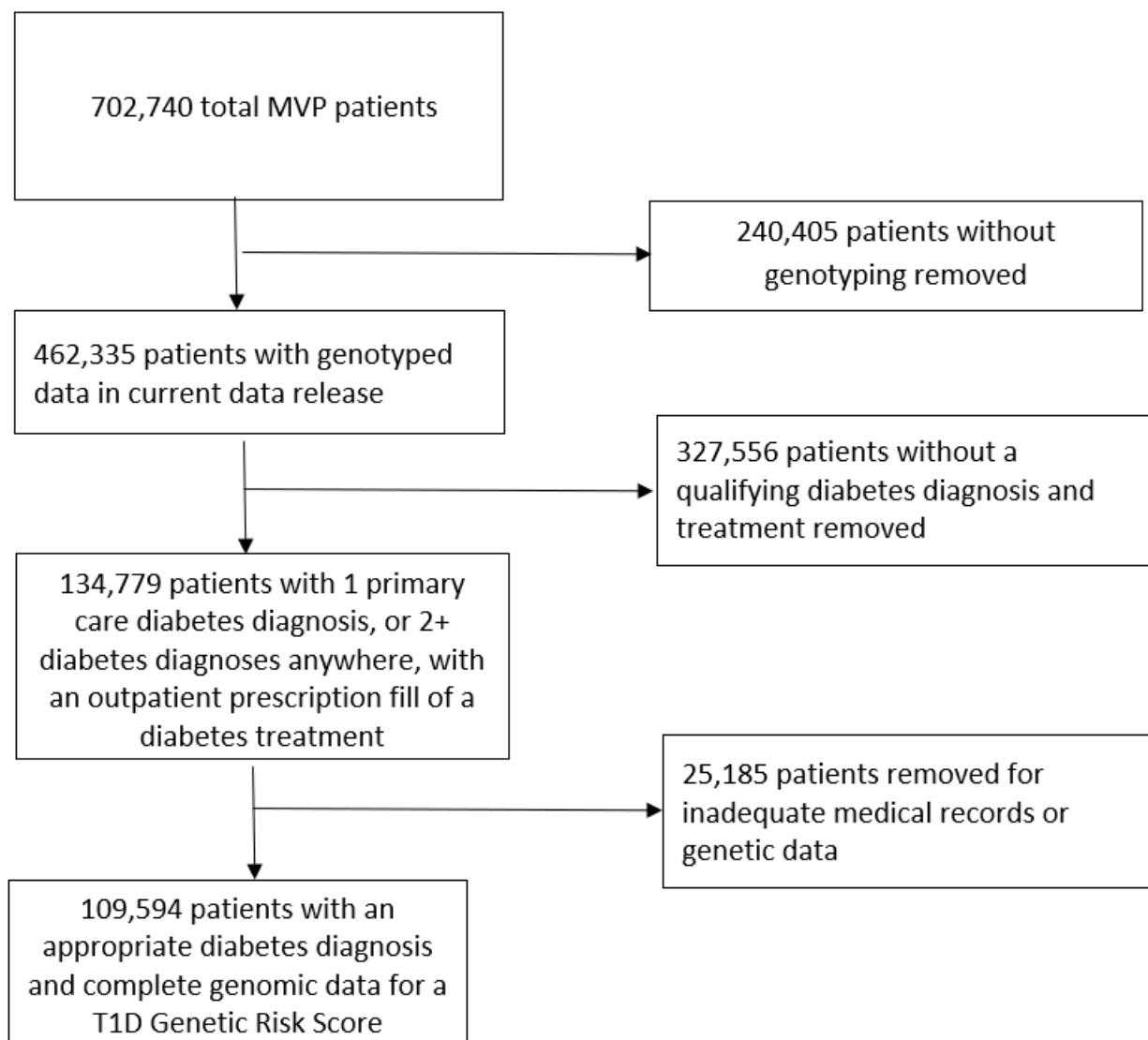


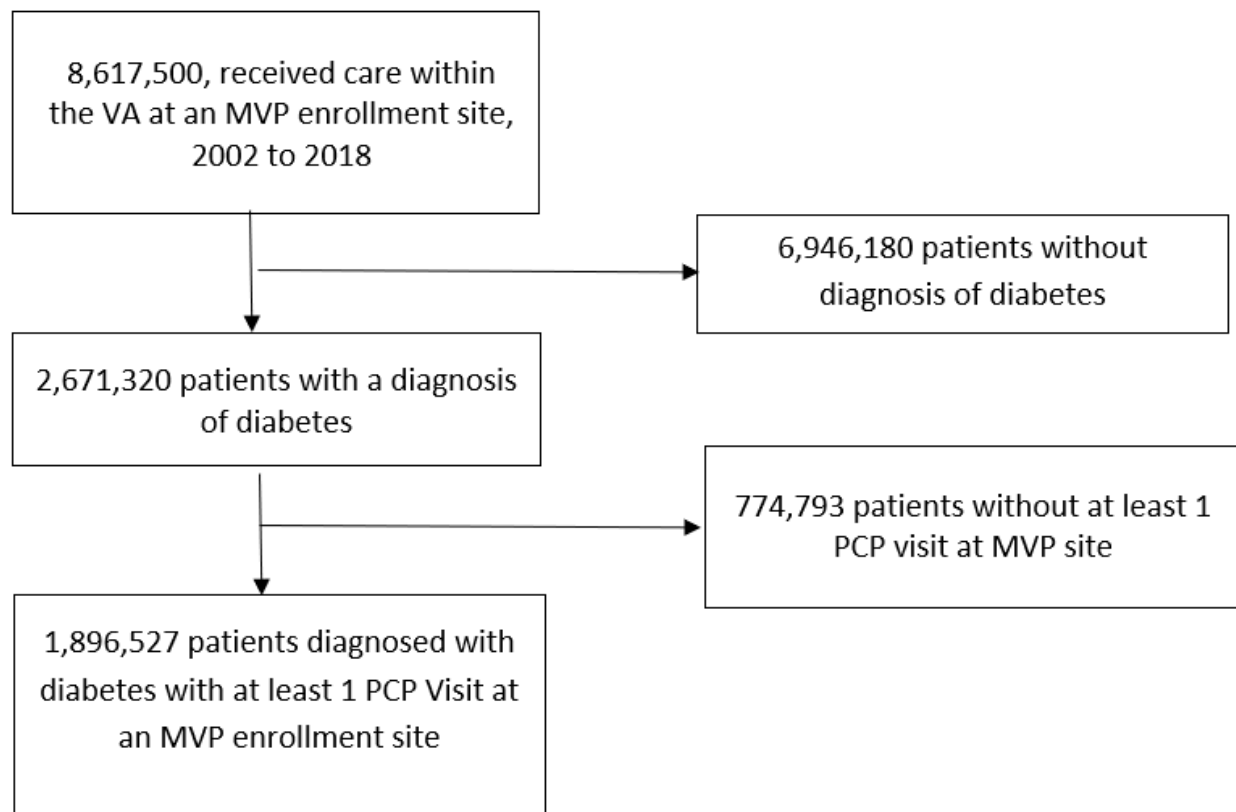
Supplements

Supplemental Figure 1 – CONSORT Diagrams of Inclusion/Exclusion into Million Veteran Program (MVP) and VA Informatics and Computing Infrastructure (VINCI) Datasets



Supplemental Figure 1a – CONSORT Diagram of Million Veteran Program Inclusion/Exclusion.

Identification = MVP recruitment; Screening identified genotyped data availability; Eligibility entailed study criteria fulfillment; Included covered the final data.



