Appendix 2 Supplementary tables [posted as supplied by author]

Table A. Baseline characteristics of included randomised controlled trials

Author (year)	International study	Number of countries involved	Number of study sites	Study phase	Total number of patients randomised	Length of follow up (weeks)	Male (n,%)	Mean age (years)	Mean BMI (kg/m²)	Mean HbA1c (%)	Mean FPG (mmol/L)	Mean diabetes duration (years)
Smaller trials												
Ahren (2013) [1]	Yes	16	133	III	680	24	293 (43.1)	54.7	32.9	8	9.3	NR
Ahren (2014) [2,3]	Yes	10	289	III	1049	164	482 (47.6)	54.5	32.6	8.1	9.2	6
Amin (2015) [4]	Yes	5	42	□	328	12	213 (64.9)	54.4	30.4	8.1	9.1	6.3
Araki (2015) [5]	No	1	35	III	361	26	258 (71.0)	56.8	26	8	8.7	8.8
Arechavaleta (2011) [6,7]	Yes	23	109	III	1035	30	563 (54.4)	56.3	30	7.5	8.1	6.8
Arjona Ferreira (2013a) [8]	Yes	12	31	III	129	54	77 (59.7)	59.5	26.8	7.9	9	17[$]
Arjona Ferreira (2013b) [9,10]	NR	NR	NR	NR	426	54	253 (59.8)	64.5	26.8	7.8	8.1	10.4
Aroda (2016) [11]	Yes	18	236	□	736	30	391 (53.2)	60.0	31.1	8.50	8.0	12.0
Aschner (2010) [12,13]	Yes	23	113	III	1050	24	484 (46.1)	56	30.8	7.3	7.9	2.4
Ba (2016) [14]	No	1	32	□	498	24	249 (50.0)	57.0	25.4	8.54	10.0	7.0
Bajaj (2014) [15]	Yes	4	52	III	272	24	132 (48.5)	53.8	28.2	8.4	8.3	NR
Barnett (2012) [16]	Yes	7	53	III	227	52	88 (38.8)	56.5	29.5	8.1	10.1	NR
Barnett (2013a) [17,18]	Yes	5	33	III	241	24	165 (68.5)	74.9	29.7	7.8	8.3	NR
Barnett (2013b) [19-21]	Yes	10	72	III	455	52	188 (41.3)	57.2	32.3	8.7	9.6	11.9
Bergenstal (2009) [22]	No	1	102	III	372	24	179 (48.1)	52.6	33.8	10.2	11.3	9
Bergenstal (2012) [23]	Yes	23	149	III	666	24	352 (55.3)	55.9	32.5	8	9.6	5.9
Blonde (2015) [24]	Yes	15	105	III	884	52	473 (53.5)	59.4	32.5	8.5	NR	12.7
Bolli (2014) [25]	Yes	15	75	III	484	≥76	225 (45.7)	56.1	32.5	8	9.5	6
Bosi (2007) [26]	Yes	4	109	III	544	24	239 (57.5)	54.2	32.7	8.4	9.9	6.3
Bosi (2009) [27]	Yes	5	＞250	III	1179	24	684 (58)	52.8	31.3	8.7	10.4	2
Buse (2011) [28,29]	Yes	5	59	III	261	30	148 (57.1)	59	33.5	8.4	8.1	NR

Chacra (2011) [30-32]	Yes	12	115	III	768	76	346 (45.1)	55.1	29.2	8.4	9.6	6.9
Davies (2012) [33]	No	1	NR	III	222	26	143 (66.2)	58.5	NR	8.4	9.8	7.5
Davies (2015) [34,35]	Yes	9	126	III	846	68	425 (50.2)	54.9	37.1	7.9	8.8	7.3
Davies (2016) [36]	Yes	6	78	III	279	26	140 (50.5)	67.2	33.9	8	9.4	15.1
DeFronzo (2008) [37,38]	Yes	16	117	III	329	26	175 (53.2)	53.4	NR	7.9	NR	NR
DeFronzo (2009) [39,40]	Yes	9	154	III	745	206	377 (50.7)	54.6	31.4	8.1	9.8	6.5
DeFronzo (2012) [41]	Yes	20	327	NR	1554	26	697 (44.9)	55.4	31.2	8.5	10	6.2
DeFronzo (2015) [42,43]	Yes	22	197	III	1363	52	721 (53.8)	55.4	31.3	8	8.7	NR
Del Prato (2014) [44,45]	Yes	32	310	III	2639	104	1312 (49.7)	55.4	31.2	7.6	NR	5.5
Diamant (2014a) [46-49]	Yes	16	72	III	467	156	243 (53.3)	58	32.3	8.3	9.8	NR
Diamant (2014b) [50,51]	Yes	17	108	III	637	30	261 (51.2)	59.5	32.4	8.2	7.1	11.5[$]
Dobs (2013) [52]	Yes	NR	41	III	278	54	111 (42.4)	54.5	30.3	8.8	10.1	9.3
Dungan (2016) [53,54]	Yes	8	31	III	300	24	132 (44.1)	58	31.2	8.4	9.8	7.6
Ferdinand (2014) [55]	Yes	3	76	III	755	26	392 (51.9)	56.5	33	7.9	NR	8.3
Ferrannini (2009) [56]	Yes	24	402	III	2789	52	1490 (53.4)	57.5	31.8	7.3	9.2	5.7
Filozof (2010) [57]	NR	NR	NR	III	1007	52	524 (52)	59.5	31	8.5	10.7	6.6
Fonseca (2007) [58]	Yes	4	68	III	296	24	152 (51.4)	59.2	33.1	8.4	9	14.7
Forst (2015) [59]	No	1	47	□	162	24	94 (58.4)	66.7	30.5	7.7	NR	8
Frederich (2012) [60,61]	Yes	4	72	III	366	76	168 (46)	55	30.5	7.9	9	1.7
Frías (2016) [62]	Yes	6	109	□	695	28	328 (47.9)	54.3	32.7	9.30	10.9	7.4
Gallwitz (2012a) [63,64]	Yes	16	209	III	1551	105	933 (60.2)	59·8	30.2	7.7	9.2	NR
Gallwitz (2012b) [65,66]	Yes	14	128	III	1029	234	524 (53.6)	56	32.5	7.5	8.8	5.7
Gao (2009) [67,68]	Yes	4	23	III	472	16	207 (44.4)	54.5	26.3	8.3	9.3	8
Garber (2008) [69]	Yes	5	114	III	515	24	241 (59.1)	58.2	31.3	8.5	10.4	7.1

Garber (2009) [70,71]	Yes	2	138	III	746	52	371 (49.7)	53	33	8.3	9.4	5.4
Giorgino (2015) [72]	Yes	21	78	III	810	78	414 (51.3)	56.7	31.6	8.1	9.1	9.1
Goke (2013) [73-75]	Yes	11	130	III	858	104	444 (51.7)	57.6	31.4	7.7	8.9	NR
Goodman (2009) [76]	Yes	2	67	III	370	24	213 (57.6)	54.8	31.5	8.6	10.9	NR
Gough (2014) [77]	Yes	19	271	III	1663	26	843 (50.8)	55	31.2	8.3	9.2	6.9
Grunberger (2012) [78]	Yes	7	44	□	164	12	74 (45.1)	56.6	32.1	7.2	NR	3.9
Haak (2012) [79,80]	Yes	14	133	III	791	24	426 (53.9)	55.3	29.1	8.6	10.9	NR
Hartley (2015) [81]	NR	NR	85	III	480	30	202 (42.1)	70.7	29.7	7.8	9.4	8.7
Henry (2011) [82]	No	1	3	III	36	12	14 (38.9)	55.6	32.9	6.8	7.1	3.1
Henry (2012) [83]	Yes	8	113	III	326	24	170 (54.3)	54.1	32.6	8.1	9.4	7.7
Henry (2014) [84,85]	NR	NR	NR	III	1615	54	759 (57)	51.8	30.9	8.8	10	4
Hermans (2012) [86,87]	Yes	7	NR	III/□	286	24	164 (57.3)	58.7	31.7	7.8	9.4	6.5
Hirose (2015) [88,89]	No	1	31	□	156	12	111 (71.2)	59.3	25.7	8.1	8.9	12.9
Hollander (2011) [90-92]	Yes	8	133	III	565	76	280 (49.6)	54	30	8.3	9	5.2
Hollander (2013) [93]	Yes	8	63	III	305	24	119 (40.8)	53.5	36.7	7.6	8.9	5.1
Home (2015) [94]	Yes	9	234	III	685	52	353 (53.2)	55.2	32.2	8.2	9.7	8.9
Idorn (2015) [95]	No	1	3	□	47	12	32 (80)	64.5	31	7.3	NR	13.6
Inagaki (2012) [96,97]	No	1	NR	III	427	26	290 (67.9)	56.8	26.2	8.5	NR	9
Iwamoto (2010) [98]	No	1	51	III	380	12	251 (66.1)	59.1	24.9	7.6	9	5.4
Kadowaki (2009) [99]	No	1	20	□	153	12	104 (68.9)	60.3	25.3	8	9.2	NR
Kadowaki (2011) [100,101]	No	1	23	III	181	24	122 (68.2)	58.4	25.5	8.2	9.1	12
Kadowaki (2013a) [102]	No	1	60	III	266	16	156 (58.6)	61.2	25.2	8.9	9.1	14
Kadowaki (2013b) [103,104]	No	1	39	III	204	12	144 (70.6)	60.4	25.9	8	8.2	NR
Kadowaki (2013c) [105,106]	No	1	56	□	324	12	213 (65.7)	58.2	24.8	7.8	8.1	6.2
Kadowaki (2014) [107]	No	1	37	III	194	12	128 (66)	59.4	24.7	8.4	9.1	8.8
Kaku (2010) [108]	No	1	49	NR	264	24	169 (64)	59.7	24.9	8.4	9.5	10.3
Kaku (2016) [109]	No	1	36	III	363	52	262 (72.8)	59.5	25.7	8.1	8.8	8

Kawamori (2012) [110-112]	No	1	47	III	561	12	395 (70.4)	60	25	8	9.1	NR
Kikuchi (2009) [113]	No	1	38	NR	291	12	195 (67)	59	24.4	7.4	9	5.3
Kikuchi (2010) [114]	No	1	29	III	202	12	144 (71.3)	59.7	24.5	7.9	9.1	9.2
Kim (2015) [115]	No	1	NR	III	204	16	109 (53.4)	55.9	NR	7.8	8.4	7.1
Kim (2016) [116]	No	1	16	□	228	16	98 (43.0)	54.5	24.9	8	8.3	5.4
Kobayashi (2014) [117]	No	1	37	III	119	24	74 (63.8)	58.4	26.1	7.6	7.6	6.8
Kothny (2013) [118]	Yes	11	67	III	449	24	229 (50.4)	59.2	29	8.8	9.4	13.1
Lavalle-Gonzalez (2013) [119,120]	Yes	22	169	III	1284	26	605 (47.1)	55.4	31.8	7.9	9.4	6.9
Liutkus (2010) [121]	Yes	1	28	III	165	26	98 (59.4)	54.7	33.7	8.2	9.1	6.3
Lukashevich (2011) [122,123]	Yes	13	108	NR	525	52	294 (57.1)	66.7	28.4	7.8	8.6	15.9
Lukashevich (2014) [124]	Yes	11	NR	III	318	24	152 (47.8)	55.1	28	8.8	9.4	7.3
Macauley (2015) [125]	NR	1	NR	□	44	26	NR	62.1	30.3	6.6	7.8	NR
Marre (2009) [126]	Yes	21	116	III	1041	26	516 (49.6)	56.1	29.9	8.4	9.8	6.6[$]
Mathieu (2014) [127]	Yes	11	119	III	177	26	116 (65.5)	61	32.2	7.7	6.2	12.3
Mathieu (2015) [128,129]	Yes	30	NR	III	660	24	315 (47.9)	58.8	32.1	8.75	9.8	13.5
Matthaei (2015) [130,131]	Yes	9	84	III	315	52	149 (47.3)	54.6	31.4	7.9	8.9	7.7
Miyagawa (2015) [132]	No	1	33	III	492	26	396 (81.0)	57.4	25.5	8.1	9.3	6.6
Moretto (2008) [133]	Yes	4	68	III	233	24	169 (56.3)	54	31	7.8	8.9	2
Mori (2016) [134]	No	1	15	NR	78	12	61 (78.2)	67.9	21.7	6.55	NR	NR
Moses (2016) [135]	Yes	9	48	III	427	24	193 (45.7)	54.9	29.1	8.4	9.2	7.8
Nauck (2007) [136,137]	Yes	13	69	III	505	52	256 (51.1)	58.5	30.4	8.6	11.2	9.9
Nauck (2009) [138,139]	Yes	15	115	III	527	26	265 (50.3)	55	32	7.9	9.5	6
Nauck (2013a) [140,141]	Yes	21	170	III	1091	104	633 (58.2)	56.7	31	8.4	10.1	7.4
Nauck (2013b) [142]	Yes	25	187	III	1049	24	549 (53.4)	58	32	8.3	11.1	NR

