Appendix: NMA of comparative efficacy of semaglutide to SGLT-2is in metformin-inadequate patients.

ADDITIONAL METHODS

PICOS statement

Table 1: PICOS study selection criteria

Criteria	Description
Population*	Adults (≥ 18 years of age) with diagnosed type 2 diabetes (T2D) either: • Inadequately controlled with metformin and/or thiazolidinediones (>94% on metformin) • Inadequately controlled with 1–2 oral anti-diabetics (OADs) • Inadequately controlled on basal insulin (with or without OADs)
Interventions	Once-weekly semaglutide 0.5 mg and 1.0 mg
Comparators	SGLT-2is: • Empagliflozin 10 mg and 25 mg once daily • Canagliflozin 100 mg and 300 mg once daily • Dapagliflozin 5 mg and 10 mg once daily Other treatments that are connected with once-weekly once-weekly semaglutide and/or a SGLT-2i
Outcomes	Efficacy: • Proportion of patients achieving composite endpoint (<7% HbA_{1c}, no weight gain and no hypoglyaemia) • Change from baseline in HbA_{1c} • Proportion of patients achieving ≤6.5% • Proportion of patients achieving <7% HbA_{1c} • Change from baseline in fasting plasma glucose (FPG) • Change from baseline in fasting postprandial plasma glucose (PPG) • Change from baseline in weight • Proportion of patients achieving ≥5% weight loss • Proportion of patients achieving ≥10% weight loss • Change from baseline in systolic blood pressure (SBP) • Change from baseline in body mass index (BMI) Safety: • Overall adverse events (AEs) • Treatment-related AEs (TRAEs)

Criteria	Description
	• Serious AEs (SAEs) • Discontinuations due to AEs (DAEs) • Nausea • Vomiting • Diarrhoea • Pancreatitis • Hypoglycemia (overall/ severe/ non-severe/nocturnal)
Study design	Randomized clinical trials (RCTs) with at least a 20-week assessment of efficacy outcomes
Other	English language From 1994 to August 2017†

*† Searches within conferences were conducted up to September 2016; *Additionally, trials that were 100% Asian were later excluded (although, studies with high percentage of Asians were included).*

Search Strategies

In this appendix, we present the specific search strategies for each of the three databases along with the hit counts for each search term. Searches were conducted on three separate occasions:

- April 5th, 2016 for studies reported between January 1st, 1994 to April 4th, 2016.
- October 3rd, 2016 for studies reported between April 5th, 2016 to October 2nd, 2016.
- August 16th, 2017 for studies reported between October 1st to August 15th, 2017.

The specific databases searched on all occasions were:

- **Medline*:** Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to present.
- **Embase***: 1974 to present.
- **Cochrane Central*:** EBM Reviews – Cochrane Central Register of Controlled Trials.

Table 2: Search strategy for EMBASE (January 1, 1994 to April 4, 2016)

Database: EMBASE **Date of search: April 5, 2016** **No.**	**Terms**	**Hits**
1	exp insulin dependent diabetes mellitus/	88360
2	((Type* adj3 ("1" or "I" or one*)) adj3 (diabete* or diabetic*)).ti,ab.	62624
3	((insulin* adj3 depend*) adj3 (diabete* or dibetic*)).ti,ab.	23902
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	64058
5	exp non insulin dependent diabetes mellitus/	171521
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	147535
7	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	163545
8	("niddm" or "t2dm").ti,ab.	26551
9	or/1-8	294456
10	exp neutral insulin/	3345
11	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	381829
12	exp human insulin/	4359
13	exp insulin aspart/	3908
14	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or (insulin aspart protamine plus insulin aspart) or (insulin aspart protamine recombinant plus insulin aspart recombinant) or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	372
15	exp insulin glulisine/	1237
16	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	445
17	exp insulin lispro/	4441
18	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	1602

Database: EMBASE Date of search: April 5, 2016 No.	Terms	Hits
19	exp insulin, short-acting/	764
20	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	1899
21	exp insulin glargine/	7000
22	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	3120
23	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	18
24	exp insulin detemir/	2749
25	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	1095
26	exp Insulin, Isophane/	6698
27	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	2140
28	exp Insulin, Long-Acting/	1516
29	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	2094
30	exp insulin degludec/	658
31	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	544
32	exp Biphasic Insulins/	669
33	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	880
34	exp insulin aspart plus insulin degludec/	35
35	((insulin degludec plus insulin aspart) or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	56
36	exp metformin/ and exp sulfonylurea derivative/	15575
37	exp 2,4 thiazolidinedione derivative/	10866
38	exp glitazone derivative/	30707
39	exp rosiglitazone/	16039
40	exp pioglitazone/	14900
41	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	16651
42	exp balaglitazone/	55
43	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	14
44	exp rivoglitazone/	59
45	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	22
46	exp Dipeptidyl-Peptidase IV Inhibitors/	10853
47	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	3162
48	exp vildagliptin/	2671
49	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	1246
50	exp sitagliptin/	5319

Database: EMBASE Date of search: April 5, 2016 No.	Terms	Hits
51	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	2649
52	exp saxagliptin/	1842
53	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	743
54	exp linagliptin/	1241
55	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	722
56	exp alogliptin/	995
57	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	459
58	exp gosogliptin/	17
59	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	14
60	exp glucagon like peptide 1 derivative/	874
61	exp liraglutide/	4260
62	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	2400
63	exp exenatide/	7274
64	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	4120
65	exp lixisenatide/	502
66	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	299
67	exp albiglutide/	428
68	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	179
69	exp taspoglutide/	201
70	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	95
71	exp dulaglutide/	318
72	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	195
73	exp nateglinide/	2359
74	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	673
75	exp repaglinide/	3178
76	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	939
77	exp mitiglinide/	307
78	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	182
79	exp alpha glucosidase inhibitor/	11682
80	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	4695
81	exp miglitol/	1312
82	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	172
83	exp acarbose/	6228
84	("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 precose or rebose).ti,ab.	131
85	exp voglibose/	925
86	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	63
87	exp sodium glucose cotransporter 2 inhibitor/	2491

Database: EMBASE Date of search: April 5, 2016 No.	Terms	Hits
88	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	1241
89	exp canagliflozin/	793
90	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	533
91	exp dapagliflozin/	1048
92	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	692
93	exp empagliflozin/	583
94	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	409
95	exp bile acid sequestrant/	1070
96	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	484
97	exp colestyramine/	9965
98	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	2790
99	exp colestipol/	2754
100	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	91
101	exp colesevelam/	1103
102	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	105
103	exp colestilan/	223
104	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	92
105	exp dopamine 2 receptor stimulating agent/	2066
106	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	629
107	exp bromocriptine/	19486
108	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	1303
109	exp bromocriptine mesilate/	2424
110	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	15977
111	exp pramlintide/	1181
112	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	73
113	(Empalina or Glyxambi or competact or janumet).ti,ab.	21
114	or/10-113	473993
115	Clinical trial/	859362
116	Randomized controlled trial/	399235
117	Randomization/	69785

Database: EMBASE Date of search: April 5, 2016 No.	Terms	Hits
118	Single blind procedure/	21790
119	Double blind procedure/	129717
120	Crossover procedure/	46573
121	Placebo/	285286
122	Randomi?ed controlled trial$.tw.	132507
123	Rct.tw.	19816
124	Random allocation.tw.	1543
125	Randomly allocated.tw.	24529
126	Allocated randomly.tw.	2117
127	(allocated adj2 random).tw.	831
128	Single blind$.tw.	17382
129	Double blind$.tw.	166720
130	((treble or triple) adj blind$).tw.	558
131	Placebo$.tw.	235298
132	Prospective study/	327502
133	Or/115-132	1573615
134	Case study/	37136
135	Case report.tw.	311905
136	Abstract report/ or letter/	973495
137	Or/134-136	1315633
138	133 not 137	1532383
139	letter.pt.	930767
140	editorial.pt.	504192
141	exp retrospective studies/	455266
142	cohort studies/	154935
143	cohort analysis/	236606
144	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	120481
145	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	469224
146	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or database or comment or clinical conference or catalogs) not ("randomized controlled trial")).pt.	3579389
147	exp Meta Analysis/	106304
148	(meta adj (analy$ or metaanalys$)).tw.	114037
149	(systematic adj (review$1 or overview$1)).tw.	96595
150	(cancerlit or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or "bids" or reference lists or bibliograph$ or hand-search$ or manual search$ or relevant journals or data extraction).ab.	108513
151	review.pt.	2144430
152	animal/	1738059
153	human/	16849272
154	152 not (152 and 153)	1305907
155	or/139-151,154	5822094
156	(9 and 114 and 138) not 155	16345
157	limit 156 to yr="1994-Current"	15292
158	limit 157 to english language	14260

Table 2: Search strategy for MEDLINE (January 1, 1994 to April 4, 2016)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: April 5, 2016		
No.	**Terms**	**Hits**
1	exp Diabetes Mellitus, Type 1/	65068
2	((Type* adj3 ("1" or "I" or one*)) adj3 (diabete* or diabetic*)).ti,ab.	42685
3	((insulin* adj3 depend*) adj3 (diabete* or dibetic*)).ti,ab.	20841
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	46587
5	exp Diabetes Mellitus, Type 2/	97228
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	97465
7	((adult or ketosis-resistant* or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable* or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	110782
8	("niddm" or "t2dm").ti,ab.	16454
9	or/1-8	202319
10	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	292902
11	exp Insulin, Regular, Human/	99
12	exp insulin aspart/	532
13	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or (insulin aspart protamine plus insulin aspart) or (insulin aspart protamine recombinant plus insulin aspart recombinant) or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	197
14	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	223
15	exp insulin lispro/	762
16	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	991
17	exp insulin, short-acting/	1260
18	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	1161
19	exp insulin glargine/	1273
20	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	1532
21	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	2
22	exp insulin detemir/	438
23	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	601
24	exp Insulin, Isophane/	921
25	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	1439
26	exp Insulin, Long-Acting/	3167
27	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	1370

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: April 5, 2016		
No.	**Terms**	**Hits**
28	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	193
29	exp Biphasic Insulins/	196
30	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	634
31	((insulin degludec plus insulin aspart) or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	18
32	exp metformin/ and exp sulfonylurea compounds/	1419
33	exp Thiazolidinediones/	10016
34	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	11309
35	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	8
36	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	12
37	exp Dipeptidyl-Peptidase IV Inhibitors/	2583
38	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	1966
39	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	684
40	exp Sitagliptin Phosphate/	821
41	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	1296
42	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	353
43	exp linagliptin/	199
44	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	341
45	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	255
46	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	6
47	exp Glucagon-Like Peptide 1/	5739
48	exp liraglutide/	729
49	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	1121
50	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	2212
51	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	130
52	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	82
53	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	49
54	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	76
55	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	454
56	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	615
57	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	123
58	exp alpha glucosidase inhibitor/	2594
59	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	3192

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: April 5, 2016		
No.	**Terms**	**Hits**
60	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	131
61	exp acarbose/	1146
62	("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 precose or rebose).ti,ab.	89
63	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	24
64	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	620
65	exp canagliflozin/	149
66	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	253
67	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	300
68	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	202
69	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	358
70	exp colestyramine/	2566
71	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	2282
72	exp colestipol/	389
73	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	72
74	exp colesevelam/	181
75	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	84
76	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	58
77	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	492
78	exp bromocriptine/	6795
79	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	940
80	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	12354
81	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	51
82	(Empalina or Glyxambi or competact or janumet).ti,ab.	14
83	or/10-82	330188
84	Randomized Controlled Trials as Topic/	101986
85	randomized controlled trial/	411394
86	Random Allocation/	86083

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: April 5, 2016		
No.	**Terms**	**Hits**
87	Double Blind Method/	134179
88	Single Blind Method/	21572
89	clinical trial/	498431
90	clinical trial, phase i.pt	15834
91	clinical trial, phase ii.pt	25604
92	clinical trial, phase iii.pt	10892
93	clinical trial, phase iv.pt	1146
94	controlled clinical trial.pt	90380
95	randomized controlled trial.pt	411394
96	multicenter study.pt	197449
97	clinical trial.pt	498431
98	exp Clinical Trials as topic/	289696
99	(clinical adj trial$).tw	252175
100	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw	140524
101	PLACEBOS/	33153
102	placebo$.tw	173802
103	randomly allocated.tw	19964
104	(allocated adj2 random$).tw	22720
105	Or/84-104	1290374
106	case report.tw	231863
107	letter/	909162
108	historical article/	328462
109	or/106-108	1456671
110	105 not 109	1259319
111	letter.pt.	909162
112	editorial.pt.	398301
113	exp retrospective studies/	570693
114	cohort studies/	190418
115	cohort analysis/	190418
116	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	80363
117	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	302983
118	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or database or comment or clinical conference or catalogs) not ("randomized controlled trial")).pt.	4075686
119	Meta-Analysis as Topic/	14664
120	meta analy$.tw.	87737
121	metaanaly$.tw.	1574
122	Meta-Analysis/	63458
123	(systematic adj (review$1 or overview$1)).tw.	77733
124	exp Review Literature as Topic/	8492
125	(cancerlit or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or "bids" or reference lists or bibliograph$ or hand-search$ or manual search$ or relevant journals or data extraction).ab.	88414
126	review.pt.	2087930
127	animal/	5808437
128	human/	15782269
129	127 not (127 and 128)	4179131

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: April 5, 2016		
No.	**Terms**	**Hits**
130	or/111-126,129	8895820
131	(9 and 83 and 110) not 130	11291
132	limit 131 to yr="1994-Current"	9851
133	limit 132 to english language	9377

Table 3: Search strategy for Cochane (January 1, 1994 to March 31, 2016)

Database: Cochrane Central Register of Controlled Trials <March 2016> Date of search: April 5, 2016 No.	Terms	Hits
1	exp Diabetes Mellitus, Type 1/	3214
2	(Type* adj3 ("1" or "I" or one*) adj3 (diabete* or diabetic*)).ti,ab.	3733
3	((insulin* adj3 depend*) adj3 (diabete* or dibetic*)).ti,ab.	1702
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	3873
5	exp Diabetes Mellitus, Type 2/	9230
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	13867
7	((adult or ketosis-resistant* or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable* or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	15212
8	("niddm" or "t2dm").ti,ab.	2853
9	or/1-8	20485
10	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	22136
11	exp Insulin, Regular, Human/	14
12	exp insulin aspart/	201
13	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or (insulin aspart protamine plus insulin aspart) or (insulin aspart protamine recombinant plus insulin aspart recombinant) or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	87
14	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	101
15	exp insulin lispro/	262
16	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	422
17	exp Insulin, Short-Acting/	459
18	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	338
19	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	705
20	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	1
21	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	200
22	exp Insulin, Isophane/	275
23	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	474
24	exp Insulin, Long-Acting/	685
25	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	226
26	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	115
27	exp Biphasic Insulins/	60