Supplemental Figure 1b – CONSORT Diagram of VA Informatics and Computing Infrastructure (VINCI) Diabetes Inclusion/Exclusion. Identification = Veterans Affairs Healthcare System participation; Screening identified diabetes diagnoses; Eligibility = study criteria fulfillment.

Supplemental Table 1 - Racial-ethnic distributions across GRS score categories using University of Exeter GRS vs University of Exeter with University of Virginia for AFR Ancestry.

	UExeter All	GRS Low	GRS Med	GRS High	GRS Highest	UExeter + UVA AFR All	GRS Low	GRS Med	GRS High	GRS Highest
GRS Groups		0-<45%	45-<90%	90-<95%	>=95%		0-<45%	45-<90%	90-<95%	>=95%
Total	109,459	63,245	36,268	4,571	5375	109,594	49,320	49,316	5,479	5,479
Race/Ethnicity										
EUR	73,872 (67.49%)	39,605 (62.62%)	26,254 (72.39%)	3,644 (79.72%)	4,369 (81.28%)	73,872 (67.41%)	34,337 (69.62%)	32,440 (65.78%)	3,538 (64.57%)	3,557 (64.92%)
AFR	25,139 (22.97%)	19,219 (30.39%)	5,500 (15.16%)	231 (5.05%)	189 (3.52%)	25,274 (23.06%)	11,376 (23.07%)	11,372 (23.06%)	1,263 (23.05%)	1,263 (23.05%)
HIS	9,537 (8.71%)	4,119 (6.51%)	3,983 (10.98%)	649 (14.20%)	786 (14.62%)	9,537 (8.70%)	3,429 (6.95%)	4,842 (9.82%)	630 (11.50%)	636 (11.61%)
ASN	911 (0.83%)	302 (0.48%)	531 (1.46%)	47 (1.03%)	31 (0.58%)	911 (0.83%)	178 (0.36%)	662 (1.34%)	48 (0.88%)	23 (0.42%)

Supplemental Table 1 - Racial-ethnic distributions across GRS score categories using University of Exeter GRS vs University of Virginia.

University of Exeter GRS was applied for all ancestry groups in both panels, except the right panel where a University of Virginia 7 SNP AFR Ancestry GRS was applied only to MVP AFR patients. Percentages represent column percentages of risk levels constructed by ventiles from the applied risk scores. EUR = non-Hispanic European Americans, AFR = non-Hispanic African Americans, HIS = Hispanic/Latino Americans, ASN = non-Hispanic Asian Americans.

Supplemental Figure 2 - ROC Curves by GAD/C-Peptide in tested patients by Ancestry (n=7433)

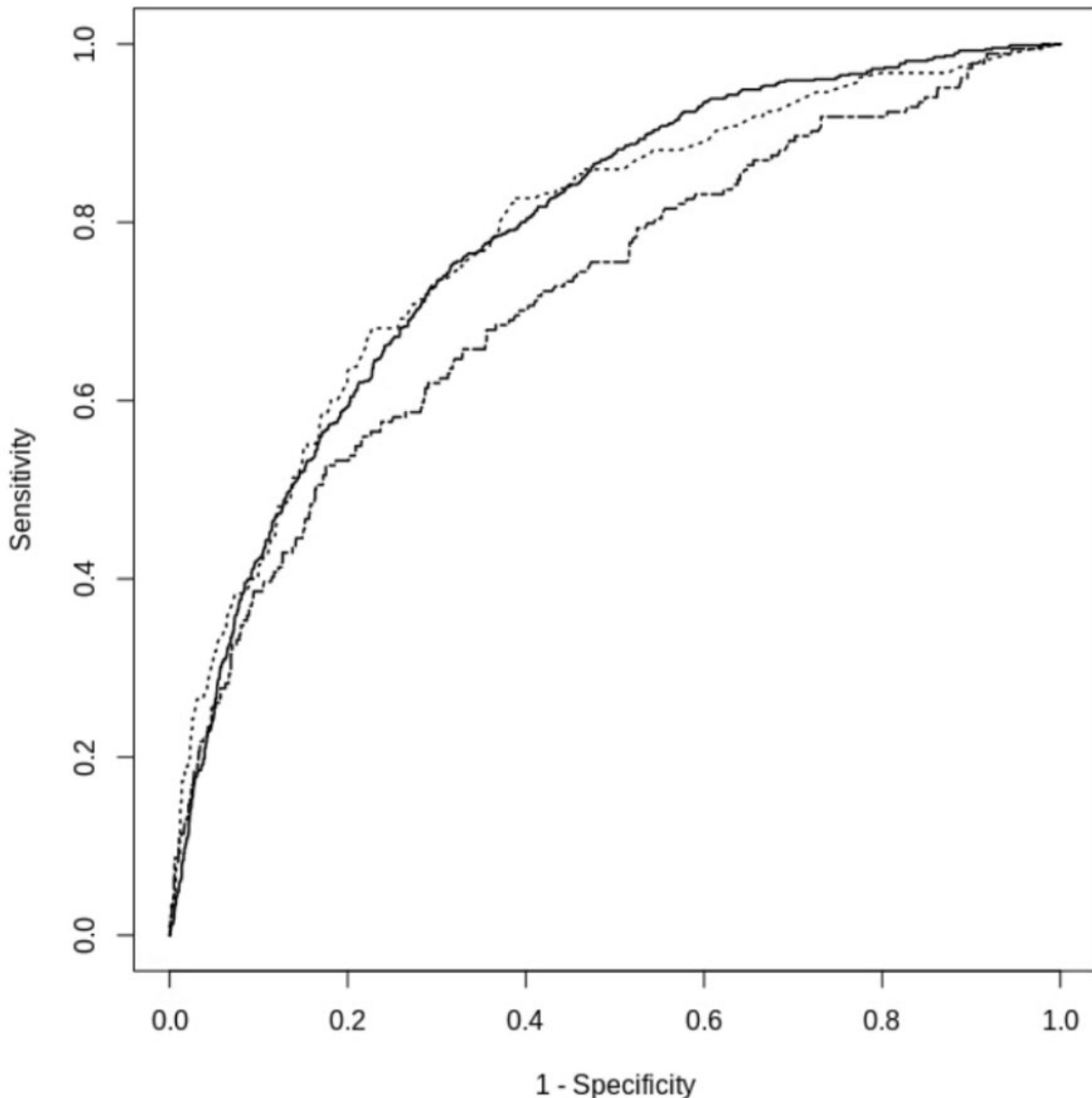


Figure 2 - GRS and T1D test positivity in EUR (n=4277) and AFR (n=2173) Ancestry Patients. HIS (n=766), and ASN Ancestry Patients (n=61) not included. EUR = non-Hispanic European Americans, AFR = non-Hispanic African Americans, HIS = Hispanic/Latino Americans, ASN = non-Hispanic Asian Americans. T1D test positivity determined by GAD Antibody level ≥ 5.0 IU/mL or C-peptide levels < 0.50 ng/ml. Ancestry determined by HARE. EUR Ancestry UExeter GRS (Solid line) AUC = 0.784, AFR Ancestry UExeter EUR GRS (Long Dash) AUC = 0.718 (P Value for difference = 0.0045), AFR Ancestry UVA AFR GRS (Dotted Line) AUC = 0.782 (P Value compared to EUR = 0.9319).

Supplemental Table 2 - Demographic and Clinical Characteristics of all Veterans with Diabetes in VA Electronic Health Records.