Nauck (2014) [143,144]	Yes	13	99	III	1098	52	521 (47.4)	54.2	31	8.1	NR	7
Nauck (2016) [145]	Yes	2	153	III	309	52	166 (55.1)	52.9	33.5	8.1	NR	4
NCT00086515 (2010) [146,147]	Yes	25	100	III	701	104	400 (57.1)	54.5	NR	8	9.5	NR
NCT00095056 (2010) [148]	Yes	16	75	III	91	54	47 (51.6)	67.9	NR	7.7	NR	NR
NCT00106704 (2010) [149,150]	Yes	23	74	III	441	24	234 (53.1)	56	NR	8.3	10.1	NR
NCT00289848 (2010) [151,152]	Yes	3	28	III	530	18	306 (57.7)	50.9	25	8.7	10.5	2
NCT00305604 (2009) [153,154]	No	1	52	III	206	24	97 (47.1)	71.9	31	7.8	9.6	7.1
NCT00337610 (2009) [155,156]	Yes	5	24	III	190	30	88 (46.3)	54.8	30.3	9.2	11.1	7.9
NCT00511108 (2010) [157,158]	Yes	8	44	□	211	12	117 (55.5)	53.6	30.9	7.9	9.8	2.4
NCT00655863 (2013) [159,160]	Yes	2	2	III	71	16	50 (70.4)	59	31.5	6.6	8.9	5.7
NCT00707993 (2013) [161,162]	Yes	11	110	III	441	52	198 (44.9)	69.9	29.8	7.5	8.1	6.1
NCT00713830 (2016) [163]	Yes	16	136	□	859	120	434 (50.5)	57.2	NR	8.25	9.6	NR
NCT00715624 (2016) [164]	Yes	15	111	□	495	125	228 (46.1)	57.2	32.1	8.40	8.1	12.5
NCT00800683 (2011) [165]	Yes	6	53	III	133	18	80 (60.2)	64.4	32	8.2	8.6	NR
NCT00819091 (2011) [166,167]	Yes	7	45	III	245	18	129 (52.7)	56.9	28.3	8.6	10	NR
NCT00839527 (2014) [168]	Yes	9	358	III	685	164	353 (53.2)	55.2	NR	NR	NR	NR
NCT00881530 (2014) [169,170]	Yes	7	132	□	659	78	334 (50.7)	58.6	29.5[#]	7.9	9.9	NR
NCT01075282 (2014) [171]	Yes	21	NR	III	807	78	414 (51.3)	56.7	31.6	8.1	9.1	9.1
NCT01318083 (2011) [172,173]	No	1	33	III	312	12	204 (65.4)	60.2	24.7	8.6	NR	9.8

NCT01644500 (2015) [174]	Yes	3	30	III	807	26	426 (53.9)	52.8	NR	NR	NR	NR
NCT01648582 (2015) [175]	Yes	5	30	III	789	52	420 (54.5)	55	NR	NR	NR	NR
NCT01682759 (2016) [176]	Yes	10	115	□	751	54	414 (55.1)	57.7	NR	7.46	8.6	NR
NCT01717313 (2016) [177]	Yes	12	NR	□	329	24	192 (58.4)	57.2	NR	NR	NR	NR
NCT01778049 (2016) [178]	Yes	11	114	III	482	24	400 (56.7)	56.8	NR	NR	NR	NR
NCT01890122 (2016) [179]	Yes	3	59	□	647	26	366 (56.6)	53.6	26.3	NR	NR	NR
Ning (2016) [180]	Yes	4	22	III	293	24	127 (43.3)	58.1	26.1	8.7	9.5	11.3
Nowicki (2011) [181-183]	Yes	14	75	III	170	52	73 (42.9)	66.5	30.7	8.3	9.9	NR
Odawara (2014) [184]	No	1	20	III	139	12	92 (66.2)	58.1	25.6	8	9.2	7.1
Oe (2015) [185]	No	1	13	NR	100	24	46 (57.5)	67.3	26.7	NR	NR	3.6
Oyama (2016) [186]	No	1	48	NR	463	108	297 (67.2)	69.3	25.1	6.96	7.6	NR
Pan (2008) [187]	Yes	3	31	III	661	24	404 (61.1)	51.8	26.2	8.6	10.1	1.2
Pan (2012) [188,189]	Yes	4	40	III	568	24	315 (55.5)	51.4	25.9	8.2	9.1	NR
Pan (2016) [190]	No	3	21	III	506	16	275 (50.8)	52.6	25.7	8	NR	4.1
Perez-Monteverde (2011) [191,192]	NR	NR	NR	III	492	12	300 (61)	51.1	29.8	9.1	10.3	NR
Pfutzner (2011) [193-195]	Yes	13	211	III	1306	76	643 (49.2)	52	30.2	9.5	11.1	1.7
Pinget (2013) [196]	Yes	13	150	III	484	24	104 (52)	55.8	33.9	8.1	9.1	8.1
Pratley (2006) [197]	Yes	2	15	III	98	12	42 (42.9)	55.7	30	8	9.6	4.3
Pratley (2009a) [198,199]	Yes	13	125	III	493	26	287 (58.2)	55.4	32.8	8	NR	7.6
Pratley (2009b) [200,201]	Yes	16	125	III	500	26	261 (52.2)	56.6	30.1	NR	NR	7.7
Pratley (2013) [202]	Yes	17	130	III	760	24	362 (48.9)	56.4	32.7	8.3	10	8.8
Pratley (2014) [203,204]	Yes	13	198	III	784	26	374 (47.7)	53.5	30.7	NR	NR	4
Probstfield (2016) [205]	No	1	12	□	102	26	64 (63.0)	62.0	33.9	7.90	NR	15.0
Raz (2012) [206]	Yes	NR	53	III	373	24	130 (36.7)	54.8	32.3	7.5	8.8	NR

Reasner (2011) [207-209]	Yes	2	229	III	1250	44	708 (56.8)	49.7	33.3	9.9	12.2	3.4
Riddle (2013) [210]	Yes	15	111	III	496	24	228 (46.1)	57	32.1	8.4	8	12.5
Roden (2015) [211-213]	Yes	9	124	III	899	24	551 (61.3)	55·0	28·4	7·88	8·42	NR
Rosenstock (2008) [214,215]	No	1	152	III	338	12	197 (58.3)	54	30.6	7.9	9.2	1.23[$]
Rosenstock (2009) [216,217]	Yes	13	110	III	390	26	161 (41.3)	55.4	32.6	9.3	10.6	12.6
Rosenstock (2013a) [218-220]	NR	6	135	III	403	206	204 (50.9)	53.5	31.7	7.9	9.7	2.6
Rosenstock (2013b) [221,222]	Yes	16	104	III	495	12	250 (50.5)	58.3	31.4	8	9.8	NR
Rosenstock (2014) [223]	Yes	16	136	III	859	24	434 (50.5)	57.3	30.2	8.3	9.5	9.3
Rosenstock (2015) [224]	Yes	9	139	III	534	24	268 (50.0)	54	31.7	8.9	10.3	7.6
Rosenstock (2016a) [225]	Yes	13	67	□	323	24	165 (51.1)	56.7	32.1	8.05	9.6	6.7
Rosenstock (2016b) [226,227]	Yes	23	240	□	1170	30	592 (50.6)	58.4	31.7	8.09	9.8	8.8
Ross (2012) [228,229]	Yes	9	81	□	491	12	280 (57)	58.6	29.6	8	9.2	NR
Russell-Jones (2012) [230]	Yes	22	124	III	820	26	484 (59)	54	31.1	8.5	NR	2.7
Scherbaum (2008) [221,232]	Yes	6	69	III	306	52	182 (59.5)	63.1	30.2	6.8	7.1	2.6
Schernthaner (2013) [233,234]	Yes	17	140	III	756	52	422 (55.9)	56.5	31.6	8.1	9.3	9.6
Schernthaner (2015) [235,236]	Yes	13	152	□	720	52	445 (61.8)	72.6	29.6	7.6	NR	7.6
Schweizer (2007) [237]	Yes	10	183	III	780	52	424 (54.4)	53.1	32.4	8.7	10.5	1.0[$]
Schweizer (2009) [238]	Yes	14	113	III	335	24	163 (48.7)	71	29.6	7.8	9.2	3
Seck (2010) [239-241]	Yes	2	173	III	1172	104	694 (59.2)	56.7	31.3	7.7	9.2	6.4
Seino (2010) [242-244]	No	1	75	III	411	24	268 (67)	58.3	24.5	8.9	11.3	8.2
Seino (2011) [245,246]	No	1	24	NR	230	12	142 (61.7)	62.1	24	8	NR	7.8
Seino (2012a) [247,248]	No	1	30	III	288	12	198 (68.8)	52.6	25.9	8	NR	NR

Seino (2012b) [249]	Yes	4	57	III	311	24	149 (47.9)	58.4	25.3	8.5	7.7	NR
Seino (2014) [250,251]	No	1	30	□	215	24	148 (69.8)	57	25.1	8.6	NR	7
Seino (2016) [252]	No	1	23	III	257	36	144 (56.0)	60.5	25.6	8.8	8.7	14.5
Sheu (2015) [253]	Yes	21	126	□	685	78	387 (56.5)	55.1	29.8	8.1	9.5	5.4
Strain (2013) [254]	Yes	7	45	III	278	24	126 (45.3)	74.8	29.8	7.9	9.8	11.4
Tajima (2011) [255]	No	1	34	III	146	12	80 (58)	60.8	24.6	8.4	8.6	9.1
Terauchi (2014) [256]	No	1	15	□	145	12	107 (73.8)	52.2	27	8	8.7	4.6
Thrasher (2014) [257,258]	No	1	93	III	226	24	121 (53.5)	53.9	32.7	8.7	10.3	NR
Umpierrez (2011) [259]	Yes	2	39	□	262	16	129 (36.4)	57	33.9	8.2	NR	NR
Umpierrez (2014) [260]	Yes	19	91	III	807	52	353 (43.7)	55.6	33.3	7.6	9	2.6
Vilsboll (2010) [261]	Yes	26	100	III	641	24	326 (50.9)	57.8	31	8.7	9.8	12.5
Wang (2016) [262]	Yes	3	19	III	306	24	152 (49.8)	55.5	25.6	8	8.9	NR
Weissman (2014) [263,264]	Yes	4	222	III	779	164	418 (56.1)	55.5	33.1	8.3	9.5	8.8
White (2014) [265,266]	Yes	4	43	III	160	12	85 (53.1)	55.4	33.1	8	9.1	NR
Williams-Herman (2010) [267-270]	Yes	NR	140	III	1091	104	539 (49.4)	53.5	32.1	8.8	11.3	4.5
Wysham (2014) [271,272]	Yes	4	89	III	976	26	570 (58.4)	55.6	33	8.1	9	8.8
Yang (2012) [273]	No	1	17	III	395	24	200 (50.6)	54.6	25.3	8.5	9.6	6.9
Yang (2015) [274]	No	1	NR	III	279	24	158 (56.6)	58.5	24.9	8.7	10.2	6.9
Yki-Jarvinen (2013) [275,276]	Yes	19	167	III	1263	52	658 (52.2)	60	31	8.3	8.3	NR
Yokoh (2015) [277]	No	1	37	NR	119	24	74 (63.8)	58.5	26.1	7.6	7.55	6.75
Yu Pan (2014) [278]	Yes	4	37	III	391	24	192 (49.2)	54.8	26.9	7.9	8.8	6.7
Zinman (2009) [279]	Yes	2	96	III	533	26	302 (56.7)	55	33.5	8.5	10.1	NR
Large cardiovascular outcomes trials												
Green (2015) (TECOS) [280]	Yes	45	673	III	14671	156*	NR	NR	NR	7.2	NR	11.6
Marso (2016) (LEADER) [281]	Yes	32	410	III	9340	197*	6003 (64.3)	64.3	32.5	NR	NR	12.9

Marso (2016) (SUSTAIN-6) (282)	Yes	20	230	III	3297	104*	2002 (60.7)	64.4	32.8	8.7	NR	13.9
Pfeffer (2015) (ELIXA) (283)	Yes	49	829	III	6068	108*	4207 (69.3)	60.3	30.2	7.7	8.2	9.3
Scirica (2013) (SAVOR-TIMI 53) (284)	Yes	26	788	□	16492	109*	11037 (66.9)	65	31.1	NR	8.7	10.3$
White (2013) (EXAMINE) (285)	Yes	55	898	□	5380	78*	3651 (67.9)	60.9	29.5	8	NR	7.2$

BMI=body mass index; FPG=fasting plasma glucose; NR=not reported.

*median follow up time (weeks); $ median diabetes duration (years); # median body mass index.