Database: Cochrane Central Register of Controlled Trials <March 2016> Date of search: April 5, 2016 No.	Terms	Hits
28	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	139
29	((insulin degludec plus insulin aspart) or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	20
30	exp metformin/ and exp sulfonylurea compounds/	402
31	exp Thiazolidinediones/	1140
32	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	1849
33	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	4
34	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	5
35	exp Dipeptidyl-Peptidase IV Inhibitors/	303
36	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	188
37	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	239
38	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	469
39	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	133
40	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	139
41	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	79
42	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	4
43	exp Glucagon-Like Peptide 1/	608
44	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	328
45	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	350
46	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	50
47	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	39
48	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	21
49	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	56
50	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	170
51	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	171
52	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	28
53	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	615
54	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	33
55	exp Acarbose/	226
56	("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 precose or rebose).ti,ab.	34
57	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	6
58	exp Sodium-Glucose Transporter 2/	88
59	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	203
60	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	103

Database: Cochrane Central Register of Controlled Trials <March 2016> Date of search: April 5, 2016 No.	Terms	Hits
61	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	155
62	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	128
63	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	29
64	exp Cholestyramine Resin/	254
65	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	361
66	exp Colestipol/	86
67	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	24
68	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	31
69	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	30
70	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	41
71	exp Bromocriptine/	455
72	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	60
73	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	1351
74	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	7
75	(Empalina or Glyxambi or competact or janumet).ti,ab.	2
76	or/10-75	26759
77	9 and 76	11576
78	limit 77 to yr="1994-Current"	10047
79	limit 78 to english language	9217

Table 4: Search strategy for EMBASE (April 1, 2016 to October 2, 2016)

Database: EMBASE Date of search: October 3, 2017 No.	Terms	Hits
1	exp insulin dependent diabetes mellitus/	94573
2	((Type* adj3 ("1" or "I" or one*)) adj3 (diabete* or diabetic*)).ti,ab.	66164
3	((insulin* adj3 depend*) adj3 (diabete* or dibetic*)).ti,ab.	24045
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	66945
5	exp non insulin dependent diabetes mellitus/	193075
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	158902
7	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	175056
8	("niddm" or "t2dm").ti,ab.	28853
9	or/1-8	312729
10	exp neutral insulin/	3403
11	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	394788
12	exp human insulin/	12946
13	exp insulin aspart/	4172
14	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or (insulin aspart protamine plus insulin aspart) or (insulin aspart protamine recombinant plus insulin aspart recombinant) or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	393
15	exp insulin glulisine/	1320
16	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	465
17	exp insulin lispro/	4684
18	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	1675
19	exp insulin, short-acting/	1009
20	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	1973
21	exp insulin glargine/	7571
22	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	3356
23	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	18
24	exp insulin detemir/	2937
25	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	1154
26	exp Insulin, Isophane/	7024
27	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	2178
28	exp Insulin, Long-Acting/	1860

Database: EMBASE Date of search: October 3, 2017 No.	Terms	Hits
29	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	2175
30	exp insulin degludec/	808
31	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	643
32	exp Biphasic Insulins/	801
33	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	901
34	exp insulin aspart plus insulin degludec/	49
35	((insulin degludec plus insulin aspart) or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	70
36	exp metformin/ and exp sulfonylurea derivative/	16641
37	exp 2,4 thiazolidinedione derivative/	12413
38	exp glitazone derivative/	32270
39	exp rosiglitazone/	16656
40	exp pioglitazone/	15803
41	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	17406
42	exp balaglitazone/	62
43	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	15
44	exp rivoglitazone/	62
45	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	22
46	exp Dipeptidyl-Peptidase IV Inhibitors/	12402
47	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	3547
48	exp vildagliptin/	2942
49	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	1374
50	exp sitagliptin/	5926
51	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	2957
52	exp saxagliptin/	2107
53	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	841
54	exp linagliptin/	1464
55	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	813
56	exp alogliptin/	1181
57	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	514
58	exp gosogliptin/	17
59	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	14
60	exp glucagon like peptide 1 derivative/	938
61	exp liraglutide/	4950
62	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	2776
63	exp exenatide/	7940
64	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	4402

Database: EMBASE Date of search: October 3, 2017 No.	Terms	Hits
65	exp lixisenatide/	648
66	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	346
67	exp albiglutide/	517
68	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	206
69	exp taspoglutide/	214
70	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	94
71	exp dulaglutide/	433
72	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	254
73	exp nateglinide/	2439
74	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	695
75	exp repaglinide/	3321
76	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	991
77	exp mitiglinide/	335
78	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	190
79	exp alpha glucosidase inhibitor/	12569
80	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	4953
81	exp miglitol/	1380
82	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	177
83	exp acarbose/	6669
84	("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 precose or rebose).ti,ab.	134
85	exp voglibose/	1000
86	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	59
87	exp sodium glucose cotransporter 2 inhibitor/	3374
88	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	1526
89	exp canagliflozin/	1063
90	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	661
91	exp dapagliflozin/	1348
92	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	842
93	exp empagliflozin/	889
94	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	591
95	exp bile acid sequestrant/	1303
96	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	499
97	exp colestyramine/	10107
98	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	2819

Database: EMBASE Date of search: October 3, 2017 No.	Terms	Hits
99	exp colestipol/	2783
100	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	92
101	exp colesevelam/	1175
102	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	106
103	exp colestilan/	237
104	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	95
105	exp dopamine 2 receptor stimulating agent/	2108
106	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	634
107	exp bromocriptine/	19816
108	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	1309
109	exp bromocriptine mesilate/	2454
110	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	16265
111	exp pramlintide/	1254
112	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	72
113	(Empalina or Glyxambi or competact or janumet).ti,ab.	24
114	or/10-113	494188
115	Clinical trial/	976474
116	Randomized controlled trial/	453207
117	Randomization/	82582
118	Single blind procedure/	25945
119	Double blind procedure/	136233
120	Crossover procedure/	53107
121	Placebo/	322901
122	Randomi?ed controlled trial$.tw.	146179
123	Rct.tw.	21841
124	Random allocation.tw.	1615
125	Randomly allocated.tw.	26254
126	Allocated randomly.tw.	2194
127	(allocated adj2 random).tw.	848
128	Single blind$.tw.	18437
129	Double blind$.tw.	173010
130	((treble or triple) adj blind$).tw.	625
131	Placebo$.tw.	245847
132	Prospective study/	378077

Database: EMBASE Date of search: October 3, 2017 No.	Terms	Hits
133	Or/115-132	1748523
134	Case study/	91139
135	Case report.tw.	322101
136	Abstract report/ or letter/	998955
137	Or/134-136	1403200
138	133 not 137	1698561
139	letter.pt.	953734
140	editorial.pt.	516852
141	exp retrospective studies/	500998
142	cohort studies/	155541
143	cohort analysis/	292412
144	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	133635
145	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	510631
146	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or database or comment or clinical conference or catalogs) not ("randomized controlled trial")).pt.	3657760
147	exp Meta Analysis/	148616
148	(meta adj (analy$ or metaanalys$)).tw.	128433
149	(systematic adj (review$1 or overview$1)).tw.	110799
150	(cancerlit or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or "bids" or reference lists or bibliograph$ or hand-search$ or manual search$ or relevant journals or data extraction).ab.	122159
151	review.pt.	2187174
152	animal/	1736531
153	human/	17854804
154	152 not (152 and 153)	1320503
155	or/139-151,154	6022212
156	(9 and 114 and 138) not 155	18534
157	limit 156 to dd=20160401-20161003	764
158	limit 157 to english language	736

Table 5: Search strategy for MEDLINE (April 1, 2016 to October 2, 2016)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: October 3, 2016		
No.	**Terms**	**Hits**
1	exp Diabetes Mellitus, Type 1/	67679
2	((Type* adj3 ("1" or "I" or one*)) adj3 (diabete* or diabetic*)).ti,ab.	45985
3	((insulin* adj3 depend*) adj3 (diabete* or dibetic*)).ti,ab.	21259
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	49532
5	exp Diabetes Mellitus, Type 2/	103432
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	107173
7	((adult or ketosis-resistant* or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable* or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	120749
8	("niddm" or "t2dm").ti,ab.	18187
9	or/1-8	217065
10	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	308581
11	exp Insulin, Regular, Human/	121
12	exp insulin aspart/	562
13	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or (insulin aspart protamine plus insulin aspart) or (insulin aspart protamine recombinant plus insulin aspart recombinant) or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	209
14	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	243
15	exp insulin lispro/	789
16	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	1044
17	exp insulin, short-acting/	1320
18	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	1237
19	exp insulin glargine/	1360
20	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	1663
21	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	3
22	exp insulin detemir/	461
23	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	629
24	exp Insulin, Isophane/	950
25	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	1486
26	exp Insulin, Long-Acting/	3323
27	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	1425

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: October 3, 2016		
No.	**Terms**	**Hits**
28	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	254
29	exp Biphasic Insulins/	199
30	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	661
31	((insulin degludec plus insulin aspart) or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	34
32	exp metformin/ and exp sulfonylurea compounds/	1498
33	exp Thiazolidinediones/	10466
34	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	12026
35	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	9
36	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	12
37	exp Dipeptidyl-Peptidase IV Inhibitors/	2860
38	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	2245
39	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	770
40	exp Sitagliptin Phosphate/	916
41	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab	1503
42	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	428
43	exp linagliptin/	219
44	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	408
45	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	303
46	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	6
47	exp Glucagon-Like Peptide 1/	6243
48	exp liraglutide/	860
49	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	1356
50	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	2445
51	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	168
52	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	99
53	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	52
54	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	111
55	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	470
56	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	652
57	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	125
58	exp alpha glucosidase inhibitor/	2704
59	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	3429

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: October 3, 2016		
No.	**Terms**	**Hits**
60	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	134
61	exp acarbose/	1180
62	("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 precose or rebose).ti,ab.	91
63	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	25
64	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	830
65	exp canagliflozin/	208
66	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	352
67	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	385
68	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	318
69	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	386
70	exp colestyramine/	2592
71	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	2344
72	exp colestipol/	392
73	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	73
74	exp colesevelam/	187
75	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	84
76	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	59
77	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	506
78	exp bromocriptine/	6877
79	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	946
80	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	12780
81	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	52
82	(Empalina or Glyxambi or competact or janumet).ti,ab.	15
83	or/10-82	348178
84	Randomized Controlled Trials as Topic/	110345
85	randomized controlled trial/	432375

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: October 3, 2016		
No.	**Terms**	**Hits**
86	Random Allocation/	89125
87	Double Blind Method/	139606
88	Single Blind Method/	22897
89	clinical trial/	506218
90	clinical trial, phase i.pt	16723
91	clinical trial, phase ii.pt	27221
92	clinical trial, phase iii.pt	11967
93	clinical trial, phase iv.pt	1247
94	controlled clinical trial.pt	91772
95	randomized controlled trial.pt	432375
96	multicenter study.pt	212194
97	clinical trial.pt	506218
98	exp Clinical Trials as topic/	302908
99	(clinical adj trial$).tw	276423
100	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw	148376
101	PLACEBOS/	33716
102	placebo$.tw	185373
103	randomly allocated.tw	21572
104	(allocated adj2 random$).tw	24443
105	Or/84-104	1364655
106	case report.tw	247959
107	letter/	943277
108	historical article/	339712
109	or/106-108	1517522
110	105 not 109	1332535
111	letter.pt.	943277
112	editorial.pt.	420398
113	exp retrospective studies/	607756
114	cohort studies/	205642
115	cohort analysis/	205642
116	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	91191
117	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	333856
118	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or database or comment or clinical conference or catalogs) not ("randomized controlled trial")).pt.	4271481
119	Meta-Analysis as Topic/	15430
120	meta analy$.tw.	103091
121	metaanaly$.tw.	1693
122	Meta-Analysis/	74054
123	(systematic adj (review$1 or overview$1)).tw.	92292
124	exp Review Literature as Topic/	9102
125	(cancerlit or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or "bids" or reference lists or bibliograph$ or hand-search$ or manual search$ or relevant journals or data extraction).ab.	104580

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: October 3, 2016		
No.	**Terms**	**Hits**
126	review.pt.	2198554
127	animal/	5991665
128	human/	16364890
129	127 not (127 and 128)	4290916
130	or/111-126,129	9270672
131	(9 and 83 and 110) not 130	12039
132	limit 131 to ed=20160401-20161003	394
133	limit 132 to english language	365

Table 6: Search strategy for Cochrane (April 1, 2016 to September 30, 2016)

Database: Cochrane Central Register of Controlled Trials <September 2016> Date of search: October 3, 2017 No.	Terms	Hits
1	exp Diabetes Mellitus, Type 1/	3271
2	(Type* adj3 ("1" or "I" or one*) adj3 (diabete* or diabetic*)).ti,ab.	3953
3	(insulin* adj3 depend* adj3 (diabete* or dibetic*)).ti,ab.	1710
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	4060
5	exp Diabetes Mellitus, Type 2/	9493
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	14717
7	((adult or ketosis-resistant* or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable* or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	16063
8	("niddm" or "t2dm").ti,ab.	3045
9	or/1-8	21576
10	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	23014
11	exp Insulin, Regular, Human/	20
12	exp insulin aspart/	201
13	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or (insulin aspart protamine plus insulin aspart) or (insulin aspart protamine recombinant plus insulin aspart recombinant) or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	93
14	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	104
15	exp insulin lispro/	266
16	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	440
17	exp Insulin, Short-Acting/	463
18	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	349
19	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	761
20	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	3
21	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	212
22	exp Insulin, Isophane/	278
23	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	482
24	exp Insulin, Long-Acting/	694
25	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	232
26	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	145
27	exp Biphasic Insulins/	60

Database: Cochrane Central Register of Controlled Trials <September 2016> Date of search: October 3, 2017 No.	Terms	Hits
28	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	146
29	((insulin degludec plus insulin aspart) or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	23
30	exp metformin/ and exp sulfonylurea compounds/	408
31	exp Thiazolidinediones/	1157
32	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	1906
33	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	4
34	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	5
35	exp Dipeptidyl-Peptidase IV Inhibitors/	312
36	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	206
37	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	249
38	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	512
39	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	151
40	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	152
41	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	87
42	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	5
43	exp Glucagon-Like Peptide 1/	630
44	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	406
45	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	384
46	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	56
47	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	43
48	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	21
49	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	63
50	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	173
51	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	173
52	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	30
53	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	630
54	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	33
55	exp Acarbose/	227
56	("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 precose or rebose).ti,ab.	34
57	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	6
58	exp Sodium-Glucose Transporter 2/	94
59	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	228