	MVP	All VA
No. of patients (had a PCP visit at an MVP recruitment site)	702,740	8,617,500
No. with diabetes*	134,779	1,896,527
Prevalence of diabetes*	29.15%	22.00%
Follow-up time in years (mean, SD) [†]	11.99 (4.89)	8.9 (5.4)
Follow-up time in years (median, 5% - 95% range) [†]	11.96 (4.30, 19.58)	8.4 (1.1, 18.5)
Age at onset (mean, SD) [†]	53.4 (9.62)	62.1 (11.4)
BMI at onset (mean, SD) [†]	33 (6.23)	32.0 (6.3)
% Male [†]	95.3%	96.5%
% White [†]	67.9%	65.9%
% African-American [†]	16.9%	16.6%
% Other or Unknown Race [†]	15.2%	17.5%
% Treated with insulin [†]	55.2%	45.3%
Time to Insulin in years (mean, SD) [†]	4.29 (4.3)	3.7 (4.4)
Time to insulin in years (median, 5% – 95% range) [†]	3.2 (0.0, 12.7)	2.1 (0.0, 12.7)
% with ketoacidosis [†]	1.3%	0.9%
% with ED visit for hypoglycemia [†]	4.0%	10.7%
% with an outpatient RPG <50 mg/dL [†]	8.3%	15.3%

Supplemental Table 2 - Demographic and Clinical Characteristics of all Veterans with Diabetes in VA Electronic Health Records. Comparison to Million Veteran Program (MVP) Subset. *Represents total MVP patients with diabetes, not 109,594 used in analysis. [†]Represents patients with diabetes and sufficient genomic data

Supplemental Table 3 – ICD codes used in Electronic Health Record Identification of Diabetes and Cardiorenal Diagnoses.

Diagnosis	ICD Codes
Diabetes (Overall)	ICD-9: 250.XX*ICD-10: E08.XX, E09.XX, E10.XX, E11.XX, E12.XX, E13.XX
Type 1 Diabetes	ICD-9: 250.01.XX, 250.03.XX, 250.11.XX, 250.13.XX, 250.21.XX, 250.23.XX, 250.31.XX, 250.33.XX, 250.41.XX, 250.43.XX, 250.51.XX, 250.53.XX, 250.61.XX, 250.63.XX, 250.71.XX, 250.73.XX, 250.81.XX, 250.83.XX, 250.91.XX, 250.93.XX; ICD-10: E10.XX
Heart Failure	ICD-9: 428.XX; ICD-10: I50.XX
Hypertension	ICD-9: 401.XX to 406.XX; ICD-10: I10.XX, I11.XX, I12.XX, I13.XX, I15.XX, I67.4.XX, I16.XX
Chronic Obstructive Pulmonary Disorder	ICD-9: 490.XX, 491.XX, 492.XX, 493.2.XX, 496.XX, 494.XX, 495.XX; ICD-10: V81.3.XX, J40.XX to J45.XX, J47.XX, J67.XX
Coronary Artery Disease	ICD-9: 410.XX to 415.XX; ICD-10: I20.XX to I26.XX
Chronic Kidney Disease	ICD-9: 403.01.XX, 403.11.XX, 403.91.XX, 404.02.XX, ; .03.XX, 404.1.XX, 404.9.XX, 584..XX, 585..XX, 586..XX, 792.5.XX; ICD-10: V42.0.XX, V45.1.XX, V56.0.XX, V56.1.XX, V56.2.XX, V56.3.XX, V56.8.XX, N18.XX
Hyperlipidemia	ICD-9: 272.XX; ICD-10: E78.0.XX, E78.01.XX, E78.1.XX, E78.2.XX, E78.3.XX, E78.4.XX, E78.5.XX, E78.6.XX, E88.1.XX, E75.21.XX, E75.22.XX, E75.249.XX, E77.0.XX, E77.1.XX, E78.81.XX, E78.89.XX, E88.89.XX, E78.9.XX
Atrial Fibrillation	ICD-9: 427.31; ICD-10: I48.0.XX, I48.1.XX, I48.2.XX, I48.91.XX
Peripheral Vascular Disease	ICD-9: 440.XX, 441.XX, 442.XX, 443.XX, 444.XX, 447.XX, 451.XX, 452.XX, 453.XX, 557.XX; ICD-10: E08.51, E08.52, E09.51, E09.52, E10.51, E10.52, E11.51, E11.52, E13.51, E13.52, I67.0.XX, I70.XX, I71.00.XX, I71.01.XX, I71.02.XX, I71.03.XX, I71.1.XX, I71.2.XX, I71.3.XX, I71.4.XX, I71.5.XX, I71.6.XX, I71.8.XX, I71.9.XX, I72.0.XX, I72.1.XX, I72.2.XX, I72.3.XX, I72.4.XX, I72.5.XX, I72.6.XX, I72.8.XX, I72.9.XX, I73.00.XX, I73.01.XX, I73.1.XX, I73.81.XX, I73.89.XX, I73.9.XX, I74.01.XX, I74.09.XX, I74.10.XX, I74.11.XX, I74.19.XX, I74.2.XX, I74.3.XX, I74.4.XX, I74.5.XX, I74.8.XX, I74.9.XX, I77.0.XX, I77.1.XX, I77.2.XX, I77.3.XX, I77.4.XX, I77.5.XX, I77.6.XX, I77.70.XX, I77.71.XX, I77.72.XX, I77.73.XX, I77.74.XX, I77.75.XX, I77.76.XX, I77.77.XX, I77.79.XX, I77.810.XX, I77.811.XX, I77.812.XX, I77.819.XX, I77.89.XX, I77.9.XX, I79.0.XX, I79.1.XX, I79.8.XX, I80.00.XX, I80.01.XX, I80.02.XX, I80.03.XX, I80.10.XX, I80.11.XX, I80.12.XX, I80.13.XX, I80.201.XX, I80.202.XX, I80.203.XX, I80.209.XX, I80.211.XX, I80.212.XX, I80.213.XX, I80.219.XX, I80.221.XX, I80.222.XX, I80.223.XX, I80.229.XX, I80.231.XX, I80.232.XX, I80.233.XX, I80.239.XX, I80.291.XX, I80.292.XX, I80.293.XX, I80.299.XX, I80.3.XX, I80.8.XX, I80.9.XX, I81.XX, I82.XX, K55.011.XX, K55.012.XX, K55.019.XX, K55.021.XX, K55.022.XX, K55.029.XX, K55.031.XX, K55.032.XX, K55.039.XX, K55.041.XX, K55.042.XX, K55.049.XX, K55.051.XX, K55.052.XX, K55.059.XX, K55.061.XX, K55.062.XX, K55.069.XX, K55.1.XX, K55.30.XX, K55.31.XX, K55.32.XX, K55.33.XX, K55.8.XX, K55.9.XX, K76.5.XX, M31.8.XX, M31.9.XX

Supplemental Table 3 – ICD codes used in Electronic Health Record Identification of Diabetes and Cardiorenal Diagnoses. List of ICD-9 and ICD-10 codes used to identify diabetes and cardiorenal

diagnoses within the VA healthcare system. *.XX denotes the range of all numbers possible after the given code.

Supplemental Table 4 - Distribution of T1D Genetic Risk Levels Across Ancestry Groups As Row Percentages.

	All	GRS Low	GRS Med	GRS High	GRS Highest
Total	109,594	49,320 (45.00%)	49,316 (45.00%)	5,479 (5.00%)	5,479 (5.00%)
HARE					
EUR	73,872	34,337 (46.48%)	32,440 (43.91%)	3,538 (4.79%)	3,557 (4.82%)
AFR	25,274	11,376 (45.01%)	11,372 (44.99%)	1,263 (5.00%)	1,263 (5.00%)
HIS	9,537	3,429 (35.95%)	4,842 (50.77%)	630 (6.61%)	636 (6.67%)
ASN	911	178 (19.54%)	662 (72.67%)	48 (5.27%)	23 (2.52%)

Supplemental Table 4 - Distribution of Genetic Risk Levels Across HARE Groups As Row Percentages.