Table B. Baseline cardiovascular disease characteristics of patients in included randomised controlled trials

Author (year)	Inclusion criteria	Including patients with established CVD or CV risk factors	Excluding patients with CVD at baseline	Specific exclusion criteria	Number of included patients with established CVD or CV risk factors											
					Obese	Smokers	Hypertension	Dyslipidaemia	CVD	Heart failure	Myocardial infarction	Stroke	Coronary artery disease	Acute coronary syndrome	Angina	Coronary revascularization
Smaller trials																
Ahren (2013) [1]	T2DM	NR	NR	NR												
Ahren (2014) [2,3]	T2DM	NR	Yes	Recent clinically significant cardiovascular and/or cerebrovascular disease (⩽2 months before screening)												
Amin (2015) [4]	T2DM	NR	Yes	Congestive heart failure (New York Heart Association class III–IV)												
Araki (2015) [5]	T2DM	Yes	Yes	Patients with a clinically significant cardiovascular disease			198/361	156/361								
Arechavaleta (2011) [6,7]	T2DM	NR	NR	NR												
Arjona Ferreira (2013a) [8]	T2DM	NR	Yes	A recent (within 3 months) cardiovascular event												
Arjona Ferreira (2013b) [9,10]	T2DM	NR	Yes	A recent (within 6 months) cardiovascular event												
Aroda (2016) [11]	T2DM	NR	NR	NR												
Aschner (2010) [12,13]	T2DM	NR	Yes	Unstable cardiac disease												
Ba (2016) [14]	T2DM	NR	Yes	Patients with new or worsening signs of coronary heart disease within 3months												
Bajaj (2014) [15]	T2DM	NR	Yes	Myocardial infarction, stroke or transient ischemic attack within 3 months before informed consent												
Barnett (2012) [16]	T2DM	NR	Yes	A major cardiovascular event within 6 months before screening; New York Heart Association class III/IV congestive heart failure and/or known left ventricular ejection fraction 540%												
Barnett (2013a) [17,18]	T2DM	NR	Yes	Myocardial infarction, stroke, or transient ischemic attack within 3 months before the study												
Barnett (2013b) [19-21]	T2DM	NR	Yes	History of significant cardiovascular disease												
Bergenstal (2009) [22]	T2DM	NR	Yes	Significant cardiac disease (New York Heart Association class III or IV congestive heart failure, unstable angina, and/or myocardial infarction) within 12 months prior to study												
Bergenstal (2012) [23]	T2DM	NR	Yes	Cardiovascular disease												
Blonde (2015)	T2DM	NR	NR	NR												

(24)								
Bolli (2014) [25]	T2DM	NR	NR	NR				
Bosi (2007) [26]	T2DM	NR	Yes	Congestive heart failure requiring pharmacologic treatment, myocardial infarction, unstable angina, or coronary artery bypass surgery within the previous 6 months				
Bosi (2009) [27]	T2DM	NR	Yes	Myocardial infarction, coronary artery bypass surgery, unstable angina or stroke within the past 6 months; congestive heart failure requiring pharmacological treatment; electrocardiogram abnormalities				
Buse (2011) (28,29)	T2DM	NR	Yes	Cardiac disease				
Chacra (2011) (30-32)	T2DM	NR	Yes	Cardiovascular event within six months of study entry, or New York Heart Association stage III/IV congestive heart failure and/or known left ventricular ejection fraction ≤40%				
Davies (2012) (33)	T2DM	NR	NR	NR				
Davies (2015) (34,35)	T2DM	Yes	NR	NR	730/846	No	586/846	564/846
Davies (2016) (36)	T2DM	NR	Yes	New York Heart Association Functional Classification IV heart failure; episode of unstable angina, acute coronary event, cerebral stroke/transient ischemic attack, or other significant cardiovascular event within the past 180 days				
DeFronzo (2008) [37,38]	T2DM	NR	NR	NR				
DeFronzo (2009) [39,40]	T2DM	NR	Yes	A cardiovascular event within 6 months before study entry or New York Heart Association stage III/IV congestive heart failure and/or known left ventricular ejection fraction ≤40%				
DeFronzo (2012) [41]	T2DM	NR	Yes	History of New York Heart Association Class III or IV heart failure, cardiac surgery, or myocardial infarction within 6 months				
DeFronzo (2015) [42,43]	T2DM	NR	Yes	Acute coronary syndrome, stroke, or transient ischemic attack within 3 months prior to consent				
Del Prato (2014) [44,45]	T2DM	NR	Yes	New York Heart Association Class III–IV heart failure, history of coronary angioplasty, coronary stent placement, coronary bypass surgery, myocardial infarction, stroke or transient ischemic attack in the previous 3 months				

Diamant (2014a) [46-49]	T2DM	NR	NR	NR					
Diamant (2014b) [50,51]	T2DM	NR	Yes	Patients with a clinically significant history of cardiac disease with functional status that is Class III or IV (New York Heart Association Class III or IV)					
Dobs (2013) [52]	T2DM	NR	Yes	Congestive heart failure (requiring pharmacological therapy or New York Heart Association Class II–IV)					
Dungan (2016) [53,54]	T2DM	NR	NR	NR					
Ferdinand (2014) [55]	T2DM	NR	Yes	A recent (<3 months) major cardiovascular event, mean seated HR<60 or >100 bpm, history of tachyarrhythmia					
Ferrannini (2009) [56]	T2DM	Yes	Yes	Serious cardiac conditions (history of torsades de pointes or ventricular tachycardia; percutaneous coronary intervention in the past 3 months; myocardial infarction, coronary artery bypass surgery, unstable angina or stroke in the past 6 months; congestive heart failure requiring pharmacological treatment; second- or third-degree atrioventricular block or prolonged QTc)	2308/2789	454/2789	1856/2789	1384/2789	541/2789
Filozof (2010) [57]	T2DM	Yes	Yes	Serious cardiac conditions (torsades de pointes, sustained and clinically relevant ventricular tachycardia or ventricular fibrillation, percutaneous coronary intervention within the past 3 months, myocardial infarction, coronary artery bypass surgery, unstable angina; or stroke within the last 6 months and congestive heart failure requiring pharmacological treatment, second- or third-degree atrioventricular block or prolonged QT_C)	534/1007				
Fonseca (2007) [58]	T2DM	NR	Yes	Serious cardiac conditions					
Forst (2015) [59]	T2DM	NR	Yes	Serious cardiac conditions					
Frederich (2012) [60,61]	T2DM	Yes	Yes	Cardiovascular event within 6 months prior to study entry or New York Heart Association stage III/IV congestive heart failure and/or known left ventricular ejection fraction $\leqslant$ 40%		212/365	64/365	32/365	19/365	49/365
Frías (2016) [62]	T2DM	NR	NR	NR					
Gallwitz (2012a) [63,64]	T2DM	NR	Yes	Myocardial infarction, stroke, or transient ischemic attack in the 6 months before screening					

Gallwitz (2012b) [65,66]	T2DM	NR	NR	NR			
Gao (2009) [67,68]	T2DM	NR	NR	NR			
Garber (2008) [69]	T2DM	NR	Yes	Myocardial infarction, unstable angina or coronary artery bypass surgery within the previous 6 months. Congestive heart failure (New York Heart Association class III or IV)			
Garber (2009) [70,71]	T2DM	NR	NR	NR			
Giorgino (2015) [72]	T2DM	NR	NR	NR			
Goke (2013) [73-75]	T2DM	NR	NR	NR			
Goodman (2009) [76]	T2DM	NR	NR	NR			
Gough (2014) [77]	T2DM	NR	NR	NR			
Grunberger (2012) [78]	T2DM	NR	Yes	Serious cardiovascular condition			
Haak (2012) [79,80]	T2DM	NR	Yes	A myocardial infarction, stroke or transient ischemic attack in the previous 6 months; had unstable or acute congestive heart failure			
Hartley (2015) [81]	T2DM	NR	Yes	Recent history of cardiovascular disease (acute coronary syndrome, coronary artery intervention, New York Heart Association Class III/ IV heart failure, stroke, transient ischemic neurologic event, or new/worsening symptoms of coronary heart disease)			
Henry (2011) [82]	T2DM	NR	Yes	Unstable condition or serious cardiovascular			
Henry (2012) [83]	T2DM	Yes	Yes	Clinically significant cardiac disease within the past 6 months abnormalities in clinical laboratory tests or electrocardiogram	35/313	197/313	176/313
Henry (2014) [84,85]	T2DM	NR	Yes	Recent (within the past 6 months) acute coronary syndrome (myocardial infarction or unstable angina),coronary artery intervention, stroke, or transient ischemic neurological disorder			
Hermans (2012) [86,87]	T2DM	NR	NR	NR			
Hirose (2015) [88,89]	T2DM	NR	Yes	Congestive heart failure (New York Heart Association Class III or IV), myocardial infarction, stroke or ischemic attacks in past 6 months			
Hollander	T2DM	NR	Yes	A cardiovascular event within 6 months before study entry or New			

(2011) [90-92]				York Heart Association stage III/IV congestive heart failure and/or known left ventricular ejection fraction of 40% or less						
Hollander (2013) [93]	T2DM	Yes	Yes	Myocardial infarction, coronary artery bypass or stroke within the past 6 months, abnormalities sin clinical laboratory tests or electrocardiogram, blood pressure >170/105 mm Hg	65/292		211/292	137/292		
Home (2015) [94]	T2DM	Yes	Yes	Recent clinically significant cardiovascular disease					28/663	
Idorn (2015) [95]	T2DM	Yes	NR	NR		27/40				
Inagaki (2012) [96,97]	T2DM	NR	NR	NR						
Iwamoto (2010) [98]	T2DM	NR	Yes	Congestive heart failure requiring pharmacological treatment, myocardial infarction, unstable angina, or coronary artery bypass surgery within 1 year						
Kadowaki (2009) [99]	T2DM	NR	Yes	Hospitalization for cardiac disease						
Kadowaki (2011) [100,101]	T2DM	NR	NR	NR						
Kadowaki (2013a) [102]	T2DM	NR	Yes	Unstable cardiovascular disease or uncontrolled severe hypertension, or body mass index (BMI) ＜18 or ＞40 kg/m^2						
Kadowaki (2013b) [103,104]	T2DM	NR	NR	NR						
Kadowaki (2013c) [105,106]	T2DM	NR	NR	NR						
Kadowaki (2014) [107]	T2DM	NR	NR	NR						
Kaku (2010) [108]	T2DM	NR	Yes	Significant cardiovascular disease (heart failure, coronary artery disease or uncontrolled hypertension)						
Kaku (2016) [109]	T2DM	NR	NR	NR						
Kawamori (2012) [110-112]	T2DM	Yes	Yes	Myocardial infarction, stroke or transient ischemic attack within the previous 6 months					294/313	
Kikuchi (2009) [113]	T2DM	NR	Yes	Myocardial infarction, unstable angina or coronary artery bypass surgery within the previous 6 months. Congestive heart failure NYHA Class II, III or IV and liver disease such as cirrhosis or chronic active hepatitis also precluded participation						
Kikuchi (2010) [114]	T2DM	NR	Yes	Myocardial infarction, unstable angina or coronary artery bypass surgery within the past 52 weeks, congestive heart failure (New York Heart Association Class III or IV						

Kim (2015) [115]	T2DM	NR	Yes	Cardiovascular significant comorbidities
Kim (2016) [116]	T2DM	NR	Yes	Myocardial infarction, unstable angina, stroke, congestive heart failure (all New York Heart Association classes I to IV)
Kobayashi (2014) [117]	T2DM	NR	Yes	A diagnosis of stroke, myocardial infarction, or other severe cardiovascular complications requiring hospitalization within the past 6 months
Kothny (2013) [118]	T2DM	NR	Yes	A myocardial infarction, coronary artery bypass surgery, percutaneous coronary intervention, stroke or transient ischemic attack within the previous 6 months, unstable angina within the previous 3 months or a current heart failure diagnosis (New York Heart Association class III or IV)
Lavalle-Gonzalez (2013) [119,120]	T2DM	NR	Yes	Cardiovascular disease (including myocardial infarction, unstable angina, revascularization procedure or cerebrovascular accident) in the 3 months before screening or uncontrolled hypertension
Liutkus (2010) [121]	T2DM	NR	NR	NR
Lukashevich (2011) [122,123]	T2DM	NR	Yes	Significant cardiovascular history within 6 months
Lukashevich (2014) [124]	T2DM	NR	Yes	Significant cardiovascular medical conditions
Macauley (2015) [125]	T2DM	NR	NR	NR
Marre (2009) [126]	T2DM	NR	NR	NR
Mathieu (2014) [127]	T2DM	NR	Yes	Stroke; heart failure New York Heart Association class III or IV; myocardial infarction; unstable angina pectoris; or coronary arterial bypass graft or angioplasty within the last 24 weeks
Mathieu (2015)[128,129]	T2DM	NR	Yes	A history of significant and active cardiovascular disease
Matthaei (2015)[130,131]	T2DM	NR	Yes	Cardiovascular disease within 3 months of screening
Miyagawa (2015)[132]	T2DM	NR	NR	NR
Moretto (2008) [133]	T2DM	NR	Yes	Presence of clinically significant cardiac disease within the year
Mori (2016)[134]	T2DM	NR	NR	NR
Moses (2016) [135]	T2DM	NR	Yes	They had a significant cardiovascular disorder within the prior 3months