Database: Cochrane Central Register of Controlled Trials <September 2016> Date of search: October 3, 2017 No.	Terms	Hits
60	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	125
61	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	180
62	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	144
63	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	29
64	exp Cholestyramine Resin/	254
65	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	363
66	exp Colestipol/	86
67	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	24
68	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	31
69	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	30
70	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	44
71	exp Bromocriptine/	459
72	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	60
73	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	1366
74	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	7
75	(Empalina or Glyxambi or competact or janumet).ti,ab.	2
76	or/10-75	27841
77	9 and 76	12159
78	limit 77 to up=201604-201610	645
79	limit 78 to english language	617

Table 7: Search strategy for EMBASE (October 1, 2016 to August 15, 2017)

Database: EMBASE Date of search: August 16, 2017 No.	Terms	Hits
1	exp insulin dependent diabetes mellitus/	99433
2	(Type* adj3 ("1" or "I" or one*) adj3 (diabete* or diabetic*)).ti,ab.	72918
3	(insulin* adj3 depend* adj3 (diabete* or dibetic*)).ti,ab.	24389
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	72660
5	exp non insulin dependent diabetes mellitus/	204226
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	179514
7	((adult or ketosis-resistant or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	196013
8	("niddm" or "t2dm").ti,ab.	33387
9	or/1-8	343362
10	exp neutral insulin/	3418
11	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	423271
12	exp human insulin/	4738
13	exp insulin aspart/	4440
14	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or insulin aspart protamine plus insulin aspart or insulin aspart protamine recombinant plus insulin aspart recombinant or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	413
15	exp insulin glulisine/	1397
16	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	498
17	exp insulin lispro/	4943
18	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	1799
19	exp insulin, short-acting/	1015
20	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	2129
21	exp insulin glargine/	8376
22	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	3793
23	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	28
24	exp insulin detemir/	3172
25	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	1255
26	exp Insulin, Isophane/	7151
27	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	2296
28	exp Insulin, Long-Acting/	1696

Database: EMBASE Date of search: August 16, 2017 No.	Terms	Hits
29	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	2327
30	exp insulin degludec/	979
31	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	818
32	exp Biphasic Insulins/	721
33	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	951
34	exp insulin aspart plus insulin degludec/	67
35	(insulin degludec plus insulin aspart or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	79
36	exp metformin/ and exp sulfonylurea derivative/	17849
37	exp 2,4 thiazolidinedione derivative/	11752
38	exp glitazone derivative/	33871
39	exp rosiglitazone/	17254
40	exp pioglitazone/	16721
41	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	18631
42	exp balaglitazone/	66
43	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	21
44	exp rivoglitazone/	62
45	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	24
46	exp Dipeptidyl-Peptidase IV Inhibitors/	14391
47	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	4130
48	exp vildagliptin/	3213
49	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	1555
50	exp sitagliptin/	6662
51	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	3424
52	exp saxagliptin/	2411
53	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	987
54	exp linagliptin/	1770
55	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	1001
56	exp alogliptin/	1378
57	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	599
58	exp gosogliptin/	17
59	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	14
60	exp glucagon like peptide 1 derivative/	1029
61	exp liraglutide/	6001
62	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	3552
63	exp exenatide/	8614
64	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	4962

Database: EMBASE Date of search: August 16, 2017 No.	Terms	Hits
65	exp lixisenatide/	906
66	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	495
67	exp albiglutide/	634
68	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	261
69	exp taspoglutide/	226
70	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	99
71	exp dulaglutide/	616
72	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	373
73	exp nateglinide/	2499
74	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	719
75	exp repaglinide/	3477
76	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	1058
77	exp mitiglinide/	346
78	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	199
79	exp alpha glucosidase inhibitor/	13321
80	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	5557
81	exp miglitol/	1425
82	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	182
83	exp acarbose/	7068
84	("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 precose or rebose).ti,ab.	136
85	exp voglibose/	1043
86	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	59
87	exp sodium glucose cotransporter 2 inhibitor/	5083
88	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	2260
89	exp canagliflozin/	1534
90	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	948
91	exp dapagliflozin/	1872
92	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	1199
93	exp empagliflozin/	1603
94	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	1060
95	exp bile acid sequestrant/	1274
96	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	543
97	exp colestyramine/	10322
98	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	2941
99	exp colestipol/	2818

Database: EMBASE Date of search: August 16, 2017 No.	Terms	Hits
100	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	93
101	exp colesevelam/	1227
102	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	106
103	exp colestilan/	243
104	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	100
105	exp dopamine 2 receptor stimulating agent/	2129
106	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	662
107	exp bromocriptine/	20104
108	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	1320
109	exp bromocriptine mesilate/	2467
110	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	16804
111	exp pramlintide/	1311
112	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	78
113	(Empalina or Glyxambi or competact or janumet).ti,ab.	30
114	or/10-113	526295
115	Clinical trial/	959136
116	Randomized controlled trial/	478804
117	Randomization/	76038
118	Single blind procedure/	29992
119	Double blind procedure/	144489
120	Crossover procedure/	53856
121	Placebo/	316121
122	Randomi?ed controlled trial$.tw.	170235
123	Rct.tw.	26180
124	Random allocation.tw.	1761
125	Randomly allocated.tw.	28944
126	Allocated randomly.tw.	2305
127	(allocated adj2 random).tw.	873
128	Single blind$.tw.	20337
129	Double blind$.tw.	184110
130	((treble or triple) adj blind$).tw.	752
131	Placebo$.tw.	264329
132	Prospective study/	411683
133	or/115-132	1848608
134	Case study/	50729
135	Case report.tw.	352037

Database: EMBASE Date of search: August 16, 2017 No.	Terms	Hits
136	Abstract report/ or letter/	1038452
137	or/134-136	1432976
138	133 not 137	1801662
139	letter.pt.	995969
140	editorial.pt.	550966
141	exp retrospective studies/	590069
142	cohort studies/	212908
143	cohort analysis/	328184
144	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	159338
145	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	592540
146	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or database or comment or clinical conference or catalogs) not "randomized controlled trial").pt.	3874720
147	exp Meta Analysis/	136183
148	(meta adj (analy$ or metaanalys$)).tw.	154441
149	(systematic adj (review$1 or overview$1)).tw.	136877
150	(cancerlit or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or "bids" or reference lists or bibliograph$ or hand-search$ or manual search$ or relevant journals or data extraction).ab.	147329
151	review.pt.	2327785
152	animal/	1817762
153	human/	18960310
154	152 not (152 and 153)	1383706
155	or/139-151,154	6481503
156	(9 and 114 and 138) not 155	19935
157	limit 156 to dd=20161001-20170816	1920
158	limit 157 to english language	1894

Table 8: Search strategy for MEDLINE (October 1, 2016 to August 15, 2017)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: August 16, 2017		
No.	**Terms**	**Hits**
1	exp Diabetes Mellitus, Type 1/	75334
2	(Type* adj3 ("1" or "I" or one*) adj3 (diabete* or diabetic*)).ti,ab.	53012
3	(insulin* adj3 depend* adj3 (diabete* or dibetic*)).ti,ab.	23255
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	56256
5	exp Diabetes Mellitus, Type 2/	119368
6	exp Diabetes Mellitus, Type 1/	75334
7	(Type* adj3 ("1" or "I" or one*) adj3 (diabete* or diabetic*)).ti,ab.	53012
8	(insulin* adj3 depend* adj3 (diabete* or dibetic*)).ti,ab.	23255
9	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	56256
10	exp Diabetes Mellitus, Type 2/	119368
11	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	125269
12	((adult or ketosis-resistant* or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable* or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	140065
13	("niddm" or "t2dm").ti,ab.	21585
14	or/6-13	247118
15	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	340809
16	exp Insulin, Regular, Human/	148
17	exp insulin aspart/	644
18	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or insulin aspart protamine plus insulin aspart or insulin aspart protamine recombinant plus insulin aspart recombinant or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	225
19	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	284
20	exp insulin lispro/	856
21	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	1120
22	exp insulin, short-acting/	1499
23	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	1400
24	exp insulin glargine/	1625
25	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	1999
26	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	9
27	exp insulin detemir/	546
28	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	718
29	exp Insulin, Isophane/	1033
30	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or	1607

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: August 16, 2017		
No.	**Terms**	**Hits**
	hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	
31	exp Insulin, Long-Acting/	3807
32	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	1583
33	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	371
34	exp Biphasic Insulins/	227
35	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	718
36	(insulin degludec plus insulin aspart or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	46
37	exp metformin/ and exp sulfonylurea compounds/	1717
38	exp Thiazolidinediones/	11320
39	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	13246
40	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	12
41	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	13
42	exp Dipeptidyl-Peptidase IV Inhibitors/	3662
43	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	2757
44	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	914
45	exp Sitagliptin Phosphate/	1157
46	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	1838
47	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	534
48	exp linagliptin/	306
49	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	528
50	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	367
51	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	6
52	exp Glucagon-Like Peptide 1/	7460
53	exp liraglutide/	1204
54	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	1863
55	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	2898
56	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	275
57	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	142
58	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	62
59	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	170
60	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	493

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: August 16, 2017		
No.	**Terms**	**Hits**
61	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	721
62	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	138
63	exp alpha glucosidase inhibitor/	3190
64	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	4045
65	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	146
66	exp acarbose/	1314
67	("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 precose or rebose).ti,ab.	96
68	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	28
69	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	1306
70	exp canagliflozin/	335
71	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	536
72	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	570
73	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	605
74	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	435
75	exp colestyramine/	2808
76	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	2604
77	exp colestipol/	432
78	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	81
79	exp colesevelam/	208
80	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	87
81	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	63
82	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	546
83	exp bromocriptine/	7457
84	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	1020
85	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	13919

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: August 16, 2017		
No.	**Terms**	**Hits**
86	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	58
87	(Empalina or Glyxambi or competact or janumet).ti,ab.	19
88	or/15-87	385446
89	Randomized Controlled Trials as Topic/	122014
90	randomized controlled trial/	497753
91	Random Allocation/	99753
92	Double Blind Method/	157698
93	Single Blind Method/	26614
94	clinical trial/	548201
95	clinical trial, phase i.pt.	20061
96	clinical trial, phase ii.pt.	32352
97	clinical trial, phase iii.pt.	15343
98	clinical trial, phase iv.pt.	1635
99	controlled clinical trial.pt.	99278
100	randomized controlled trial.pt.	497753
101	multicenter study.pt.	249622
102	clinical trial.pt.	548201
103	exp Clinical Trials as topic/	332580
104	(clinical adj trial$).tw.	322095
105	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	167927
106	PLACEBOS/	36441
107	placebo$.tw.	209384
108	randomly allocated.tw.	25117
109	(allocated adj2 random$).tw.	28281
110	or/89-109	1544067
111	case report.tw.	275839
112	letter/	1024285
113	historical article/	356206
114	or/111-113	1641756
115	110 not 114	1508913
116	letter.pt.	1024285
117	editorial.pt.	464772
118	exp retrospective studies/	709964
119	cohort studies/	233640
120	cohort analysis/	233640
121	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab.	111041
122	(retrospective adj7 (study or studies or design or analysis or analyses or cohort or data or review)).ti,ab.	392808
123	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or database or comment or clinical conference or catalogs) not "randomized controlled trial").pt.	4686839
124	Meta-Analysis as Topic/	17171
125	meta analy$.tw.	128678
126	metaanaly$.tw.	1925
127	Meta-Analysis/	92162
128	(systematic adj (review$1 or overview$1)).tw.	118135
129	exp Review Literature as Topic/	10205

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) Date of search: August 16, 2017		
No.	**Terms**	**Hits**
130	(cancerlit or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or "bids" or reference lists or bibliograph$ or hand-search$ or manual search$ or relevant journals or data extraction).ab.	129079
131	review.pt.	2446279
132	animal/	6514291
133	human/	17835009
134	132 not (132 and 133)	4647558
135	or/116-131,134	10182129
136	(14 and 88 and 115) not 135	14296
137	limit 136 to yr="1994-Current"	12648
138	limit 137 to english language	12093
139	limit 138 to ed=20161001-20170816	797

Table 9: Search strategy for Cochrane (October 1, 2016 to July 31, 2017)

Database: Cochrane Central Register of Controlled Trials <July 2017> Date of search: August 16, 2017 No.	Terms	Hits
1	exp Diabetes Mellitus, Type 1/	3441
2	(Type* adj3 ("1" or "I" or one*) adj3 (diabete* or diabetic*)).ti,ab.	4718
3	(insulin* adj3 depend* adj3 (diabete* or dibetic*)).ti,ab.	1757
4	(type 1 diabete$ or type 1 diabetic* or diabetes mellitus, type 1 or juvenile diabete$ or insulin dependent diabete$ mellitus).ti,ab.	4685
5	exp Diabetes Mellitus, Type 2/	10476
6	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*)).ti,ab.	18033
7	((adult or ketosis-resistant* or matur* or late or non-insulin depend* or noninsulin depend* or non insulin* or slow or stable* or "type 2" or "type II" or lipoatrophic) adj3 (diabete* or diabetic*)).ti,ab.	19417
8	("niddm" or "t2dm").ti,ab.	3823
9	or/1-8	25691
10	(actrapid or berlinsulin or endopancrine or hoe 21 gh or hoe 21 ph or humulin s or insulin recombinant purified human or insulin or novo actrapid or novoactrapid or insulin novopen or nuralin or orgasuline or umuline velasulin or velosulin or velosulin br or velosulin br human).ti,ab.	26491
11	exp Insulin, Regular, Human/	28
12	exp insulin aspart/	232
13	(insulin aspart protamine or "NovoLOG Mix 70/30" or "NovoLog Mix 70/30 FlexPen" or "NovoLog Mix 70/30 PenFill" or "b28 asp insulin" or "insulin b28asp" or "b28-asp-insulin" or "b28asp insulin" or "biphasic insulin aspart 30" or insulin aspart protamine plus insulin aspart or insulin aspart protamine recombinant plus insulin aspart recombinant or insulin aspart recombinant or novolog innolet or novolog mix or "novolog mix 50/50" or "novomix 30" or novorapid or novorapide or novo?rapid or (faster?acting adj2 aspart)).ti,ab.	107
14	(insulin glulisine or glulisine insulin or Glulisine or Apidra or apidra solostar or insulin glulisine recombinant).ti,ab.	113
15	exp insulin lispro/	277
16	(Lispro or Lyspro or Humalog or Liprolog or insulin lispro humalog or "lispro eli lilly brand of insulin lispro" or "28b-lys-29b-pro-insulin" or "insulin lysyl28b-prolyl28b-" or lispro insulin or lyspro insulin or "lys28b-pro29b-").ti,ab.	491
17	exp Insulin, Short-Acting/	507
18	(short acting insulin* or short-acting insulin or insulin short-acting or quick acting insulin* or rapid acting insulin* or rapid-acting insulin or rapidly acting insulin* or fast acting insulin* or quick acting analog* or rapid acting analog* or rapidly acting analog* or short acting analog* or fast acting analog* or insulin rapid-acting).ti,ab.	403
19	((insulin adj2 glargine*) or abasria or lantus or to?jeo or abasaglar or Lantus OptiClik Cartridge or Lantus Solostar Pen or basaglar or glargine insulin or hoe901 or hoe 901 or lantus solostar or "ly 2963016" or "ly2963016" or optisulin or optisulin depot or optisulin long or trujeo).ti,ab.	941
20	((biosimilar adj2 glargine) or lantus solostar).ti,ab.	4
21	((insulin adj2 detemir) or insulin detemir or insulin detemir recombinant or levemir or levemir flexpen or levemir flextouch or levemir innolet or levemir penfill or "nn 304" or "nn304").ti,ab.	250
22	exp Insulin, Isophane/	292
23	(NPH insulin or insulin NPH or Humulin or Novolin or novolin$ge or humalog or "Humulin N" or "Novolin N" or Insulin isophane or zinc insulin protamine or neutral protamine hagedorn insulin or hagedorn insulin protamine or isophane insulin regular or isophane insulin or protamine zinc insulin or regular isophane insulin or protamine hagedorn insulin or insulin protamine zinc or insulin isophane).ti,ab.	515
24	exp Insulin, Long-Acting/	738
25	(long acting insulin* or long acting analog* or intermediate acting insulin* or intermediate acting analog* or slow* acting insulin* or slow* acting analog* or insulin semilente or long acting insulin or insulin long acting or insulin long-acting or semilente insulin or long-acting insulin).ti,ab.	259
26	(degludec or degludec insulin or insulin degludec? or tresiba or "IDeg" or "nn 1250" or "nn1250").ti,ab.	221
27	exp Biphasic Insulins/	72

