET + CAN		0.45 (0.00 to 48.56)	0.45 (0.00 to 47.28)	–0.07 (–2.28 to 2.54)
MET + DAP		1.45 (0.02 to 122.20)	1.44 (0.02 to 114.50)	0.06 (–2.06 to 6.45)
MET + EMP		0.18 (0.00 to 8.45)	0.19 (0.00 to 8.39)	–0.12 (–2.22 to 0.82)
MET + EXE		0.60 (0.00 to 166.60)	0.60 (0.00 to 145.10)	–0.04 (–2.12 to 11.14)
MET + ROS		0.31 (0.00 to 54.18)	0.31 (0.00 to 51.44)	–0.09 (–2.27 to 3.24)
MET + PIO		5.54 (0.15 to 365.40)	5.45 (0.15 to 310.30)	0.80 (–1.30 to 17.27)
MET + IGA		19.82 (0.30 to 4,234.00)	18.65 (0.30 to 1,293.00)	3.34 (–0.76 to 78.64)
MET + SIT	MET + LIN	15.45 (0.15 to 2,950.00)	15.36 (0.16 to 2,927.00)	0.46 (–2.41 to 1.63)
MET + VIL		1.69 (0.00 to 964.80)	1.69 (0.00 to 953.70)	0.01 (–2.94 to 1.76)
MET + CAN		2.16 (0.00 to 1,502.00)	2.16 (0.00 to 1,478.00)	0.03 (–2.82 to 2.62)
MET + DAP		8.24 (0.03 to 3,182.00)	8.20 (0.03 to 3,044.00)	0.19 (–2.54 to 6.56)
MET + EMP		1.05 (0.02 to 49.59)	1.05 (0.02 to 49.42)	0.00 (–2.66 to 0.73)
MET + EXE		3.15 (0.00 to 3,460.00)	3.14 (0.00 to 3,151.00)	0.05 (–2.59 to 11.26)
MET + ROS		1.55 (0.00 to 1,208.00)	1.55 (0.00 to 1,180.00)	0.01 (–2.82 to 3.36)
MET + PIO		32.27 (0.13 to 12,360.00)	31.58 (0.14 to 10,500.00)	0.95 (–2.05 to 17.55)
MET + IGA		119.70 (0.40 to 107,400.00)	107.20 (0.41 to 45,930.00)	3.49 (–0.64 to 78.78)
MET + VIL	MET + SIT	0.11 (0.00 to 4.85)	0.11 (0.00 to 4.78)	–0.44 (–1.65 to 1.35)
MET + CAN		0.18 (0.00 to 5.32)	0.18 (0.00 to 5.22)	–0.38 (–1.54 to 2.01)
MET + DAP		0.54 (0.01 to 20.16)	0.54 (0.01 to 18.92)	–0.22 (–1.53 to 6.27)
MET + EMP		0.07 (0.00 to 2.38)	0.07 (0.00 to 2.36)	–0.47 (–1.64 to 0.58)
MET + EXE		0.24 (0.00 to 22.01)	0.24 (0.00 to 19.63)	–0.31 (–1.45 to 10.73)
MET + ROS		0.13 (0.00 to 7.62)	0.13 (0.00 to 7.41)	–0.40 (–1.58 to 2.86)
MET + PIO		1.93 (0.12 to 53.85)	1.92 (0.13 to 44.96)	0.48 (–1.05 to 17.18)
MET + IGA		6.71 (0.36 to 585.00)	6.46 (0.36 to 137.10)	3.07 (–0.40 to 78.22)
MET + CAN	MET + VIL	1.47 (0.00 to 1,100.00)	1.47 (0.00 to 1,084.00)	0.01 (–1.64 to 2.57)
MET + DAP		4.88 (0.04 to 2,804.00)	4.86 (0.04 to 2,721.00)	0.18 (–1.53 to 6.59)
MET + EMP		0.65 (0.00 to 288.50)	0.65 (0.00 to 286.40)	–0.01 (–1.78 to 1.05)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + EXE		1.87 (0.00 to 2,586.00)	1.87 (0.00 to 2,408.00)	0.03 (–1.58 to 11.36)
MET + ROS		1.05 (0.00 to 916.30)	1.05 (0.00 to 864.00)	0.00 (–1.68 to 3.35)
MET + PIO		17.40 (0.19 to 10,840.00)	17.05 (0.19 to 9,103.00)	0.93 (–1.02 to 17.65)
MET + IGA		72.64 (0.50 to 68,820.00)	65.85 (0.50 to 30,490.00)	3.50 (–0.38 to 78.83)
MET + DAP	MET + CAN	3.59 (0.02 to 6,950.00)	3.58 (0.02 to 6,630.00)	0.15 (–2.36 to 6.49)
MET + EMP		0.47 (0.00 to 1,070.00)	0.47 (0.00 to 1,062.00)	–0.03 (–2.64 to 0.98)
MET + EXE		1.64 (0.00 to 2,906.00)	1.63 (0.00 to 2,703.00)	0.02 (–2.36 to 11.20)
MET + ROS		0.79 (0.00 to 2,376.00)	0.79 (0.00 to 2,305.00)	–0.01 (–2.56 to 3.27)
MET + PIO		13.76 (0.13 to 19,390.00)	13.45 (0.14 to 18,470.00)	0.87 (–1.67 to 17.53)
MET + IGA		48.78 (0.39 to 131,700.00)	43.72 (0.40 to 60,990.00)	3.39 (–0.76 to 78.78)
MET + EMP	MET + DAP	0.13 (0.00 to 16.92)	0.13 (0.00 to 16.69)	–0.21 (–6.62 to 0.83)
MET + EXE		0.41 (0.00 to 150.30)	0.41 (0.00 to 136.40)	–0.09 (–6.37 to 11.00)
MET + ROS		0.19 (0.00 to 55.84)	0.20 (0.00 to 53.84)	–0.16 (–6.47 to 3.10)
MET + PIO		3.97 (0.04 to 410.70)	3.91 (0.04 to 344.70)	0.64 (–5.60 to 17.20)
MET + IGA		14.90 (0.12 to 4126.00)	13.79 (0.12 to 1,388.00)	3.09 (–3.76 to 78.11)
MET + EXE	MET + EMP	3.26 (0.00 to 1,933.00)	3.25 (0.00 to 1,781.00)	0.06 (–0.88 to 11.32)
MET + ROS		1.61 (0.00 to 876.40)	1.61 (0.00 to 824.30)	0.01 (–0.99 to 3.40)
MET + PIO		30.50 (0.36 to 6,798.00)	29.86 (0.36 to 5,822.00)	0.99 (–0.42 to 17.62)
MET + IGA		115.70 (0.85 to 49,270.00)	105.20 (0.85 to 20,900.00)	3.57 (–0.04 to 78.87)
MET + ROS	MET + EXE	0.51 (0.00 to 1,980.00)	0.51 (0.00 to 1,897.00)	–0.02 (–11.29 to 3.05)
MET + PIO		8.32 (0.12 to 18,080.00)	8.09 (0.13 to 17,040.00)	0.64 (–7.18 to 15.58)
MET + IGA		35.44 (0.14 to 124,800.00)	30.92 (0.15 to 65,620.00)	3.05 (–5.91 to 77.12)
MET + PIO	MET + ROS	18.38 (0.09 to 44,280.00)	17.94 (0.10 to 41,320.00)	0.89 (–2.38 to 17.47)
MET + IGA		68.25 (0.27 to 347,500.00)	60.84 (0.28 to 160,500.00)	3.40 (–1.32 to 78.83)
MET + IGA	MET + PIO	3.61 (0.04 to 626.20)	3.44 (0.05 to 188.80)	2.04 (–12.84 to 76.52)
Random-effects model	Residual deviance	25.52 vs. 35 data points		
	Deviance information criteria	128.376		

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; EMP = empagliflozin; EXE = exenatide; IGA = insulin glargine; GLI = glipizide; GLM = glimepiride; LIN = linagliptin; MET = metformin; OR = odds ratio; PIO = pioglitazone; RD = risk difference; ROS = rosiglitazone; RR = relative risk; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 40: Consistency Plot for Unstable Angina (Individual-Drug Case Analysis)



Weight

Table 61: Weight: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + GLC	MET	1.59 (–1.31 to 4.44)
MET + GLM		2.21 (1.70 to 2.73)
MET + GLY		2.33 (–8.40 to 13.82)
MET + GLI		2.56 (1.68 to 3.45)
MET + GLL		1.65 (–0.02 to 3.34)
MET + REP		3.27 (1.46 to 5.07)
MET + NAT		0.90 (–0.37 to 2.19)
MET + MIT		0.39 (–0.89 to 1.68)
MET + SAX		0.30 (–0.34 to 0.95)
MET + ALO		0.28 (–0.52 to 1.06)
MET + LIN		–0.42 (–1.71 to 0.88)
MET + SIT		0.23 (–0.22 to 0.67)
MET + VIL		0.10 (–0.56 to 0.73)
MET + CAN		–2.21 (–2.95 to –1.45)
MET + DAP		–2.16 (–2.90 to –1.42)
MET + EMP		–2.17 (–2.92 to –1.42)
MET + LIR		–1.47 (–2.37 to –0.53)
MET + EXE		–2.13 (–2.91 to –1.36)
MET + DUL		–0.82 (–1.90 to 0.29)
MET + LIX		–0.89 (–1.57 to –0.20)
MET + PIO		2.93 (2.29 to 3.58)