Nauck (2007) (136,137)	T2DM	NR	NR	NR				
Nauck (2009) (138,139)	T2DM	NR	Yes	New York Heart Association Class III or IV heart failure; or history of coronary angioplasty, coronary stent placement, coronary bypass surgery or myocardial infarction within 6 months				
Nauck (2013a) (140,141)	T2DM	NR	NR	NR				
Nauck (2013b) (142)	T2DM	Yes	Yes	Myocardial infarction or stroke within 6 months, recent unstable hypertension	759/1028	586/1028		
Nauck (2014) (143,144)	T2DM	NR	NR	NR				
Nauck (2016) (145)	T2DM	Yes	Yes	Recent cardiovascular and/or cerebrovascular disease			9/301	
NCT00086515 (2010) (146,147)	T2DM	NR	NR	NR				
NCT00095056 (2010) (148)	T2DM	NR	Yes	Patient has had heart problems (such as a heart attack or chest pain) or stroke within the past 6 months or any condition				
NCT00106704 (2010) (149,150)	T2DM	NR	NR	NR				
NCT00289848 (2010) (151,152)	T2DM	NR	Yes	Unstable cardiac disease				
NCT00305604 (2009) (153,154)	T2DM	NR	Yes	A recent change in cardiovascular status (such as acute coronary syndrome, coronary artery intervention, worsening congestive heart failure, stroke, a transient ischemic neurologic event, or worsening symptoms of coronary artery disease)				
NCT00337610 (2009) (155,156)	T2DM	NR	NR	NR				
NCT00511108 (2010) (157,158)	T2DM	NR	Yes	A significant cardiovascular disorder				
NCT00655863 (2013) (159,160)	T2DM	NR	Yes	Any coronary interventions or history of myocardial infarction within the past 6 months				
NCT00707993 (2013) (161,162)	T2DM	NR	Yes	History of coronary angioplasty, coronary stent placement, coronary bypass surgery, or myocardial infarction within the 6 months prior to Screening				
NCT00713830 (2016)(163)	T2DM	NR	Yes	Patients with history of myocardial infarction, stroke, or heart failure requiring hospitalization				
NCT00715624 (2016) (164)	T2DM	NR	Yes	Patients with cardiovascular disease				
NCT00800683 (2011) (165)	T2DM	NR	Yes	Myocardial infarction, stroke or transient ischemic attack within 6 months prior to informed consent,				

				unstable or acute congestive heart failure
NCT00819091 (2011) [166,167]	T2DM	NR	Yes	A myocardial infarction, stroke, or transient ischemic attack in the previous 6 months; unstable or acute congestive heart failure
NCT00839527 (2014) [168]	T2DM	NR	Yes	Current symptomatic heart failure (NYHA Class II-IV)
NCT00881530 (2014) [169,170]	T2DM	NR	NR	NR
NCT01075282 (2014) [171]	T2DM	NR	Yes	History of Heart Failure New York Heart Classification III or IV, or acute myocardial infarction, or stroke within 2 months of screening
NCT01318083 (2011) [172,173]	T2DM	NR	Yes	Serious cardiovascular disorders
NCT01644500 (2015) [174]	T2DM	NR	Yes	Have cardiac disorder defined as unstable angina, myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention, heart failure, arrhythmia, transient ischemic attack, or stroke
NCT01648582 (2015) [175]	T2DM	NR	Yes	Have cardiac disorder defined as unstable angina, myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention, heart failure, arrhythmia, transient ischemic attack, or stroke
NCT01682759 (2016) [176]	T2DM	NR	Yes	Patients with new or worsening coronary heart disease, congestive heart failure, myocardial infarction, unstable angina, coronary artery intervention, stroke or transient ischemic neurological disorder within the past 3 months
NCT01717313 (2016) [177]	T2DM	NR	Yes	Patients with new or worsening coronary heart disease or congestive heart failure within the past 3 months, or has any of the following disorders within the past 3 months: acute coronary syndrome, coronary artery intervention, stroke or transient ischemic neurological disorder
NCT01778049 (2016) [178]	T2DM	NR	Yes	Acute coronary syndrome and stroke within 3 months of informed consent
NCT01890122 (2016) [179]	T2DM	NR	Yes	Patients with heart failure, history of coronary angioplasty, coronary stent placement, coronary bypass surgery, or myocardial infarction within 6 months prior to Screening
Ning (2016) [180]	T2DM	NR	Yes	Congestive heart failure (New York Heart Association Class III or IV)

Nowicki (2011) (181-183)	T2DM	NR	NR	NR								
Odawara (2014) (184)	T2DM	NR	Yes	Congestive heart failure (New York Heart Association Class III or IV), myocardial infarction, stroke or transient ischemic attacks in the past 6 months								
Oe (2015) (185)	T2DM patients with left ventricular diastolic dysfunction	Yes	Yes	Myocardial infarction or stroke within the previous 24 weeks, significant left ventricular hypertrophy, atrial fibrillation at baseline		10/80	69/80			7/80		
Oyama (2016) (186)	T2DM	NR	Yes	Patients with heart failure and a history of myocardial infarction, angina pectoris, percutaneous transluminal coronary angioplasty, or bypass surgery			347/442	311/442	41/442	101/442	57/442	35/442
Pan (2008) (187)	T2DM	Yes	Yes	Myocardial infarction, unstable angina or coronary artery bypass surgery within the previous 6 months. Congestive heart failure, New York Heart Association Class III or IV	83/661							
Pan (2012) (188,189)	T2DM	NR	Yes	New York Heart Association class III or IV congestive heart failure or left ventricular ejection fraction of ≤40%, or a significant cardiovascular history within 6 months								
Pan (2016) (190)	T2DM	NR	Yes	New York Heart Association Class III or IV heart failure or a history of coronary angioplasty, coronary stent placement, coronary bypass surgery or myocardial infarction within 6 months								
Perez-Monteverde (2011) (191,192)	T2DM	NR	NR	NR								
Pfutzner (2011) (193-195)	T2DM	NR	Yes	Cardiovascular event within 6 months before study entry or New York Heart Association stage III/IV congestive heart failure and/or known left ventricular ejection fraction ≤40%								
Pinget (2013) (196)	T2DM	NR	NR	NR								
Pratley (2006) (197)	T2DM	NR	Yes	Clinically significant cardiovascular abnormalities								
Pratley (2009a) (198,199)	T2DM	NR	Yes	They had active heart failure (New York Heart Association Class III or IV) or had undergone an invasive coronary procedure or had a myocardial infarction within 6 months before screening								
Pratley (2009b) (200,201)	T2DM	NR	Yes	New York Heart Association classes III or IV heart failure; a history of coronary angioplasty, coronary stent placement, coronary bypass surgery, or myocardial infarction within 6								

				months	
Pratley (2013) (202)	T2DM	NR	Yes	Clinically relevant QTc prolongation (e.g. QTc >480ms) or family history of Long QT Syndrome	
Pratley (2014) (203,204)	T2DM	NR	Yes	Heart failure (New York Heart Association Class III-IV); coronary angioplasty, stent placement, bypass surgery or myocardial infarction within 3 months of screening	
Probstfield (2016) (205)	T2DM patients with high cardiovascular risk	Yes	Yes	Patients with current symptomatic heart failure, history of New York Heart Association Functional Classification III or IV congestive heart failure at any time or left ventricular ejection fraction < 25%	
Raz (2012) (206)	T2DM	NR	Yes	Cardiac disease within the past 6 months	
Reasner (2011) (207-209)	T2DM	NR	Yes	Unstable cardiac disease	
Riddle (2013) (210)	T2DM	Yes	NR	NR	297/495
Roden (2015) (211-213)	T2DM	NR	NR	NR	
Rosenstock (2008) (214,215)	T2DM	NR	Yes	Congestive heart failure, recent cardiovascular illness	
Rosenstock (2009) (216,217)	T2DM	NR	Yes	Coronary angioplasty, coronary stent placement, coronary bypass surgery or myocardial infarction within the previous 6 months. New York Heart Association class III or IV heart failure	
Rosenstock (2013a) (218-220)	T2DM	NR	NR	NR	
Rosenstock (2013b) (221,222)	T2DM	NR	Yes	History of myocardial infarction, stroke or transient ischemic attack within 6 months	
Rosenstock (2014) (223)	T2DM	NR	Yes	History of myocardial infarction, stroke, or heart failure requiring hospitalization within the previous 6 months	
Rosenstock (2015) (224)	T2DM	NR	Yes	Cardiovascular disease within 3 months of screening, congestive heart failure (New York Heart Association functional class IV)	
Rosenstock (2016a) (225)	T2DM	NR	NR	NR	
Rosenstock (2016b) (226,227)	T2DM	NR	NR	NR	
Ross (2012) (228,229)	T2DM	NR	Yes	A major cardiovascular event (myocardial infarction, stroke or transient ischemic attack) within the previous six months	
Russell-Jones (2012) (230)	T2DM	NR	NR	NR	

Scherbaum (2008) [231,232]	T2DM	Yes	Yes	A history of significant cardiac arrhythmia, congestive heart failure, New York Heart Association Class III or IV or liver disease such as cirrhosis	83/131						
Schernthaner (2013) [233,234]	T2DM	NR	Yes	Cardiovascular disease							
Schernthaner (2015) [235,236]	T2DM	Yes	NR	NR	317/720	555/720	433/720	40/720	54/720	67/720	38/720
Schweizer (2007) [237]	T2DM	NR	Yes	Congestive heart failure requiring pharmacological treatment, or myocardial infarction, unstable angina, or coronary artery bypass surgery within the previous 6 months							
Schweizer (2009) [238]	T2DM	Yes	Yes	Congestive heart failure requiring pharmacological treatment or myocardial infarction, unstable angina or stroke or coronary artery bypass surgery within the past 6 months	138/335						
Seck (2010) [239-241]	T2DM	NR	NR	NR							
Seino (2010) [242-244]	T2DM	NR	Yes	Significant cardiovascular disease (heart failure, coronary artery disease or uncontrolled hypertension)							
Seino (2011) [245,246]	T2DM	NR	Yes	Serious cardiovascular disorders							
Seino (2012a) [247,248]	T2DM	NR	Yes	Patients with severe cardiovascular function impairment							
Seino (2012b) [249]	T2DM	NR	Yes	History within the previous 6 months of myocardial infarction, stroke or heart failure requiring hospitalization							
Seino (2014) [250,251]	T2DM	NR	Yes	Cardiovascular/cerebrovascular disease							
Seino (2016) [252]	T2DM	NR	NR	NR							
Sheu (2015) [253]	T2DM	NR	Yes	A history of significant cardiovascular disease							
Strain (2013) [254]	T2DM	NR	Yes	Myocardial infarction, coronary artery bypass surgery, or stroke within 6 months; unstable angina within 3 months; congestive heart failure (New York Heart Association classification of III or IV)							
Tajima (2011) [255]	T2DM	NR	Yes	Unstable cardiovascular disease							
Terauchi (2014) [256]	T2DM	NR	NR	NR							
Thrasher (2014) [257,258]	T2DM	NR	Yes	A history of myocardial infarction, stroke, or transient ischemic attack within 3 months before screening							

Umpierrez (2011) [259]	T2DM	NR	Yes	Cardiovascular disorders				
Umpierrez (2014) [260]	T2DM	NR	NR	NR				
Vilsboll (2010) [261]	T2DM	NR	Yes	Unstable cardiac disease (including new or worsening signs or symptoms of coronary heart disease within 3 months of study entry or any of the following within 6 months of study entry: acute coronary syndrome, stroke or ischemic event; coronary artery intervention, or New York Heart Association Class II-IV congestive heart failure)				
Wang (2016) [262]	T2DM	NR	Yes	Patients had experienced myocardial infarction, stroke, or transient ischemic attack ≤6 months prior to informed consent; had unstable or acute congestive heart failure				
Weissman (2014) [263,264]	T2DM	Yes	Yes	Recent significant cardiovascular (within 2 months) or cerebrovascular (within 1 month) events	532/745		37/745	
White (2014) [265,266]	T2DM	NR	Yes	A cardiovascular event within 3 months of screening, congestive heart failure New York Heart Association class III/IV, known ejection fraction ≤40%				
Williams-Herman (2010) [267-270]	T2DM	NR	Yes	Unstable cardiac disease				
Wysham (2014) [271,272]	T2DM	NR	NR	NR				
Yang (2012) [273]	T2DM	NR	Yes	Congestive heart failure, unstable coronary heart disease				
Yang (2015) [274]	T2DM	NR	Yes	Patients with congestive heart failure (New York Heart Association Class III or IV)				
Yki-Jarvinen (2013) [275,276]	T2DM	NR	Yes	A myocardial infarction, stroke, or transient ischemic attack within 6 months before informed consent				
Yokoh (2015) [277]	T2DM	NR	Yes	Myocardial infarction, or other severe cardiovascular complications requiring hospitalization within the past 6 months				
Yu Pan (2014) [278]	T2DM	NR	NR	NR				
Zinman (2009) [279]	T2DM	NR	NR	NR				
Large cardiovascular outcomes trials								
Green (2015) (TECOS) [280]	T2DM patients with established or pre-existing	Yes, including patients who had established CVD (major coronary artery disease, ischemic cerebrovascular disease, or atherosclerotic	NR	NR	7522/14735	10863/14735	6255/14735	9378/14735

	CVD	peripheral arterial disease) or were at least 50 years of age, with a glycated hemoglobin level of 6.5 to 8.0% when treated with stable doses of one or two oral anti-hyperglycemic agents (metformin, pioglitazone, or sulfonylurea) or insulin (with or without metformin)											
Marso (2016) (LEADER) [281]	T2DM patients with high CVD risk	Yes, including patients with cardiovascular coexisting condition or cardiovascular risk factors	Yes	The occurrence of an acute coronary or cerebrovascular event within 14 days before screening and randomisation			9340/9340	1305/9340	2864/9340				3638/6068
Marso (2016) (SUSTAIN-6) [282]	T2DM patients with established cardiovascular disease, or with at least one cardiovascular risk factor	Yes, including patients with established cardiovascular disease, or with at least one cardiovascular risk factor	Yes	A history of an acute coronary or cerebrovascular event within 90 days before randomisation; planned revascularization of a coronary, carotid, or peripheral artery	1804/3297	3059/3297		777/3297	1072/3297	491/3297	1994/3297		
Pfeffer (2015) (ELIXA) [283]	T2DM patients with acute coronary syndrome	Yes, including patients with acute coronary syndrome	Yes	Coronary-artery bypass graft surgery for the qualifying event, planned coronary revascularization procedure within 90 days after screening	709/6068	4635/6068		1358/6068		331/6068	818/6068	6068/6068	4586/6068
Scirica (2013) (SAVOR-TIMI 53) [284]	T2DM patients who had a history of, or were at risk for, cardiovascular events	Yes, including patients with a history of established CVD or multiple risk factors for vascular disease	NR	NR		13492/16492	11739/16492	2105/16492	6237/16492				7123/16492
White (2013) (EXAMINE) [285]	T2DM patients with acute coronary syndrome	Yes, including patients with acute coronary syndrome	Yes	Unstable cardiac disorders (e.g., New York Heart Association class IV heart failure, refractory angina, uncontrolled arrhythmias, critical valvular heart disease	367/5380	4469/5380		1501/5380	4734/5380	388/5380	5380/5380		4060/16492

T2DM=type 2 diabetes mellitus; CVD=cardiovascular disease; CV=cardiovascular; NR=not reported.