Database: Cochrane Central Register of Controlled Trials <July 2017> Date of search: August 16, 2017 No.	Terms	Hits
28	((biphasic adj2 insulin*) or novomix or insulin novo rapitard or rapitard or rapitard insulin or rapitard mc or "humulin$ 70/30" or "humulin$ 50/50" or "novolin?ge 10/90" or "novolin?ge 20/80" or "novolin?ge 30/70" or "novolin?ge 40/60" or "novolin?ge 50/50" or "novolog? mix 70/30" or "humalog? mix 75/25" or "humalog? mix 50/50").ti,ab.	169
29	(insulin degludec plus insulin aspart or IDegAsp or ryzodeg or "nn 5401" or "nn5401" or degludecplus).ti,ab.	43
30	exp metformin/ and exp sulfonylurea compounds/	441
31	exp Thiazolidinediones/	1206
32	(glitazone* or thiazolidinedione* or pioglitazone* or rosiglitazone* or actos or avandia or avandamet or avandaryl).ti,ab.	2128
33	(balaglitazone* or "drf 2593" or "drf2593" or "nn 2344" or "nn2344").ti,ab.	9
34	("cs 011" or "cs011" or "rivoglitazone" or rivoglitazone hydrochloride).ti,ab.	5
35	exp Dipeptidyl-Peptidase IV Inhibitors/	371
36	((dpp adj IV adj inhibitor*) or (Dipeptidyl-Peptidase adj IV adj inhibitor*) or DPP-4 inhibitors or dipeptidyl peptidase-4 inhibitors).ti,ab.	325
37	(vildagliptin or galvus or jalra or xiliarx or "laf-237" or "laf 237" or "laf237" or "nvp laf-237" or "nvp laf 237" or "nvp laf237" or gliptin or incretin agent*).ti,ab.	314
38	("sitagliptin?" or Januvia or Janumet or "mk 0431" or "mk 431" or "mk0431" or "mk431" or "ono 5435" or "ono5435" or ristaben or sitagliptin phosphate or sitagliptin phosphate monohydrate or tesavel or xelevia).ti,ab.	719
39	("saxagliptin?" or Onglyza or saxagliptin hydrochloride or saxagliptin monohydrate or "bms 477118" or "bms-477118" or "bms477118" or 3-hydroxyadamantylglycine-4,5-methanoprolinenitrile).ti,ab.	193
40	(linagliptin or Tradjenta or Trajenta or "BI-1356" or "BI1356" or "BI 1356" or ondero).ti,ab.	216
41	(alogliptin or "SYR-322" or "SYR322" or Nesina or dutogliptin or vipidia or alogliptin benzoate).ti,ab.	113
42	(gosogliptin or "pf 734200" or "pf734200").ti,ab.	6
43	exp Glucagon-Like Peptide 1/	717
44	("liraglutide?" or victoza or saxenda or "nn 2211" or "nn2211").ti,ab.	686
45	("exenatide?" or exendin 4 or "ac 2993" or "ac 2993a" or "ac2993" or "ac2993a" or bydureon or byetta or exenatide synthetic or "ly 2148568" or "ly2148568").ti,ab.	513
46	("lixisenatide?" or "ave 0010" or "ave0010" or lyxumia or "zp 10" or "zp10").ti,ab.	88
47	(albiglutide or eperzan or tanzeum or syncria or naliglutide or albugon).ti,ab.	58
48	("taspoglutide?" or "R-1583" or "R1583" or "BIM51077" or "BIM-51077" or "itm 077" or "itm077" or "r 1583" or "r1583" or "ro 5073031" or "ro5073031").ti,ab.	21
49	("dulaglutide?" or "ly 2189265" or "ly2189265" or trulicity).ti,ab.	99
50	("nateglinide?" or "a 4166" or "a4166" or "ay 4166" or "ay4166" or "djn 608" or "djn608" or fastic or glinate or "sdz djn 608" or "sdz djn608" or senaglinide or starlix or starsis or trazec or "ym 026" or "ym026").ti,ab.	185
51	("repaglinide?" or "2 ethoxy 4" or actulin or "ag ee 388" or "ag ee 623" or "ag ee 623 zw" or "ag ee388" or "ag ee623" or "ag ee623 zw" or "ag-ee623zw" or enyglid or gluconorm or novonorm or prandin or rapilan or sestrine or surepost or novonorm).ti,ab.	188
52	("mitiglinide?" or glufast or "kad 1229" or "kad1229" or "mitiglinide calcium" or "mitiglinide calcium hydrate" or "s 21403" or "s21403").ti,ab.	33
53	((alph* adj glucos* adj inhibit*) or (alf* adj glucos* adj inhibit*) or acarbose or glucobay or precose or prandase or akarbose or "miglitol*" or glyset or diastabol or voglibose).ti,ab.	723
54	("bay 1099" or "bay m 1099" or "bay m1099" or "bay1099" or diastabol or glyset or nojirimycin).ti,ab.	35
55	exp Acarbose/	243
56	("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 precose or rebose).ti,ab.	39
57	("ao 128" or "ao128" or basen or "en 116 077" or "en 116077" or "en116 077" or "en116077" or glustat).ti,ab.	6
58	exp Sodium-Glucose Transporter 2/	122
59	("sodium glucose co-transporter 2 inhibitor?" or "gliflozin*" or gliflozin derivative or gliflozins or "SGLT2 inhibitor" or "SGLT2 inhibitors").ti,ab.	349
60	("canagliflozin?" or invokana or "jnj 28431754" or "jnj28431754" or "ta 7284" or "ta7284").ti,ab.	191

Database: Cochrane Central Register of Controlled Trials <July 2017> Date of search: August 16, 2017 No.	Terms	Hits
61	("dapagliflozin?" or "bms 512148" or "bms512148" or dapagliflozin propanediol or dapagliflozin propanediol monohydrate or farxiga or forxiga).ti,ab.	260
62	("empagliflozin?" or "bi 10773" or "bi10773" or "1,5 anhydro 1" or "1,5 anhydro 1 c" or jardiance).ti,ab.	245
63	(bile acid sequestering agent or bile acid sequestrants).ti,ab.	34
64	exp Cholestyramine Resin/	255
65	(chol-less or choles or cholesthexal or cholestyramin or cholestyramine or cholestyramine chloride or cholestyramine light or cholestyramine resin or cholybar or cholytar or colestepril or colestiramina or colestran or colestrol or colestyramin or cuemid or lipocol-merz or lismol or locholest or locholest light or prevalite or quantalan or quantalan zuckerfrei or questran or questran light or questran lite or questran loc or resincoles-tiramina or resincolestiramina or vasosan p-granulat or vasosan s-granulat).ti,ab.	368
66	exp Colestipol/	86
67	(cholestabyl or cholestipol or colestid or colestid flavored or colestipol hydrochloride or diethylenetriamine epichlorohydrin copolymer or "diethylenetriamine polymer with 1 chloro 2,3 epoxypropane" or "epichlorohydrin copolymer with diethylenetriamine" or flavored colestid or lestid or "u 26,597a" or "u 26597 a" or "u 26597a" or "u-26,597a").ti,ab.	24
68	(cholestagel or colesevelam hydrochloride or "gt 31 104" or "gt 31 104hb" or "gt 31-104" or "gt 31-104hb" or "gt31 104" or "gt31 104hb" or "gt31-104" or "gt31-104hb" or welchol).ti,ab.	31
69	(bindren or cholebine or colestilan chloride or colestimide or "mci 196" or "mci196").ti,ab.	32
70	("agonist,dopamine d2" or "dopamine 2 agonist" or "dopamine 2 receptor agonist" or "dopamine 2 receptor stimulator" or "dopamine D2 agonist" or "dopamine D2 receptor agonist" or "dopamine D2 receptor stimulating agent" or "dopamine D2 receptor stimulator").ti,ab.	50
71	exp Bromocriptine/	462
72	("2 bromo alpha ergocriptine" or "2 bromo alpha ergocryptin" or "2 bromo alpha ergocryptine" or "2 bromoergocryptine" or antipark or bromed or bromergon or bromocriptin or bromocryptine or bromoergocriptine or bromoergocryptine or bromokin or bromopar or "cb 154" or "cb154" or ergobromocriptine or ergoset or serocryptin).ti,ab.	60
73	("2 bromo alpha ergocriptine mesilate" or "2 bromo alpha ergocryptine mesylate" or "2 bromo alpha ergokryptine methanesulfonate" or alpha-bromocriptine or antilactin or apo-bromocriptine or axialit or bagren or barlolin or brameston or brocaden or bromidine or bromo-kin or bromocorn or bromocrel or bromocriptine or mesylate or bromocriptine methanesulfonate or bromocryptine mesylate or bromocryptine methanesulfonate or bromohexal or butin or "cb 154 mesylate" or cryocriptina or cycloset or demil or deprolac or diken or elkrip or ergolactin or kripton or lactismine or medocriptine or parilac or parlodel or "parlodel la" or "parlodel lar" or "parlodel p" or parlodel snaptabs or pravidel or provasyn or ronalin or suplac or umprel or zolac).ti,ab.	1436
74	("ac 137" or "ac137" or pramlintide acetate or symlin).ti,ab.	7
75	(Empalina or Glyxambi or competact or janumet).ti,ab.	2
76	or/10-75	32230
77	9 and 76	14407
78	limit 77 to yr="1994-Current"	12858
79	limit 78 to english language	10533
80	limit 79 to up=201610-201708	1551

Data conversion

For categorical variables, typically dichotomous, conversions consisted of calculating unreported proportions or event counts. If the number of patients with an event was reported without a percentage, it was divided by the sample size, multiplied by 100 and rounded to one or two decimal places to obtain the percentage. In cases where number of events was not reported, but a percentage or proportion was, the number of events was calculated from this information by multiplying the proportion/percentage by the total sample size. The value was rounded to the nearest whole number.

For continuous outcomes, the standard error was converted based on the following formulae:

- *Standard deviations*
  - $SE = SD/\sqrt{N}$
- *95% confidence intervals*
  - $SE = \frac{upper\ limit - lower\ limit}{3.92}$
- *Inter-quartile range*
  - $SE = (\frac{upper\ limit - lower\ limit}{1.35}) /\sqrt{N}$
- *Range*
  - $SE = (\frac{upper\ limit - lower\ limit}{5}) /\sqrt{N}$
- *P-values from absolute difference measures*
  - *SE = effect estimate / Z, where Z is the standard normal deviate corresponding to the reported p-value*

Similarly, for patient characteristics, measures of dispersion (confidence intervals, standard ranges, etc.), were converted to standard deviations by using slightly modified versions of the equations above.

In cases where change from baseline was not reported but measurements at baseline and time of measurement were provided, the difference in measures of the endpoint was used as a measure of change. In such cases, the standard error of change was estimated by combining the standard errors at both time points and using an outcome specific correlation coefficient (ρ) in the following equation:

$$SE(\theta) = \sqrt{Var(Y_1) + Var(Y_2) - 2SD_1SD_2\rho}\ /\sqrt{n}$$

Although the outcome specific correlation can be obtained by first deriving the correlation from studies that reported both change and measurements at the both time points, typically this is not feasible and as such the correlation was assumed to be 0.5. In cases where interquartile ranges (IQR) were provided, the length of the IQR was divided by 1.35 to estimate standard deviation.

For variables with multiple units of measure, all data were converted to the same unit.

For outcomes with missing measures of dispersion, the standard errors were imputed by using the average standard deviation among trials reporting dispersion of the outcome of interest. The mean standard deviation was then converted to standard error using study-specific sample sizes.