Race/Ethnicity determined using HARE Algorithm. EUR = non-Hispanic European, AFR = non-Hispanic African, HIS = Hispanic/Latino, ASN = non-Hispanic Asian.

Supplemental Table 5 -Demographic and Clinical Characteristics across GRS score categories using Wellcome Trust Centiles.

	All	GRS Low	GRS Med	GRS High	GRS Highest	<i>P Value</i>
Oram GRS cutoffs	(0.8552, 0.3429)	(0.8552, 0.2340)	(0.2340, 0.2700)	(0.2700, 0.2800)	(0.2800, 0.3429)	
Total	109,459	63,245	36,268	4,571	5,375	
Sex						<0.0001
Male	104,231 (95.22%)	60,058 (94.96%)	34,662 (95.57%)	4,359 (95.36%)	5,152 (95.85%)	
Female	5,228 (4.78%)	3,187 (5.04%)	1,606 (4.43%)	212 (4.64%)	223 (4.15%)	
Age Category						
Age, Mean (SD)	65.16 (9.83)	65.06 (9.72)	65.41 (9.88)	65.05 (10.20)	64.91 (10.47)	<0.0001
20-29	131 (0.12%)	55 (0.09%)	32 (0.09%)	12 (0.26%)	32 (0.60%)	<0.0001
30-39	1,219 (1.11%)	616 (0.97%)	433 (1.19%)	71 (1.55%)	99 (1.84%)	
40-49	5,346 (4.88%)	3,089 (4.88%)	1,753 (4.83%)	245 (5.36%)	259 (4.82%)	
50-59	19,453 (17.77%)	11,778 (18.62%)	6,016 (16.59%)	747 (16.34%)	912 (16.97%)	
60-69	52,253 (47.74%)	30,099 (47.59%)	17,382 (47.93%)	2,215 (48.46%)	2,557 (47.57%)	
70-79	22,426 (20.49%)	12,761 (20.18%)	7,675 (21.16%)	913 (19.97%)	1,077 (20.04%)	
80+	8575 (7.83%)	4810 (7.61%)	2960 (8.16%)	367 (8.03%)	438 (8.15%)	
Race/Ethnicity[†]						<0.0001
EUR	73,872 (67.49%)	39,605 (62.62%)	26,254 (72.39%)	3,644 (79.72%)	4,369 (81.28%)	
AFR	25,139 (22.97%)	19,219 (30.39%)	5,500 (15.16%)	231 (5.05%)	189 (3.52%)	
HIS	9,537 (8.71%)	4,119 (6.51%)	3,983 (10.98%)	649 (14.20%)	786 (14.62%)	
ASN	911 (0.83%)	302 (0.48%)	531 (1.46%)	47 (1.03%)	31 (0.58%)	
Diabetes-related Variables						
Taking Insulin	60,366 (55.15%)	34,489 (54.53%)	19,939 (54.98%)	2,619 (57.30%)	3,319 (61.75%)	<0.0001
Taking Sulfonylurea	76,228 (69.64%)	44,734 (70.73%)	25,100 (69.21%)	3,042 (66.55%)	3,352 (62.36%)	<0.0001
Diabetic Ketoacidosis	1,434 (1.31%)	674 (1.07%)	485 (1.34%)	88 (1.93%)	187 (3.48%)	<0.0001
Hypoglycemia Dx at ED	4,401 (4.02%)	2,507 (3.96%)	1,393 (3.84%)	205 (4.48%)	296 (5.51%)	<0.0001
Outpatient Glucose <50 mg/dL	9,096 (8.31%)	5,114 (8.09%)	2,902 (8.00%)	409 (8.95%)	671 (12.48%)	<0.0001
Years to Insulin (Median)	3.22 (3.17, 3.27)	3.4 (3.32, 3.47)	3.25 (3.15, 3.34)	2.68 (2.41, 2.99)	1.37 (1.15, 1.62)	<0.0001
Years to Insulin (Mean)	3.29 (4.30)	4.4 (4.30)	4.3 (4.31)	3.99 (4.28)	3.38 (4.16)	<0.0001

Years to Sulfonylurea (Median)	0.51 (0.49, 0.53)	0.51 (0.48, 0.53)	0.52 (0.48, 0.54)	0.53 (0.44, 0.67)	0.5 (0.39, 0.57)	0.525
eGFR at Enrollment (Mean)	73.12 (26.17)	73.27 (26.15)	72.86 (26.50)	73.35 (24.72)	72.87 (25.11)	0.107
A1c at Diabetes Onset (Mean)	7.74 (2.22)	7.75 (2.10)	7.72 (2.45)	7.71 (1.97)	7.84 (2.03)	0.0044
BMI at Diabetes Onset (Mean)	33.01 (6.23)	33.08 (6.18)	33.05 (6.26)	32.86 (6.44)	32.07 (6.40)	<0.0001
Age at Diabetes Onset (Mean)	53.48 (9.62)	53.41 (9.51)	53.73 (9.64)	53.40 (9.96)	52.94 (10.43)	<0.0001
Years of follow-up (Mean)	11.99 (4.88)	11.96 (4.88)	12.00 (4.86)	11.96 (4.92)	12.29 (5.04)	<0.0001
T1D Diagnostic						
T1D ICD Code Any Use	19,371 (17.70%)	10,475 (16.56%)	6,454 (17.8%)	954 (20.87%)	1,488 (27.68%)	<0.0001
T1D ICD Code at Least 50%	1,583 (1.45%)	404 (0.64%)	585 (1.61%)	156 (3.41%)	438 (8.15%)	<0.0001
GAD Tested	2,627 (2.40%)	1,238 (1.96%)	892 (2.46%)	161 (3.52%)	336 (6.25%)	<0.0001
%Positive if GAD Tested [†]	517 (19.68%)	109 (8.80%)	206 (23.09%)	52 (32.30%)	150 (44.64%)	<0.0001
C-peptide Tested	6,243 (5.70%)	3,312 (5.24%)	2,068 (5.70%)	318 (6.96%)	545 (10.14%)	<0.0001
%Low C-peptide If Tested [‡]	547 (8.76%)	95 (2.87%)	208 (10.06%)	62 (19.50%)	182 (33.39%)	<0.0001

Supplemental Table 5 -Demographic and Clinical Characteristics across GRS score categories using Wellcome Trust Centiles. **P Values* determined to assess trend using ANOVA for continuous variables and Multinomial Cochrane-Armitage tests for categorical variables. [†]Race/Ethnicity determined using HARE Genetic Ancestry Algorithm. EUR = European, AFR = African, HIS = Admixed Hispanic/Latino, ASN = Asian. [‡]GAD Antibody level ≥5.0 IU/mL or C-peptide levels <0.50 ng/ml were indicative of Type 1 Diabetes. EUR = non-Hispanic European, AFR = non-Hispanic African, HIS = Hispanic/Latino, ASN = non-Hispanic Asian.

Supplemental Table 6 – Demographic and Clinical Characteristics Across GRS Score Categories Stratified by HARE Ancestry

Supplemental Table 6a - Demographics and T1D Characteristics by HARE African Ancestry.