Table C. Interventions tested and event rates in randomised controlled trials in patients with type 2 diabetes mellitus

Author (year)	Medications used across groups	Incretin		Control		Duration of treatment (weeks)
		Type	Events	Type	Events	
Smaller trials						
Ahren (2013) [1]	Metformin	Lixisenatide	0/510	Placebo	0/170	24
Ahren (2014) [2,3]	Metformin	Sitagliptin	0/302	Placebo	0/101	164
		Albiglutide	1/302	Glimepiride	0/307	
Amin (2015) [4]	None	Sitagliptin	0/55	Placebo	0/54	12
		Sitagliptin	0/55	Ertugliflzin	0/219	
Araki (2015) [5]	SU ± biguanide	Dulaglutide	0/181	Insulin glargine	0/180	26
Arechavaleta (2011) [6,7]	Metformin	Sitagliptin	0/516	Glimepiride	1/518	30
Arjona Ferreira (2013a) [8]	None	Sitagliptin	4/64	Glipizide	6/65	54
Arjona Ferreira (2013b) [9,10]	None	Sitagliptin	3/210	Glipizide	7/212	54
Aroda (2016) [11]	Insulin glargine	Lixisenatide	1/365	No additional drugs	2/365	30
Aschner (2010) [12,13]	None	Sitagliptin	1/528	Metformin	0/522	24
Ba (2016) [14]	SU ± metformin	Sitagliptin	0/248	Placebo	0/249	24
Bajaj (2014) [15]	Metformin + pioglitazone	Linagliptin	0/183	Placebo	1/89	24
Barnett (2012) [16]	None	Linagliptin	1/151	Placebo	0/76	52
Barnett (2013a) [17,18]	Metformin, sulfonylureas, or basal insulin, or combinations of these drugs	Linagliptin	0/162	Placebo	0/79	24
Barnett (2013b) [19-21]	Insulin ± metformin	Saxagliptin	2/304	Canagliflozin	0/151	52
Bergenstal (2009) [22]	Metformin + SU	Exenatide	0/124	Biphasic insulin aspart 70/30 (BIAsp 30)	1/128	24

Bergenstal (2012) [23]	Metformin	Sitagliptin	0/184	Placebo	0/90	24
		Taspoglutide	0/379	Placebo	0/90	
Blonde (2015) [24]	Metformin	Dulaglutide	2/588	Glargine	3/296	52
Bolli (2014) [25]	Metformin	Lixisenatide	2/322	Placebo	2/160	≥76
Bosi (2007) [26]	Metformin	Vildagliptin	0/360	Placebo	0/181	24
Bosi (2009) [27]	None	Vildagliptin	0/297	Metformin	0/292	24
	Metformin	Vildagliptin	1/292	No additional drugs	0/292	
Buse (2011) [28,29]	Insulin glargine	Exenatide	0/137	Placebo	1/122	30
Chacra (2011) [30-32]	Glyburide	Saxagliptin	1/501	Placebo	4/267	76
Davies (2012) [33]	None	Exenatide	0/111	Insulin detemir	0/105	26
Davies (2015) [34,35]	None	Liraglutide	1/632	Placebo	0/212	68
Davies (2016) [36]	Monotherapy or dual-therapy combinations of metformin and/or SU and/or pioglitazone	Liraglutide	4/140	Placebo	1/137	26
DeFronzo (2008) [37,38]	None	Alogliptin	0/264	Placebo	0/64	26
DeFronzo (2009) [39,40]	Metformin	Saxagliptin	1/564	Placebo	2/179	206
DeFronzo (2012) [41]	Metformin	Alogliptin	0/257	Placebo	0/129	26
	Metformin + pioglitazone	Alogliptin	0/780	No additional drugs	1/387	
DeFronzo (2015) [42,43]	Metformin + empagliflozin	Linagliptin	1/269	No additional drugs	1/277	52
	Empagliflozin	Linagliptin	1/272	No additional drugs	4/270	

Del Prato (2014) [44,45]	Metformin	Alogliptin	6/1751	Glipizide	5/869	104
Diamant (2014a) [46-49]	Metformin ± SU	Exenatide	1/233	Insulin glargine	1/223	156
Diamant (2014b) [50,51]	Insulin glargine + metformin	Exenatide	1/315	Insulin lispro	0/312	30
Dobs (2013) [52]	Rosiglitazone + metformin	Sitagliptin	0/170	Placebo	0/92	54
Dungan (2016) [53,54]	glimepiride	Dulaglutide	1/239	Placebo	0/60	24
Ferdinand (2014) [55]	None	Dulaglutide	0/505	Placebo	0/250	26
Ferrannini (2009) [56]	Metformin	Vildagliptin	2/1389	Glimepiride	3/1383	52
Filozof (2010) [57]	Metformin	Vildagliptin	1/510	Glimepiride	1/493	52
Fonseca (2007) [58]	Insulin	Vildagliptin	1/144	Placebo	1/152	24
Forst (2015) [59]	Glimepiride	Vildagliptin	0/82	NPH insulin	1/79	24
Frederich (2012) [60,61]	None	Saxagliptin	2/291	Placebo	0/74	76
Frías (2016) [62]	Metformin + dapagliflozin	Exenatide	3/231	No additional drugs	1/233	28
	Metformin	Exenatide	1/230	Dapagliflozin	1/233	
Gallwitz (2012a) [63,64]	Metformin	Linagliptin	4/776	Glimepiride	4/775	105
Gallwitz (2012b) [65,66]	Metformin	Exenatide	5/511	Glimepiride	5/508	234
Gao (2009) [67,68]	Metformin ± SU	Exenatide	0/234	Placebo	0/231	16
Garber (2008) [69]	Glimepiride	Vildagliptin	0/339	Placebo	0/176	24
Garber (2009) [70,71]	None	Liraglutide	0/497	Glimepiride	1/248	52
Giorgino (2015) [72]	Metformin + glimepiride	Dulaglutide	1/545	Insulin Glargine	2/262	78
Goke (2013) [73-75]	Metformin	Saxagliptin	4/428	Glipizide	2/430	104
Goodman (2009) [76]	Metformin	Vildagliptin	0/248	Placebo	0/122	24

Gough (2014) [77]	Metformin + pioglitazone	Liraglutide	0/412	Insulin degludec	0/412	26
Grunberger (2012) [78]	Metformin	Dulaglutide	0/132	Placebo	0/32	12
Haak (2012) [79,80]	None	Linagliptin	0/142	Placebo	0/72	24
	Metformin	Linagliptin	0/286	No additional drugs	1/291	
Hartley (2015) [81]	None	Sitagliptin	0/241	Glimepiride	0/236	32
Henry (2011) [82]	None	Saxagliptin	0/20	Placebo	0/16	12
Henry (2012) [83]	Metformin + pioglitazone	Taspoglutide	0/223	Placebo	0/101	24
Henry (2014) [84,85]	Pioglitazone	Sitagliptin	3/581	No additional drugs	1/565	54
Hermans (2012) [86,87]	Metformin 1500 mg	Saxagliptin	1/147	Metformin 500 mg, once or twice daily	1/139	24
Hirose (2015) [88,89]	Insulin ± metformin	Vildagliptin	0/78	Placebo	0/78	12
Hollander (2011) [90-92]	Thiazolidinedione	Saxagliptin	2/381	Placebo	0/184	76
Hollander (2013) [93]	Metformin	Taspoglutide	0/154	Placebo	1/150	24
Home (2015) [94]	Metformin + glimepiride	Albiglutide	0/271	Placebo	1/115	52
		Albiglutide	0/271	Pioglitazone	3/277	
Idorn (2015) [95]	Metformin	Liraglutide	0/25	Placebo	0/22	12
Inagaki (2012) [96,97]	None	Exenatide	1/215	Insulin glargine	0/212	26
Iwamoto (2010) [98]	None	Vildagliptin	0/188	Voglibose	0/192	12
Kadowaki (2009) [99]	None	Exenatide	0/111	Placebo	0/40	12
Kadowaki (2011) [100,101]	None	Exenatide	0/144	Placebo	0/35	24
Kadowaki (2013a) [102]	Insulin	Sitagliptin	0/129	Placebo	0/137	16
Kadowaki (2013b) [103,104]	Pioglitazone	Teneligliptin	0/103	Placebo	0/101	12
Kadowaki (2013c) [105,106]	None	Teneligliptin	0/244	Placebo	1/80	12
Kadowaki (2014) [107]	Glimepiride	Teneligliptin	0/96	Placebo	0/98	12

Kaku (2010) [108]	SU	Liraglutide	0/176	Placebo	0/84	24
Kaku (2016) [109]	Glinide, metformin, a-glucosidase inhibitor or thiazolidinedione	Liraglutide	1/240	An additional OAD	0/120	52
Kawamori (2012) [110-112]	None	Linagliptin	0/319	Placebo	0/80	12
		Linagliptin	0/319	Voglibose	0/162	
Kikuchi (2009) [113]	None	Vildagliptin	0/219	Placebo	0/72	12
Kikuchi (2010) [114]	Glimepiride	Vildagliptin	0/102	Placebo	0/100	12
Kim (2015) [115]	Metformin	Teneligliptin	0/136	Placebo	0/68	16
Kim (2016) [116]	Metformin	Vildagliptin	0/117	Pioglitazone	0/111	16
Kobayashi (2014) [117]	Metformin or pioglitazone	Sitagliptin	0/58	Alpha-glucosidase inhibitor	0/58	24
Kothny (2013) [118]	Insulin ±Metformin	Vildagliptin	0/227	Placebo	1/221	24
Lavalle-Gonzalez (2013) [119,120]	Metformin	Sitagliptin	0/366	Canagliflozin	1/735	26
		Sitagliptin	0/366	Placebo	0/183	
Liutkus (2010) [121]	Thiazolidinediones ± metformin	Exenatide	0/111	Placebo	0/54	26
Lukashevich (2011) [122,123]	Metformin	Vildagliptin	8/287	Placebo	6/226	52
Lukashevich (2014) [124]	None	Vildagliptin	0/157	Placebo	1/160	24
Macauley (2015) [125]	Metformin	Vildagliptin	0/22	Placebo	0/22	26
Marre (2009) [126]	Glimepiride	Liraglutide	0/695	Placebo	0/114	26
		Liraglutide	0/695	Rosiglitazone	0/231	
Mathieu (2014) [127]	Insulin degludec (IDeg) + Metformin	Liraglutide	0/87	Insulin aspart	0/86	26
Mathieu (2015) [128,129]	None	Sitagliptin	2/329	Placebo	1/329	24