ADDITIONAL RESULTS

Trial characteristics tables

Table 10: Trial characteristics including treatment duration, trial phase, blinding, counties, number of study sites, and study sponsor(s)

Trial ID	Treatment duration, weeks	Trial Phase	Blinding	Country (s)	Study sites, n	Sponsor (s)
Bailey et al, 2010[1]	102	Phase 3	Double blind	USA, Canada, Argentina, Mexico, Brazil	80	AstraZeneca and Bristol-Myers Squibb
Bolinder et al, 2012[2]	102	Phase 3	Double blind	Bulgaria, Czech Republic, Hungary, Poland, Sweden	40	AstraZeneca and Bristol-Myers Squibb
CANTATA-D[3]	52	Phase 3	Double blind	International	169	Janssen
CANTATA-SU[4]	52	Phase 3	Double blind	International (19 countries)	157	Janssen
DeFronzo et al, 2015[5]	52	Phase 3	Double blind	International (22 countries)	197	Boehringer Ingelheim
EMPA-REG MET[7] and EMPA-REG EXTEND MET[6]	24	Phase 3	Double blind	Canada, China, France, Germany, India, Korea, Mexico, Slovakia, Slovenia, Taiwan, Turkey, USA	148	Boehringer Ingelheim
SUSTAIN 2[9]	56	Phase 3	Double blind	Argentina, Bulgaria, Czech Republic, Hong Kong, Hungary, India, Japan, Mexico, Norway, Portugal, Romania, Russia, South Africa, Spain, Sweden, Thailand, Turkey, Ukraine	18	Novo Nordisk
SUSTAIN 7[8]	40	Phase 3	Open label	Bulgaria, Croatia, Finland, Germany, Greece, Hong Kong, India, Ireland, Latvia, Lithuania, Portugal, Romania, Slovakia, Spain, United Kingdom, United States	198	Novo Nordisk

Table 11: Treatment arms of the trials included in the evidence base

Trial ID	Main Treatment				
	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Bailey et al, 2010[1]	Placebo	Dapagliflozin 5mg QD	Dapagliflozin 10mg QD		--
Bolinder et al, 2012[2]	Placebo	Dapagliflozin 10mg QD	--	--	--
CANTATA-D[3]	Placebo	Sitagliptin 100mg QD	Canagliflozin 100mg QD	Canagliflozin 300mg QD	--
CANTATA-SU[4]	Canagliflozin 100mg QD	Canagliflozin 300mg QD	--	--	--
DeFronzo et al, 2015[5]	Empagliflozin 10mg QD	Empagliflozin 25mg QD	--	--	--
EMPA-REG MET[7] and EMPA-REG EXTEND MET[6]	Placebo	Empagliflozin 10mg QD	Empagliflozin 25mg QD	--	--
SUSTAIN 2[9]	Once-weekly semaglutide 0.5mg QW	Once-weekly semaglutide 1.0mg QW	Sitagliptin 100mg QD	--	--
SUSTAIN 7[8]	Once-weekly semaglutide 0.5mg QW	Once-weekly semaglutide 1.0mg QW	--	--	--

Legend: *--: not applicable; DQ: once daily; BID: twice daily; QW: once weekly.*

Patient characteristic tables

Table 12: Baseline demographic characteristics of trials in the evidence base

Trial ID	Treatment	N	Number of female subjects	Number of caucasian subjects	Number of Black subjects	Number of Hispanic subjects	Number of Asian subjects	Number of other subjects
Bailey et al, 2010[1]	Placebo	137	61 (45.00)	--	--	--	--	--
	Dapagliflozin 5mg QD	137	68 (50.00)	--	--	--	--	--
	Dapagliflozin 10mg QD	137	58 (43.00)	--	--	--	--	--
Bolinder et al, 2012[2]	Placebo	91	40 (44.00)	91 (100.00)	--	--	--	--
	Dapagliflozin 10mg QD	91	40 (44.90)	89 (100.00)	--	--	--	--
CANTATA-D[3]	Placebo	183	89 (48.60)	129 (70.50)	3 (1.60)	--	30 (16.40)	21 (11.50)
	Sitagliptin 100mg QD	366	194 (53.00)	264 (72.10)	13 (3.60)	--	41 (11.20)	48 (13.10)
	Canagliflozin 100mg QD	368	194 (52.70)	252 (68.50)	16 (4.30)	--	51 (13.90)	49 (13.30)
	Canagliflozin 300mg QD	367	202 (55.00)	256 (69.80)	13 (3.50)	--	60 (16.30)	38 (10.40)
CANTATA-SU[4]	Canagliflozin 100mg QD	483	231 (48.00)	323 (67.00)	20 (4.00)	--	99 (21.00)	41 (9.00)
	Canagliflozin 300mg QD	485	244 (50.00)	333 (69.00)	19 (4.00)	--	92 (19.00)	41 (9.00)
DeFronzo et al, 2015[5]	Empagliflozin 10mg QD	140	59 (43.10)	104 (75.90)	--	--	19 (13.90)	14 (10.20)
	Empagliflozin 25mg QD	141	75 (53.60)	100 (71.40)	--	--	20 (14.30)	20 (14.30)
EMPA-REG EXTEND MET[6]	Placebo	207	91 (44.00)	113 (54.60)	2 (1.00)	--	92 (44.40)	0 (0.00)
	Empagliflozin 10mg QD	217	92 (42.40)	112 (51.60)	4 (1.80)	--	99 (45.60)	2 (0.90)
	Empagliflozin 25mg QD	214	93 (43.70)	113 (53.10)	0 (0.00)	--	98 (46.00)	2 (0.90)
EMPA-REG MET[7]	Placebo	207	91 (44.00)	113 (55.00)	2 (1.00)	--	92 (44.00)	0 (0.00)
	Empagliflozin 10mg QD	217	92 (42.00)	112 (52.00)	4 (2.00)	--	99 (46.00)	2 (1.00)
	Empagliflozin 25mg QD	214	93 (44.00)	113 (53.00)	0 (0.00)	--	98 (46.00)	2 (1.00)
SUSTAIN 2[9]	Once-weekly semaglutide 0.5mg	410	202 (49.40)	279 (68.20)	18 (4.40)	69 (16.90)	106 (25.90)	6 (1.50)
	Once-weekly semaglutide 1.0mg	410	204 (49.90)	279 (68.20)	24 (5.90)	67 (16.40)	99 (24.20)	7 (1.70)

Trial ID	Treatment	N	Number of female subjects	Number of caucasian subjects	Number of Black subjects	Number of Hispanic subjects	Number of Asian subjects	Number of other subjects
	Sitagliptin 100mg QD	411	199 (48.90)	281 (69.00)	17 (4.20)	73 (17.90)	102 (25.10)	7 (1.70)
SUSTAIN 7[8]	Once-weekly semaglutide 0.5mg	301	132 (43.90)	233 (77.40)	17 (5.60)	29 (9.60)	50 (16.60)	1 (0.30)
	Once-weekly semaglutide 1.0mg	300	138 (46.00)	243 (81.00)	18 (6.00)	35 (11.70)	38 (12.70)	1 (0.30)

Legend: *no symbol: standard deviation; --: no estimate reported.*

Table 13: Baseline clinical characteristics of trials in the evidence base

Trial ID	Treatment	N	Estimated age (years)	Estimated weight at baseline (kg)	Estimated BMI at baseline (kg/m^2)	Estimated HbA1c at baseline (%)	Estimated postprandial glucose at baseline (mmol/L)	Estimated duration of disease (years)	Estimated fasting plasma glucose at baseline (mmol/L)	Estimated systolic blood pressure at baseline (mmHg)
Bailey et al, 2010[1]	Placebo	137	53.70 (0.88)	87.70 (1.64)	31.80 (0.45)	8.11 (0.08)	--	5.80 (0.44)	9.19 (0.22)	127.70 (1.25)
	Dapagliflozin 5mg QD	137	54.30 (0.80)	84.70 (1.39)	31.40 (0.43)	8.17 (0.08)	--	6.40 (0.50)	9.39 (0.23)	126.90 (1.22)
	Dapagliflozin 10mg QD	137	52.70 (0.85)	86.30 (1.50)	31.20 (0.44)	7.92 (0.07)	--	6.10 (0.46)	8.66 (0.18)	126.00 (1.36)
Bolinder et al, 2012[2]	Placebo	91	60.80 (0.72)	90.90 (1.44)	31.70 (0.41)	7.16 (0.06)	--	5.50 (0.56)	8.30 (0.15)	133.30 (1.49)#
	Dapagliflozin 10mg QD	91	60.60 (0.86)	92.10 (1.48)	32.10 (0.41)	7.19 (0.05)	--	6.00 (0.47)	8.21 (0.14)	135.90 (1.49)#
CANTATA-D[3]	Placebo	183	55.30 (0.72)	86.60 (1.66)	31.10 (0.45)	8.00 (0.07)	13.80 (0.27)	6.80 (0.39)	9.10 (0.16)	128.00 (0.94)
	Sitagliptin 100mg QD	366	55.50 (0.50)	87.70 (1.13)	32.00 (0.32)	7.90 (0.05)	14.20 (0.19)	6.80 (0.27)	9.40 (0.12)	128.00 (0.71)
	Canagliflozin 100mg QD	368	55.50 (0.49)	88.70 (1.16)	32.40 (0.33)	7.90 (0.05)	14.30 (0.20)	6.70 (0.28)	9.30 (0.12)	128.00 (0.66)
	Canagliflozin 300mg QD	367	55.30 (0.48)	85.40 (1.09)	31.40 (0.33)	7.90 (0.05)	14.50 (0.21)	7.10 (0.28)	9.60 (0.13)	128.70 (0.68)
CANTATA-SU[4]	Canagliflozin 100mg QD	483	56.40 (0.43)	86.90 (0.91)	31.00 (0.24)	7.80 (0.04)	--	6.50 (0.25)	9.20 (0.10)	130.00 (0.56)
	Canagliflozin 300mg QD	485	55.80 (0.42)	86.60 (0.89)	31.20 (0.25)	7.80 (0.04)	--	6.70 (0.25)	9.10 (0.09)	130.00 (0.63)
DeFronzo et al, 2015[5]	Empagliflozin 10mg QD	140	56.10 (0.89)	86.10 (1.54)	30.90 (0.46)	8.00 (0.08)	--	--	8.97 (0.16)	131.60 (1.22)
	Empagliflozin 25mg QD	141	55.50 (0.84)	87.70 (1.48)	31.80 (0.45)	8.02 (0.07)	--	--	8.88 (0.18)	129.20 (1.13)
EMPA-REG EXTEND MET[6]	Placebo	207	56.00 (0.67)	79.70 (1.29)	28.70 (0.36)	7.90 (0.06)	--	--	8.70 (0.13)	128.60 (1.02)
	Empagliflozin 10mg QD	217	55.50 (0.67)	81.60 (1.26)	29.10 (0.37)	7.94 (0.05)	--	--	8.60 (0.14)	129.60 (0.96)
	Empagliflozin 25mg QD	214	55.60 (0.70)	82.20 (1.32)	29.70 (0.39)	7.86 (0.06)	--	--	8.30 (0.12)	130.00 (1.03)
EMPA-REG MET[7]	Placebo	207	56.00 (0.67)	79.70 (1.29)	28.70 (0.36)	7.90 (0.06)	--	--	8.66 (0.13)	128.60 (1.02)
	Empagliflozin 10mg QD	217	55.50 (0.67)	81.60 (1.26)	29.10 (0.37)	7.94 (0.05)	--	--	8.58 (0.13)	129.60 (0.96)
	Empagliflozin 25mg QD	214	55.60 (0.70)	82.20 (1.32)	29.70 (0.39)	7.86 (0.06)	--	--	8.29 (0.12)	130.00 (1.03)
SUSTAIN 2[9]	Once-weekly semaglutide 0.5mg	410	54.30 (0.80)	84.70 (1.39)	32.50 (0.34)^	8.00 (0.05)^	--	6.40 (0.24)^	9.33 (0.18)^	132.60 (0.70)#
	Once-weekly semaglutide 1.0mg	410	52.70 (0.85)	86.30 (1.50)	32.50 (0.37)^	8.00 (0.05)^	--	6.70 (0.38)^	9.29 (0.15)^	132.60 (0.70)#

Trial ID	Treatment	N	Estimated age (years)	Estimated weight at baseline (kg)	Estimated BMI at baseline (kg/m^2)	Estimated HbA1c at baseline (%)	Estimated postprandial glucose at baseline (mmol/L)	Estimated duration of disease (years)	Estimated fasting plasma glucose at baseline (mmol/L)	Estimated systolic blood pressure at baseline (mmHg)
	Sitagliptin 100mg QD	411	60.80 (0.72)	90.90 (1.44)	32.50 (0.29)^	8.20 (0.05)^	--	6.60 (0.33)^	9.60 (0.13)^	132.60 (0.70)#
SUSTAIN 7[8]	Once-weekly semaglutide 0.5mg	301	56.00 (10.90)	96.40 (24.38)	33.70 (7.12)	8.30 (0.96)	--	7.70 (5.92)	9.80 (2.54)	--
	Once-weekly semaglutide 1.0mg	300	55.00 (10.60)	95.50 (20.90)	33.60 (6.49)	8.20 (0.92)	--	7.30 (5.66)	9.80 (2.58)	--

Legend: *no symbol: standard deviation; *: standard error; ^: range; #: imputed; --: no estimate reported.*

Table 14: Number of trials reporting data for each outcome for which NMA was feasible at the 26-week time point

Outcomes	Number of trials reporting
Change from baseline in HbA_{1c}	8
HbA_{1c} <7.0%	5
Change from baseline in fasting plasma glucose	8
Change from baseline in weight	7
Change from baseline in systolic blood pressure	6

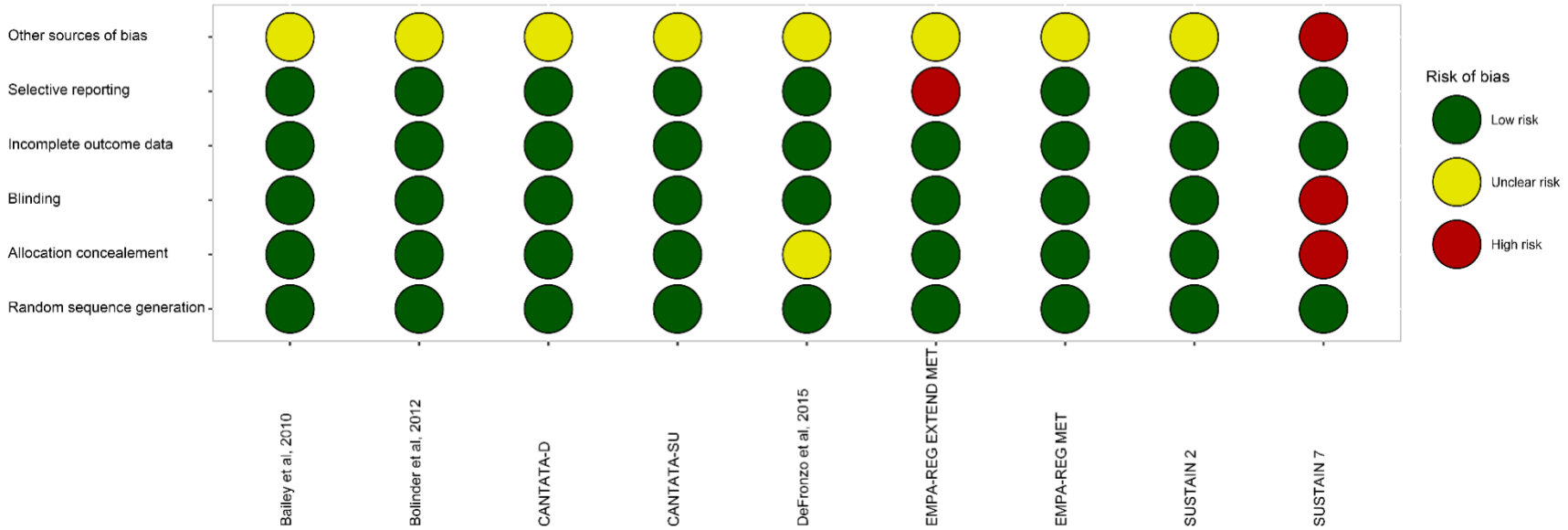
Note: *For data available in the form of figures, trial authors were contacted in order to obtain the actual 26-week data values; if data was not provided, the 26-week data was extracted from the curves using DigitizeIt.*

Table 15: The number of patients in analysis populations and prior treatments at time of randomization