Treatment	Reference	MD (95% CrI)
MET + ROS		2.31 (1.26 to 3.39)
MET + IAS		4.03 (–7.85 to 16.19)
MET + IGA		2.31 (1.29 to 3.39)
MET + IND		2.89 (1.20 to 4.63)
MET + DSP		2.34 (0.58 to 4.17)
MET + GLM	MET + GLC	0.62 (–2.26 to 3.54)
MET + GLY		0.74 (–10.31 to 12.62)
MET + GLI		0.98 (–2.00 to 3.97)
MET + GLL		0.06 (–3.21 to 3.29)
MET + REP		1.68 (–1.67 to 5.10)
MET + NAT		–0.69 (–3.84 to 2.46)
MET + MIT		–1.19 (–4.33 to 1.96)
MET + SAX		–1.29 (–4.19 to 1.67)
MET + ALO		–1.31 (–4.25 to 1.64)
MET + LIN		–2.01 (–5.16 to 1.16)
MET + SIT		–1.36 (–4.24 to 1.54)
MET + VIL		–1.49 (–4.40 to 1.43)
MET + CAN		–3.80 (–6.71 to –0.83)
MET + DAP		–3.75 (–6.70 to –0.77)
MET + EMP		–3.76 (–6.69 to –0.79)
MET + LIR		–3.06 (–6.06 to –0.04)
MET + EXE		–3.72 (–6.66 to –0.78)
MET + DUL		–2.41 (–5.46 to 0.66)
MET + LIX		–2.48 (–5.38 to 0.45)
MET + PIO		1.34 (–1.47 to 4.15)
MET + ROS		0.73 (–2.33 to 3.80)
MET + IAS		2.44 (–9.94 to 14.69)
MET + IGA		0.72 (–2.29 to 3.76)
MET + IND		1.30 (–2.02 to 4.68)
MET + DSP		0.75 (–2.56 to 4.14)
MET + GLY	MET + GLM	0.12 (–10.59 to 11.62)
MET + GLI		0.35 (–0.61 to 1.31)
MET + GLL		–0.56 (–2.26 to 1.13)
MET + REP		1.06 (–0.81 to 2.93)
MET + NAT		–1.31 (–2.68 to 0.07)
MET + MIT		–1.82 (–3.20 to –0.45)
MET + SAX		–1.91 (–2.62 to –1.20)
MET + ALO		–1.93 (–2.85 to –1.04)
MET + LIN		–2.63 (–3.80 to –1.41)
MET + SIT		–1.98 (–2.54 to –1.43)
MET + VIL		–2.11 (–2.83 to –1.42)
MET + CAN		–4.42 (–5.29 to –3.54)

Treatment	Reference	MD (95% CrI)
MET + DAP		–4.37 (–5.25 to –3.51)
MET + EMP		–4.38 (–5.18 to –3.59)
MET + LIR		–3.68 (–4.63 to –2.74)
MET + EXE		–4.34 (–5.19 to –3.50)
MET + DUL		–3.03 (–4.16 to –1.90)
MET + LIX		–3.10 (–3.91 to –2.32)
MET + PIO		0.72 (0.01 to 1.42)
MET + ROS		0.10 (–1.04 to 1.28)
MET + IAS		1.82 (–10.13 to 13.97)
MET + IGA		0.10 (–0.96 to 1.22)
MET + IND		0.68 (–1.05 to 2.44)
MET + DSP		0.13 (–1.68 to 1.99)
MET + GLI	MET + GLY	0.23 (–11.21 to 10.96)
MET + GLL		–0.68 (–12.24 to 10.09)
MET + REP		0.94 (–10.69 to 11.70)
MET + NAT		–1.43 (–13.02 to 9.32)
MET + MIT		–1.93 (–13.44 to 8.89)
MET + SAX		–2.03 (–13.55 to 8.72)
MET + ALO		–2.05 (–13.50 to 8.68)
MET + LIN		–2.75 (–14.32 to 7.96)
MET + SIT		–2.10 (–13.56 to 8.58)
MET + VIL		–2.23 (–13.73 to 8.41)
MET + CAN		–4.54 (–16.02 to 6.18)
MET + DAP		–4.49 (–15.97 to 6.27)
MET + EMP		–4.50 (–16.02 to 6.22)
MET + LIR		–3.80 (–15.28 to 6.93)
MET + EXE		–4.46 (–15.96 to 6.26)
MET + DUL		–3.15 (–14.64 to 7.57)
MET + LIX		–3.22 (–14.62 to 7.49)
MET + PIO		0.60 (–10.89 to 11.31)
MET + ROS		–0.02 (–11.48 to 10.61)
MET + IAS		1.70 (–14.91 to 18.73)
MET + IGA		–0.02 (–11.42 to 10.77)
MET + IND		0.56 (–11.04 to 11.43)
MET + DSP		0.01 (–11.54 to 10.82)
MET + GLL	MET + GLI	–0.92 (–2.78 to 0.95)
MET + REP		0.71 (–1.29 to 2.72)
MET + NAT		–1.66 (–3.21 to –0.10)
MET + MIT		–2.17 (–3.74 to –0.60)
MET + SAX		–2.26 (–3.15 to –1.38)
MET + ALO		–2.29 (–3.20 to –1.40)
MET + LIN		–2.98 (–4.50 to –1.44)

Treatment	Reference	MD (95% CrI)
MET + SIT		–2.34 (–3.22 to –1.45)
MET + VIL		–2.46 (–3.56 to –1.42)
MET + CAN		–4.77 (–5.89 to –3.63)
MET + DAP		–4.72 (–5.84 to –3.63)
MET + EMP		–4.73 (–5.86 to –3.58)
MET + LIR		–4.04 (–5.23 to –2.81)
MET + EXE		–4.70 (–5.83 to –3.58)
MET + DUL		–3.39 (–4.73 to –2.02)
MET + LIX		–3.46 (–4.53 to –2.38)
MET + PIO		0.37 (–0.65 to 1.39)
MET + ROS		–0.25 (–1.61 to 1.13)
MET + IAS		1.47 (–10.38 to 13.63)
MET + IGA		–0.25 (–1.55 to 1.10)
MET + IND		0.33 (–1.54 to 2.24)
MET + DSP		–0.22 (–2.16 to 1.77)
MET + REP	MET + GLL	1.62 (–0.81 to 4.10)
MET + NAT		–0.75 (–2.81 to 1.37)
MET + MIT		–1.25 (–3.37 to 0.86)
MET + SAX		–1.35 (–3.13 to 0.43)
MET + ALO		–1.37 (–3.21 to 0.46)
MET + LIN		–2.07 (–4.12 to 0.02)
MET + SIT		–1.42 (–3.15 to 0.29)
MET + VIL		–1.55 (–3.11 to –0.01)
MET + CAN		–3.86 (–5.70 to –2.02)
MET + DAP		–3.81 (–5.66 to –2.00)
MET + EMP		–3.82 (–5.64 to –2.00)
MET + LIR		–3.12 (–4.98 to –1.24)
MET + EXE		–3.78 (–5.61 to –1.95)
MET + DUL		–2.47 (–4.46 to –0.49)
MET + LIX		–2.54 (–4.33 to –0.74)
MET + PIO		1.28 (–0.44 to 3.02)
MET + ROS		0.67 (–1.34 to 2.68)
MET + IAS		2.38 (–9.70 to 14.69)
MET + IGA		0.66 (–1.31 to 2.66)
MET + IND		1.24 (–1.11 to 3.68)
MET + DSP		0.69 (–1.72 to 3.17)
MET + NAT	MET + REP	–2.37 (–4.58 to –0.16)
MET + MIT		–2.88 (–5.09 to –0.65)
MET + SAX		–2.97 (–4.88 to –1.05)
MET + ALO		–2.99 (–4.96 to –1.01)
MET + LIN		–3.69 (–5.88 to –1.47)
MET + SIT		–3.04 (–4.90 to –1.19)