	All	GRS Low	GRS Med	GRS High	GRS Highest	P -Value*
Total	25,274	11,376	11,372	1,263	1,263	
Sex						0.1433
Male	23,327 (92.3%)	10,486 (92.18%)	10,498 (92.31%)	1,187 (93.98%)	1,156 (91.53%)	
Female	1,949 (7.71%)	890 (7.82%)	874 (7.69%)	78 (6.18%)	107 (8.47%)	
Age Category						
Age, Mean (SD)	61.74 (9.65)	61.84 (9.65)	61.69 (9.58)	61.83 (9.82)	61.11 (10.07)	0.0704
20-29 (%)	34 (0.13%)	14 (0.12%)	17 (0.15%)	2 (0.16%)	1 (0.08%)	0.3294
30-39 (%)	383 (1.52%)	171 (1.50%)	165 (1.45%)	22 (1.74%)	25 (1.98%)	
40-49 (%)	2,005 (7.93%)	870 (7.65%)	907 (7.98%)	104 (8.23%)	124 (9.82%)	
50-59 (%)	7,431 (29.40%)	3,376 (29.68%)	3,335 (29.33%)	357 (28.27%)	363 (28.74%)	
60-69 (%)	10,971 (43.41%)	4,923 (43.28%)	4,958 (43.60%)	562 (44.50%)	528 (41.81%)	
70-79 (%)	3,385 (13.39%)	1,519 (13.35%)	1,542 (13.56%)	149 (11.80%)	175 (13.86%)	
80+ (%)	1,044 (4.13%)	493 (4.33%)	439 (3.86%)	65 (5.15%)	47 (3.72%)	
Diabetes-related Variables						
Taking Insulin	14,665 (58.02%)	6,601 (58.03%)	6,520 (57.33%)	750 (59.38%)	794 (62.87%)	0.0015
Taking Sulfonylurea	17,372 (68.73%)	7,971 (70.07%)	7,727 (67.95%)	852 (67.46%)	822 (65.08%)	<0.0001
Diabetic Ketoacidosis	498 (1.97%)	175 (1.54%)	237 (2.08%)	32 (2.53%)	54 (4.28%)	<0.0001
Hypoglycemia Dx at ED	1,495 (5.92%)	645 (5.67%)	663 (5.83%)	93 (7.36%)	94 (7.44%)	0.0096
Outpatient Glucose <50 mg/dL	3,067 (12.14%)	1,287 (11.31%)	1,405 (12.35%)	167 (13.22%)	208 (16.47%)	<0.0001
Years to Insulin (Median)	2.71 (2.55, 2.83)	2.89 (2.72, 3.03)	2.74 (2.52, 2.90)	2.06 (1.56, 2.55)	1.81 (1.26, 2.22)	<0.0001
Years to Insulin (Mean)	3.96 (4.24)	4.10 (4.30)	3.94 (4.21)	3.60 (4.16)	3.37 (3.99)	<0.0001
Years to Sulfonylurea (Median)	0.34 (0.30, 0.39)	0.33 (0.27, 0.40)	0.34 (0.29, 0.41)	0.48 (0.25, 0.73)	0.35 (0.21, 0.51)	0.394
eGFR at Enrollment (Mean)	76.90 (30.22)	76.64 (28.63)	77.20 (32.07)	77.05 (28.86)	76.44 (28.49)	0.547
A1c at Diabetes Onset (Mean)	8.21 (2.95)	8.18 (2.44)	8.18 (2.49)	8.34 (2.55)	8.59 (7.65)	<0.0001
BMI at Diabetes Onset (Mean)	32.40 (6.16)	32.44 (6.11)	32.44 (6.20)	32.03 (6.09)	31.93 (6.26)	0.008
Age at Diabetes Onset (Mean)	49.98 (9.47)	50.04 (9.39)	49.99 (9.44)	50.07 (9.74)	49.23 (10.06)	0.0347

Years of Follow-Up (Mean)	12.07 (5.00)	12.12 (4.98)	12.01 (5.02)	12.07 (4.97)	12.19 (5.11)	0.285
T1D Diagnostic						
T1D ICD Code Any Use	4,725 (18.70%)	2,030 (17.84%)	2,092 (18.40%)	283 (22.41%)	320 (25.34%)	<0.0001
T1D ICD Code at Least 50%	263 (1.04%)	67 (0.59%)	122 (1.07%)	30 (2.38%)	44 (3.48%)	<0.0001
GAD Tested	800 (3.17%)	327 (2.87%)	350 (3.08%)	49 (3.88%)	74 (5.86%)	0.0027
%Positive of GAD Tested†	107 (13.38%)	18 (5.50%)	47 (13.43%)	8 (16.33%)	34 (45.95%)	<0.0001
C-peptide Tested	1,877 (7.43%)	804 (7.07%)	822 (7.23%)	116 (9.18%)	135 (10.69%)	<0.0001
%Low C-peptide If Tested†	106 (5.65%)	6 (0.75%)	48 (5.84%)	16 (13.79%)	36 (26.67%)	<0.0001

Supplemental Table 6a - Demographics and T1D Characteristics by HARE African Ancestry. **P Values* determined to assess trend using ANOVA for continuous variables and Multinomial Cochrane-Armitage tests for categorical variables. †GAD Antibody level ≥ 5.0 IU/mL or C-peptide levels <0.50 ng/ml were indicative of Type 1 Diabetes.

Supplemental Table 6b - Demographics and T1D Characteristics by HARE European Ancestry.

	All	GRS Low	GRS Med	GRS High	GRS Highest	<i>P Value</i> *
Total	73,872	34,337	32,440	3,538	3,557	
Sex						0.3244
Male	70,975 (96.08%)	33,025 (96.18%)	31,159 (96.05%)	3,386 (95.70%)	3,405 (95.73%)	
Female	2,897 (3.92%)	1,312 (3.82%)	1,281 (3.95%)	152 (4.30%)	152 (4.27%)	
Age Category						
Age, Mean (SD)	66.68 (9.45)	66.85 (9.23)	66.74 (9.49)	65.70 (9.99)	65.44 (10.38)	<0.0001
20-29 (%)	65 (0.09%)	14 (0.04%)	20 (0.06%)	9 (0.25%)	22 (0.62%)	<0.0001
30-39 (%)	552 (0.75%)	204 (0.59%)	243 (0.75%)	47 (1.33%)	58 (1.63%)	
40-49 (%)	2,605 (3.53%)	1,138 (3.31%)	1,147 (3.54%)	162 (4.58%)	158 (4.44%)	
50-59 (%)	9,822 (13.30%)	4,418 (12.87%)	4,334 (13.36%)	520 (14.70%)	550 (15.46%)	
60-69 (%)	36,358 (49.22%)	17,069 (49.71%)	15,845 (48.84%)	1,750 (49.46%)	1,694 (47.62%)	
70-79 (%)	17,442 (23.61%)	8,243 (24.01%)	7,689 (23.70%)	744 (21.03%)	766 (21.54%)	
80+ (%)	6,995 (9.47%)	3,232 (9.41%)	3,150 (9.71%)	305 (8.62%)	308 (8.66%)	
Diabetes-related Variables						
Taking Insulin	39,970 (54.11%)	18,129 (52.80%)	1,754 (5.41%)	2,038 (57.60%)	2,260 (63.54%)	<0.0001
Taking Sulfonylurea	51,433 (69.62%)	24,529 (71.44%)	22,488 (69.32%)	2,280 (64.44%)	2,136 (60.05%)	<0.0001
Diabetic Ketoacidosis	788 (1.07%)	247 (0.72%)	334 (1.03%)	83 (2.35%)	124 (3.49%)	<0.0001