Trial ID	Treatment	Randomized, n	Completed, n	Withdrawal, n	Safety Population, n
Bailey et al, 2010[1]	Placebo	137	119	18	137
	Dapagliflozin 5mg	137	122	15	137
	Dapagliflozin 10mg	137	121	14	135
Bolinder et al, 2012[2]	Placebo	91	86	5	91
	Dapagliflozin 10mg	91	83	8	91
CANTATA-D[3]	Placebo	183	155	28	183
	Sitagliptin 100mg	366	319	47	366
	Canagliflozin 100mg	368	322	46	368
	Canagliflozin 300mg	367	323	44	367
CANTATA-SU[7]	Canagliflozin 100mg	483	395	88	483
	Canagliflozin 300mg	485	380	105	485
DeFronzo et al, 2015[8]	Empagliflozin 10mg	140	118	22	137
	Empagliflozin 25mg	141	125	16	140
EMPA-REG EXTEND MET[11]	Placebo	207	121	17	206
	Empagliflozin 10mg	217	162	11	217
	Empagliflozin 25mg	214	139	13	214
SUSTAIN 2[44]	Semaglutide 0.5mg	410	387	54	409
	Semaglutide 1.0mg	410	388	65	409
	Sitagliptin 100mg	411	388	36	407
SUSTAIN 7[46]	Semaglutide 0.5mg	301	279	22	301
	Semaglutide 1.0mg	300	279	21	300

Risk of Bias

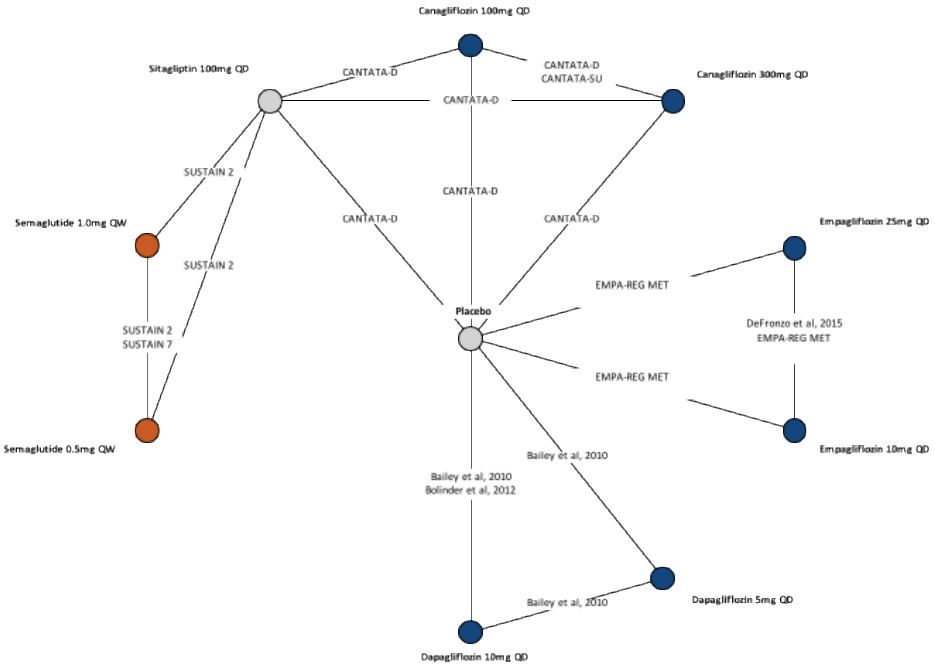
Figure 1: Risk of bias by trial



Additional Figures

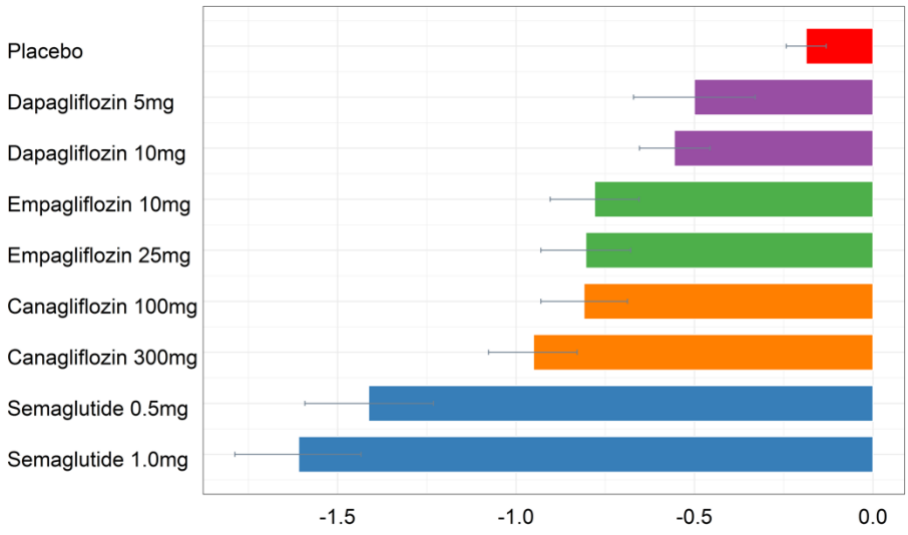
Change from baseline in HbA1c

Figure 2: Network of evidence informing HbA_{1c}



Legend: *Circles represent each treatment included in the network, with orange for once-weekly once-weekly semaglutide, dark blue for SGLT-2is, and grey for others.*

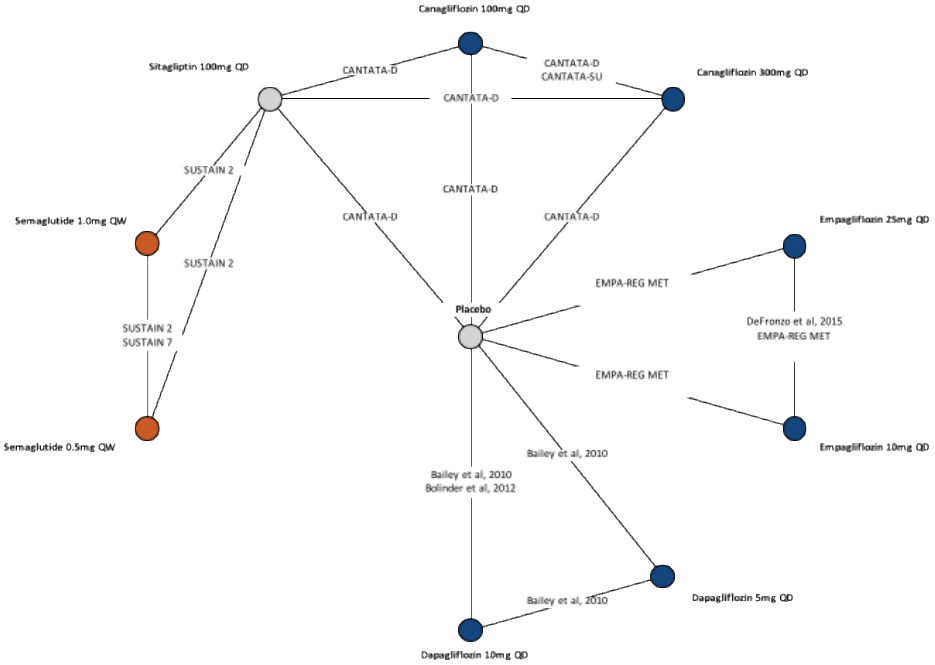
Figure 3: Modelled change from baseline for HbA_{1c} according to the fixed-effects NMA



Legend*: Error bars represent 95% credible intervals*

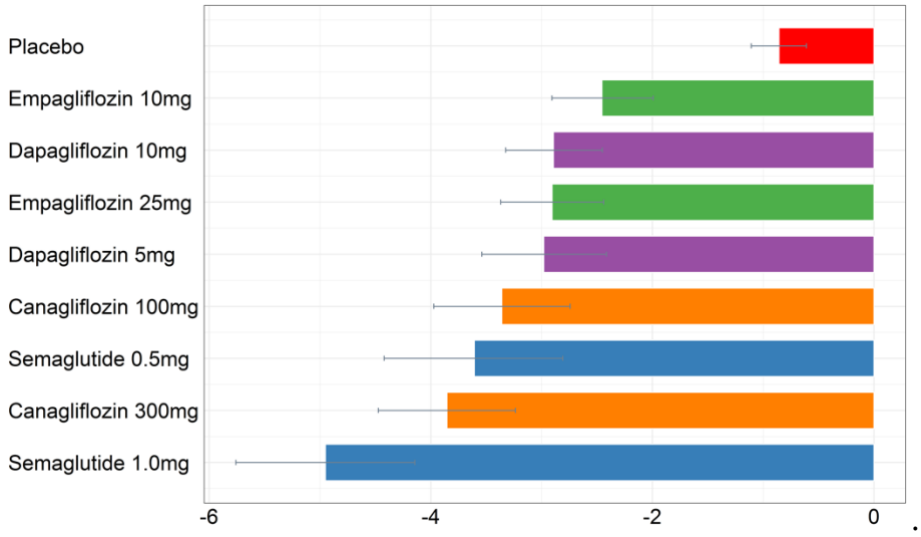
Change from baseline in weight

Figure 4: Network of evidence informing weight



Legend: *Circles represent each treatment included in the network, with orange for once-weekly once-weekly semaglutide, dark blue for SGLT-2is, and grey for others.*

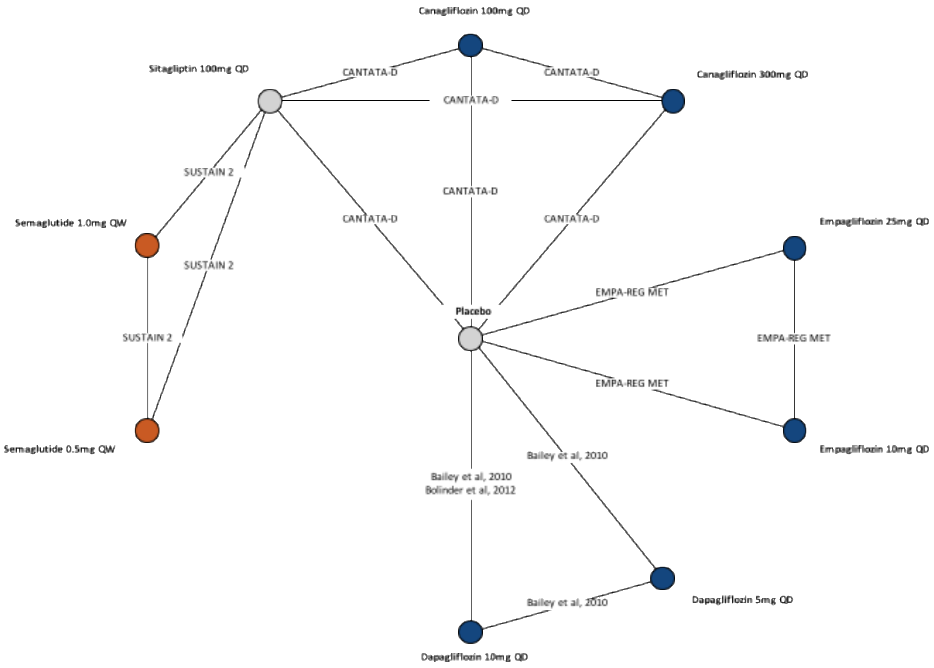
Figure 5: Modelled responses for change from baseline weight according to the fixed-effects NMA



Legend*: Error bars represent 95% credible intervals*

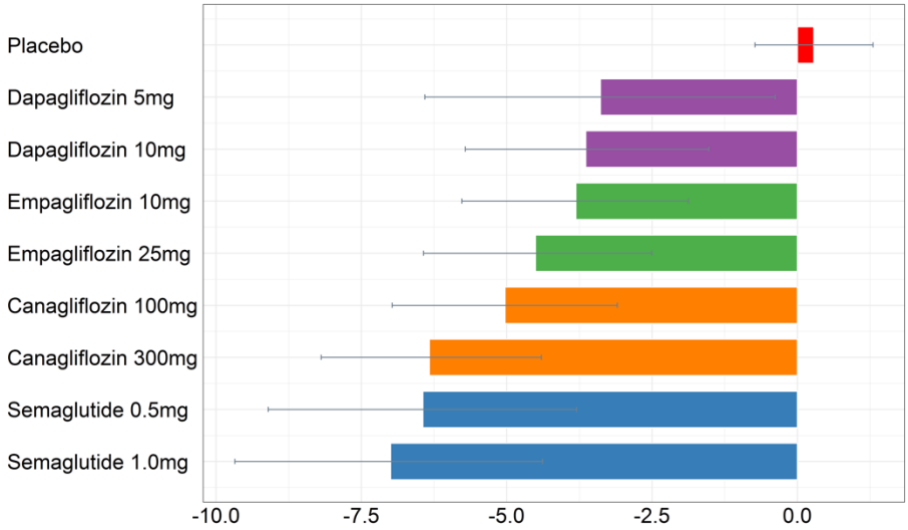
Change in systolic blood pressure (SBP)

Figure 6: Network of evidence informing changes in baseline to SBP



Legend: *Circles represent each treatment included in the network, with orange for once-weekly once-weekly semaglutide, dark blue for SGLT-2is, and grey for others.*

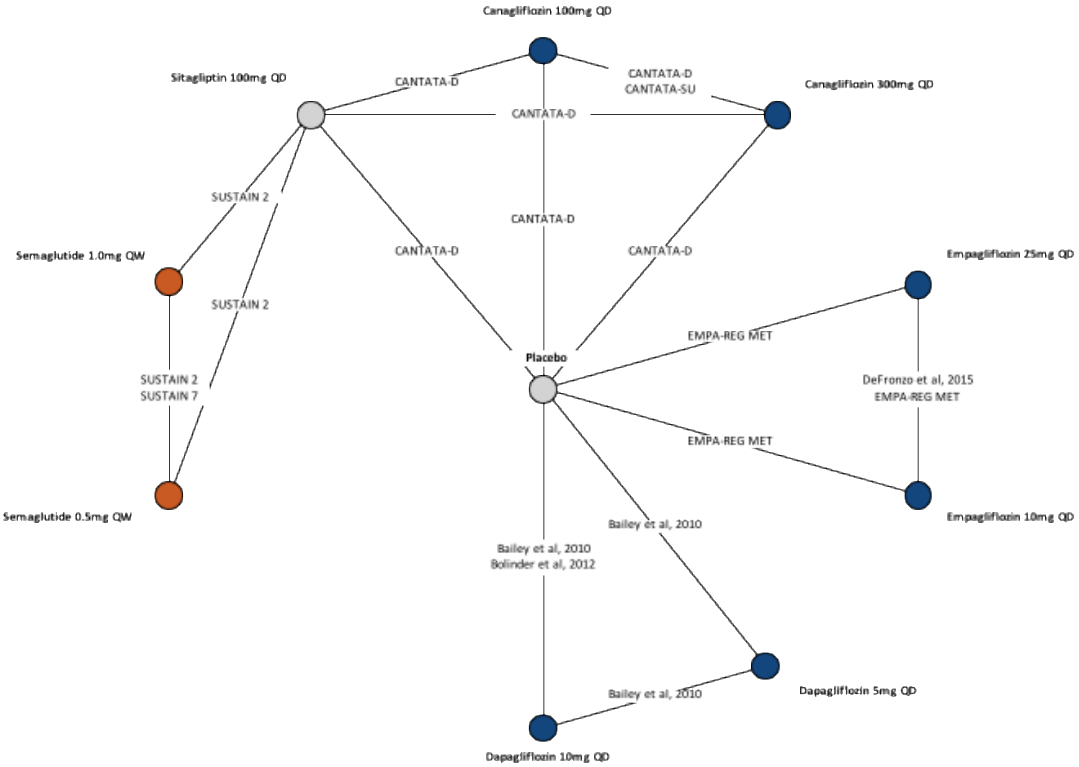
Figure 7: Modelled change from baseline for SBP according to the fixed-effects NMA