Treatment	Reference	MD (95% CrI)
MET + VIL		–3.17 (–5.09 to –1.28)
MET + CAN		–5.48 (–7.42 to –3.52)
MET + DAP		–5.43 (–7.38 to –3.48)
MET + EMP		–5.44 (–7.39 to –3.47)
MET + LIR		–4.74 (–6.75 to –2.70)
MET + EXE		–5.41 (–7.37 to –3.44)
MET + DUL		–4.09 (–6.19 to –2.00)
MET + LIX		–4.16 (–6.11 to –2.22)
MET + PIO		–0.34 (–2.23 to 1.58)
MET + ROS		–0.96 (–3.05 to 1.15)
MET + IAS		0.76 (–11.34 to 13.00)
MET + IGA		–0.96 (–3.05 to 1.14)
MET + IND		–0.38 (–2.88 to 2.11)
MET + DSP		–0.93 (–3.44 to 1.63)
MET + MIT	MET + NAT	–0.51 (–2.32 to 1.31)
MET + SAX		–0.60 (–2.04 to 0.84)
MET + ALO		–0.63 (–2.14 to 0.84)
MET + LIN		–1.32 (–3.13 to 0.52)
MET + SIT		–0.68 (–2.03 to 0.67)
MET + VIL		–0.80 (–2.25 to 0.60)
MET + CAN		–3.11 (–4.58 to –1.65)
MET + DAP		–3.06 (–4.55 to –1.59)
MET + EMP		–3.07 (–4.55 to –1.61)
MET + LIR		–2.37 (–3.93 to –0.79)
MET + EXE		–3.04 (–4.54 to –1.55)
MET + DUL		–1.73 (–3.39 to –0.04)
MET + LIX		–1.80 (–3.24 to –0.34)
MET + PIO		2.03 (0.59 to 3.45)
MET + ROS		1.41 (–0.24 to 3.07)
MET + IAS		3.13 (–8.92 to 15.30)
MET + IGA		1.41 (–0.21 to 3.09)
MET + IND		1.99 (–0.14 to 4.16)
MET + DSP		1.44 (–0.74 to 3.70)
MET + SAX	MET + MIT	–0.09 (–1.52 to 1.34)
MET + ALO		–0.12 (–1.65 to 1.40)
MET + LIN		–0.81 (–2.62 to 1.01)
MET + SIT		–0.17 (–1.52 to 1.18)
MET + VIL		–0.30 (–1.75 to 1.12)
MET + CAN		–2.60 (–4.08 to –1.11)
MET + DAP		–2.55 (–4.04 to –1.07)
MET + EMP		–2.56 (–4.03 to –1.08)
MET + LIR		–1.87 (–3.43 to –0.28)

CADTH

Treatment	Reference	MD (95% CrI)
MET + EXE		–2.53 (–4.02 to –1.02)
MET + DUL		–1.22 (–2.88 to 0.49)
MET + LIX		–1.29 (–2.74 to 0.18)
MET + PIO		2.53 (1.11 to 3.97)
MET + ROS		1.92 (0.26 to 3.62)
MET + IAS		3.64 (–8.35 to 15.91)
MET + IGA		1.92 (0.27 to 3.59)
MET + IND		2.50 (0.36 to 4.65)
MET + DSP		1.95 (–0.23 to 4.21)
MET + ALO	MET + SAX	–0.03 (–0.98 to 0.90)
MET + LIN		–0.72 (–2.12 to 0.67)
MET + SIT		–0.08 (–0.75 to 0.60)
MET + VIL		–0.20 (–1.11 to 0.64)
MET + CAN		–2.51 (–3.47 to –1.55)
MET + DAP		–2.46 (–3.32 to –1.62)
MET + EMP		–2.47 (–3.42 to –1.52)
MET + LIR		–1.78 (–2.83 to –0.70)
MET + EXE		–2.44 (–3.40 to –1.48)
MET + DUL		–1.13 (–2.33 to 0.09)
MET + LIX		–1.20 (–2.10 to –0.29)
MET + PIO		2.63 (1.76 to 3.47)
MET + ROS		2.01 (0.79 to 3.25)
MET + IAS		3.73 (–8.16 to 15.88)
MET + IGA		2.01 (0.86 to 3.22)
MET + IND		2.59 (0.80 to 4.40)
MET + DSP		2.04 (0.18 to 3.96)
MET + LIN	MET + ALO	–0.69 (–2.18 to 0.81)
MET + SIT		–0.05 (–0.90 to 0.83)
MET + VIL		–0.18 (–1.18 to 0.81)
MET + CAN		–2.48 (–3.55 to –1.39)
MET + DAP		–2.43 (–3.51 to –1.37)
MET + EMP		–2.45 (–3.53 to –1.35)
MET + LIR		–1.75 (–2.90 to –0.53)
MET + EXE		–2.41 (–3.48 to –1.34)
MET + DUL		–1.10 (–2.40 to 0.25)
MET + LIX		–1.17 (–2.20 to –0.13)
MET + PIO		2.65 (1.75 to 3.57)
MET + ROS		2.04 (0.71 to 3.40)
MET + IAS		3.75 (–8.13 to 15.92)
MET + IGA		2.04 (0.78 to 3.36)
MET + IND		2.61 (0.78 to 4.52)
MET + DSP		2.07 (0.15 to 4.05)

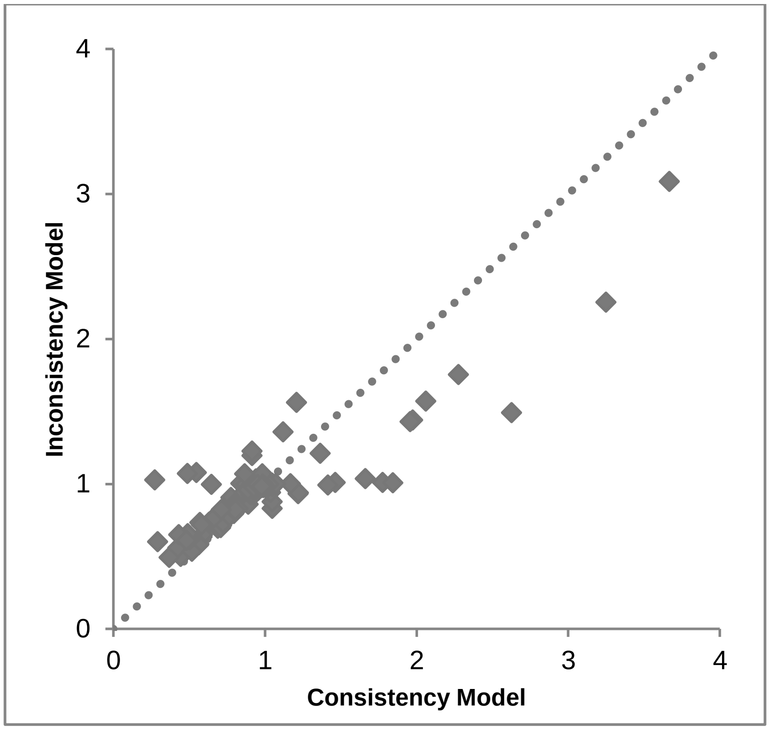
Treatment	Reference	MD (95% CrI)
MET + SIT	MET + LIN	0.64 (–0.68 to 1.95)
MET + VIL		0.52 (–0.90 to 1.88)
MET + CAN		–1.79 (–3.29 to –0.32)
MET + DAP		–1.74 (–3.24 to –0.27)
MET + EMP		–1.75 (–3.21 to –0.33)
MET + LIR		–1.05 (–2.56 to 0.45)
MET + EXE		–1.72 (–3.18 to –0.28)
MET + DUL		–0.41 (–2.06 to 1.21)
MET + LIX		–0.47 (–1.90 to 0.96)
MET + PIO		3.35 (1.97 to 4.72)
MET + ROS		2.73 (1.07 to 4.41)
MET + IAS		4.45 (–7.56 to 16.64)
MET + IGA		2.73 (1.15 to 4.35)
MET + IND		3.31 (1.21 to 5.41)
MET + DSP		2.76 (0.58 to 4.97)
MET + VIL	MET + SIT	–0.13 (–0.88 to 0.60)
MET + CAN		–2.43 (–3.22 to –1.66)
MET + DAP		–2.38 (–3.24 to –1.55)
MET + EMP		–2.40 (–3.24 to –1.55)
MET + LIR		–1.70 (–2.54 to –0.83)
MET + EXE		–2.36 (–3.14 to –1.59)
MET + DUL		–1.05 (–2.06 to –0.01)
MET + LIX		–1.12 (–1.82 to –0.41)
MET + PIO		2.70 (2.00 to 3.40)
MET + ROS		2.09 (1.03 to 3.18)
MET + IAS		3.80 (–8.14 to 15.93)
MET + IGA		2.09 (1.11 to 3.11)
MET + IND		2.66 (1.01 to 4.34)
MET + DSP		2.12 (0.38 to 3.90)
MET + CAN	MET + VIL	–2.31 (–3.27 to –1.32)
MET + DAP		–2.26 (–3.22 to –1.29)
MET + EMP		–2.27 (–3.20 to –1.30)
MET + LIR		–1.57 (–2.62 to –0.46)
MET + EXE		–2.23 (–3.17 to –1.25)
MET + DUL		–0.92 (–2.14 to 0.33)
MET + LIX		–0.99 (–1.89 to –0.06)
MET + PIO		2.83 (2.06 to 3.63)
MET + ROS		2.21 (0.99 to 3.48)
MET + IAS		3.93 (–8.00 to 16.06)
MET + IGA		2.21 (1.04 to 3.46)
MET + IND		2.79 (1.03 to 4.64)
MET + DSP		2.24 (0.39 to 4.15)