Hypoglycemia Dx at ED	2,489 (3.37%)	1,040 (3.03%)	1,105 (3.41%)	148 (4.18%)	196 (5.51%)	<0.0001
Outpatient Glucose <50 mg/dL	5,357 (7.25%)	2,210 (6.44%)	2,365 (7.29%)	315 (8.90%)	467 (13.13%)	<0.0001
Years to Insulin (Median)	3.41 (3.34, 3.49)	3.74 (3.62, 3.74)	3.41 (3.28, 3.51)	2.48 (2.17, 2.80)	1.17 (0.94, 1.44)	<0.0001
Years to Insulin (Mean)	4.41 (4.32)	4.61 (4.32)	4.39 (4.32)	3.93 (4.29)	3.26 (4.15)	<0.0001
Years to Sulfonylurea (Median)	0.57 (0.54, 0.60)	0.60 (0.56, 0.64)	0.55 (0.52, 0.59)	0.63 (0.48, 0.80)	0.52 (0.41, 0.64)	0.872
eGFR at Enrollment (Mean)	71.25 (24.18)	71.22 (24.31)	71.08 (24.05)	72.47 (24.09)	71.90 (24.11)	0.0070
A1c at Diabetes Onset (Mean)	7.54 (1.87)	7.28 (1.85)	7.30 (1.88)	7.44 (1.86)	7.49 (1.93)	<0.0001
BMI at Diabetes Onset (Mean)	33.30 (6.26)	33.48 (6.17)	33.30 (6.28)	32.88 (6.49)	31.93 (6.45)	<0.0001
Age at Diabetes Onset (Mean)	55.01 (9.25)	55.25 (9.01)	55.07 (9.27)	54.02 (9.84)	53.35 (10.43)	<0.0001
Years of Follow-Up (Mean)	11.97 (4.82)	11.91 (4.80)	11.99 (4.81)	11.99 (4.85)	12.41 (5.03)	<0.0001
T1D Diagnostic						
T1D ICD Code Any Use	13,057 (17.68%)	5,447 (15.86%)	5,711 (17.60%)	800 (22.61%)	1,099 (30.90%)	<0.0001
T1D ICD Code at Least 50%	1,242 (1.68%)	198 (0.58%)	529 (1.63%)	157 (4.44%)	358 (10.06%)	<0.0001
GAD Tested	1,556 (2.11%)	499 (1.45%)	677 (2.09%)	130 (3.67%)	250 (7.03%)	<0.0001
%Positive of GAD Tested [†]	374 (24.04%)	41 (8.22%)	166 (24.52%)	50 (38.46%)	117 (46.80%)	<0.0001
C-peptide Tested	3,648 (4.94%)	1,449 (4.22%)	1,574 (4.85%)	246 (6.95%)	379 (10.66%)	<0.0001
%Low C-peptide If Tested [†]	423 (11.6%)	34 (2.35%)	179 (11.37%)	64 (26.02%)	146 (38.52%)	0.0002

Supplemental Table 6b - Demographics and T1D Characteristics by HARE European Ancestry. *P Values determined to assess trend using ANOVA for continuous variables and Multinomial Cochrane-Armitage tests for categorical variables. [†]GAD Antibody level ≥5.0 IU/mL or C-peptide levels <0.50 ng/ml were indicative of Type 1 Diabetes.

Supplemental Table 6c - Demographics and T1D Characteristics by HARE Admixed Hispanic/Latino Ancestry.

	All	GRS Low	GRS Med	GRS High	GRS Highest	P-Value*
Total	9,537	3,429	4,842	630	636	
Sex						0.9709
Male	9,180 (96.26%)	3,302 (96.3%)	4,661 (96.26%)	607 (96.35%)	610 (95.91%)	
Female	357 (3.74%)	127 (3.70%)	181 (3.74%)	23 (3.65%)	26 (4.09%)	
Age Category						

Age, Mean (SD)	62.84 (10.18)	63.06 (9.98)	62.69 (10.21)	62.92 (10.27)	62.80 (10.90)	0.4465
20-29 (%)	28 (0.29%)	7 (0.20%)	12 (0.25%)	5 (0.79%)	4 (0.63%)	0.3098
30-39 (%)	240 (2.52%)	73 (2.13%)	129 (2.66%)	14 (2.22%)	24 (3.77%)	
40-49 (%)	645 (6.76%)	224 (6.53%)	339 (7.00%)	47 (7.46%)	35 (5.50%)	
50-59 (%)	2063 (21.63%)	731 (21.32%)	1070 (22.10%)	125 (19.84%)	137 (21.54%)	
60-69 (%)	4,607 (48.31%)	1,678 (48.94%)	2,307 (47.65%)	316 (50.16%)	306 (48.11%)	
70-79 (%)	1,472 (15.43%)	540 (15.75%)	753 (15.55%)	91 (14.44%)	88 (13.84%)	
80+ (%)	480 (5.03%)	174 (5.07%)	232 (4.79%)	32 (5.08%)	42 (6.60%)	
Diabetes-related Variables						
Taking Insulin	5,412 (56.75%)	1,935 (56.43%)	2,759 (56.98%)	346 (54.92%)	372 (58.49%)	0.5952
Taking Sulfonylurea	6,913 (72.49%)	2,495 (72.76%)	3,510 (72.49%)	468 (74.29%)	440 (69.18%)	0.2006
Diabetic Ketoacidosis	143 (1.50%)	42 (1.22%)	68 (1.40%)	11 (1.75%)	22 (3.46%)	0.0003
Hypoglycemia Dx at ED	402 (4.22%)	148 (4.32%)	201 (4.15%)	27 (4.29%)	26 (4.09%)	0.9824
Outpatient Glucose <50 mg/dL	661 (6.93%)	217 (6.33%)	340 (7.02%)	42 (6.67%)	62 (9.75%)	0.0196
Years to Insulin (Median)	3.24 (3.07, 3.41)	3.41 (3.12, 3.76)	3.24 (2.98, 3.46)	3.07 (2.44, 3.97)	2.68 (1.60, 3.26)	0.141
Years to Insulin (Mean)	4.31 (4.28)	4.43 (4.35)	4.27 (4.21)	4.41 (4.40)	3.91 (4.37)	0.141
Years to Sulfonylurea (Median)	0.35 (0.30, 0.43)	0.37 (0.27, 0.48)	0.37 (0.28, 0.50)	0.35 (0.14, 0.59)	0.27 (0.12, 0.51)	0.442
eGFR at Enrollment (Mean)	77.37 (27.68)	76.51 (27.66)	77.89 (27.73)	78.03 (26.73)	77.36 (28.24)	0.166
A1c at Diabetes Onset (Mean)	8.08 (2.23)	8.06 (2.24)	8.05 (2.20)	8.19 (2.24)	8.27 (2.36)	0.0948
BMI at Diabetes Onset (Mean)	32.72 (6.10)	32.65 (6.01)	32.79 (6.16)	33.03 (6.36)	32.20 (5.88)	0.0835
Age at Diabetes Onset (Mean)	51.17 (9.77)	51.37 (9.60)	51.04 (9.77)	51.20 (9.94)	51.14 (10.47)	0.512
Years of Follow-Up (Mean)	11.99 (5.03)	12.00 (5.05)	11.97 (4.98)	12.02 (5.21)	11.99 (5.07)	0.989
T1D Diagnostic						
T1D ICD Code Any Use	1,516 (15.90%)	526 (15.34%)	786 (16.23%)	88 (13.97%)	116 (18.24%)	0.1347
T1D ICD Code at Least 50%	76 (0.80%)	13 (0.38%)	37 (0.76%)	7 (1.11%)	19 (2.99%)	<0.0001
GAD Tested	244 (2.56%)	72 (2.10%)	127 (2.62%)	19 (3.02%)	26 (4.09%)	0.1606
%Positive of GAD Tested [†]	34 (13.93%)	3 (4.17%)	18 (14.17%)	5 (26.32%)	8 (30.77%)	0.0025
C-peptide Tested	676 (7.09%)	223 (6.50%)	349 (7.21%)	43 (6.83%)	61 (9.59%)	0.0120

%Low C-peptide If Tested [†]	17 (2.51%)	4 (1.79%)	8 (2.30%)	0 (0.00%)	5 (8.20%)	0.0300
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Supplemental Table 6c - Demographics and T1D Characteristics by HARE Admixed Hispanic/Latino Ancestry. **P Values* determined to assess trend using ANOVA for continuous variables and Multinomial Cochrane-Armitage tests for categorical variables. [†]GAD Antibody level ≥5.0 IU/mL or C-peptide levels <0.50 ng/ml were indicative of Type 1 Diabetes.

