

Supplementary Table 3. *P* values for diabetes status (normoglycemia, prediabetes, and diabetes) 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	683	0.568	0.545	887	0.466	0.493	683	0.919	0.937	887	0.177	0.208
Fat mass, kg	652	0.22	0.198	856	0.551	0.625	652	0.634	0.908	856	0.226	0.302
Body fat percentage, %	652	0.311	0.344	856	0.706	0.831	652	0.494	0.908	856	0.055	0.064
Waist circumference, cm	683	0.245	0.198	886	0.603	0.749	683	0.8	0.807	886	0.295	0.295
Lean body mass, kg	652	0.409	0.198	856	0.52	0.64	652	0.747	0.628	856	0.927	0.919
Triglycerides, mmol/L	682	0.829	0.699	886	0.252	0.103	682	0.048	0.056	886	0.738	0.761
Total cholesterol, mmol/L	682	0.719	0.725	886	0.576	0.488	682	0.562	0.638	886	0.67	0.634
HDL-C, mmol/L	682	0.244	0.33	886	0.848	0.894	682	0.861	0.719	886	0.168	0.295
LDL-C, mmol/L	672	0.987	0.988	876	0.771	0.67	672	0.724	0.733	876	0.329	0.194
Apolipoprotein A, mmol/L	682	0.039	0.044	886	0.831	0.625	682	0.817	0.611	886	0.525	0.491
Apolipoprotein B, mmol/L	682	0.954	0.866	885	0.422	0.279	682	0.831	0.869	885	0.593	0.377
Lipoprotein A, mmol/L	682	0.604	0.654	885	0.307	0.338	682	0.073	0.079	885	0.723	0.659
Fasting plasma glucose, mmol/L	683	0.813	0.778	887	0.974	0.942	683	0.735	0.69	887	0.183	0.251
30-min glucose, mmol/L	666	0.382	0.41	862	0.685	0.613	666	0.269	0.229	862	0.491	0.639
120-min glucose, mmol/L	668	0.849	0.92	865	0.268	0.254	668	0.159	0.158	865	0.916	0.959
Fasting plasma insulin, mmol/L	683	0.554	0.774	887	0.258	0.21	683	0.54	0.39	887	0.9	0.835
30-min insulin, mmol/L	667	0.381	0.385	863	0.645	0.662	667	0.855	0.831	863	0.965	0.958
120-min insulin, mmol/L	668	0.664	0.677	865	0.298	0.235	668	0.455	0.537	865	0.585	0.756
HOMA-IR	683	0.466	0.692	887	0.299	0.259	683	0.366	0.27	887	0.723	0.668
HOMA-β	683	0.827	0.824	887	0.154	0.146	683	0.905	0.992	887	0.493	0.487
IGI	666	0.825	0.907	860	0.832	0.862	666	0.408	0.456	860	0.999	0.968
IGF-1, ng/mL	233	0.811	0.841	220	0.855	0.66	233	0.015	0.01	220	0.777	0.638
IGFBP-1, ng/mL	233	0.283	0.165	220	0.879	0.947	233	0.944	0.82	220	0.34	0.431
IGFBP-3, ng/mL	233	0.924	0.968	220	0.244	0.382	233	0.266	0.163	220	0.731	0.807

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.