

Supplementary Table 2. *P* values for diabetes medication by hePRS-IR and mePRS-IR interaction on cardiometabolic outcomes in men and women

Variable	<i>P</i> of diabetes medication × hePRS-IR interaction						<i>P</i> of diabetes medication × mePRS-IR interaction					
	Men			Women			Men			Women		
	No.	Crude	Adjusted	No.	Crude	Adjusted	No.	Crude	Adjusted	No.	Crude	Adjusted
Body mass index, kg/m ²	684	0.802	0.82	889	0.79	0.743	684	0.793	0.43	889	0.102	0.125
Fat mass, kg	653	0.716	0.48	858	0.99	0.89	653	0.891	0.671	858	0.117	0.156
Body fat percentage, %	653	0.652	0.581	858	0.969	0.834	653	0.845	0.583	858	0.308	0.455
Waist circumference, cm	684	0.578	0.571	888	0.193	0.264	684	0.779	0.388	888	0.804	0.657
Lean body mass, kg	653	0.941	0.958	858	0.805	0.816	653	0.604	0.486	858	0.148	0.162
Triglycerides, mmol/L	683	0.768	0.792	888	0.327	0.169	683	0.985	0.983	888	0.634	0.477
Total cholesterol, mmol/L	683	0.755	0.748	888	0.467	0.42	683	0.845	0.996	888	0.274	0.355
HDL-C, mmol/L	683	0.671	0.715	888	0.581	0.345	683	0.798	0.694	888	0.982	0.704
LDL-C, mmol/L	673	0.929	0.85	878	0.261	0.257	673	0.819	0.797	878	0.182	0.265
Apolipoprotein A, mmol/L	683	0.193	0.298	888	0.294	0.142	683	0.299	0.626	888	0.679	0.84
Apolipoprotein B, mmol/L	683	0.729	0.759	887	0.593	0.542	683	0.942	0.978	887	0.328	0.463
Lipoprotein A, mmol/L	683	0.893	0.906	887	0.767	0.817	683	0.178	0.171	887	0.5	0.544
Fasting plasma glucose, mmol/L	684	0.072	0.066	889	0.769	0.78	684	0.352	0.328	889	0.981	0.987
30-min glucose, mmol/L	666	0.378	0.298	864	0.639	0.73	666	0.673	0.58	864	0.185	0.21
120-min glucose, mmol/L	668	0.408	0.36	865	0.449	0.494	668	0.575	0.498	865	0.574	0.53
Fasting plasma insulin, mmol/L	684	0.865	0.768	889	0.678	0.648	684	0.308	0.191	889	0.513	0.531
30-min insulin, mmol/L	667	0.731	0.702	865	0.669	0.873	667	0.367	0.651	865	0.167	0.224
120-min insulin, mmol/L	668	0.686	0.649	867	0.714	0.724	668	0.278	0.482	867	0.426	0.509
HOMA-IR	684	0.422	0.343	889	0.573	0.556	684	0.17	0.104	889	0.522	0.523
HOMA-β	684	0.485	0.561	889	0.662	0.835	684	0.695	0.899	889	0.97	0.934
IGI	666	0.493	0.454	862	0.281	0.64	666	0.563	0.48	862	0.754	0.756
IGF-1, ng/mL	233	0.552	0.446	221	0.925	0.796	233	0.967	0.957	221	0.253	0.134
IGFBP-1, ng/mL	233	0.666	0.571	221	0.862	0.735	233	0.55	0.975	221	0.573	0.744
IGFBP-3, ng/mL	233	0.373	0.491	221	0.811	0.747	233	0.953	0.808	221	0.751	0.668

Crude models are adjusted for age and population stratification. Fully adjusted models are additionally adjusted for age, smoking, alcohol consumption, socioeconomic status, presence of chronic diseases, birth weight, and leisure-time physical activity.

hePRS-IR, polygenic risk score for the hippocampal-insulin receptor; mePRS-IR, polygenic risk score for the mesocorticolimbic-insulin receptor; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostatic model of assessment of insulin resistance; HOMA-β, homeostatic model of assessment of β-cell function; IGI, insulinogenic index; IGF-1, insulin growth factor 1; IGFBP-1, insulin growth factor-binding protein 1; IGFBP-3, insulin growth factor-binding protein 3.