Matthaei (2015) [130,131]	Dapagliflozin +metformin	Saxagliptin	0/153	Placebo	1/162	52
Miyagawa (2015) [132]	None	Dulaglutide	0/280	Placebo	0/70	26
		Liraglutide	0/137	Placebo	0/70	
Moretto (2008) [133]	None	Exenatide	0/155	Placebo	0/77	24
Mori (2016)[134]	None	Linagliptin	0/40	Voglibose	1/38	12
Moses (2016) [135]	Sulfonylurea + metformin	Sitagliptin	0/210	Placebo	1/212	24
Nauck (2007) [136,137]	Sulfonylurea + metformin	Exenatide	2/253	Biphasic insulin aspart	1/248	52
Nauck (2009) [138,139]	Metformin	Alogliptin	1/423	Placebo	0/104	26
Nauck (2013a) [140,141]	Metformin	Liraglutide	2/724	Placebo	0/121	104
		Liraglutide	2/724	Glimepiride	0/242	
Nauck (2013b) [142]	Metformin	Taspoglutide	1/715	Insulin glargine	2/322	24
Nauck (2014) [143,144]	Metformin	Dulaglutide	1/606	Placebo	0/177	52
		Sitagliptin	2/315	Placebo	0/177	
Nauck (2016) [145]	None	Albiglutide	3/200	Placebo	0/101	52
NCT00086515 (2010) [146,147]	None	Sitagliptin	2/464	Glipizide	0/237	104
NCT00095056 (2010) [148]	None	Sitagliptin	1/65	Placebo	0/26	54
NCT00106704 (2010) [149,150]	Glimepiride ± metformin	Sitagliptin	2/222	Placebo	1/219	24
NCT00289848 (2010) [151,152]	None	Sitagliptin	1/352	Placebo	0/178	18
NCT00305604 (2009) [153,154]	None	Sitagliptin	0/102	Placebo	0/104	24
NCT00337610 (2009) [155,156]	Metformin	Sitagliptin	0/96	Placebo	1/94	30
NCT00511108 (2010)	None	Sitagliptin	0/52	Placebo	0/53	12

(157,158)	Pioglitazone	Sitagliptin	0/52	No additional drugs	0/54	
NCT00655863 (2013) (159,160)	None	Alogliptin	0/25	Placebo	0/24	16
NCT00707993 (2013) (161,162)	None	Alogliptin	0/222	Glipizide	0/219	52
NCT00713830 (2016) (163)	None	Lixisenatide	1/574	Placebo	0/285	24
NCT00715624 (2016) (164)	None	Lixisenatide	1/328	Placebo	0/167	24
NCT00800683 (2011) (165)	Insulin	Linagliptin	1/68	Placebo	1/65	18
NCT00819091 (2011) (166,167)	SU	Linagliptin	1/161	Placebo	0/84	18
NCT00839527 (2014) (168)	Metformin + glimepiride	Albiglutide	1/271	Placebo	0/115	164
		Albiglutide	1/271	Pioglitazone	0/227	
NCT00881530 (2014) (169,170)	Metformin	Sitagliptin	0/56	No additional drugs	1/56	78
		Sitagliptin	0/56	Empagliflozin	0/332	
NCT01075282 (2014) (171)	Metformin +glimepiride	Dulaglutide	0/545	Insulin Glargine	1/262	78
NCT01318083 (2011) (172,173)	Glimepiride	Alogliptin	2/209	Placebo	0/103	12
NCT01644500 (2015) (174)	None	Dulaglutide	1/536	Glimepiride	0/269	26
NCT01648582 (2015) (175)	Metformin ±sulfonylurea	Dulaglutide	1/526	Insulin Glargine	0/257	52
NCT01682759 (2016) (176)	None	Omarigliptin	2/375	Glimepiride	1/375	54
NCT01717313 (2016) (177)	Metformin	Omarigliptin	0/165	Placebo	1/164	24
NCT01778049 (2016) (178)	Empagliflozin + Metformin	Linagliptin	0/238	Placebo	0/240	24
NCT01890122 (2016) (179)	None	Alogliptin	0/162	Placebo	1/161	26
	Metformin	Alogliptin	0/158	No additional drugs	0/161	
Ning (2016) (180)	Insulin ± metformin	Vildagliptin	0/146	Placebo	0/147	24
Nowicki (2011) (181-183)	None	Saxagliptin	3/85	Placebo	4/85	52
Odawara (2014) (184)	Metformin	Vildagliptin	0/69	Placebo	0/70	12

Oe (2015) [185]	None	Sitagliptin	0/40	Voglibose	0/40	24
Oyama (2016) [186]	Conventional therapy	Sitagliptin	3/222	No additional drugs	2/220	108
Pan (2008) [187]	None	Vildagliptin	0/431	Acarbose	0/216	24
Pan (2012) [188,189]	None	Saxagliptin	1/284	Placebo	0/284	24
Pan (2016) [190]	Metformin or pioglitazone	Alogliptin	0/252	Placebo	0/253	16
Perez-Monteverde (2011) [191,192]	None	Sitagliptin	0/244	Pioglitazone	0/248	12
Pfutzner (2011) [193-195]	None	Saxagliptin	2/335	Metformin	5/328	76
	Metformin	Saxagliptin	3/643	No additional drugs	5/328	
Pinget (2013) [196]	Pioglitazone ± metformin.	Lixisenatide	0/323	Placebo	2/161	24
Pratley (2006) [197]	None	Vildagliptin	0/70	Placebo	0/28	12
Pratley (2009a) [198,199]	Pioglitazone	Alogliptin	1/397	Placebo	0/97	26
Pratley (2009b) [200,201]	Glyburide	Alogliptin	0/401	Placebo	0/99	26
Pratley (2013) [202]	Metformin + SU	Taspoglutide	0/494	Pioglitazone	0/257	24
Pratley (2014) [203,204]	None	Alogliptin	0/222	Placebo	0/106	26
	Metformin	Alogliptin	0/220	No additional drugs	0/220	
Probstfield (2016) [205]	Metformin + insulin analogs	Exenatide	1/47	No additional drugs	0/45	26
Raz (2012) [206]	None	Taspoglutide	0/239	Placebo	0/129	24
Reasner (2011) [207-209]	Metformin	Sitagliptin	1/625	No additional drugs	2/621	44
Riddle (2013) [210]	Basal insulin ± metformin	Lixisenatide	1/328	Placebo	0/167	24
Roden (2015) [211-213]	None	Sitagliptin	1/223	Placebo	1/229	24
		Sitagliptin	1/223	Empagliflozin	0/447	
Rosenstock (2008) [214,215]	None	Saxagliptin	0/271	Placebo	0/67	12
Rosenstock (2009) [216,217]	Insulin ± metformin	Alogliptin	1/260	Placebo	0/129	26

Rosenstock (2013a) [218-220]	None	Saxagliptin	0/306	Placebo	1/95	206
Rosenstock (2013b) [221,222]	Metformin	Sitagliptin	0/71	Placebo	0/71	12
		Sitagliptin	0/71	Empagliflozin	0/353	
Rosenstock (2014) [223]	None	Lixisenatide	1/574	Placebo	0/285	24
Rosenstock (2015) [224]	Metformin	Saxagliptin	0/176	Dapagliflozin	0/179	24
		Saxagliptin	0/179	Placebo	0/179	
Rosenstock (2016a) [225]	Metformin + insulin glargine	Lixisenatide	0/161	No additional drugs	0/162	24
Rosenstock (2016b) [226,227]	None	Lixisenatide	1/233	Insulin Glargine	3/467	30
Ross (2012) [228,229]	Metformin	Linagliptin	0/447	Placebo	0/44	12
Russell-Jones (2012) [230]	None	Exenatide	0/248	Metformin	1/246	26
		Sitagliptin	0/163	Pioglitazone	0/163	
Scherbaum (2008) [231,232]	None	Vildagliptin	0/156	Placebo	1/150	52
Schernthaner (2013) [233,234]	Metformin + SU	Sitagliptin	0/378	Canagliflozin	2/377	52
Schernthaner (2015) [235,236]	None	Saxagliptin	1/359	Glimepiride	1/359	52
Schweizer (2007) [237]	None	Vildagliptin	2/511	Metformin	2/249	52
Schweizer (2009) [238]	None	Vildagliptin	1/167	Metformin	0/165	24
Seck (2010) [239-241]	Metformin	Sitagliptin	1/588	Glipizide	8/584	104
Seino (2010) [242-244]	None	Liraglutide	1/268	Glibenclamide	0/132	24
Seino (2011) [245,246]	Voglibose	Alogliptin	0/155	Placebo	0/75	12
Seino (2012a) [247,248]	Metformin	Alogliptin	0/188	Placebo	0/100	12
Seino (2012b) [249]	Insulin regimen ± SU	Lixisenatide	0/154	Placebo	1/157	24
Seino (2014) [250,251]	None	Albiglutide	0/159	Placebo	0/53	24
Seino (2016) [252]	Insulin	Liraglutide	0/127	Placebo	0/130	36
Sheu (2015) [253]	None	Omarigliptin	4/405	Placebo	1/80	78

Strain (2013) [254]	None	Vildagliptin	1/139	Placebo	1/139	24
Tajima (2011) [255]	Glimepiride	Sitagliptin	0/71	Placebo	0/67	12
Terauchi (2014) [256]	None	Dulaglutide	1/108	Placebo	0/37	16
Thrasher (2014) [257,258]	None	Linagliptin	0/106	Placebo	0/120	24
Umpierrez (2011) [259]	None	Dulaglutide	0/196	Placebo	0/66	16
Umpierrez (2014) [260]	None	Dulaglutide	0/539	Metformin	0/268	52
Vilsboll (2010) [261]	Insulin + metformin	Sitagliptin	0/322	Placebo	0/319	24
Wang (2016) [262]	Metformin	Linagliptin	0/205	Placebo	0/100	24
Weissman (2014) [263,264]	Metformin ± SU	Albiglutide	3/504	Insulin glargine	3/241	164
White (2014) [265,266]	Metformin	Saxagliptin	0/74	Placebo	0/86	12
Williams-Herman (2010) [267-270]	None	Sitagliptin	0/179	Metformin	2/176	104
	Metformin	Sitagliptin	3/372	No additional drugs	0/364	
Wysham (2014) [271,272]	Metformin + pioglitazone	Dulaglutide	2/559	Placebo	0/141	26
		Exenatide	0/276	Placebo	0/141	
Yang (2012) [273]	Metformin	Sitagliptin	0/197	Placebo	0/198	24
Yang (2015) [274]	Glimepiride	Vildagliptin	0/143	Placebo	0/136	24
Yki-Jarvinen (2013) [275,276]	Basal insulin	Linagliptin	5/631	Placebo	5/630	52
Yokoh (2015) [277]	Metformin ± pioglitazone	Sitagliptin	0/58	Alpha-glucosidase inhibitor	0/58	24
Yu Pan (2014) [278]	Metformin ± SU	Lixisenatide	0/196	Placebo	0/194	24
Zinman (2009) [279]	Metformin + rosiglitazone	Liraglutide	0/356	Placebo	0/177	26
Large cardiovascular outcomes trials						
Green (2015) (TECOS) [280]	OADs (Metformin, pioglitazone, or sulfonylurea) or insulin (with or without metformin)	Sitagliptin	547/7332	Placebo	537/7339	156*
Marso (2016) (LEADER)	Standard of care treatment	Liraglutide	381/4668	Placebo	447/4672	197*

(281)	(none, or treated with one or more OAD, or human NPH insulin, or long-acting insulin analogue (alone or in combination with OAD(s)))					
Marso (2016) (SUSTAIN-6) (282)	Standard of care treatment (none; or treated with one or two OAD; or basal insulin (human NPH insulin, or long-acting insulin analogue) or premixed insulin, alone or in combination with one or two OAD(s))	Semaglutide	62/1648	Placebo	60/1649	104*
Pfeffer (2015) (ELIXA) (283)	Metformin, SU, TZD, insulin, or other diabetes medications	Lixisenatide	211/3034	Placebo	223/3034	108*
Scirica (2013) (SAVOR-TIMI 53) (284)	Antihyperglycemic drugs (metformin, SU, TZD, insulin, other antihyperglycemic medications, or none)	Saxagliptin	420/8280	Placebo	378/8212	109*
White (2013) (EXAMINE) (285)	Standard of care treatment for type 2 diabetes mellitus (e.g. metformin, SU, insulin, TZD)	Alogliptin	153/2701	Placebo	173/2679	78*

SU=sulphonylurea; TZD thiazolidinedione; OADs oral antidiabetic drugs; NPH=Neutral Protamine Hagedorn.

*median treatment time (weeks).

