

Supplementary Materials

for

The Clinical relevance of Polygenic Risk Scores to Type 2 Diabetes Mellitus in Korean Population

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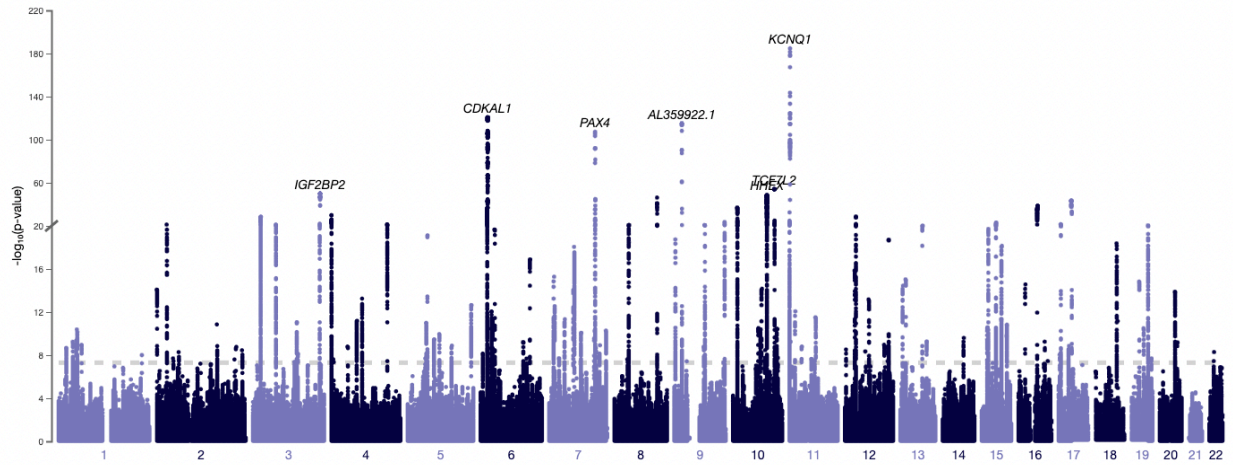
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Seoul National University, Seoul, South Korea

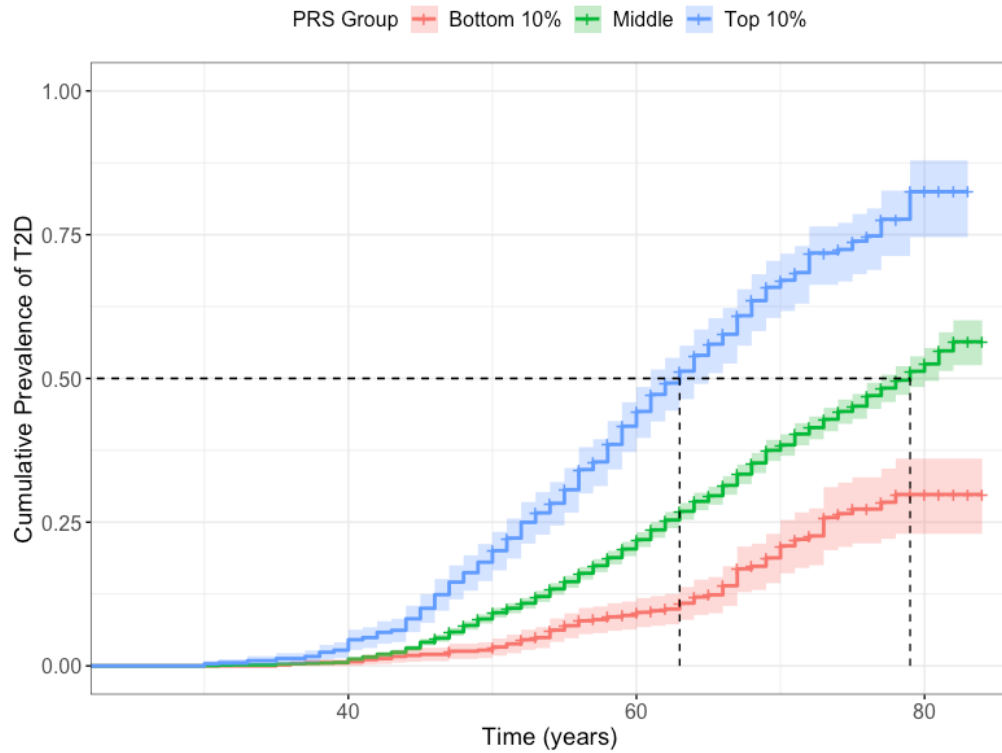
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Supplementary Figures