Treatment	Reference	MD (95% CrI)
MET + DAP	MET + CAN	0.05 (–1.00 to 1.09)
MET + EMP		0.04 (–1.01 to 1.09)
MET + LIR		0.74 (–0.40 to 1.89)
MET + EXE		0.07 (–0.97 to 1.10)
MET + DUL		1.38 (0.11 to 2.65)
MET + LIX		1.32 (0.34 to 2.28)
MET + PIO		5.14 (4.16 to 6.09)
MET + ROS		4.52 (3.24 to 5.82)
MET + IAS		6.24 (–5.73 to 18.44)
MET + IGA		4.52 (3.31 to 5.77)
MET + IND		5.10 (3.30 to 6.95)
MET + DSP		4.55 (2.67 to 6.49)
MET + EMP	MET + DAP	–0.01 (–1.04 to 1.03)
MET + LIR		0.69 (–0.46 to 1.87)
MET + EXE		0.02 (–1.03 to 1.09)
MET + DUL		1.33 (0.05 to 2.66)
MET + LIX		1.27 (0.28 to 2.27)
MET + PIO		5.09 (4.13 to 6.06)
MET + ROS		4.47 (3.18 to 5.80)
MET + IAS		6.19 (–5.81 to 18.43)
MET + IGA		4.47 (3.24 to 5.78)
MET + IND		5.05 (3.22 to 6.93)
MET + DSP		4.50 (2.61 to 6.47)
MET + LIR	MET + EMP	0.70 (–0.45 to 1.86)
MET + EXE		0.04 (–1.01 to 1.09)
MET + DUL		1.35 (0.06 to 2.66)
MET + LIX		1.28 (0.28 to 2.28)
MET + PIO		5.10 (4.15 to 6.05)
MET + ROS		4.48 (3.19 to 5.79)
MET + IAS		6.20 (–5.72 to 18.36)
MET + IGA		4.48 (3.25 to 5.76)
MET + IND		5.06 (3.22 to 6.92)
MET + DSP		4.51 (2.62 to 6.47)
MET + EXE	MET + LIR	–0.66 (–1.79 to 0.41)
MET + DUL		0.65 (–0.38 to 1.65)
MET + LIX		0.58 (–0.37 to 1.52)
MET + PIO		4.40 (3.31 to 5.45)
MET + ROS		3.79 (2.43 to 5.15)
MET + IAS		5.50 (–6.48 to 17.64)
MET + IGA		3.78 (2.51 to 5.06)
MET + IND		4.36 (2.51 to 6.21)
MET + DSP		3.81 (1.89 to 5.74)

Treatment	Reference	MD (95% CrI)
MET + DUL	MET + EXE	1.31 (0.08 to 2.57)
MET + LIX		1.24 (0.39 to 2.09)
MET + PIO		5.06 (4.17 to 5.95)
MET + ROS		4.45 (3.17 to 5.76)
MET + IAS		6.17 (–5.75 to 18.27)
MET + IGA		4.45 (3.46 to 5.48)
MET + IND		5.02 (3.37 to 6.72)
MET + DSP		4.48 (2.72 to 6.28)
MET + LIX	MET + DUL	–0.07 (–1.25 to 1.10)
MET + PIO		3.75 (2.52 to 4.96)
MET + ROS		3.14 (1.69 to 4.62)
MET + IAS		4.85 (–7.19 to 17.00)
MET + IGA		3.14 (1.74 to 4.55)
MET + IND		3.71 (1.77 to 5.67)
MET + DSP		3.17 (1.15 to 5.19)
MET + PIO	MET + LIX	3.82 (2.93 to 4.72)
MET + ROS		3.21 (1.97 to 4.47)
MET + IAS		4.92 (–7.00 to 17.02)
MET + IGA		3.20 (2.10 to 4.36)
MET + IND		3.78 (2.05 to 5.56)
MET + DSP		3.24 (1.42 to 5.09)
MET + ROS	MET + PIO	–0.62 (–1.83 to 0.63)
MET + IAS		1.10 (–10.82 to 13.25)
MET + IGA		–0.62 (–1.73 to 0.57)
MET + IND		–0.04 (–1.79 to 1.76)
MET + DSP		–0.59 (–2.39 to 1.30)
MET + IAS	MET + ROS	1.72 (–10.31 to 13.97)
MET + IGA		0.00 (–1.44 to 1.45)
MET + IND		0.58 (–1.40 to 2.54)
MET + DSP		0.03 (–2.02 to 2.09)
MET + IGA	MET + IAS	–1.72 (–13.76 to 10.08)
MET + IND		–1.14 (–13.16 to 10.74)
MET + DSP		–1.69 (–13.88 to 10.21)
MET + IND	MET + IGA	0.58 (–0.78 to 1.93)
MET + DSP		0.03 (–1.43 to 1.47)
MET + DSP	MET + IND	–0.55 (–2.54 to 1.44)
Random-effects model	Residual deviance	148.4 vs. 152 data points
	Deviance information criteria	311.804

ALO = alogliptin; CAN = canagliflozin; CrI = credible interval; DAP = dapagliflozin; DSP = insulin deludec/insulin aspart mix; DUL = dulaglutide; EMP = empagliflozin; EXE = exenatide; GLC = glicazide; GLI = glipizide; GLL = gliclazide; GLM = glimepiride; GLY = glyburide; IAS = insulin aspart; IGA = insulin glargine; IND = insulin degludec; LIN = linagliptin; LIR = liraglutide; LIX = lixisenatide; MD = mean difference; MET = metformin; MIT = mitiglinide; NAT = nateglinide; PIO = pioglitazone; REP = repaglinide; ROS = rosiglitazone; SAX = saxagliptin; SIT = sitagliptin; VIL = vildagliptin; vs. = versus.

Figure 41: Consistency Plot for Weight (Individual-Drug Case Analysis)



Appendix 12: Sensitivity Analyses — Reference Case

Glycated Hemoglobin (A1C)

Table 62: Sensitivity A1C: Mean Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	MD (95% CrI)
MET + SUL	MET	**–0.93 (–1.24 to –0.62)**
MET + MEG		**–0.51 (–1.17 to 0.17)**
MET + DPP-4		**–0.92 (–1.23 to –0.62)**
MET + SGLT-2		**–0.60 (–1.26 to 0.07)**
MET + GLP-1		**–0.73 (–1.15 to –0.29)**
MET + TZD		**–1.02 (–1.33 to –0.71)**
MET + INS-BA		**–0.93 (–1.76 to –0.09)**
MET + INS-BI		**–1.27 (–2.37 to –0.15)**
MET + MEG	MET + SUL	0.42 (–0.31 to 1.17)
MET + DPP-4		0.00 (–0.34 to 0.35)
MET + SGLT-2		0.33 (–0.40 to 1.06)
MET + GLP-1		0.20 (–0.28 to 0.70)
MET + TZD		–0.09 (–0.39 to 0.21)
MET + INS-BA		0.00 (–0.87 to 0.87)
MET + INS-BI		–0.35 (–1.47 to 0.81)
MET + DPP-4	MET + MEG	–0.42 (–1.17 to 0.32)
MET + SGLT-2		–0.09 (–1.04 to 0.85)
MET + GLP-1		–0.22 (–1.01 to 0.58)
MET + TZD		–0.51 (–1.25 to 0.22)
MET + INS-BA		–0.42 (–1.48 to 0.66)
MET + INS-BI		–0.77 (–2.05 to 0.54)
MET + SGLT-2	MET + DPP-4	0.33 (–0.40 to 1.05)
MET + GLP-1		0.20 (–0.31 to 0.72)
MET + TZD		–0.09 (–0.49 to 0.29)
MET + INS-BA		0.00 (–0.89 to 0.87)
MET + INS-BI		–0.35 (–1.48 to 0.82)
MET + GLP-1	MET + SGLT-2	–0.13 (–0.91 to 0.66)
MET + TZD		–0.42 (–1.15 to 0.31)
MET + INS-BA		–0.33 (–1.39 to 0.74)
MET + INS-BI		–0.68 (–1.95 to 0.62)
MET + TZD	MET + GLP-1	–0.29 (–0.81 to 0.21)
MET + INS-BA		–0.20 (–0.92 to 0.50)

Treatment	Reference	MD (95% CrI)
MET + INS-BI		–0.55 (–1.57 to 0.49)
MET + INS-BA	MET + TZD	0.09 (–0.80 to 0.98)
MET + INS-BI		–0.26 (–1.39 to 0.90)
MET + INS-BI	MET + INS-BA	–0.35 (–1.07 to 0.40)
Random-effects model	Residual deviance	48.77 vs. 55 data points
	Deviance information criteria	–25.194

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MD = mean difference; MEG = meglitinide; MET = metformin; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Nonsevere Hypoglycemia

