

Supplementary Table 9. Incremental value of polygenic risk score in predicting gestational diabetes, above and beyond the clinical risk factors

Stage	Cohort	Ethnicity	Population	Study design	PCs and clinical factors	Number		ROC curve analysis								Continuous NRI (95% CI)	P _{NRI}
								Model 1: PRS only		Model 2 (base model): PCs and clinical risk factors		Model 3: PRS, PCs and clinical risk factors		Comparison of AUC Model 3 vs. Model 2			
						GDM case	Non-GDM control	AUC (95% CI)	P value	AUC (95% CI)	P value	AUC (95% CI)	P value	Increased AUC	P _{increase}		
Discovery	HAPO-HK Study	East Asian	Chinese pregnant women	Population-based	PCs, age, and BMI	149	811	0.692 (0.646–0.738)	4.3×10 ⁻¹⁴	0.675 (0.630–0.720)	5.3×10 ⁻¹²	0.753 (0.711–0.795)	4.4×10 ⁻²³	0.0779	1.4×10 ⁻⁴	57.4 (39.6 to 75.3)	<0.05
						145	776	0.695 (0.649–0.742)	4.0×10 ⁻¹⁴	0.695 (0.647–0.742)	4.9×10 ⁻¹⁴	0.767 (0.725–0.809)	9.4×10 ⁻²⁵	0.0722	2.7×10 ⁻⁴	58.1 (36.7 to 74.1)	<0.05
	Tianjin Study	East Asian	Chinese pregnant women	Case-control	PCs, age, and BMI	229	226	0.625 (0.574–0.676)	2.0×10 ⁻⁶	0.643 (0.593–0.694)	6.3×10 ⁻⁸	0.693 (0.645–0.741)	5.1×10 ⁻¹³	0.0499	0.0134	35.6 (18.4 to 59.3)	<0.05
	TGDM-NDM Study	East Asian	Cases: Chinese pregnant women; Controls: Chinese non-pregnant women	Case-control	PCs, age, and BMI	86	180	0.643 (0.575–0.712)	8.0×10 ⁻⁵	0.785 (0.731–0.838)	3.0×10 ⁻¹⁴	0.810 (0.758–0.861)	1.6×10 ⁻¹⁶	0.0250	0.0596	25.8 (1.4 to 60.8)	<0.05
De novo replication	Guangzhou Study	East Asian	Chinese pregnant women	Case-control	Age, and BMI	344	436	0.543 (0.503–0.584)	0.0192	0.647 (0.608–0.685)	9.5×10 ⁻¹³	0.651 (0.613–0.690)	1.9×10 ⁻¹³	0.0046	0.4568	10.8 (-2.5 to 24.9)	NS
In silico replication	HAPO-Thai Study	East Asian	Thai pregnant women	Population-based	PCs, age, and BMI	260	933	0.542 (0.503–0.581)	0.0191	0.638 (0.600–0.676)	4.5×10 ⁻¹²	0.640 (0.602–0.678)	2.6×10 ⁻¹²	0.0016	0.6199	9.8 (-5.7 to 24.5)	NS
						134	459	0.531 (0.477–0.584)	0.1414	0.711 (0.661–0.761)	4.7×10 ⁻¹⁴	0.711 (0.661–0.761)	4.8×10 ⁻¹⁴	3.25E-05	0.9830	-1.6 (-10.2 to 26.2)	NS
	HAPO-Hispanic Study	Hispanic	Hispanic pregnant women	Population-based	PCs, age, and BMI	207	596	0.570 (0.524–0.616)	1.3×10 ⁻³	0.713 (0.673–0.754)	2.8×10 ⁻²⁰	0.729 (0.689–0.769)	5.1×10 ⁻²³	0.0153	0.0595	29.9 (12.7 to 47.1)	<0.05
						194	556	0.561 (0.513–0.609)	5.6×10 ⁻³	0.735 (0.694–0.776)	1.1×10 ⁻²²	0.742 (0.701–0.783)	5.7×10 ⁻²⁴	0.0070	0.2863	26.2 (5.8 to 45.6)	<0.05

ROC curve analysis: Model 1 includes the PRS only; Model 2 (base model) includes the principal components and the clinical risk factors; Model 3 includes both models 1 and 2. AUC (95% CI) and related changes were estimated based on the risk prediction models (i.e., models 1–3) computed by logistic regression. P tests the null hypothesis that “AUC is equal to zero.” P_{increase} tests the null hypothesis that “difference in AUC between models 2 and 3 is equal to zero.”

Reclassification analysis: Old model includes the principal components and the clinical risk factors. New model includes old model and PRS. P_{NRI} tests the null hypothesis that “continuous NRI is equal to zero.”

PC, principal component; GDM, gestational diabetes mellitus; ROC, receiver operating characteristic; PRS, polygenic risk score; AUC, area under the curve; NRI, net reclassification improvement; CI, confidence interval; HAPO-HK, Hyperglycemia and Adverse Pregnancy Outcome-Hong Kong; BMI, body mass index; GWG, gestational weight gain; SBP, systolic blood pressure; DBP, diastolic blood pressure; TGDM-NDM, Treated GDM Cases vs. Non-diabetes Controls; NS, not significant.