Supplementary Fig. S1 Manhattan plot of meta-analysis of East Asian T2DM

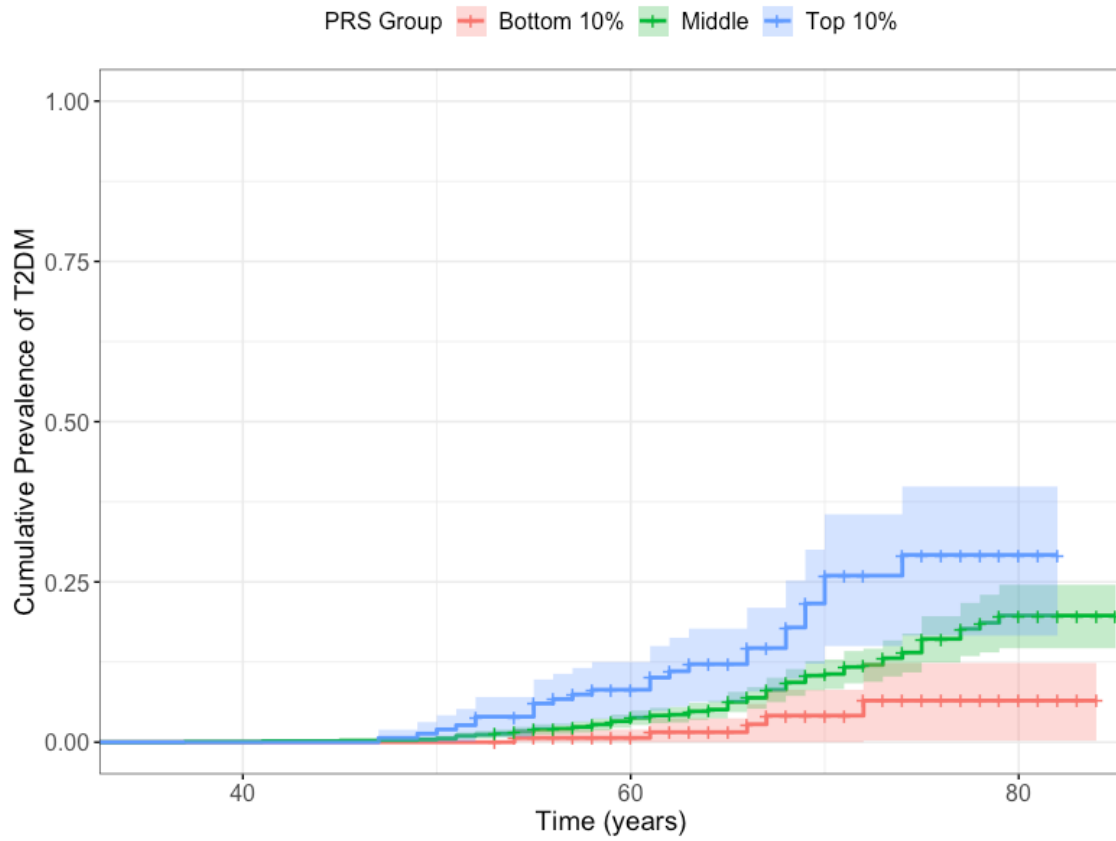


Supplementary Fig. S2 KoGES Ansan and Ansung: Kaplan-Meier curve for cumulative prevalence of T2DM by PRS group