Table 63: Diabetes Outcomes — Sensitivity Nonsevere Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + SUL	MET	**13.49 (8.26 to 23.20)**	11.88 (7.56 to 19.26)	11.70 (7.34 to 18.33)
MET + MEG		**9.88 (4.70 to 20.84)**	9.01 (4.50 to 17.52)	8.65 (3.87 to 16.73)
MET + DPP-4		0.97 (0.62 to 1.56)	0.97 (0.63 to 1.55)	–0.03 (–0.49 to 0.51)
MET + SGLT-2		1.22 (0.68 to 2.12)	1.21 (0.68 to 2.09)	0.23 (–0.40 to 1.08)
MET + GLP-1		0.93 (0.57 to 1.56)	0.93 (0.57 to 1.55)	–0.08 (–0.54 to 0.55)
MET + TZD		0.99 (0.36 to 2.55)	0.99 (0.36 to 2.51)	–0.01 (–0.76 to 1.55)
MET + INS-BA		**4.56 (2.57 to 8.25)**	4.39 (2.52 to 7.70)	3.64 (1.68 to 6.96)
MET + INS-BI		**10.81 (5.33 to 21.66)**	9.76 (5.07 to 18.07)	9.41 (4.53 to 17.55)
MET + MEG	MET + SUL	0.74 (0.34 to 1.49)	0.76 (0.38 to 1.41)	–2.96 (–10.13 to 4.58)
MET + DPP-4		0.07 (0.05 to 0.10)	0.08 (0.06 to 0.11)	–11.75 (–18.09 to –7.50)
MET + SGLT-2		0.09 (0.04 to 0.17)	0.10 (0.05 to 0.19)	–11.46 (–18.05 to –7.07)
MET + GLP-1		0.07 (0.04 to 0.11)	0.08 (0.05 to 0.13)	–11.79 (–18.22 to –7.49)
MET + TZD		0.07 (0.02 to 0.19)	0.08 (0.03 to 0.21)	–11.62 (–18.21 to –7.22)
MET + INS-BA		0.34 (0.21 to 0.55)	0.37 (0.23 to 0.58)	–8.01 (–13.38 to –4.22)
MET + INS-BI		0.80 (0.44 to 1.41)	0.82 (0.48 to 1.34)	–2.28 (–7.89 to 4.14)
MET + DPP-4	MET + MEG	0.10 (0.05 to 0.22)	0.11 (0.06 to 0.23)	–8.67 (–16.72 to –3.88)
MET + SGLT-2		0.12 (0.05 to 0.30)	0.13 (0.06 to 0.31)	–8.41 (–16.53 to –3.55)
MET + GLP-1		0.09 (0.04 to 0.22)	0.10 (0.05 to 0.23)	–8.73 (–16.78 to –3.90)
MET + TZD		0.10 (0.03 to 0.32)	0.11 (0.03 to 0.34)	–8.56 (–16.75 to –3.62)
MET + INS-BA		0.46 (0.21 to 1.09)	0.48 (0.23 to 1.08)	–4.96 (–12.80 to 0.49)
MET + INS-BI		1.08 (0.45 to 2.79)	1.07 (0.49 to 2.51)	0.69 (–7.74 to 9.67)
MET + SGLT-2	MET + DPP-4	1.25 (0.67 to 2.20)	1.25 (0.67 to 2.17)	0.26 (–0.43 to 1.10)
MET + GLP-1		0.95 (0.58 to 1.56)	0.95 (0.59 to 1.55)	–0.05 (–0.55 to 0.51)
MET + TZD		1.03 (0.35 to 2.58)	1.03 (0.36 to 2.54)	0.03 (–0.80 to 1.53)
MET + INS-BA		4.68 (2.87 to 7.65)	4.50 (2.80 to 7.18)	3.67 (1.82 to 6.80)
MET + INS-BI		11.10 (5.94 to 19.93)	10.03 (5.62 to 16.81)	9.44 (4.64 to 17.43)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET + GLP-1	MET + SGLT-2	0.76 (0.38 to 1.59)	0.76 (0.39 to 1.58)	–0.31 (–1.23 to 0.53)
MET + TZD		0.82 (0.27 to 2.38)	0.82 (0.27 to 2.34)	–0.23 (–1.34 to 1.39)
MET + INS-BA		3.74 (1.85 to 8.06)	3.61 (1.83 to 7.56)	3.38 (1.36 to 6.73)
MET + INS-BI		8.88 (4.00 to 20.71)	8.03 (3.79 to 17.52)	9.15 (4.26 to 17.30)
MET + TZD	MET + GLP-1	1.08 (0.37 to 2.89)	1.08 (0.37 to 2.85)	0.07 (–0.81 to 1.59)
MET + INS-BA		4.92 (2.87 to 8.20)	4.73 (2.81 to 7.74)	3.71 (1.87 to 6.76)
MET + INS-BI		11.63 (5.92 to 22.49)	10.48 (5.57 to 19.02)	9.49 (4.70 to 17.45)
MET + INS-BA	MET + TZD	4.55 (1.63 to 13.82)	4.37 (1.60 to 13.02)	3.57 (1.26 to 6.93)
MET + INS-BI		10.84 (3.71 to 34.73)	9.75 (3.49 to 30.07)	9.34 (4.34 to 17.48)
MET + INS-BI	MET + INS-BA	2.38 (1.43 to 3.80)	2.23 (1.40 to 3.40)	5.72 (1.88 to 11.97)
Random-effects model	Residual deviance	94.33 vs. 98 data points		
	Deviance information criteria	463.356		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; INS-BA = basal insulin; INS-BI = biphasic insulin; MEG = meglitinide; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Appendix 13: Research Question 2 — Detailed Network Meta-Analysis Results for the Reference-Case Analysis

Major Adverse Cardiovascular Events (MACE)

Table 64: Major Adverse Cardiovascular Events: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
DPP-4	Placebo	0.99 (0.68 to 1.45)
SGLT-2		0.86 (0.46 to 1.67)
GLP-1		0.87 (0.45 to 1.65)
SGLT-2	DPP-4	0.87 (0.41 to 1.88)
GLP-1		0.88 (0.41 to 1.83)
GLP-1	SGLT-2	1.01 (0.39 to 2.46)
Random-effects model	Total residual deviance	4.053 vs. 5 data points
	Deviance information criteria	–9.193

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; HR = hazard ratio; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; vs. = versus.

Cardiovascular Death (CV)

Table 65: Cardiovascular Death: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
DPP-4	Placebo	0.97 (0.33 to 2.68)
SGLT-2		0.58 (0.14 to 2.55)
GLP-1		0.86 (0.30 to 2.47)
TZD		0.83 (0.20 to 3.73)
SGLT-2	DPP-4	0.60 (0.10 to 3.72)
GLP-1		0.89 (0.22 to 4.03)
TZD		0.86 (0.15 to 5.27)
GLP-1	SGLT-2	1.48 (0.25 to 8.94)
TZD		1.42 (0.18 to 11.65)
TZD	GLP-1	0.96 (0.15 to 6.20)
Random-effects model	Total residual deviance	6.063 vs. 6 data points
	Deviance information criteria	–2.803

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; HR = hazard ratio; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; TZD = thiazolidinedione; vs. = versus.

All-Cause Mortality

Table 66: All-Cause Mortality: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
DPP-4	Placebo	1.02 (0.83 to 1.20)
SGLT-2		0.67 (0.47 to 0.95)
GLP-1		0.89 (0.71 to 1.12)
TZD		0.91 (0.71 to 1.16)
SGLT-2	DPP-4	0.66 (0.45 to 0.99)
GLP-1		0.87 (0.67 to 1.19)
TZD		0.90 (0.67 to 1.24)
GLP-1	SGLT-2	1.32 (0.89 to 2.03)
TZD		1.36 (0.90 to 2.09)
TZD	GLP-1	1.03 (0.74 to 1.42)
Random-effects model	Total residual deviance	7.678 vs. 8 data points
	Deviance information criteria	–10.022

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; HR = hazard ratio; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; TZD = thiazolidinedione; vs. = versus.

Hospitalization for Unstable Angina

Table 67: Hospitalization for Unstable Angina: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
DPP-4	Placebo	1.03 (0.05 to 20.01)
SGLT-2		0.96 (0.01 to 62.12)
GLP-1		0.97 (0.02 to 68.10)
SGLT-2	DPP-4	0.92 (0.01 to 141.88)
GLP-1		0.94 (0.01 to 175.04)
GLP-1	SGLT-2	1.02 (0.00 to 410.76)
Random-effects model	Total residual deviance	3.995 vs. 4 data points
	Deviance information criteria	–0.18

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; HR = hazard ratio; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; vs. = versus.

Hospitalization for Heart Failure

Table 68: Hospitalization for Heart Failure: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
DPP-4	Placebo	1.13 (0.43 to 2.93)
SGLT-2		0.68 (0.18 to 2.75)
GLP-1		0.91 (0.35 to 2.40)
SGLT-2	DPP-4	0.60 (0.12 to 3.35)
GLP-1		0.80 (0.21 to 3.13)
GLP-1	SGLT-2	1.34 (0.24 to 6.86)
Random-effects model	Total residual deviance	5.03 vs. 5 data points
	Deviance information criteria	–3.26

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; HR = hazard ratio; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; vs. = versus.