Table D. Risk of bias of randomised controlled trials of incretin treatment in type 2 diabetes mellitus

Author (year)	Adequate randomisation sequence generation	Adequate allocation concealment	Blinding of participants and caregivers	Blinding of outcome assessors and outcome adjudicators	Free of infrequent missing outcome data#	Free of selective outcome reporting	Free of other sources of bias
Smaller trials							
Ahren (2013) [1]	**Probably yes** Randomised, double-blind*	**Probably yes** Randomised, double-blind†	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**‡	**Probably yes** There were 10.4% (53/510) and 7.1% (12/158) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**§	**Probably yes** Generally balanced baseline characteristics across groups
Ahren (2014) [2,3]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 32.0% (201/628) and 33.5% (141/421) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Amin (2015) [4]	**Definitely yes** Using a computer-generated random permuted block method	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 5.5% (3/55) and 14.3% (39/273) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Araki (2015) [5]	**Definitely yes** Using a computer-generated random sequence with an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely no** Open-label	**Definitely yes**	**Definitely yes** There were 4.4% (8/181) and 1.7% (3/180) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Arechavaleta (2011) [6,7]	**Definitely yes** Using a concealed computer-generated allocation schedule	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 9.3% (48/516) and 9.2% (51/519) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Arjona Ferreira (2013a) [8]	**Definitely yes** Using a computer-generated randomisation schedule	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 26.6% (17/64) and 30.8% (20/65) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Arjona Ferreira (2013b) [9,10]	**Definitely yes** Using a computer-generated randomisation schedule	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 22.3% (47/211) and 19.8% (42/212) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Aroda (2016) [11]	**Definitely yes** Using an interactive voice/web response system	**Definitely yes** Using an interactive voice/web response system	**Definitely no** Open-label	**Definitely yes**	**Probably yes** There were 8.4% (31/367) and 3.8% (14/369) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Aschner (2010) [12,13]	**Definitely yes** Using a computer-generated allocation schedule	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 11.6% (61/528) and 14.4% (75/522) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Ba (2016) [14]	**Definitely yes** Using a computer-generated allocation schedule	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 7.6% (19/249) and 15.7% (39/249) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Bajaj (2014) [15]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive voice response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 9.8% (18/183) and 14.6% (13/89) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Barnett (2012) [16]	**Definitely yes** Using an interactive voice response system using a centrally blocked randomisation schedule	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 11.8% (36/304) and 11.3% (17/151) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Barnett (2013a) [17,18]	**Definitely yes** Using computer-generated randomisation sequence	**Definitely yes** Using a central interactive voice-web response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 9.9% (16/162) and 6.3% (5/79) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Barnett (2013b) [19-21]	**Definitely yes** Using computer-generated blocked randomisation schedule	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.1% (58/304) and 17.2% (26/151) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Bergenstal (2009) [22]	**Definitely yes** Using a telephone interactive voice response system and/or interactive web-based randomisation system	**Definitely yes** Using a telephone interactive voice response system and/or interactive web-based randomisation system	**Definitely no** Open-label	**Definitely yes**	**Definitely no** More subjects had missing outcome data in the exenatide group (30%) than in the biphasic insulin aspart 70/30 QD group (16%) and biphasic insulin aspart 70/30 BID group (19%)	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Bergenstal (2012) [23]	**Definitely yes** Using either a telephone- or web-based system	**Definitely yes** Using a telephone- or web-based system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.9% (114/573) and 10.8% (10/93) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Blonde (2015) [24]	**Definitely yes** Using a computer-generated randomisation sequence	**Definitely yes** Using an interactive voice-response system	**Definitely no** Open-label	**Definitely yes**	**Definitely no** There were 21.7% (70/322) and 21.6% (35/162) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Bolli (2014) [25]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 24.1% (142/588) and 20.3% (60/296) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Bosi (2007) [26]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 14.4% (52/362) and 16.5% (30/182) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Bosi (2009) [27]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 15.3% (135/885) and 16.7% (49/294) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Buse (2011) [28,29]	**Definitely yes** Using a centralized, computer-generated, random-sequence	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.0% (26/137) and 18.0% (22/122) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Chacra (2011) [30-32]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 25.7% (129/501) and 30.7% (82/267) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Davies (2012) [33]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely no** Open-label	**Definitely yes**	**Probably no** There were 17.1% (19/111) and 11.7% (12/111) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Davies (2015) [34,35]	**Definitely yes** Using a centralized manner via an interactive voice/web response system	**Definitely yes** Using an interactive voice/web response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 26.8% (170/634) and 34.0% (72/212) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Davies (2016) [36]	**Definitely yes** Using a sponsor-provided telephone or web-based randomisation system	**Definitely yes** Using a sponsor-provided telephone or web-based randomisation system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 26.8% (25/140) and 24.5% (34/139) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
DeFronzo (2008) [37,38]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.7% (52/264) and 38.5% (25/65) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
DeFronzo (2009) [39,40]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 23.6% (133/564) and 37.4% (67/179) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
DeFronzo (2012) [41]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 15.3% (159/1037) and 31.5% (163/517) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
DeFronzo (2015) [42,43]	**Definitely yes** Using a third-party interactive voice and web response system	**Definitely yes** Using a third-party interactive voice and web response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 11.6% (47/405) and 13.5% (38/281) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Del Prato (2014) [44,45]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 20.8% (368/1765) and 25.3% (221/874) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Diamant (2014a) [46-49]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive voice-response system	**Definitely no** Open-label	**Definitely yes**	**Definitely no** There were 36.9% (86/233) and 34.2% (80/234) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Diamant (2014b) [50,51]	**Definitely yes** Using block randomisation with computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely no** Open-label	**Definitely yes**	**Probably no** There were 15.9% (50/315) and 11.9% (37/312) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Dobs (2013) [52]	**Definitely yes** Using a computer-generated schedule	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 21.6% (21/97) and 12.7% (23/181) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Dungan (2016)[53,54]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 10.4% (25/240) and 6.7% (4/60) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Ferdinand (2014) [55]	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 16.0% (81/505) and 17.6% (44/250) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Ferrannini (2009) [56]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 15.9% (222/1396) and 19.7% (275/1393) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Filozof (2010) [57]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 20.5% (105/513) and 16.6% (82/494) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Fonseca (2007) [58]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 20.1% (29/144) and 17.8% (27/152) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Forst (2015) [59]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely no** Open-label	**Definitely yes**	**Definitely no** There were 27.7% (23/83) and 10.1% (8/79) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Frederich (2012) [60,61]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 37.1% (108/291) and 35.1% (26/74) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Frías (2016)[62]	**Definitely yes** Using a central interactive voice and web-response system	**Definitely yes** Using an interactive voice and web-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 12.1% (56/462) and 9.9% (23/233) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Gallwitz (2012a) [63,64]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using a central interactive voice or web response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 24.4% (189/776) and 22.1% (171/775) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Gallwitz (2012b) [65,66]	**Definitely yes** Using a computer-generated randomisation sequence	**Probably no** Allocation concealment was not reported and this study is an open-label trial††	**Definitely no** Open-label	**Definitely yes**	**Definitely no** There were 33.8% (174/515) and 24.9% (128/514) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Gao (2009) [67,68]	**Definitely yes** Using a computerized random-number generator	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 18.9% (45/238) and 11.1% (26/234) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Garber (2008) [69]	**Definitely yes** Using a health authority–inspected and validated system that automates the random assignment of treatment groups to randomisation numbers	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 33.9% (115/339) and 38.6% (68/176) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Garber (2009) [70,71]	**Definitely yes** Using a telephone-based or web-based systems	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 32.8% (163/498) and 38.7% (96/248) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Giorgino (2015)[72]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive voice response system	**Definitely no** Open label	**Definitely yes**	**Probably no** There were 11.0% (60/545) and 10.3% (27/262) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Goke (2013) [73-75]	**Definitely yes** Using a balanced block randomisation schedule	**Definitely yes** Using an interactive Web-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 61.4% (263/428) and 65.8% (283/430) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Goodman (2009) [76]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 20.6% (51/248) and 26.2% (32/122) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Gough (2014) [77]	**Definitely yes** Using an interactive voice or web response system	**Definitely yes** Using an interactive voice or web response system	**Definitely no** Open label	**Definitely yes**	**Probably no** There were 11.8% (98/834) and 11.6% (48/414) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Grunberger (2012) [78]	**Definitely yes** Using an interactive voice or web response system	**Definitely yes** Using an interactive voice or web response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 8.9% (12/135) and 6.3% (2/32) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Haak (2012) [79,80]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 11.2% (48/428) and 15.4% (56/363) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Hartley (2015) [81]	**Definitely yes** Using a computer-generated allocation schedule	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 15.4% (37/241) and 16.3% (39/239) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Henry (2011) [82]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 15.0% (3/20) and 6.3% (1/16) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Henry (2012) [83]	**Definitely yes** Using a central randomisation system (by site)	**Definitely yes** Using a central randomisation system (by site)	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 15.2% (34/224) and 13.7% (14/102) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Henry (2014) [84,85]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 24.9% (191/767) and 30.0% (169/565) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Hermans (2012) [86,87]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.0% (28/147) and 23% (32/139) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Hirose (2015) [88,89]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 2.6% (2/78) and 3.9% (3/76) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Hollander (2011) [90-92]	**Definitely yes** Using a blocked randomisation schedule	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 21.5% (82/381) and 25.0% (46/184) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Hollander (2013) [93]	**Definitely yes** Using a central randomisation system (by site)	**Definitely yes** Using a central randomisation system (by site); the randomisation code was not broken until the end of the study	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 9.9% (15/151) and 22.1% (34/154) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Home (2015) [94]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 18.1% (51/281) and 22.0% (89/404) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Idorn (2015) [95]	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 24% (6/25) and 9.0% (2/22) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Inagaki (2012) [96,97]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive voice response system	**Definitely no** Open label	**Definitely yes**	**Probably yes** There were 10.2% (22/215) and 5.2% (11/212) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Iwamoto (2010) [98]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 4.8% (9/188) and 5.2% (10/192) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kadowaki (2009) [99]	**Definitely yes** Using a dynamic allocation algorithm	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 13.3% (15/113) and 2.5% (1/40) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kadowaki (2011) [100,101]	**Definitely yes** Using a dynamic allocation algorithm	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 18.6% (27/145) and 5.6% (2/36) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kadowaki (2013a) [102]	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 3.1% (4/129) and 5.8% (8/137) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

					groups		
Kadowaki (2013b) [103,104]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 4.9% (5/103) and 3.0% (3/101) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kadowaki (2013c) [105,106]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 3.7% (9/244) and 3.8% (3/80) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kadowaki (2014) [107]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 1.0% (1/96) and 3.1% (3/98) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kaku (2010) [108]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 5.1% (9/176) and 16.0% (14/88) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kaku (2016) [109]	**Definitely yes** Using an interactive voice/web response system	**Definitely yes** Using an interactive voice/web response system	**Definitely no** Open label	**Definitely yes**	**Probably yes** There were 9.1% (22/243) and 7.5% (9/120) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kawamori (2012) [110-112]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely yes** There were 2.5% (8/319) and 4.1% (10/242) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kikuchi (2009) [113]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 2.7% (6/219) and 8.3% (6/72) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

					groups		
Kikuchi (2010) [114]	**Definitely yes** Using a dynamic randomisation	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely yes** There were 2.9% (3/102) and 4.0% (4/100) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kim (2015) [115]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 12.5% (17/136) and 14.7% (10/68) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kim (2016) [116]	**Probably yes** Randomised, double-blind	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 12.0% (14/117) and 25.2% (28/111) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kobayashi (2014) [117]	**Definitely yes** Using a minimization method through a website	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Probably no** There were 11.7% (7/60) and 11.9% (7/59) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Kothny (2013) [118]	**Definitely yes** Using an interactive response technology	**Definitely yes** Using an interactive response technology	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 8.8% and 13.6% patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Lavalle-Gonzalez (2013) [119,120]	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 12.8% (47/366) and 12.9% (118/918) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Liutkus (2010) [121]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 13.5% (15/111) and 7.4% (4/54) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Lukashevich (2011) [122,123]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 11.8% (34/289) and 11.9% (27/226) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Lukashevich (2014) [124]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 8.9% (14/158) and 3.1% (5/160) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Macauley (2015) [125]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 9% (2/22) and 13.6% (3/22) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Marre (2009) [126]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 11.2% (78/695) and 19.9% (69/346) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Mathieu (2014) [127]	**Probably yes** Randomised, double-blind	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Probably no** There were 13.6% (12/88) and 15.7% (14/89) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Mathieu (2015) [128,129]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 10.6% (35/330) and 8.2% (27/330) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Matthaei (2015) [130,131]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 7.2% (11/153) and 3.7% (6/162) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Miyagawa (2015) [132]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 5.5% (23/417) and 10% (7/70) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Moretto (2008) [133]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 13.5% (21/155) and 11.5% (9/78) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Mori (2016)[134]	**Probably yes** Randomised, double-blind	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 7.5% (3/40) and 15.8% (6/38) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Moses (2016) [135]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 6.6% (14/213) and 11.7% (25/214) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nauck (2007) [136,137]	**Definitely yes** Using a computer-generated randomisation table	**Definitely yes** Using an automated voice response system	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 22.0% (56/255) and 10.8% (27/250) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nauck (2009) [138,139]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.4% (82/423) and 30.8% (32/104) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nauck (2013a) [140,141]	**Definitely yes** Using a telephone-based or web-based randomisation system	**Definitely yes** Using a telephone-based or web-based randomisation system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 47.3% (343/725) and 60.6% (222/366) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nauck (2013b) [142]	**Probably no** Randomised, open label**	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 21.2% (152/717) and 11.7% (39/332) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nauck (2014) [143,144]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 21.9% (212/921) and 36.7% (65/177) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nauck (2016) [145]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 21.1% (43/204) and 24.8% (26/105) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00086515 (2010) [146,147]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 56.0% (260/464) and 53.6% (127/237) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