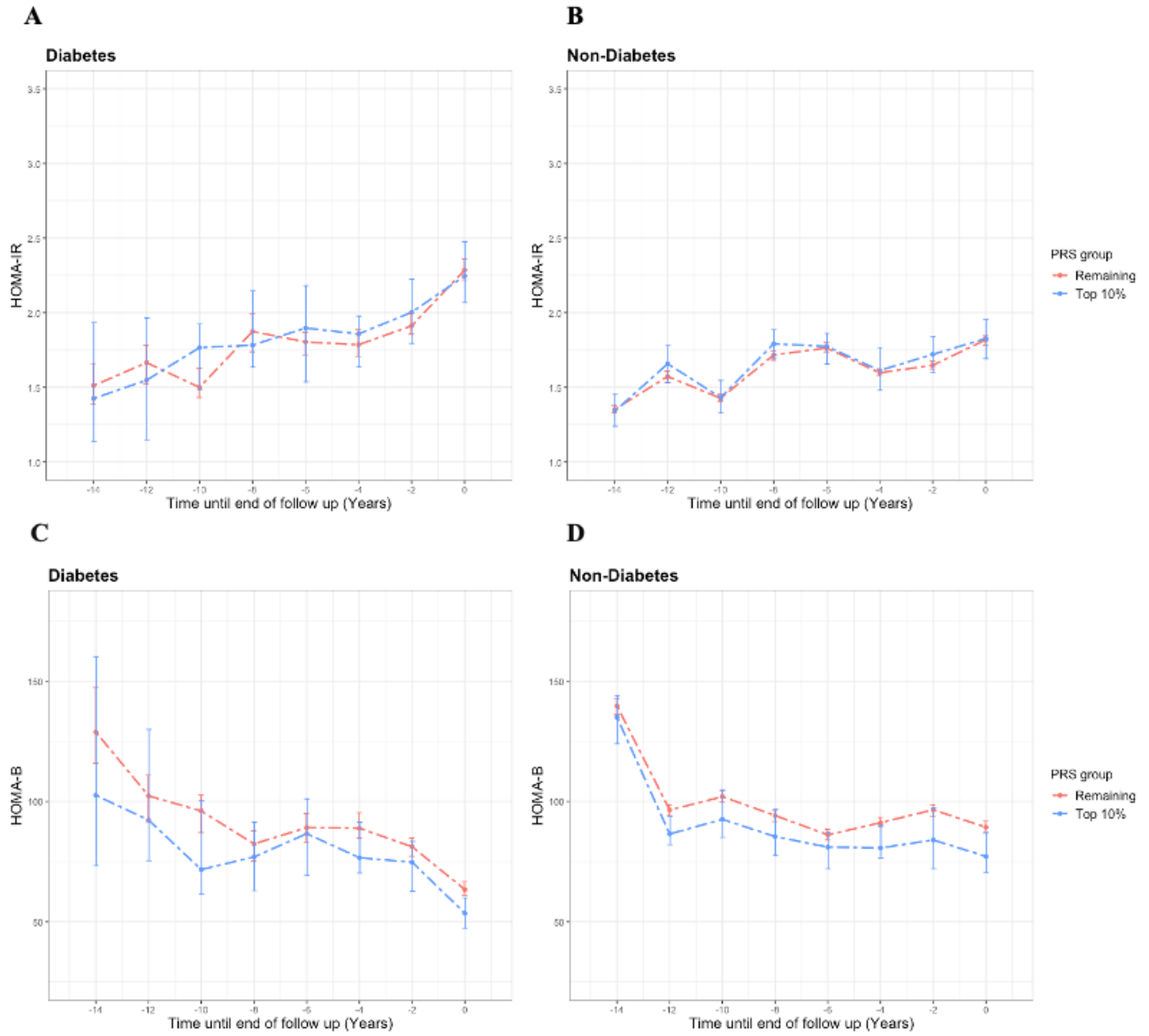
Each shaded area represents 95% confidence band for each curve. Each dash line indicates median age-at-T2DM diagnosis for each PRS group.