Supplemental Table 6d - Demographics and T1D Characteristics by HARE Asian Ancestry.

	All	GRS Low	GRS Med	GRS High	GRS Highest	P-Value
Total	911	178	662	48	23	
Sex						0.0056
Male	880 (96.60%)	168 (94.38%)	646 (97.58%)	43 (89.58%)	23 (100.00%)	
Female	31 (3.40%)	10 (5.62%)	16 (2.42%)	5 (10.42%)	0 (0.00%)	
Age Category						
Age, Mean (SD)	62.84 (10.18)	63.06 (9.98)	62.69 (10.21)	62.92 (10.27)	62.80 (10.90)	0.391
20-29 (%)	6 (0.66%)	1 (0.56%)	5 (0.76%)	0 (0.00%)	0 (0.00%)	0.3695
30-39 (%)	45 (4.94%)	11 (6.18%)	30 (4.53%)	3 (6.25%)	1 (4.35%)	
40-49 (%)	103 (11.31%)	21 (11.80%)	73 (11.03%)	6 (12.50%)	3 (13.04%)	
50-59 (%)	182 (19.98%)	36 (20.22%)	132 (19.94%)	8 (16.67%)	6 (26.09%)	
60-69 (%)	375 (41.16%)	81 (45.51%)	264 (39.88%)	22 (45.83%)	8 (34.78%)	
70-79 (%)	142 (15.59%)	22 (12.36%)	110 (16.62%)	6 (12.50%)	4 (17.39%)	
80+ (%)	58 (6.37%)	6 (3.37%)	48 (7.25%)	3 (6.25%)	1 (4.35%)	
Diabetes-related Variables						
Taking Insulin	407 (44.68%)	85 (47.75%)	288 (43.50%)	22 (45.83%)	12 (52.17%)	0.6597
Taking Sulfonylurea	612 (67.18%)	115 (64.61%)	451 (68.13%)	31 (64.58%)	15 (65.22%)	0.8035
Diabetic Ketoacidosis	7 (0.77%)	0 (0.00%)	5 (0.76%)	1 (2.08%)	1 (4.35%)	0.9648
Hypoglycemia Dx at ED	24 (2.63%)	3 (1.69%)	20 (3.02%)	1 (2.08%)	0 (0.00%)	0.6391
Outpatient Glucose <50 mg/dL	33 (3.62%)	4 (2.25%)	27 (4.08%)	2 (4.17%)	0 (0.00%)	0.5195
Years to Insulin (Median)	3.24 (3.07, 3.41)	3.41 (3.12, 3.76)	3.24 (2.98, 3.46)	3.07 (2.44, 3.97)	2.68 (1.60, 3.26)	0.344
Years to Insulin (Mean)	4.31 (4.28)	4.43 (4.35)	4.27 (4.21)	4.41 (4.40)	3.91 (4.37)	0.344
Years to Sulfonylurea (Median)	0.35 (0.30, 0.43)	0.37 (0.27, 0.48)	0.37 (0.28, 0.50)	0.35 (0.14, 0.59)	0.27 (0.12, 0.51)	0.994
eGFR at Enrollment (Mean)	77.37 (27.68)	76.51 (27.66)	77.89 (27.73)	78.03 (26.73)	77.36 (28.24)	0.0671
a1c at Enrollment (Mean)	7.76 (1.74)	7.74 (1.77)	7.77 (1.72)	7.72 (1.68)	7.78 (1.82)	0.858
a1c at Diabetes Onset (Mean)	8.08 (2.23)	8.06 (2.24)	8.05 (2.20)	8.19 (2.24)	8.27 (2.36)	0.863

BMI at Enrollment (Mean)	32.46 (6.79)	32.23 (6.24)	32.64 (7.19)	32.85 (6.60)	32.03 (6.68)	0.977
BMI at Diabetes Onset (Mean)	32.72 (6.10)	32.65 (6.01)	32.79 (6.16)	33.03 (6.36)	32.20 (5.88)	0.936
Age at Diabetes Onset (Mean)	51.17 (9.77)	51.37 (9.60)	51.04 (9.77)	51.20 (9.94)	51.14 (10.47)	0.492
Years of Follow-Up (Mean)	11.99 (5.03)	12.00 (5.05)	11.97 (4.98)	12.02 (5.21)	11.99 (5.07)	0.623
T1D Diagnostic						
T1D Code Any Use	104 (11.42%)	25 (14.04%)	68 (10.27%)	7 (14.58%)	4 (17.39%)	0.3392
T1D Code at Least 50%	6 (0.66%)	2 (1.12%)	3 (0.45%)	1 (2.08%)	0 (0.00%)	0.4476
GAD Tested	32 (3.51%)	4 (2.25%)	23 (3.47%)	3 (6.25%)	2 (8.70%)	0.2674
%Positive of GAD Tested	2 (6.25%)	0 (0.00%)	2 (8.70%)	0 (0.00%)	0 (0.00%)	0.8411
C-peptide Tested	52 (5.71%)	10 (5.62%)	36 (5.44%)	4 (8.33%)	2 (8.7%)	0.8442
%Positive of CPep Tested	2 (3.85%)	0 (0.00%)	2 (5.56%)	0 (0.00%)	0 (0.00%)	0.7384

Supplemental Table 6d - Demographics and T1D Characteristics by HARE Asian Ancestry. **P* Values determined to assess trend using ANOVA for continuous variables and Multinomial Cochran-Armitage tests for categorical variables. GAD Antibody level ≥ 5.0 IU/mL or C-peptide levels <0.50 ng/ml were indicative of Type 1 Diabetes.

Supplemental Table 7 - Median Years to Hypoglycemia-Level Random Plasma Glucose Readings by Genetic Risk Levels.

	<70 mg/dL	<65 mg/dL	<60 mg/dL	<55 mg/dL	<50 mg/dL
GRS Low	5.68 (5.59, 5.79)	6.31 (6.17, 6.44)	6.88 (6.75, 7.01)	7.44 (7.26, 7.61)	7.98 (7.80, 8.22)
GRS Med	5.62 (5.51, 5.71)	6.18 (6.04, 6.28)	6.77 (6.66, 6.90)	7.12 (6.97, 7.27)	7.49 (7.30, 7.71)
GRS High	5.26 (4.95, 5.49)	5.78 (5.46, 6.09)	6.39 (6.02, 7.07)	6.96 (6.40, 7.44)	7.27 (6.64, 7.72)
GRS Highest	4.72 (4.49, 5.03)	5.10 (4.81, 5.50)	5.73 (5.36, 6.15)	6.13 (5.63, 6.45)	6.53 (6.14, 7.07)

Supplemental Table 7 - Median Years to Hypoglycemia-Level Random Plasma Glucose Readings by Genetic Risk Levels. Median years to hypoglycemia reported with 95% confidence intervals. All *P*-Values <0.0001 in tests for trend across glucose levels.

Supplemental Table 8 - Mean Time to Insulin Across Genetic Risk Categories and GAD/C-Peptide Testing.