Total Adverse Events

Table 69: Total Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
DPP-4	Placebo	1.08 (0.40 to 2.85)	1.01 (0.76 to 1.15)	1.14 (–18.83 to 12.02)
SGLT-2		0.86 (0.33 to 2.33)	0.97 (0.71 to 1.13)	–2.53 (–23.26 to 10.31)
GLP-1		1.07 (0.41 to 2.97)	1.01 (0.78 to 1.15)	1.03 (–17.84 to 12.25)
SGLT-2	DPP-4	0.80 (0.20 to 3.36)	0.96 (0.69 to 1.30)	–3.60 (–26.05 to 19.10)
GLP-1		1.00 (0.25 to 4.11)	1.00 (0.76 to 1.33)	–0.06 (–20.71 to 21.49)
GLP-1	SGLT-2	1.24 (0.31 to 5.02)	1.05 (0.78 to 1.45)	3.54 (–18.39 to 26.05)
Random-effects model	Residual deviance	6.006 vs. 6 data points		
	Deviance information criteria	59.719		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; vs. = versus.

Withdrawals Due to Adverse Events

Table 70: Withdrawals Due to Adverse Events: Odds Ratios, Relative Risks and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
MET	Placebo	0.33 (0.05 to 1.76)	0.35 (0.06 to 1.66)	–5.22 (–7.61 to 5.24)
SUL		0.67 (0.21 to 1.98)	0.69 (0.22 to 1.84)	–2.49 (–6.27 to 6.66)
DPP-4		0.97 (0.50 to 1.87)	0.97 (0.52 to 1.74)	–0.23 (–3.85 to 5.97)
GLP-1		1.49 (0.96 to 2.39)	1.44 (0.96 to 2.15)	3.49 (–0.30 to 9.21)
TZD		1.19 (0.60 to 2.28)	1.17 (0.62 to 2.07)	1.36 (–3.05 to 8.56)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
SUL	MET	2.01 (0.58 to 8.24)	1.95 (0.61 to 7.76)	2.35 (–3.87 to 8.56)
DPP-4		2.95 (0.48 to 20.04)	2.79 (0.51 to 18.08)	4.82 (–5.76 to 11.16)
GLP-1		4.54 (0.81 to 29.39)	4.13 (0.83 to 25.47)	8.53 (–2.16 to 14.63)
TZD		3.63 (0.76 to 18.98)	3.38 (0.78 to 17.22)	6.30 (–2.47 to 12.22)
DPP-4	SUL	1.44 (0.40 to 5.54)	1.41 (0.44 to 5.03)	2.21 (–7.34 to 9.22)
GLP-1		2.23 (0.70 to 7.77)	2.09 (0.73 to 6.86)	5.91 (–3.67 to 12.58)
TZD		1.78 (0.73 to 4.54)	1.70 (0.75 to 4.20)	3.71 (–3.04 to 8.76)
GLP-1	DPP-4	1.54 (0.70 to 3.54)	1.48 (0.73 to 3.14)	3.69 (–3.30 to 10.38)
TZD		1.23 (0.48 to 3.11)	1.20 (0.51 to 2.81)	1.58 (–5.78 to 9.49)
TZD	GLP-1	0.80 (0.34 to 1.72)	0.82 (0.38 to 1.60)	–2.12 (–9.33 to 5.60)
Random-effects model	Residual deviance	12.14 vs. 12 data points		
	Deviance information criteria	99.864		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; MET = metformin; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Serious Adverse Events

Table 71: Serious Adverse Events: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
SUL	Placebo	0.81 (0.37 to 1.77)	0.87 (0.48 to 1.39)	–4.66 (–18.55 to 13.88)
DPP-4		0.92 (0.58 to 1.47)	0.95 (0.68 to 1.26)	–1.88 (–11.38 to 9.20)
SGLT-2		0.94 (0.58 to 1.50)	0.96 (0.68 to 1.27)	–1.52 (–11.38 to 9.76)
GLP-1		0.95 (0.68 to 1.33)	0.97 (0.77 to 1.19)	–1.17 (–8.30 to 6.68)
TZD		0.92 (0.57 to 1.49)	0.94 (0.67 to 1.27)	–1.99 (–11.70 to 9.58)
DPP-4	SUL	1.13 (0.46 to 2.83)	1.09 (0.62 to 2.11)	2.71 (–17.52 to 20.63)
SGLT-2		1.15 (0.46 to 2.85)	1.10 (0.62 to 2.11)	3.12 (–17.30 to 20.40)
GLP-1		1.17 (0.50 to 2.72)	1.11 (0.66 to 2.08)	3.42 (–16.10 to 19.07)
TZD		1.13 (0.61 to 2.11)	1.08 (0.74 to 1.72)	2.58 (–11.51 to 14.05)
SGLT-2	DPP-4	1.02 (0.52 to 1.97)	1.01 (0.65 to 1.55)	0.40 (–14.34 to 14.82)
GLP-1		1.03 (0.58 to 1.81)	1.02 (0.71 to 1.50)	0.72 (–12.13 to 12.89)
TZD		0.99 (0.51 to 1.94)	1.00 (0.64 to 1.54)	–0.12 (–14.70 to 14.42)
GLP-1	SGLT-2	1.02 (0.57 to 1.83)	1.01 (0.70 to 1.51)	0.38 (–13.00 to 12.92)
TZD		0.98 (0.50 to 1.96)	0.99 (0.64 to 1.55)	–0.47 (–15.05 to 14.82)
TZD	GLP-1	0.96 (0.54 to 1.73)	0.98 (0.66 to 1.42)	–0.85 (–12.87 to 12.36)
Random-effects model	Residual deviance	11.8 vs. 12 data points		
	Deviance information criteria	117.501		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; SUL = sulfonylurea; TZD = thiazolidinedione; vs. = versus.

Severe Hypoglycemia

Table 72: Severe Hypoglycemia: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
DPP-4	Placebo	1.18 (0.91 to 1.54)	1.18 (0.91 to 1.53)	0.18 (–0.09 to 0.51)
SGLT-2		0.82 (0.45 to 1.47)	0.82 (0.46 to 1.47)	–0.18 (–0.55 to 0.44)
GLP-1		0.71 (0.49 to 0.99)	0.71 (0.49 to 0.99)	–0.28 (–0.51 to 0.00)
TZD		2.05 (1.11 to 3.98)	2.03 (1.10 to 3.88)	1.00 (0.11 to 2.53)
SGLT-2		0.69 (0.36 to 1.33)	0.69 (0.37 to 1.33)	–0.35 (–0.86 to 0.33)
GLP-1	DPP-4	0.60 (0.38 to 0.92)	0.60 (0.38 to 0.92)	–0.45 (–0.87,–0.08)
TZD		1.74 (0.89 to 3.51)	1.72 (0.89 to 3.43)	0.82 (–0.15 to 2.37)
GLP-1	SGLT-2	0.87 (0.43 to 1.70)	0.87 (0.44 to 1.69)	–0.10 (–0.76 to 0.34)
TZD		2.52 (1.07 to 5.98)	2.49 (1.07 to 5.83)	1.16 (0.08 to 2.71)
TZD	GLP-1	2.89 (1.44 to 6.24)	2.86 (1.43 to 6.06)	1.27 (0.36 to 2.81)
Random-effects model	Residual deviance	13.86 vs. 16 data points		
	Deviance information criteria	114.457		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; TZD = thiazolidinedione; vs. = versus.

Pancreatitis

Table 73: Pancreatitis: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
DPP-4	Placebo	1.60 (0.97 to 2.66)	1.60 (0.97 to 2.65)	0.15 (–0.01 to 0.37)
GLP-1		0.73 (0.37 to 1.39)	0.73 (0.37 to 1.38)	–0.07 (–0.18 to 0.09)
GLP-1	DPP-4	0.45 (0.20 to 1.03)	0.45 (0.20 to 1.03)	–0.22 (–0.46 to 0.01)
Random-effects model	Residual deviance	7.972 vs. 10 data points		
	Deviance information criteria	59.869		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; vs. = versus.

Bone Fractures

Table 74: Bone Fractures: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
DPP-4	Placebo	1.00 (0.39 to 2.47)	1.00 (0.40 to 2.38)	–0.01 (–1.59 to 3.64)
SGLT-2		0.95 (0.37 to 2.48)	0.95 (0.37 to 2.39)	–0.13 (–1.67 to 3.66)
TZD		1.39 (0.50 to 3.65)	1.37 (0.50 to 3.41)	0.98 (–1.34 to 6.23)

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
SGLT-2	DPP-4	0.96 (0.24 to 3.67)	0.96 (0.26 to 3.54)	–0.11 (–3.82 to 3.69)
TZD		1.39 (0.35 to 5.24)	1.38 (0.36 to 4.86)	0.97 (–3.16 to 6.09)
TZD	SGLT-2	1.46 (0.36 to 5.60)	1.44 (0.37 to 5.23)	1.08 (–3.10 to 6.15)
Random-effects model	Residual deviance	6.002 vs. 6 data points		
	Deviance information criteria	50.27		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; SGLT-2 = sodium-glucose cotransporter-2 inhibitor; vs. = versus.