Supplementary Fig. S3 UKBB East Asian validation: Kaplan-Meier curve for cumulative prevalence of T2DM by PRS Group



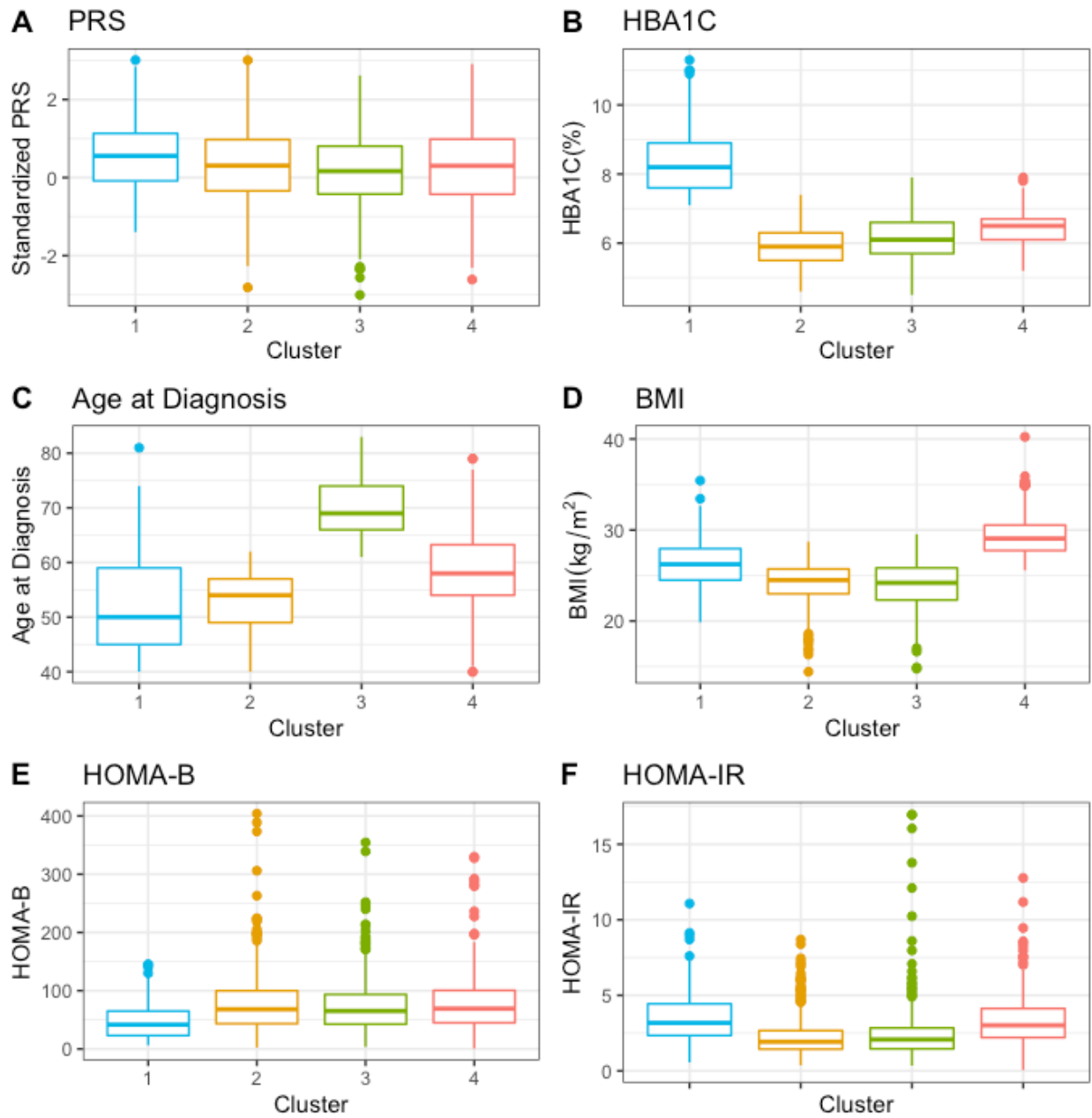
Each shaded area represents 95% confidence band for each curve.

Supplementary Fig. S4 Retrograde trajectory of HOMA-IR and HOMA-B. A. Diabetes (HOMA-IR) B. Non-Diabetes (HOMA-IR) C. Diabetes (HOMA-B) D. Non-Diabetes (HOMA-B)



Each bar represents 95% confidence interval at each time point.