Legend*: Error bars represent 95% credible intervals*

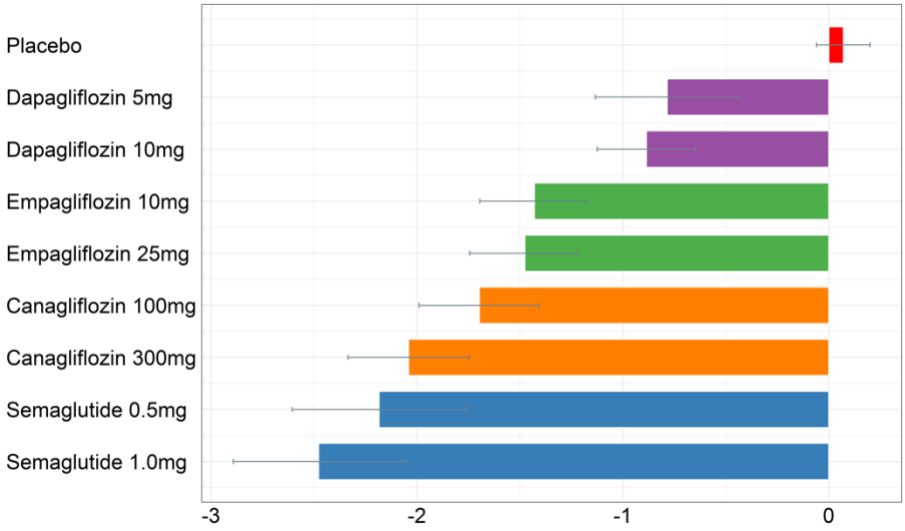
Change in fasting blood glucose (FPG)

Figure 8: Network of evidence informing changes in baseline to FPG



Legend: *Circles represent each treatment included in the network, with orange for once-weekly once-weekly semaglutide, dark blue for SGLT-2is, and grey for others.*

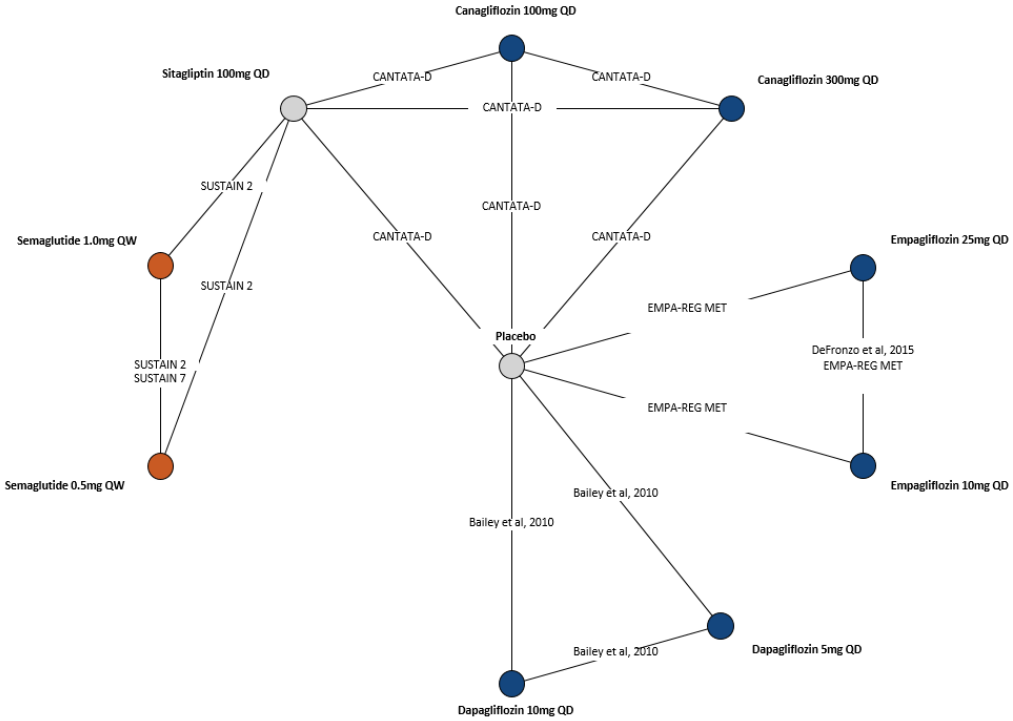
Figure 9: Modelled change from baseline for FPG according to the fixed-effects NMA



Legend*: Error bars represent 95% credible intervals*

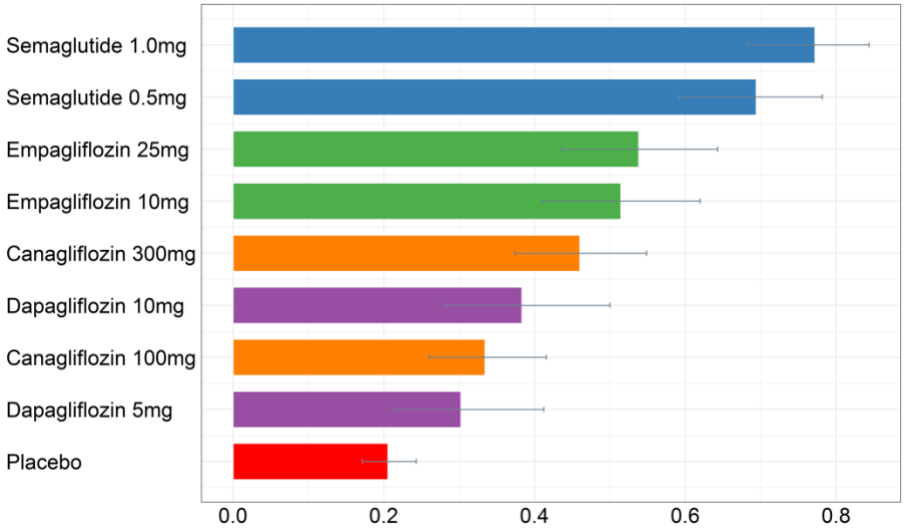
Proportion of patients achieving <7% HbA1c

Figure 10: Network of evidence informing proportions of patients attaining HbA_{1c} <7.0%



Legend: *Circles represent each treatment included in the network, with orange for once-weekly once-weekly semaglutide, dark blue for SGLT-2is, and grey for others.*

Figure 11: Modelled proportion of patients achieving HbA1c <7.0% according to the fixed-effects NMA



Legend*: Error bars represent 95% credible intervals*

Model Selection

In this appendix we present the DIC values for each competing analysis specific to an outcome at a given time point. The competing analyses included fixed- and random-effects, meta-regression adjustments to the principal analyses, and sensitivity analyses (without meta-regression adjustments). Meta-regression adjustments were carried out individually on four covariates: sex, weight, disease duration, and HbA1c. Each covariate was coded as a categorical variable so as to minimize the risk of ecological fallacy bias. For sex, weight, and disease duration, and HbA1c, the median value was used to dichotomize the covariates. Sensitivity analyses included removing trials with 40% or more subjects of Asian ethnicity, and analyzing safety outcomes at the longest reported follow-up for each trial.

Table 16: Model selection for change in HbA1c from baseline amongst competing base case and sensitivity analyses

	Deviance	pD	DIC
Fixed-Effects	22.08	17.02	39.10
Random-Effects	20.69	19.44	40.13
Gender FE	22.11	17.02	39.13
Gender RE	20.65	19.33	39.98
Weight FE	18.86	17.99	36.85
Weight RE	19.22	19.36	38.58
Dis. duration FE	18.91	17.98	36.89
Dis. duration RE	19.46	19.31	38.77
HbA1c FE	22.10	16.99	39.09
HbA1c RE	20.58	19.49	40.07
	Sensitivity Analyses		
Ethnicity ≥ 40% FE	17.07	13.02	30.09
Ethnicity ≥ 40% RE	15.76	15.20	30.96

OAD: oral antidiabetic; FE: fixed-effects; RE: random-effects; pD: effective number of parameters; DIC: deviance information criterion. Note: gender, weight, disease duration, and HbA1c were dichotomized at the median.

Table 17: Model selection for proportion of subjects achieving <7% HbA1c amongst competing base case and sensitivity analyses

	Deviance	pD	DIC
Fixed-Effects	13.87	14.00	27.87
Random-Effects	14.13	14.85	28.98
Gender FE	13.9	13.99	27.89
Gender RE	14.23	14.67	28.90
Weight FE	13.82	14.03	27.85
Weight RE	14.24	14.82	29.06
Dis. duration FE	13.91	14.00	27.91
Dis. duration RE	14.23	14.72	28.95
HbA1c FE	13.93	14.02	27.95
HbA1c RE	14.23	14.71	28.94
	Sensitivity Analyses		
Ethnicity ≥ 40% FE	9.35	9.96	19.31
Ethnicity ≥ 40% RE	9.38	9.93	19.31

OAD: oral antidiabetic; FE: fixed-effects; RE: random-effects; pD: effective number of parameters; DIC: deviance information criterion. Note: sex, weight and disease duration were dichotomized at the median.

Table 18: Model selection for change in weight from baseline amongst competing base case and sensitivity analyses

	Deviance	pD	DIC
Fixed-Effects	19.00	16.00	35.00
Random-Effects	17.98	18.00	35.98
Gender FE	18.95	16.00	34.95
Gender RE	18.16	17.89	36.05
Weight FE	19.91	17.05	36.96
Weight RE	18.39	18.79	37.18
Dis. duration FE	19.98	16.97	36.95
Dis. duration RE	18.47	18.73	37.20
HbA1c FE	18.98	16.00	34.98
HbA1c RE	18.06	17.88	35.94
	Sensitivity Analyses		
Ethnicity ≥ 40% FE	14.72	12.01	26.73
Ethnicity ≥ 40% RE	13.30	13.61	26.91

OAD: oral antidiabetic; FE: fixed-effects; RE: random-effects; pD: effective number of parameters; DIC: deviance information criterion. Note: gender, weight, disease duration, and HbA1c were dichotomized at the median.

Table 19: Model selection for change in SBP from baseline amongst competing base case and sensitivity analyses

	Deviance	pD	DIC
Fixed-Effects	15.18	14.94	30.12
Random-Effects	15.63	16.13	31.76
Gender FE	15.26	15.02	30.28
Gender RE	15.88	16.13	32.01
Weight FE	15.58	16.01	31.59
Weight RE	16.01	16.69	32.70
Dis. duration FE	15.48	16.07	31.55
Dis. duration RE	16.07	16.80	32.87
HbA1c FE	15.09	14.97	30.06
HbA1c RE	15.71	16.10	31.81
	Sensitivity Analyses		
Ethnicity ≥ 40% FE	12.07	12.00	24.07
Ethnicity ≥ 40% RE	12.58	13.19	25.77

OAD: oral antidiabetic; FE: fixed-effects; RE: random-effects; pD: effective number of parameters; DIC: deviance information criterion. Note: gender, weight, disease duration, and HbA1c were dichotomized at the median.

Table 20: Model selection for change in FPG from baseline amongst competing base case and sensitivity analyses

	Deviance	pD	DIC
Fixed-Effects	23.60	17.01	40.61
Random-Effects	20.29	19.80	40.09
Gender FE	23.71	17.05	40.76
Gender RE	20.51	19.81	40.32
Weight FE	24.77	17.96	42.73
Weight RE	20.71	20.55	41.26
Dis. duration FE	24.52	18.03	42.55
Dis. duration RE	20.68	20.52	41.20
HbA1c FE	23.65	17.02	40.67
HbA1c RE	20.29	19.69	39.98
	Sensitivity Analyses		
Ethnicity ≥ 40% FE	18.67	13.00	31.67
Ethnicity ≥ 40% RE	15.51	15.41	30.92

OAD: oral antidiabetic; FE: fixed-effects; RE: random-effects; pD: effective number of parameters; DIC: deviance information criterion. Note: gender, weight, disease duration, and HbA1c were dichotomized at the median.

Rank Probabilities

In this appendix, we present the rankings for each analysis, along with the SUCRA in brackets. The SUCRA (surface under the cumulative ranking curve) is a parameter used for ranking that varies from 0 to 1, where 0 implies being ranked last and having no probability of being ranked other than last and 1 implies treatment has full probability of being ranked first. Semaglutide 1.0mg once-weekly was ranked first for all efficacy outcomes with a consistently high SUCRA.