	GAD not tested	GAD tested and negative*	GAD tested and positive*
GRS Low	4.53 (4.33)	2.60 (3.54)	1.98 (3.00)
GRS Med	4.37 (4.30)	2.27 (3.42)	1.02 (2.02)
GRS High	4.06 (4.32)	1.62 (2.92)	1.23 (1.97)
GRS Highest	3.61 (4.23)	1.19 (2.25)	0.88 (1.94)
Figure 2B: Time to Insulin			
	C-peptide not tested	C-peptide tested and not low*	C-peptide tested and low*
GRS Low	4.56 (4.34)	3.50 (3.99)	0.64 (1.62)
GRS Med	4.40 (4.32)	3.26 (3.83)	0.81 (1.84)
GRS High	4.11 (4.34)	2.89 (3.61)	0.58 (1.41)
GRS Highest	3.60 (4.26)	2.21 (3.22)	0.58 (1.69)

Supplemental Table 8 - Mean Time to Insulin Across Genetic Risk Categories and GAD/C-Peptide Testing. Means reported with standard deviations. *GAD Antibody level ≥ 5.0 IU/mL or C-peptide levels < 0.50 ng/ml were indicative of Type 1 Diabetes.

Supplemental Table 9 - Mean Time to Insulin by Genetic Risk for AFR and non-AFR Ancestries.

	AFR	Non-AFR
GRS Low	4.10 (4.31)	4.59 (4.32)
GRS Med	3.94 (4.21)	4.38 (4.31)
GRS High	3.60 (4.16)	4.00 (4.31)
GRS Highest	3.37 (3.99)	3.35 (4.18)

Supplemental Table 9 - Mean Time to Insulin by Genetic Risk for AFR and non-AFR Ancestries. Means reported with standard deviations.

Supplemental Table 10 - Demographic and Clinical Characteristics across GRS score categories in Patients Without Use of Insulin for 3 Months After Diabetes Onset.

	All	GRS Low	GRS Med	GRS High	GRS Highest	P-Value*
Total	49,384	22,391	22,076	2,457	2,460	
Sex						0.1959
Male	47,090 (95.35%)	21,346 (95.33%)	21,077 (95.47%)	2,342 (95.32%)	2,325 (94.51%)	
Female	2,294 (4.65%)	1,045 (4.67%)	999 (4.53%)	115 (4.68%)	135 (5.49%)	
Age Category						
Age, Mean (SD)	64.29 (9.64)	64.48 (9.41)	64.29 (9.70)	63.60 (10.14)	63.31 (10.62)	<0.0001
20-29	76 (0.15%)	16 (0.07%)	28 (0.13%)	12 (0.49%)	20 (0.81%)	<0.0001
30-39	613 (1.24%)	215 (0.96%)	285 (1.29%)	49 (1.99%)	64 (2.60%)	
40-49	2,660 (5.39%)	1,177 (5.26%)	1,193 (5.40%)	141 (5.74%)	149 (6.06%)	
50-59	9,595 (19.43%)	4,315 (19.27%)	4,311 (19.53%)	499 (20.31%)	470 (19.11%)	
60-69	24,126 (48.85%)	11,037 (49.29%)	10,703 (48.48%)	1,208 (49.17%)	1,178 (47.89%)	
70-79	9,307 (18.85%)	4,267 (19.06%)	4,196 (19.01%)	396 (16.12%)	448 (18.21%)	
80+	2,984 (6.04%)	1,355 (6.05%)	1,349 (6.11%)	149 (6.06%)	131 (5.33%)	
Race/Ethnicity[†]						0.0025
EUR	32,582 (65.98%)	15,238 (68.05%)	14,244 (64.52%)	1,558 (63.41%)	1,542 (62.68%)	
AFR	11,987 (24.27%)	5,478 (24.47%)	5,304 (24.03%)	595 (24.22%)	610 (24.80%)	
HIS	4,474 (9.06%)	1,604 (7.16%)	2,282 (10.34%)	289 (11.76%)	299 (12.15%)	
ASN	341 (0.69%)	71 (0.32%)	246 (1.11%)	15 (0.61%)	9 (0.37%)	
Diabetes-related Variables						
Taking Insulin	50,384 (100%)	23,391 (100%)	22,076 (100%)	2,457 (100%)	2,460 (100%)	0.0002
Taking Sulfonylurea	40,150 (81.30%)	18,485 (82.56%)	17,905 (81.11%)	1,906 (77.57%)	1,854 (75.37%)	<0.0001
Diabetic Ketoacidosis	957 (1.94%)	353 (1.58%)	424 (1.92%)	79 (3.22%)	101 (4.11%)	<0.0001
Hypoglycemia Dx at ED	2,587 (5.24%)	1,139 (5.09%)	1,161 (5.26%)	151 (6.15%)	136 (5.53%)	0.1359
Outpatient Glucose <50 mg/dL	5,220 (10.57%)	2,269 (10.13%)	2,340 (10.60%)	283 (11.52%)	328 (13.33%)	<0.0001

Years to Insulin (Median)	4.57 (4.53, 4.63)	4.67 (4.59, 4.76)	4.60 (4.53, 4.68)	4.23 (4.03, 4.49)	3.74 (3.48, 4.04)	<0.0001
Years to Insulin (Mean)	5.24 (4.21)	5.33 (4.21)	5.24 (4.19)	5.00 (4.25)	4.68 (4.22)	
Years to Sulfonylurea (Median)	0.21 (0.19, 0.23)	0.22 (0.19, 0.24)	0.20 (0.17, 0.22)	0.27 (0.19, 0.34)	0.21 (0.14, 0.28)	0.6550
eGFR at Enrollment (Mean)	71.56 (27.23)	71.21 (27.03)	71.56 (27.47)	72.88 (26.79)	83.34 (27.26)	0.0003
A1c at Diabetes Onset (Mean)	8.19 (2.29)	8.14 (2.26)	8.20 (2.31)	8.24 (2.80)	8.39 (2.33)	<0.0001
BMI at Diabetes Onset (Mean)	33.11 (6.29)	33.34 (6.25)	33.05 (6.29)	32.72 (6.37)	31.87 (6.36)	<0.0001
Age at Diabetes Onset (Mean)	51.46 (9.28)	51.62 (9.11)	51.46 (9.31)	50.95 (9.64)	50.56 (10.09)	<0.0001
Years of follow-up (Mean)	13.14 (4.60)	13.17 (4.59)	13.14 (4.59)	12.94 (4.71)	13.07 (4.67)	0.1040
T1D Diagnostic						
T1D ICD Code Any Use	13,561 (27.46%)	5,955 (26.60%)	6,023 (27.28%)	747 (30.40%)	836 (33.98%)	<0.0001
T1D ICD Code at Least 50%	594 (1.20%)	122 (0.54%)	259 (1.17%)	72 (2.93%)	141 (5.73%)	<0.0001
GAD Tested	1,694 (3.43%)	620 (2.77%)	760 (3.44%)	125 (5.09%)	189 (7.68%)	<0.0001
%Positive of GAD Tested [‡]	306 (18.06%)	42 (6.77%)	135 (17.76%)	45 (36.00%)	84 (44.44%)	<0.0001
C-peptide Tested	4,084 (8.27%)	1,709 (7.63%)	1,808 (8.19%)	250 (10.18%)	317 (12.89%)	<0.0001
%Low C-peptide If Tested [‡]	218 (5.34%)	22 (1.29%)	93 (5.14%)	33 (13.20%)	70 (22.08%)	<0.0001

Supplemental Table 10 - Demographic and Clinical Characteristics across GRS score categories in Patients Without Use of Insulin for 3 Months After Diabetes Onset. **P Values* determined to assess trend using ANOVA for continuous variables and Multinomial Cochrane-Armitage tests for categorical variables. [†]Race/Ethnicity determined using HARE Algorithm. EUR = non-Hispanic European, AFR = non-Hispanic African, HIS = Hispanic/Latino, ASN = non-Hispanic Asian. [‡]GAD Antibody level ≥ 5.0 IU/mL or C-peptide levels <0.50 ng/ml were indicative of Type 1 Diabetes.