Supplementary Fig. S5 Novel diabetic subgroup characteristics



Supplementary Tables

Supplementary Table S1 Area under the receiver operating characteristics curve (AUC) of different methods

	T2DM ~ PRS	T2DM ~ PRS + sex + age
Lassosum	0.64859	0.67599
PRS-CS	0.64766	0.67691

Supplementary Table S2 Dropout rate of Participants of Koges_Anсан and Ansong dataset

Follow-up	Baseline	1st	2nd	3rd	4th	5th	6th	7th
Dropout Rate (%)	0	5.14	10.66	15.12	14.48	15.45	17.81	11.57

Supplementary Table S3 Cumulative prevalence of T2DM for baseline and each follow-up of Koges_Ansan and Ansung dataset

Follow-up	Baseline	1st	2nd	3rd	4th	5th	6th	7th
NGT	2572	2539	1821	1351	975	838	711	600
Prediabetes	2172	2015	2544	2832	3043	3039	3048	2995
Diabetes	746	936	1125	1307	1472	1613	1731	1895

Supplementary Table S4 Results of Cox regression analysis for cumulative prevalence of T2DM by PRS group

PRS	Hazard Ratio	95% CI	P-value
Categorized PRS			
Bottom Decile	0.45	<i>0.36 – 0.56</i>	<i>2.84E-13</i>
Middle (10-90%)	1.00 (reference)		
Top Decile	2.290	<i>12.02 – 2.59</i>	<i>2.00E-16</i>

In the Cox regression model, sex was included as a predictor.

Supplementary Table S5 Results of Cox regression analysis for predicting T2DM complication

T2DM Complications	PRS	Hazard Ratio	95% CI	P-value
Macrovascular Complications	Categorized PRS			
	Bottom Decile	0.6047	0.2233 – 1.637	0.322
	Middle (10-90%)	1.00 (reference)		
	Top Decile	0.7980	0.5325 – 1.196	0.275
	Standardized PRS	0.9816	0.8415 – 1.145	0.813
Nephropathy	Categorized PRS			
	Bottom Decile	0.9122	0.4675 – 1.780	0.788
	Middle (10-90%)	1.00 (reference)		
	Top Decile	0.8548	0.6197 – 1.179	0.339
	Standardized PRS	0.9177	0.8110 – 1.038	0.173

specified as macrovascular complications and nephropathy

Macrovascular complications include myocardial infarction, coronary artery disease, congestive heart failure, cerebrovascular disease, peripheral artery disease.

Supplementary Table S6 Characteristics at the baseline of the KoGES_Anсан and Anսung non-diabetic population dataset

	PRS Bottom Decile (n = 348)	Middle (10-90%) (n = 2075)	PRS Top Decile (n = 149)	P-value
Basic Information				
Male (%)	173 (49.71)	941 (45.35)	66 (44.30)	0.295
Age (year)	50.73 ± 8.24	49.69 ± 8.46	48.61 ± 7.41	0.014
Physical Measurements				
BMI (kg/m ²)	24.08 ± 2.89	24.10 ± 2.87	24.41 ± 2.80	0.424
SBP (mmHg)	117.62 ± 16.03	117.98 ± 17.07	118.74 ± 18.08	0.796
DBP (mmHg)	79.03 ± 10.74	78.85 ± 11.41	79.03 ± 11.85	0.95
Clinical Risk Factors				
HDL (mg/dL)	50.07 ± 11.75	50.48 ± 11.69	50.01 ± 11.39	0.764
LDL (mg/dL)	115.64 ± 30.30	115.72 ± 31.63	115.55 ± 29.62	0.997
TG (mg/dL)	133.18 ± 81.57	152.93 ± 111.57	126.77 ± 61.24	0.759
Fasting Glucose (mg/dL)	84.29 ± 11.47	131.97 ± 93.41	87.20 ± 7.00	6.06e-05
Fasting Insulin (μIU/mL)	7.05 ± 3.58	7.29 ± 4.76	7.74 ± 7.61	0.348
HbA1C (%)	5.29 ± 0.32	5.34 ± 0.22	5.34 ± 0.22	0.00719
Others				
Current Smoking (%)	89 (25.58)	460 (22.17)	30 (20.13)	0.254
Family History (%)	21 (6.03)	200 (9.64)	15 (10.07)	0.091

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HDL:

High-Density Lipoprotein; LDL: Low-Density Lipoprotein; TG: Triglyceride. Obtained P-value

using one-way ANOVA analysis.