

Appendix 10 Meta-regression for network meta-analyses compared with placebo

Table 1 Results of univariate meta-regression

Variables (No. of studies) Scale	Comparison	Regression coefficient	Standard error	Proportional change in OR (95% CI)	P value
Age Per 10 years	Incretin VS Placebo	-0.221095	0.496844	0.80(0.30,2.12)	0.656
	Insulin VS Placebo	-0.150506	8.926956	0.86(2.17e-08,3.41e+07)	0.987
	Met VS Placebo	6.914018	1258.909	NA	0.996
	SU VS Placebo	0.784092	1.270383	2.19(0.18,26.42)	0.537
	TZD VS Placebo	-0.717931	729.8827	NA	0.999
BMI (123) Per 1 kg/m ²	Incretin VS Placebo	-0.006005	0.1044931	0.99(0.81,660.64)	0.954
	Insulin VS Placebo	0.019944	3.30275	1.02(0.002,1.03)	0.995
	Met VS Placebo	0.8499565	154.0751	2.34(1.7e-131,3.3e+131)	0.996
	SU VS Placebo	-0.2408509	0.2750153	0.79(0.46,1.35)	0.381
	TZD VS Placebo	0.0183281	55.13116	1.02(1.20e-47,8.62e+46)	1.000
HbA1c (124) Per 1%	Incretin VS Placebo	0.1155811	0.2208454	1.12(0.73,1.73)	0.601
	Insulin VS Placebo	0.965176	2.432701	1.10(0.01,129.61)	0.968
	Met VS Placebo	0.0060799	371.0757	NA	1.000
	SU VS Placebo	0.4554837	1.723957	1.58(0.054,46.27)	0.792
	TZD VS Placebo	0.0473053	431.689	NA	1.000
DM duration (111) Per 1 years	Incretin VS Placebo	0.0387145	0.0685746	1.04(0.91,1.19)	0.572
	Insulin VS Placebo	0.0432332	0.5767707	1.04(0.34,3.23)	0.940
	Met VS Placebo	-0.0176436	156.9235	0.98(2.6e-134,3.7e+133)	1.000
	SU VS Placebo	0.1842336	0.2126941	1.20(0.79,1.82)	0.386
	TZD VS Placebo	0.0528398	104.0614	1.05(2.79e-89,3.98e+88)	1.000

Note: Due to the limited number of SGLT-2 and a-Glu compared to incretin-based therapies, they were not included in meta-regression.

Met: metformin; SU: sulphonylureas; TZD: thiazolidinediones.

Table 2 Results of multivariate meta-regression

Comparison	Variables	Scale	Regression coefficient	Standard error	Proportional change in OR (95% CI)	P value
Incretin vs Placebo	Age	Per 10 years	-1.458008	0.8245859	0.23(0.05,1.17)	0.077
	BMI	Per 1 kg/m ²	-0.2004523	0.1457966	0.82(0.61,1.09)	0.169
	HbA1c	Per 1%	0.1672979	0.2730721	1.18(0.69,2.02)	0.540
	DM duration	Per 1 years	0.1994348	0.3477171	1.28(1.00,1.65)	0.048
Insulin vs Placebo	Age	Per 10 years	NA	NA	NA	NA
	BMI	Per 1 kg/m ²	NA	NA	NA	NA
	HbA1c	Per 1%	-2.625439	817.0785	NA	0.997
	DM duration	Per 1 years	-0.5357169	193.7626	0.58(6.9e-166,5.0e+164)	0.998
Met vs Placebo	Age	Per 10 years	NA	NA	NA	NA
	BMI	Per 1 kg/m ²	NA	NA	NA	NA
	HbA1c	Per 1%	0.5927973	529.8334	NA	0.999
	DM duration	Per 1 years	0.140215	191.4408	0.99(1.3e-163,1.0e+163)	0.999
SU vs Placebo	Age	Per 10 years	-9.708239	11496.93	NA	0.999
	BMI	Per 1 kg/m ²	-1.92131	3713.346	0.58(2.3e-211,1.5e+210)	0.998
	HbA1c	Per 1%	1.445007	1625.121	NA	1.000
	DM duration	Per 1 years	0.5672268	83.20875	NA	0.999
TZD vs Placebo	Age	Per 10 years	NA	NA	NA	NA
	BMI	Per 1 kg/m ²	0.9771629	581.3705	NA	0.999
	HbA1c	Per 1%	NA	NA	NA	NA
	DM duration	Per 1 years	1.928063	1112.619	NA	0.999

Note: Due to the limited number of AGIs compared to incretin-based therapies, they were not included in meta-regression.

Met: metformin; SU: sulphonylureas; TZD: thiazolidinediones.

Table 3 Results of network meta-analysis before and after regression

Comparison	Before adjustment	x1	x2	x3	x4	x1 x2 x3 x4
Incretin vs Placebo	0.87(0.71,1.05)	1.03(0.54,1.99)	0.91(0.69,1.21)	0.92(0.71,1.19)	0.79(0.48,1.30)	1.22(0.62,2.41)
Insulin vs Placebo	1.00(0.31,3.20)	1.03(0.08,13.20)	0.87(0.00,62926.63)	0.93(0.04,19.82)	0.79(0.03,23.03)	NA
Met vs Placebo	2.69(0.62,11.66)	NA	NA	NA	NA	NA
SGLT-2 vs Placebo	0.16(0.02,1.47)	NA	NA	NA	NA	NA
SU vs Placebo	0.68(0.35,1.32)	1.27(0.41,3.91)	1.35(0.50,3.64)	1.41(0.23,8.60)	0.90(0.26,3.10)	NA
TZD vs Placebo	2.04(0.60,6.95)	NA	NA	NA	NA	NA
AGIs vs Placebo	0.29(0.01,7.19)	NA	NA	NA	NA	NA