Table 21: Table of rankings and supporting SUCRA scores for efficacy outcomes

Treatment	HbA1c	HbA1c <7.0%	Fasting plasma glucose	Weight	Systolic blood pressure
Placebo	10 (0.00)	10 (0.00)	10 (0.00)	9 (0.06)	10 (0.00)
Once-weekly semaglutide 0.5mg	2 (0.89)	2 (0.88)	2 (0.86)	2 (0.83)	3 (0.81)
Once-weekly semaglutide 1.0mg	1 (1.00)	1 (1.00)	1 (1.00)	1 (1.00)	1 (0.91)
Canagliflozin 100mg	6 (0.49)	8 (0.22)	4 (0.64)	4 (0.56)	4 (0.59)
Canagliflozin 300mg	3 (0.76)	5 (0.55)	3 (0.81)	3 (0.75)	2 (0.83)
Dapagliflozin 5mg	8 (0.19)	7 (0.36)	8 (0.20)	5 (0.54)	7 (0.37)
Dapagliflozin 10mg	9 (0.14)	9 (0.16)	9 (0.15)	7 (0.48)	8 (0.34)
Empagliflozin 10mg	7 (0.45)	4 (0.65)	6 (0.48)	8 (0.25)	6 (0.38)
Empagliflozin 25mg	5 (0.51)	3 (0.72)	5 (0.52)	6 (0.49)	5 (0.52)
Sitagliptin 100mg	4 (0.56)	6 (0.46)	7 (0.34)	10 (0.05)	9 (0.25)

Consistency verification

Figure 12: Direct versus indirect evidence from NMA for change from baseline in HbA1c

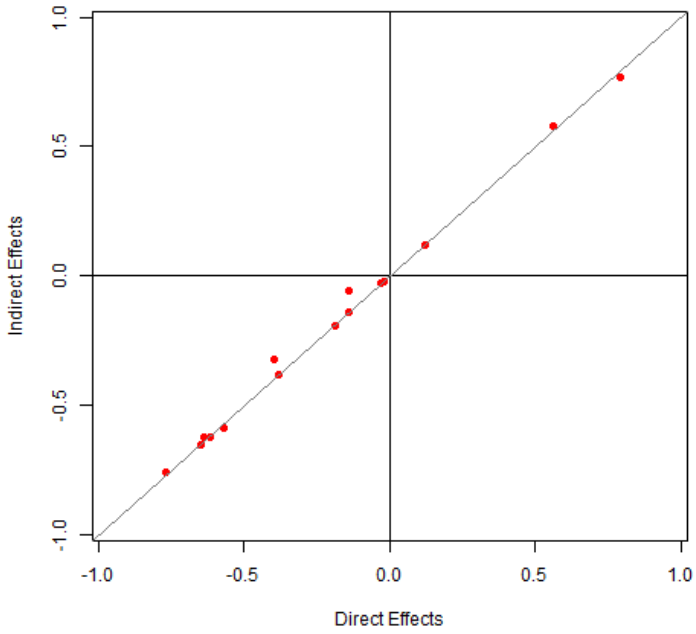


Figure 13: Direct versus indirect evidence from NMA for percent of patients achieving HbA1c < 7%

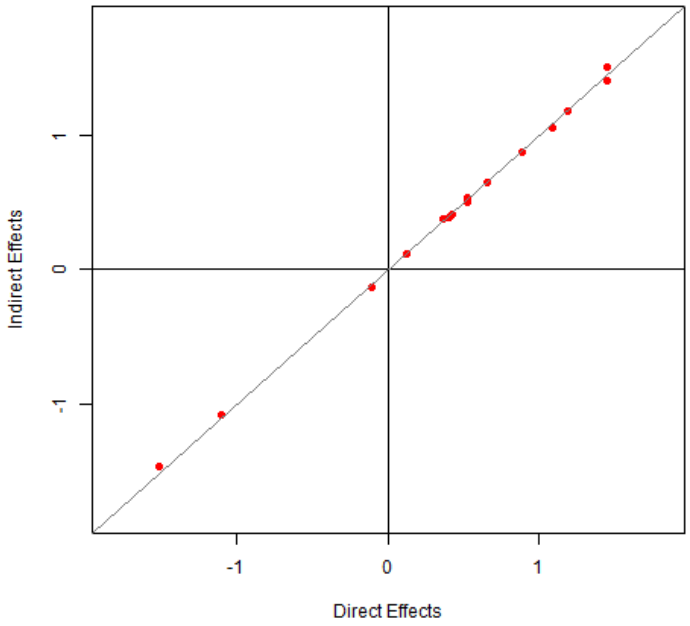


Figure 14: Direct versus indirect evidence from NMA for change from baseline in weight

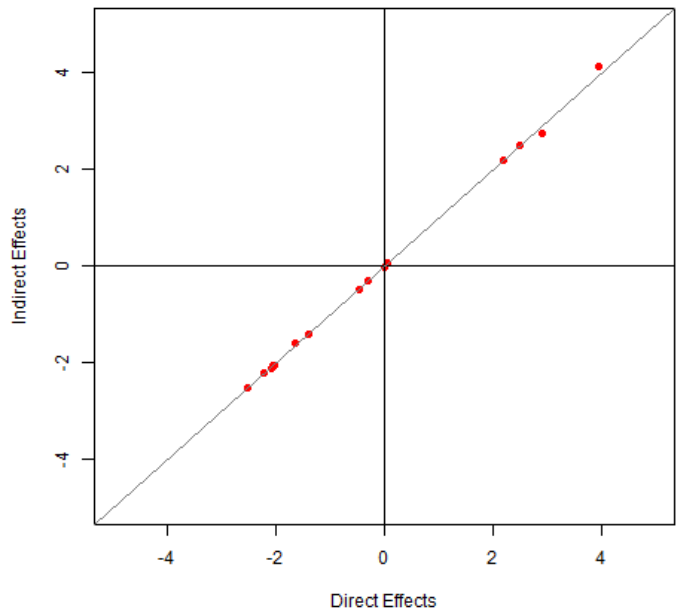


Figure 15: Direct versus indirect evidence from NMA for change from baseline in SBP

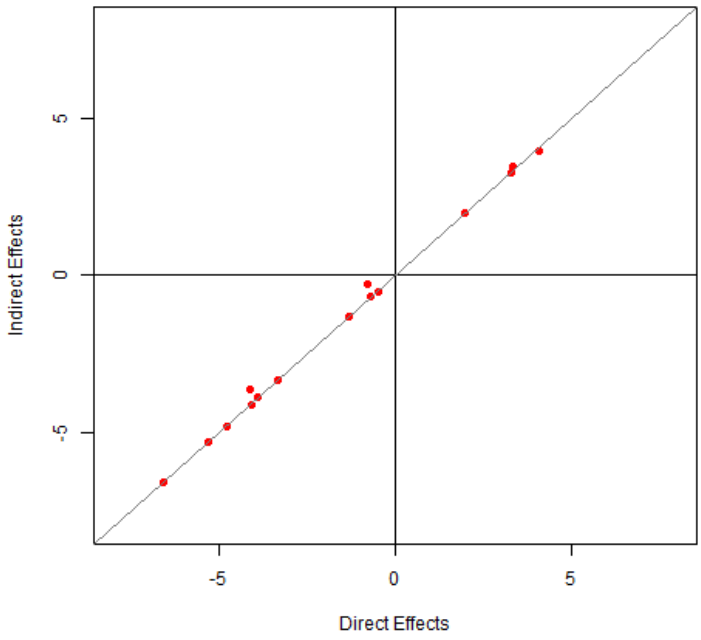
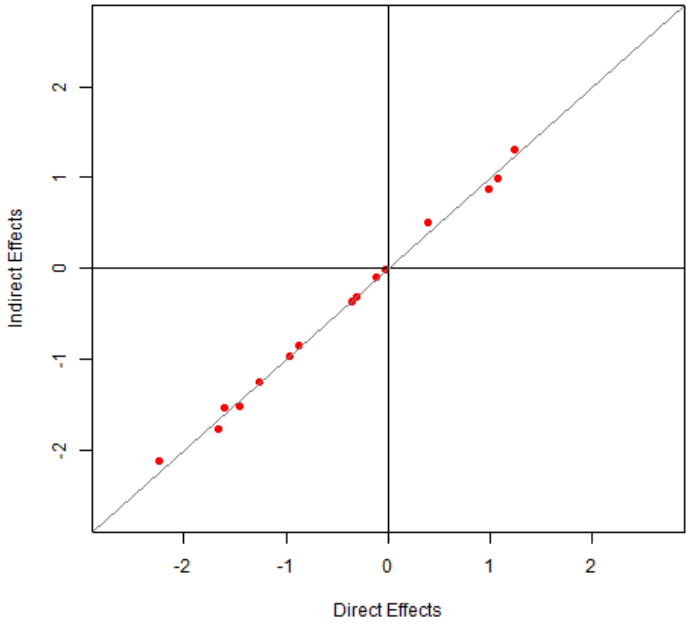


Figure 6: Direct versus indirect evidence from NMA for change from baseline in FPG



Sensitivity Analyses

Excluding trials with ≥ 40% Asian patients

Table 22: Mean differences of change in HbA1c at baseline comparing semaglutide to SGLT-2 estimated by a random-effects NMA and restricted to trials without 40% or more patients of Asian ethnicity

	Placebo	Once-weekly semaglutide 0.5mg	Once-weekly semaglutide 1.0mg
Placebo	--	**-1.23 (-1.42, -1.04)**	**-1.42 (-1.61, -1.24)**
Once-weekly semaglutide 0.5mg	**1.23 (1.04, 1.42)**	--	**-0.20 (-0.29, -0.10)**
Once-weekly semaglutide 1.0mg	**1.42 (1.24, 1.61)**	**0.20 (0.10, 0.29)**	--
Canagliflozin 100mg once daily	**0.62 (0.48, 0.76)**	**-0.61 (-0.77, -0.44)**	**-0.80 (-0.96, -0.64)**
Canagliflozin 300mg once daily	**0.77 (0.63, 0.90)**	**-0.46 (-0.63, -0.30)**	**-0.66 (-0.82, -0.49)**
Dapagliflozin 5mg once daily	**0.31 (0.13, 0.50)**	**-0.91 (-1.18, -0.65)**	**-1.11 (-1.37, -0.85)**
Dapagliflozin 10mg once daily	**0.37 (0.26, 0.48)**	**-0.86 (-1.08, -0.64)**	**-1.05 (-1.27, -0.84)**

Each cell represents the comparison (mean difference and 95% CrI) of the column treatment versus the row treatment. All bolded values are statistically meaningful at the 0.05 significance level.

Table 23: Odds ratios of proportion of patients achieving <7% HbA1c comparing semaglutide vs SGLT-2s estimated by a fixed-effects NMA and restricted to trials without 40% or more patients of Asian ethnicity

	Placebo	Once-weekly semaglutide 0.5mg	Once-weekly semaglutide 1.0mg
Placebo	--	**8.79 (5.45, 14.21)**	**13.18 (8.09, 21.41)**
Once-weekly semaglutide 0.5mg	**0.11 (0.07, 0.18)**	--	**1.49 (1.09, 2.05)**
Once-weekly semaglutide 1.0mg	**0.08 (0.05, 0.12)**	**0.67 (0.49, 0.92)**	--
Canagliflozin 100mg once daily	**0.52 (0.35, 0.75)**	**4.54 (3.01, 6.85)**	**6.75 (4.44, 10.42)**
Canagliflozin 300mg once daily	**0.30 (0.21, 0.44)**	**2.67 (1.76, 4.03)**	**3.99 (2.59, 6.13)**
Dapagliflozin 5mg once daily	0.60 (0.35, 1.01)	**5.27 (2.61, 10.82)**	**7.83 (3.83, 16.12)**
Dapagliflozin 10mg once daily	**0.42 (0.24, 0.70)**	**3.65 (1.79, 7.45)**	**5.44 (2.64, 11.10)**

Each cell represents the comparison (odds ratio and 95% CrI) of the column treatment versus the row treatment. All bolded values are statistically meaningful at the 0.05 significance level.

Table 24: Mean differences of change in FPG from baseline comparing semaglutide to SGLT-2 estimated by a fixed-effects NMA and restricted to trials without 40% or more patients of Asian ethnicity

	Placebo	Once-weekly semaglutide 0.5mg	Once-weekly semaglutide 1.0mg
Placebo	--	**-2.26 (-2.71, -1.82)**	**-2.55 (-2.99, -2.10)**
Once-weekly semaglutide 0.5mg	**2.26 (1.82, 2.71)**	--	**-0.29 (-0.52, -0.05)**
Once-weekly semaglutide 1.0mg	**2.55 (2.10, 2.99)**	**0.29 (0.05, 0.52)**	--
Canagliflozin 100mg once daily	**1.77 (1.44, 2.10)**	**-0.49 (-0.88, -0.11)**	**-0.78 (-1.17, -0.40)**
Canagliflozin 300mg once daily	**2.11 (1.78, 2.44)**	-0.15 (-0.54, 0.24)	**-0.44 (-0.82, -0.05)**
Dapagliflozin 5mg once daily	**0.85 (0.47, 1.24)**	**-1.41 (-2.00, -0.81)**	**-1.69 (-2.28, -1.10)**
Dapagliflozin 10mg once daily	**0.96 (0.67, 1.24)**	**-1.30 (-1.84, -0.77)**	**-1.59 (-2.12, -1.06)**

Each cell represents the comparison (mean difference and 95% CrI) of the column treatment versus the row treatment. All bolded values are statistically meaningful at the 0.05 significance level.

Table 25: Mean differences of change in weight from baseline comparing semaglutide to SGLT-2 estimated by a fixed-effects NMA and restricted to trials without 40% or more patients of Asian ethnicity

	Placebo	Once-weekly semaglutide 0.5mg	Once-weekly semaglutide 1.0mg
Placebo	--	**-2.75 (-3.48, -1.99)**	**-4.09 (-4.83, -3.32)**
Once-weekly semaglutide 0.5mg	**2.75 (1.99, 3.48)**	--	**-1.35 (-1.78, -0.90)**
Once-weekly semaglutide 1.0mg	**4.09 (3.32, 4.83)**	**1.35 (0.90, 1.78)**	--
Canagliflozin 100mg once daily	**2.20 (1.64, 2.76)**	-0.55 (-1.29, 0.22)	**-1.89 (-2.64, -1.13)**
Canagliflozin 300mg once daily	**2.50 (1.95, 3.05)**	-0.24 (-1.00, 0.52)	**-1.59 (-2.34, -0.84)**
Dapagliflozin 5mg once daily	**2.12 (1.49, 2.75)**	-0.63 (-1.61, 0.35)	**-1.98 (-2.95, -0.98)**
Dapagliflozin 10mg once daily	**2.03 (1.53, 2.54)**	-0.72 (-1.63, 0.20)	**-2.06 (-2.97, -1.14)**

Each cell represents the comparison (mean difference and 95% CrI) of the column treatment versus the row treatment. All bolded values are statistically meaningful at the 0.05 significance level.

Table 26: Mean differences of change in SBP from baseline comparing semaglutide to SGLT-2 estimated by a fixed-effects NMA and restricted to trials without 40% or more patients of Asian ethnicity

	Placebo	Once-weekly semaglutide 0.5mg	Once-weekly semaglutide 1.0mg
Placebo	--	**-6.71 (-9.41, -4.10)**	**-7.26 (-9.85, -4.64)**
Once-weekly semaglutide 0.5mg	**6.71 (4.10, 9.41)**	--	-0.55 (-2.01, 0.96)
Once-weekly semaglutide 1.0mg	**7.26 (4.64, 9.85)**	0.55 (-0.96, 2.01)	--
Canagliflozin 100mg once daily	**5.28 (3.37, 7.25)**	-1.43 (-3.83, 1.00)	-1.96 (-4.37, 0.45)
Canagliflozin 300mg once daily	**6.60 (4.66, 8.54)**	-0.12 (-2.52, 2.28)	-0.67 (-3.02, 1.75)
Dapagliflozin 5mg once daily	**3.67 (0.38, 6.94)**	-3.06 (-7.22, 1.18)	-3.59 (-7.71, 0.63)
Dapagliflozin 10mg once daily	**3.97 (1.36, 6.58)**	-2.75 (-6.45, 0.93)	-3.30 (-6.92, 0.39)

Each cell represents the comparison (mean difference and 95% CrI) of the column treatment versus the row treatment. All bolded values are statistically meaningful at the 0.05 significance level.