

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									
							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			
							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	GDM case	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
						Non-GDM control	776 (0.649-0.742)	0.695 (0.647-0.742)	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)
In silico replication	Tanjun Study	East Asian	Chinese pregnant women	Case-control	PCs, age, and BMI	GDM case	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
						Non-GDM control	226 (0.575-0.712)	0.643 (0.731-0.838)	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)
De novo replication	Guangzhou Study	East Asian	Chinese pregnant women	Case-control	Age, and BMI	GDM case	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
						Non-GDM control	436 (0.503-0.581)	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)
In silico replication	HAPO-Thai Study	East Asian	Thai pregnant women	Population-based	PCs, age, and BMI	GDM case	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
						Non-GDM control	459 (0.524-0.616)	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)
HAPO-Hispanic Study	Hispanic	Hispanic	Hispanic pregnant women	Population-based	PCs, age, and BMI	GDM case	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
						Non-GDM control	556 (0.513-0.609)	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)

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.