NCT00095056 (2010) (148)	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 10.7% (13/121) and 9.8% (5/51) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00106704 (2010) (149,150)	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 58.1% (129/222) and 68.5% (150/219) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00289848 (2010) (151,152)	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 12.8% (45/352) and 25.3% (45/178) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00305604 (2009) (153,154)	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 31.4% (32/102) and 45.2% (47/104) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00337610 (2009) (155,156)	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 17.7% (17/96) and 14.9% (14/94) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00511108 (2010) (157,158)	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 10.6% (11/104) and 6.5% (7/107) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00655863 (2013) (159,160)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 2.1% (1/47) and 0% (0/24) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00707993 (2013) (161,162)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 40.0% (89/222) and 42.9% (94/219) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00713830 (2016) (163)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 30.9% (177/573) and 28.7% (82/286) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

NCT00715624 (2016) (164)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 35.2% (116/329) and 31.1% (52/167) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00800683 (2011) (165)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 27.9% (19/68) and 26.1% (17/65) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00819091 (2011) (166,167)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 6.2% (10/161) and 8.3% (7/84) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00839527 (2014) (168)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 66.8% (181/271) and 66.8% (262/392) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT00881530 (2014) (169,170)	**Probably no** Randomised, open label	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Probably yes** There were 3.6% (2/56) and 7.8% (47/603) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01075282 (2014) (171)	**Probably no** Randomised, open label	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Probably no** There were 11.0% (60/545) and 9.4% (25/265) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01318083 (2011) (172,173)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 3.8% (8/209) and 4.9% (5/103) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01644500 (2015) (174)	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 9.5% (51/536) and 6.3% (18/271) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

NCT01648582 (2015) [175]	**Probably no** Randomised, open label	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 13.1% (69/526) and 7.6% (2/263) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01682759 (2016) [176]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 17.8% (67/376) and 18.4% (69/375) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01717313 (2016) [177]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 18.8% (31/165) and 17.1% (28/164) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01778049 (2016) [178]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 11.3% (27/240) and 7.9% (19/242) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
NCT01890122 (2016) [179]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 15.5% (50/322) and 26.5% (86/325) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Ning (2016) [180]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 4.9% (13/263) and 6.8% (18/265) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Nowicki (2011) [181-183]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 50.6% (43/85) and 41.2% (35/85) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Odawara (2014) [184]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 2.9% (2/69) and 14.3% (10/70) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Oe (2015) [185]	**Definitely yes** Using computer-generated and a	**Definitely yes** Using computer-generated and a web-based system	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 24.0% (12/50) and 22.0% (11/50) patients in incretin and control groups with missing outcome data,	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

	web-based system				respectively		
Oyama (2016) [186]	**Probably no** Randomised, open label	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 17.2% (40/232) and 16.5% (38/231) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pan (2008) [187]	**Definitely yes** Using computer-generated and a web-based system	**Definitely yes** Using computer-generated and a web-based system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 9.5% (42/441) and 12.7% (28/220) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pan (2012) [188,189]	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 7.7% (22/284) and 12.7% (36/284) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pan (2016) [190]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 7.5% (19/252) and 9.1% (23/254) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Perez-Monteverde (2011) [191,192]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 23.3% (57/244) and 19.3% (48/248) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pfutzner (2011) [193-195]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 31.6% (309/978) and 33.2% (109/328) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pinget (2013) [196]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 10.8% (35/323) and 14.9% (24/161) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pratley (2006) [197]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 9.7% (7/72) and 7.1% (2/28) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Pratley (2009a) [198,199]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 11.6% (46/396) and 14.4% (14/97) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pratley (2009b) [200,201]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 12.5% (50/401) and 37.4% (37/99) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pratley (2013) [202]	**Definitely yes** Using a central randomisation system	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 20.4% (102/499) and 12.6% (33/261) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pratley (2014) [203,204]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 24.2% (107/442) and 12.0% (69/326) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Probstfield (2016) [205]	**Probably no** Randomised, open label	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Probably yes** There were 5.8% (3/52) and 6.0% (3/50) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Raz (2012) [206]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 10.0% (25/249) and 10.5% (13/124) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Reasner (2011) [207-209]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 22.7% (142/625) and 22.4% (139/621) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Riddle (2013) [210]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 16.1% (53/329) and 12.0% (20/167) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Roden (2015) [211-213]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 61.0% (136/223) and 39.5% (267/676) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Rosenstock (2008) [214,215]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 16.2% (44/271) and 17.9% (12/67) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2009) [216,217]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 18.5% (48/260) and 17.7% (23/130) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2013a) [218-220]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 24.8% (76/306) and 25.3% (24/95) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2013b) [221,222]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 4.5% (19/424) and 7.0% (66/71) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2014) [223]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 12.9%(74/573) and 10.8% (31/286) patients in incretin and control groups with missing outcome data, respectively, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2015) [224]	**Definitely yes** Using a centralized blocked randomisation schedule	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 7.0%(25/355) and 10.6% (19/179) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2016a) [225]	**Definitely yes** Using an interactive voice/Web response system (IVRS/IWRS)	**Definitely yes** Using an interactive voice/Web response system (IVRS/IWRS)	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 6.8%(11/161) and 1.9% (3/162) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Rosenstock (2016b) [226,227]	**Definitely yes** Using an interactive voice/Web response system generated patient randomisation	**Definitely yes** Using an interactive voice/Web response system	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 6.0%(56/936) and 12.4% (29/234) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Ross (2012) [228,229]	**Definitely yes** Using a central interactive voice/web response system	**Definitely yes** Using a central interactive voice/web response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 5.8% (26/447) and 2.3% (1/44) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Russell-Jones (2012) [230]	**Definitely yes** Using a computer-generated random sequence using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 10.0% (66/657) and 11.0% (18/163) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Scherbaum (2008) [231,232]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 14.7% (10/68) and 20.6% (13/63) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Schernthaner (2013) [233,234]	**Definitely yes** Using a computer-generated randomisation schedule	**Definitely yes** Using an Interactive Voice Response System/ Interactive Web Response System	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 44.4% (168/378) and 32.6% (123/377) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Schernthaner (2015) [235,236]	**Definitely yes** Using an interactive web response system	**Definitely yes** Using an interactive web response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.7% (71/360) and 20.8% (75/360) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Schweizer (2007) [237]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 28.1% (148/526) and 24.8% (63/254) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Schweizer (2009) [238]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 16.6% (28/169) and 16.3% (27/166) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Seck (2010) [239-241]	**Definitely yes** Using computer-generated allocation schedule	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely yes** There were 2.0% (12/588) and 4.3% (25/584) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Seino (2010) [242-244]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 9.4% (26/272) and 9.6% (19/139) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Seino (2011) [245,246]	**Definitely yes** Using computer generated codes which were kept in a secure area	**Probably no** Randomised, open label	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 31.8% (107/337) with missing outcome data	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Seino (2012a) [247,248]	**Definitely yes** Using an interactive voice or web-activated response system	**Definitely yes** Using an interactive voice or web-activated response system	**Definitely no** Open label	**Definitely yes**	**Definitely no** There were 21.2% (25/118) and 15.3% (20/131) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Seino (2012b) [249]	**Definitely yes** Using an interactive voice response system	**Definitely yes** Using an interactive voice response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably no** There were 13.6% (21/154) and 8.3% (13/157) patients in incretin and control groups with missing outcome data	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Seino (2014) [250,251]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 8.1% (13/161) and 7.4% (4/54) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Seino (2016) [252]	**Definitely yes** Using an interactive voice-/web-responsive service	**Definitely yes** Using an interactive voice-/web-responsive service	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 4.7% (6/127) and 3.8% (5/130) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Sheu (2015) [253]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 47.4% (54/114) and 39.3% (257/571) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Strain (2013) [254]	**Definitely yes** Using a validated automated system	**Definitely yes** Using an interactive response technology provider	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 5.8% (8/139) and 5.8% (8/139) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Tajima (2011) [255]	**Definitely yes** Using a computer-generated randomisation scheme	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 13.3% (8/60) and 18.8% (13/69) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Terauchi (2014) [256]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely yes** There were 4.8% (7/145) with missing outcome data	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Thrasher (2014) [257,258]	**Definitely yes** Using a validated pseudorandom number	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 8.3% (10/120) and 7.5% (8/106) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Umpierrez (2011) [259]	**Definitely yes** Using a computer-generated random sequence	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 12.2% (24/196) and 9.0% (6/66) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Umpierrez (2014) [260]	**Definitely yes** Using a computer generated random sequence	**Definitely yes** Using an interactive Voice Response System	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 7.8% (37/475) and 20.5% (55/268) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were not balanced across treatment groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Vilsboll (2010) [261]	**Definitely yes** Using a computer-generated allocation schedule	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 12.7% (41/322) and 11.3% (36/319) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Wang (2016) [262]	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 7.0% (14/205) and 12.0% (13/101) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Weissman (2014) [263,264]	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 10.8% (8/74) and 9.3% (8/86) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

White (2014) [265,266]	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 22.6% (666/2679) and 20.9% (564/2701) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Williams-Herman (2010) [267-270]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely no** There were 26.6% (242/915) and 11.9% (21/176) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Wysham (2014) [271,272]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably no** There were 12.0% (100/835) and 14.2% (20/141) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Yang (2012) [273]	**Definitely yes** Using a computer-generated schedule	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 11.7% (23/197) and 8.0% (16/198) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Yang (2015) [274]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 6.3% (9/143) and 7.4% (10/136) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Yki-Jarvinen (2013) [275,276]	**Definitely yes** Using a computer-generated random sequence	**Definitely yes** Using an interactive Voice Response System	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 2.1% (13/630) and 2.1% (13/631) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Yokoh (2015) [277]	**Probably yes** Randomised, double-blind	**Probably no** Randomised, open label	**Definitely no** Open label	**Definitely yes**	**Probably no** There were 11.7% (7/60) and 11.7% (7/59) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Yu Pan (2014) [278]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Probably yes** There were 8.4% (17/196) and 5.6% (11/195) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

Zinman (2009) [279]	**Definitely yes** Using a telephone- or Web-based randomisation system	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 19.7% (70/356) and 29.2% (50/171) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Large cardiovascular outcomes trials							
Green (2015) (TECOS) [280]	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Using an interactive voice-response system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 4.9% (360/7332) and 5.9% (434/7339) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Marso (2016) (LEADER) [281]	**Definitely yes** Using the interactive voice/web response system	**Definitely yes** Using the interactive voice/web response system	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely yes** There were 1.5% (25/1648) and 2.4% (40/1649) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Marso (2016) (SUSTAIN-6) [282]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Probably yes** Double-blind (details not reported)	**Definitely yes**	**Definitely yes** There were 3.0% (139/4668) and 3.4% (159/4672) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Pfeffer (2015) (ELIXA) [283]	**Definitely yes** Using a centralized assignment system	**Definitely yes** Using a centralized assignment system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Probably yes** There were 5.7% (204/3034) and 7.8% (231/3034) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
Scirica (2013) (SAVOR-TIMI 53) [284]	**Definitely yes** Using a central computerized telephone or Web-based system	**Definitely yes** Using a central computerized telephone or Web-based system	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely yes** There were 2.4% (202/8280) and 2.6% (214/8212) patients in incretin and control groups with missing outcome data, respectively; missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups
White (2013) (EXAMINE) [285]	**Probably yes** Randomised, double-blind	**Probably yes** Randomised, double-blind	**Definitely yes** Double-blind (participant, investigator)	**Definitely yes**	**Definitely no** There were 22.6% (606/2679) and 21.9% (564/2701) patients in incretin and control groups with missing outcome data, respectively	**Definitely yes**	**Probably yes** Generally balanced baseline characteristics across groups

* Method for allocation concealment not clearly reported. We judged that concealed allocation was likely achieved given it was a randomised double blinded trial, according to instructions. We followed this rule throughout the review.

** Method for generating randomisation sequence not clearly reported. We judged that randomisation sequence generation was likely not achieved given it was a randomised open label trial, according to instructions. We followed this rule throughout the

review.

† Method for allocation concealment not clearly reported. We judged that concealed allocation was likely achieved given it was a randomised double blinded trial, according to instructions. We followed this rule throughout the review.

†† Method for allocation concealment not clearly reported. We judged that concealed allocation was likely not achieved given it was a randomised open label trial, according to instructions. We followed this rule throughout the review.

‡ As death is definitely an objective outcome, the risk of bias is unlikely introduced even without blinding of outcome assessors. This principle applies to all the included trials.

We used the following rules to judge the free of infrequent missing outcome data for all included trials throughout the review: definitely yes: there were less than 5% patients with missing outcome data, and missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups; probably yes: there were 5 to 10% patients with missing outcome data, and missing outcome data were generally balanced across treatment groups, with similar reasons for missing data across groups; probably no: there were 10% to 15% of missing outcome data; definitely no: there were over 15% patients with missing outcome data, or there were more than 5% absolute difference of missing outcome data between groups.

§ Death data was clearly reported. This applied to all the included trials.

References of included trials

1. Ahren B, Dimas AL, Miossec P, Saubadu S, Aronson R. Efficacy and safety of lixisenatide once-daily morning or evening injections in type 2 diabetes inadequately controlled on metformin (GetGoal-M). *Diabetes Care* 2013; **36**: 2543-2550.
2. GlaxoSmithKline. Efficacy and safety of albiglutide in treatment of type 2 diabetes. National Library of Medicine (US), 2000. http://clinicaltrials.gov/show/NCT00838903 (accessed March 10, 2017).
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