Pancreatic Cancer

Table 75: Pancreatic Cancer: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
DPP-4	Placebo	0.53 (0.19 to 1.46)	0.53 (0.19 to 1.46)	–0.06 (–0.14 to 0.05)
GLP-1		1.09 (0.34 to 3.10)	1.09 (0.34 to 3.09)	0.01 (–0.10 to 0.27)
TZD		0.13 (0.01 to 0.75)	0.13 (0.01 to 0.75)	–0.11 (–0.18 to –0.03)
GLP-1	DPP-4	2.04 (0.44 to 9.01)	2.04 (0.44 to 8.99)	0.07 (–0.08 to 0.33)
TZD		0.24 (0.02 to 1.89)	0.24 (0.02 to 1.89)	–0.05 (–0.17 to 0.04)
TZD	GLP-1	0.12 (0.01 to 0.97)	0.12 (0.01 to 0.97)	–0.12 (–0.38 to 0.00)
Random-effects model	Residual deviance	16.92 vs. 12 data points		
	Deviance information criteria	64.97		

CrI = credible interval; DPP-4 = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; TZD = thiazolidinedione; vs. = versus.

Bladder Cancer

Table 76: Bladder Cancer: Odds Ratios, Relative Risks, and Risk Difference for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	OR (95% CrI)	RR (95% CrI)	RD% (95% CrI)
GLP-1	Placebo	1.25 (0.44 to 3.78)	1.25 (0.44 to 3.76)	0.05 (–0.14 to 0.56)
TZD		1.86 (0.75 to 4.67)	1.85 (0.75 to 4.64)	0.19 (–0.07 to 0.62)
TZD	GLP-1	1.50 (0.36 to 5.84)	1.49 (0.36 to 5.81)	0.13 (–0.45 to 0.61)
Random-effects model	Residual deviance	5.652 vs. 6 data points		
	Deviance information criteria	35.228		

CrI = credible interval; GLP-1 = glucagon-like peptide-1 agonist; OR = odds ratio; RD = risk difference; RR = relative risk; TZD = thiazolidinedione; vs. = versus.

Appendix 14: Research Question 2 — Detailed Network Meta-Analysis Results FOR THE Individual Drug Analysis

Hospitalization for Heart Failure

Table 77: Hospitalization for Heart Failure: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
Saxagliptin 5	Placebo	1.28 (0.00 to 657.21)
Sitagliptin 100		1.00 (0.00 to 501.70)
Empaglaflozin 25		0.67 (0.00 to 340.02)
Liraglutide 1.8		0.87 (0.00 to 459.44)
Lixisenatide		0.97 (0.00 to 473.90)
Sitagliptin 100	Saxagliptin 5	0.79 (0.00 to 5,244.84)
Empaglaflozin 25		0.53 (0.00 to 3,229.23)
Liraglutide 1.8		0.68 (0.00 to 5,819.68)
Lixisenatide		0.76 (0.00 to 5,497.23)
Empaglaflozin 25	Sitagliptin 100	0.66 (0.00 to 3,415.23)
Liraglutide 1.8		0.87 (0.00 to 6,254.15)
Lixisenatide		0.97 (0.00 to 6,747.99)
Liraglutide 1.8	Empaglaflozin 25	1.32 (0.00 to 10,721.43)
Lixisenatide		1.46 (0.00 to 9,246.50)
Lixisenatide	Liraglutide 1.8	1.11 (0.00 to 6,981.37)
Random-effects model	Total residual deviance	4.989 vs. 5 data points
	Deviance information criteria	–3.007

CrI = credible interval; HR = hazard ratio; vs. = versus.

Note: number denotes amount in milligrams unless otherwise indicated.

Hospitalization for Unstable Angina

Table 78: Hospitalization for Unstable Angina: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
Saxagliptin 5	Placebo	1.18 (0.00 to 560.04)
Sitagliptin 100		0.89 (0.00 to 460.36)
Empaglaflozin 25		0.97 (0.00 to 466.85)
Liraglutide 1.8		0.97 (0.00 to 485.90)
Sitagliptin 100	Saxagliptin 5	0.76 (0.00 to 4,870.73)
Empaglaflozin 25		0.81 (0.00 to 5,602.68)

Treatment	Reference	HR (95% CrI)
Liraglutide 1.8		0.82 (0.00 to 6,335.98)
Empagliflozin 25	Sitagliptin 100	1.08 (0.00 to 6,995.34)
Liraglutide 1.8		1.10 (0.00 to 7,331.97)
Liraglutide 1.8	Empagliflozin 25	1.02 (0.00 to 7,201.18)
Random-effects model	Total residual deviance	3.983 vs. 4 data points
	Deviance information criteria	–0.163

CrI = credible interval; HR = hazard ratio; vs. = versus.

Note: number denotes amount in milligrams unless otherwise indicated.

All-Cause Mortality

Table 79: All-Cause Death: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
Saxagliptin 5	Placebo	1.11 (0.00 to 541.31)
Alogliptin 25		0.88 (0.00 to 464.98)
Sitagliptin 100		1.02 (0.00 to 513.89)
Empagliflozin 25		0.67 (0.00 to 335.63)
Liraglutide 1.8		0.85 (0.00 to 421.15)
Lixisenatide 0.02		0.94 (0.00 to 440.98)
Rosiglitazone 8		0.86 (0.00 to 431.38)
Pioglitazone 45		0.96 (0.00 to 508.77)
Alogliptin 25	Saxagliptin 5	0.79 (0.00 to 5,469.81)
Sitagliptin 100		0.93 (0.00 to 5,404.57)
Empagliflozin 25		0.61 (0.00 to 4,048.09)
Liraglutide 1.8		0.76 (0.00 to 4,870.73)
Lixisenatide 0.02		0.86 (0.00 to 4,438.18)
Rosiglitazone 8		0.77 (0.00 to 4,875.61)
Pioglitazone 45		0.87 (0.00 to 5,585.90)
Sitagliptin 100	Alogliptin 25	1.17 (0.00 to 8,014.44)
Empagliflozin 25		0.77 (0.00 to 4,500.75)
Liraglutide 1.8		0.97 (0.00 to 6,542.01)
Lixisenatide 0.02		1.07 (0.00 to 7,302.70)
Rosiglitazone 8		0.98 (0.00 to 6,118.06)
Pioglitazone 45		1.09 (0.00 to 8,299.91)
Empagliflozin 25	Sitagliptin 100	0.65 (0.00 to 3,920.60)
Liraglutide 1.8		0.85 (0.00 to 6,173.37)
Lixisenatide 0.02		0.92 (0.00 to 5,399.17)
Rosiglitazone 8		0.84 (0.00 to 5,324.11)
Pioglitazone 45		0.94 (0.00 to 6,118.06)
Liraglutide 1.8	Empagliflozin 25	1.26 (0.00 to 7,638.83)

Treatment	Reference	HR (95% CrI)
Lixisenatide 0.02		1.40 (0.00 to 9,976.62)
Rosiglitazone 8		1.30 (0.00 to 7,215.60)
Pioglitazone 45		1.44 (0.00 to 9,376.86)
Lixisenatide 0.02	Liraglutide 1.8	1.10 (0.00 to 6,247.90)
Rosiglitazone 8		1.00 (0.00 to 6,399.66)
Pioglitazone 45		1.13 (0.00 to 6,809.00)
Rosiglitazone 8	Lixisenatide 0.02	0.92 (0.00 to 5,497.23)
Pioglitazone 45		1.03 (0.00 to 6,911.90)
Pioglitazone 45	Rosiglitazone 8	1.12 (0.00 to 7,998.43)
Random-effects model	Total residual deviance	8.027 vs. 8 data points
	Deviance information criteria	–7.819

CrI = credible interval; HR = hazard ratio; vs. = versus.

Note: number denotes amount in milligrams unless otherwise indicated.

Major Adverse Cardiovascular Events

Table 80: Major Adverse Cardiovascular Events: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
Saxagliptin 5	Placebo	1.00 (0.00 to 506.74)
Alogliptin 25		0.98 (0.00 to 470.13)
Sitagliptin 100		0.98 (0.00 to 500.20)
Empaglaflozin 25		0.86 (0.00 to 479.14)
Liraglutide 1.8		0.87 (0.00 to 407.89)
Alogliptin 25	Saxagliptin 5	0.97 (0.00 to 5,790.65)
Sitagliptin 100		0.98 (0.00 to 6,463.98)
Empaglaflozin 25		0.86 (0.00 to 7,237.27)
Liraglutide 1.8		0.87 (0.00 to 6,148.72)
Sitagliptin 100	Alogliptin 25	1.01 (0.00 to 5,530.31)
Empaglaflozin 25		0.89 (0.00 to 6,707.62)
Liraglutide 1.8		0.88 (0.00 to 5,350.79)
Empaglaflozin 25	Sitagliptin 100	0.88 (0.00 to 7,172.43)
Liraglutide 1.8		0.89 (0.00 to 5,329.43)
Liraglutide 1.8	Empaglaflozin 25	1.00 (0.00 to 6,057.18)
Random-effects model	Total residual deviance	4.988 vs. 5 data points
	Deviance information criteria	–7.292

CrI = credible interval; HR = hazard ratio; vs. = versus.

Note: number denotes amount in milligrams unless otherwise indicated.

