

Supplementary Table S1. Comparison of Baseline Characteristics between the Selected Individuals for this Study and the Full Type 2 Diabetes Population in GoDARTS.

	Current Study (n=5,152)	GoDARTS Type 2 Diabetes Cases (n=8,698)
Age (years)	65	67
Male (%)	56.1	56.3
Body Mass Index (kg/m ²)	32	31
Smoking history (%)	51	63
Systolic blood pressure (mmHg)	139	141
Diastolic blood pressure (mmHg)	77	77
Glycated Haemoglobin (mmol/mol)	59.6	60.7
Glycated Haemoglobin (%)	7.6	7.7
Total Cholesterol (mmol/l)	4.4	4.3
HDL-Cholesterol (mmol/l)	1.3	1.3

GoDARTS Type 2 diabetes baseline data taken from Hebert et al., 2018 (reference 20 in the manuscript)

Supplementary Table S2. Association between Retinal Risk Score and Major Adverse Cardiovascular Events Across Genetic and Clinical Risk Tertiles

	Adjusted Hazard Ratio (95% CI)	p value	Interaction p value
Polygenic Risk Score Tertile			0.13
1	1.17 (1.03-1.32)	0.014	
2	1.08 (0.97-1.22)	0.17	
3	1.08 (0.97-1.19)	0.15	
Pooled Cohort Equations Risk Score Tertile			0.09
1	1.17 (1.01-1.35)	0.031	
2	1.18 (1.06-1.31)	0.002	
3	1.03 (0.93-1.14)	0.62	

Multivariable model included: age, sex, glycated haemoglobin, duration of diabetes, retinal risk score

PCE and CHD PRS. All hazard ratios per standard deviation increase.

Supplementary Table S3. Area Under the Curve, Integrated Discrimination Improvement and Continuous Net Reclassification for Retinal Risk Score and CHD PRS versus the Pooled Cohort Equations ASCVD Risk Score for Prediction of Major Adverse Cardiovascular Events at 10 Years.

	Model 1	Model 2		Model 3		Model 4		Model 5	
	PCE only (baseline)	Retinal Risk Score + Age + Sex	p value	CHD PRS + Age + Sex	p value	CHD PRS + Retinal Risk Score + Age + Sex	p value	CHD PRS + Retinal Risk Score + ASCVD Risk Score + Age + Sex	p value
AUC	0.658 (0.640-0.677)	0.663 (0.645-0.681)	0.33	0.683 (0.665-0.701)	<0.001	0.686 (0.667-0.704)	<0.001	0.690 (0.672-0.708)	<0.001
IDI (vs. PCE only)	-	0.001 (-0.003-0.004)	0.79	0.018 (0.012-0.023)	<0.001	0.019 (0.013-0.025)	<0.001	0.023 (0.018-0.028)	<0.001
Continuous NRI (vs. PCE only)	-	0.080 (0.010-0.150)	0.024	0.216 (0.147-0.285)	<0.001	0.240 (0.171-0.309)	<0.001	0.319 (0.251- 0.388)	<0.001

AUC – Area Under the Curve; PCE – Pooled Cohort Equations Atherosclerotic Cardiovascular Disease Risk Score; PRS – Coronary Heart Disease Genetic Risk Score; IDI – Integrated Discrimination Improvement; NRI – Net Reclassification Index.

Bold indicates p<0.05. All p values vs. Model 1.

Supplementary Table S4. List of Abbreviations.

AI – artificial intelligence

ASCVD – atherosclerotic cardiovascular disease

AUC – area under the curve

CHD – coronary heart disease

CRAE – central retinal arteriolar equivalent

CRVE – central retinal venular equivalent

CVD – cardiovascular disease

DRS – diabetes retinal screening

EHR – electronic health record

FD(a/v) – fractal dimension (arterial/venous)

GoDARTS – Genetics of Diabetes Audit and Research Tayside Study

HbA1c – glycated haemoglobin

HR – hazard ratio

ICD – International Classification of Diseases

IDI – integrated discrimination index

MACE – major adverse cardiovascular events

MI – myocardial infarction

NRI – net reclassification index

PCE – pooled cohort equations

PRS – polygenic risk score

ROC – receiver operator characteristic

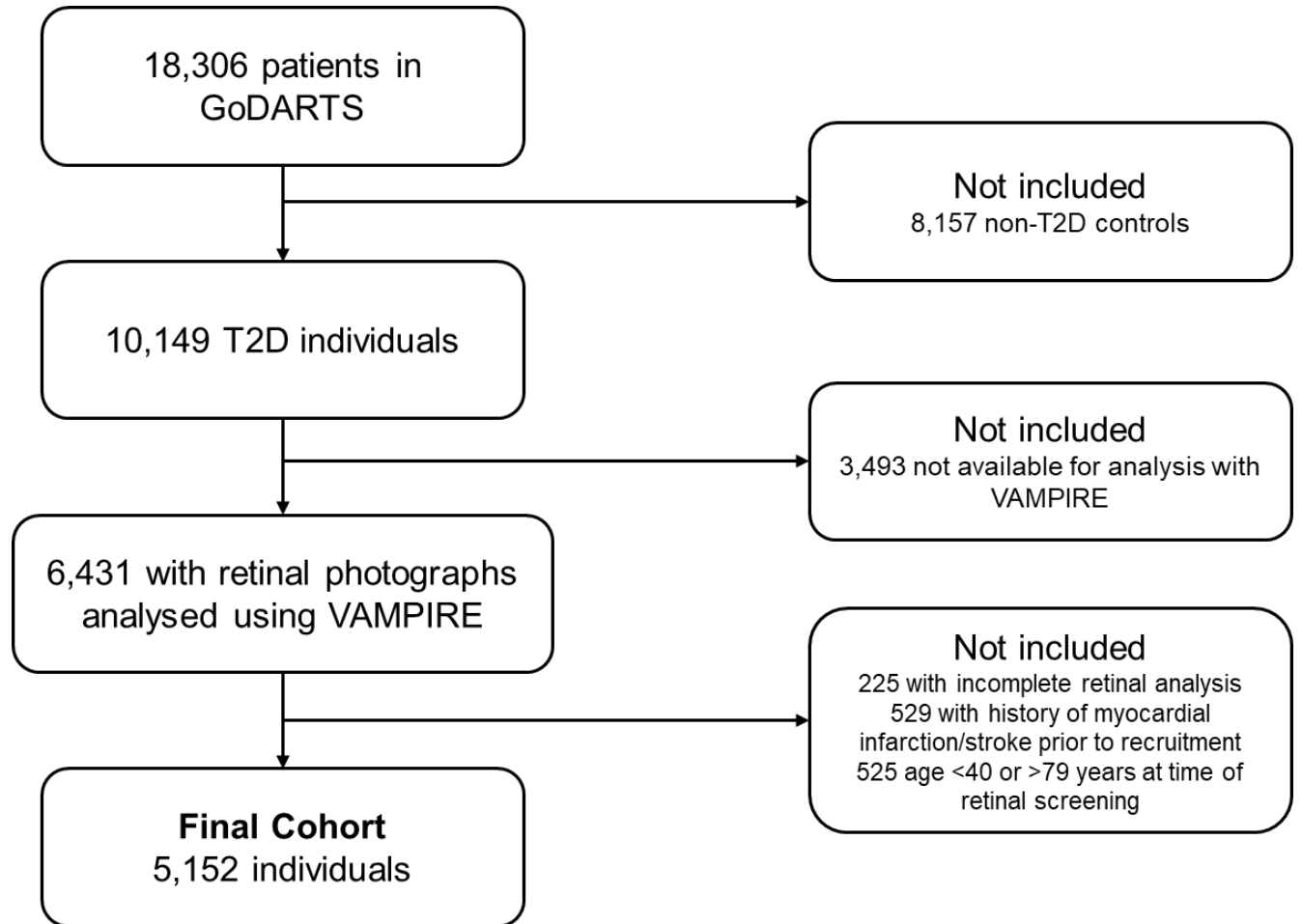
SNP – single nucleotide polymorphism

Tort (a/v) – tortuosity (arterial/venous)