Cardiovascular Death

Table 81: Cardiovascular Death: Hazard Ratio for All Treatment Comparisons — Random-Effects Model

Treatment	Reference	HR (95% CrI)
Saxagliptin 5	Placebo	1.03 (0.00 to 452.14)
Alogliptin 25		0.88 (0.00 to 502.20)
Empagliflozin 25		0.59 (0.00 to 315.13)
Liraglutide 1.8		0.78 (0.00 to 407.48)
Lixisenatide 20 mcg		0.97 (0.00 to 456.23)
Rosiglitazone 8		0.84 (0.00 to 492.26)
Alogliptin 25	Saxagliptin 5	0.86 (0.00 to 6,747.99)
Empagliflozin 25		0.57 (0.00 to 4,129.87)
Liraglutide 1.8		0.76 (0.00 to 5,074.58)
Lixisenatide 20 mcg		0.94 (0.00 to 5,636.40)
Rosiglitazone 8		0.83 (0.00 to 6,399.66)
Empagliflozin 25	Alogliptin 25	0.67 (0.00 to 4,934.47)
Liraglutide 1.8		0.88 (0.00 to 5,843.00)
Lixisenatide 20 mcg		1.11 (0.00 to 7,093.97)
Rosiglitazone 8		0.95 (0.00 to 6,849.97)
Liraglutide 1.8	Empagliflozin 25	1.31 (0.00 to 8,857.32)
Lixisenatide 20 mcg		1.66 (0.00 to 10,270.18)
Rosiglitazone 8		1.43 (0.00 to 8,604.15)
Lixisenatide 20 mcg	Liraglutide 1.8	1.25 (0.00 to 6,836.29)
Rosiglitazone 8		1.09 (0.00 to 7,646.47)
Rosiglitazone 8	Lixisenatide 20 mcg	0.87 (0.00 to 5,223.90)
Random-effects model	Total residual deviance	5.988 vs. 6 data points
	Deviance information criteria	–2.628

CrI = credible interval; HR = hazard ratio; vs. = versus.

Note: number denotes amount in milligrams unless otherwise indicated.

Appendix 15: Results of Pharmacoeconomic Sensitivity Analyses

Table 82: Base-Case Results (Using Cost of NPH Insulin for Basal Insulin)

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,648	8.8369		
SU	$39,251	8.8784	$38,643	$38,643
SGLT-2 inhibitors	$49,308	8.9530	$100,459	$134,861
GLP-1 agonists	$55,946	8.9894	$119,997	$182,263
DPP-4 inhibitors	$48,859	8.8998	$178,127	Extended dominance[a]
Basal insulin	$54,852	8.8898	$324,968	Dominated[b]
Biphasic insulin	$63,719	8.9340	$268,496	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; NPH = neutral protamine Hagedorn; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2.

[c] Dominated by SGLT-2, GLP-1.

Table 83: Using Price of a More Costly and Widely Utilized Sulfonylurea ($0.0931 per Gliclazide 30 mg SR Tablet, Instead of Price for Glyburide 5 mg Tablet $0.0574) With Ontario Drug Benefit Blood Glucose Test Strip Limits

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$36,408	8.8369		
SU	$39,455	8.8784	$73,417	$73,417
SGLT-2 inhibitors	$48,055	8.9530	$100,341	$115,325
GLP-1 agonists	$54,687	8.9894	$119,871	$182,113
DPP-4 inhibitors	$47,614	8.8998	$178,035	Extended dominance[a]
Basal insulin	$54,886	8.8898	$281,615	Dominated[b]
Biphasic insulin	$63,753	8.9340	$349,027	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SR = slow release; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2, GLP-1.

[c] Dominated by SGLT-2, GLP-1.

Table 84: Lower Disutility for Mild or Moderate Hypoglycemia (–0.0052 Instead of –0.014) Based on NICE Guidance on Insulin Analogues

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,648	8.8388		
SU	$39,251	8.8824	$36,733	$36,733
SGLT-2 inhibitors	$49,308	8.9549	$100,441	$138,839
GLP-1 agonists	$55,946	8.9913	$119,974	$182,221
DPP-4 inhibitors	$48,859	8.9017	$178,102	Extended dominance[a]
Basal insulin	$54,852	8.8965	$298,188	Dominated[b]
Biphasic insulin	$63,719	8.9407	$255,897	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; NICE = National Institute for Health and Care Excellence; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2.

[c] Dominated by GLP-1, SGLT-2.

Table 85: Lower Disutility for Severe Hypoglycemia (–0.01 Instead of –0.047) Based on NICE Guidance for Type 2 Diabetes

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,648	8.8371		
SU	$39,251	8.8822	$35,539	$35,539
SGLT-2 inhibitors	$49,308	8.9532	$100,457	$141,746
GLP-1 agonists	$55,946	8.9896	$119,994	$182,259
DPP-4 inhibitors	$48,859	8.9000	$178,124	Extended dominance[a]
Basal insulin	$54,852	8.9369	$172,423	Dominated[b]
Biphasic insulin	$63,719	8.9812	$180,893	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; NICE = National Institute for Health and Care Excellence; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by SGLT-2.

[c] Dominated by GLP-1.

Table 86: Lower Disutility for Hypoglycemia (–0.0052 for Mild and Moderate; –0.01 for Severe Hypoglycemia)

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,648	8.8390		
SU	$39,251	8.8863	$33,917	$33,917
SGLT-2 inhibitors	$49,308	8.9551	$100,439	$146,148
GLP-1 agonists	$55,946	8.9915	$119,971	$182,217

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
DPP-4 inhibitors	$48,859	8.9019	$178,099	Extended dominance[a]
Basal insulin	$54,852	8.9435	$164,580	Dominated[b]
Biphasic insulin	$63,719	8.9879	$175,085	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by SGLT-2.

[c] Dominated by GLP-1.

Table 87: Utility Estimates for Diabetes Complications from Clarke et al. (2004)

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,648	8.7058		
SU	$39,251	8.7474	$38,561	$38,561
SGLT-2 inhibitors	$49,308	8.8302	$93,724	$121,422
GLP-1 agonists	$55,946	8.8639	$115,749	$197,121
DPP-4 inhibitors	$48,859	8.7735	$165,693	Extended dominance[a]
Basal insulin	$54,852	8.7630	$300,671	Dominated[b]
Biphasic insulin	$63,719	8.8076	$256,172	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2.

[c] Dominated by SGLT-2, GLP-1.

Table 88: Cost for Mild or Moderate Hypoglycemia ($93 Per Event Instead of Zero Cost) Based on Brod et al. (2011)

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,668	8.8369		
SU	$39,294	8.8784	$39,192	$39,192
SGLT-2 inhibitors	$49,328	8.9530	$100,461	$134,558
GLP-1 agonists	$55,966	8.9894	$119,998	$182,263
DPP-4 inhibitors	$48,879	8.8998	$178,128	Extended dominance[a]
Basal insulin	$54,922	8.8898	$325,916	Dominated[b]
Biphasic insulin	$63,789	8.9340	$269,015	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2.

[c] Dominated by SGLT-2, GLP-1.

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Table 89: Base-Case Results Using Cost of Insulin Glargine for Basal Insulin

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$37,648	8.8369		
SU	$39,251	8.8784	$38,643	$38,643
SGLT-2 inhibitors	$49,308	8.9530	$100,459	$134,861
GLP-1 agonists	$55,946	8.9894	$119,997	$182,263
DPP-4 inhibitors	$48,859	8.8998	$178,127	Extended dominance[a]
Basal insulin	$60,109	8.8898	$424,272	Dominated[b]
Biphasic insulin	$63,719	8.9340	$268,496	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; QALY = quality-adjusted life-year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2, GLP-1.

[c] Dominated by SGLT-2, GLP-1.

Table 90: Base-Case Results Using Costs for Fatal Events for Ischemic Heart Disease and Heart Failure

Treatment	Costs	QALYs	ICUR (Versus Metformin Monotherapy)	Sequential ICUR
MET	$38,107	8.8369		
SU	$39,732	8.8784	$39,177	$39,177
SGLT-2 inhibitors	$49,768	8.9530	$100,468	$134,578
GLP-1 agonists	$56,393	8.9894	$119,919	$181,906
DPP-4 inhibitors	$49,360	8.8998	$178,795	Extended dominance[a]
Basal insulin	$55,321	8.8898	$325,156	Dominated[b]
Biphasic insulin	$64,180	8.9340	$268,519	Dominated[c]

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1 receptor; ICUR = incremental cost-utility ratio; MET = metformin; QALY = quality-adjusted life year; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; vs. = versus.

Note: A dominated strategy is associated with more costs and less benefits than the previous most effective strategy. An extendedly dominated strategy has an ICUR higher than that of the next most effective strategy; therefore, an extendedly dominated strategy produces additional gains in effectiveness at incremental costs higher than those of the next most effective strategy.

[a] Subject to extended dominance through MET and SGLT-2, SU and SGLT-2, MET and GLP-1, SU and GLP-1.

[b] Dominated by DPP-4, SGLT-2.

[c] Dominated by SGLT-2, GLP-1.