VAMPIRE – Vascular Assessment and Measurement Platform for Images of the Retina

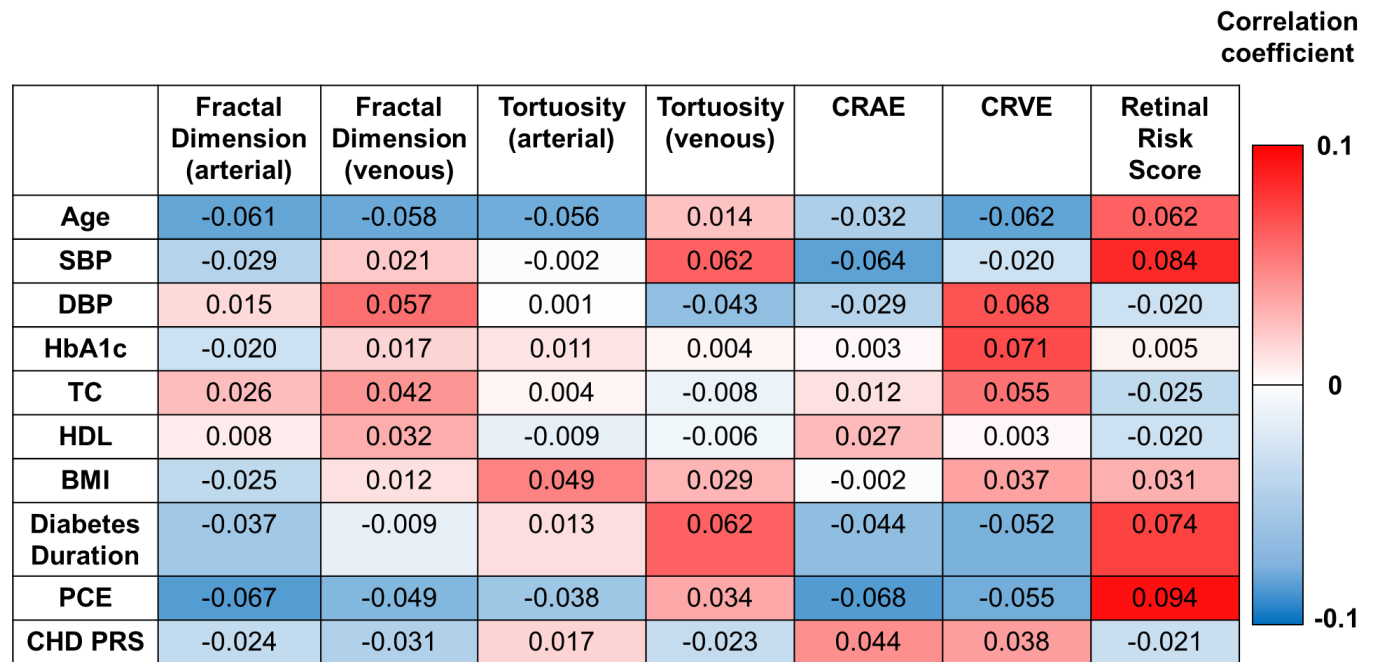
Supplementary Figure 1. Study Flowchart.

Cohort derivation.



Supplementary Figure 2. Correlations between Retinal Vascular Parameters and Continuous Clinical and Genomic Risk Factors.

Correlation matrix showing correlation coefficient (Pearson r) between Retinal Vascular Parameters and Continuous Clinical and Genomic Risk Factors.



SBP – systolic blood pressure; DBP – diastolic blood pressure; HbA1c – glycated haemoglobin; TC – total cholesterol; HDL – high-density lipoprotein cholesterol; BMI – body mass index; PCE – pooled cohort equations atherosclerotic cardiovascular risk score; CHD PRS – coronary heart disease polygenic risk score; CRAE – central retinal arterial equivalent; CRVE – central retinal venous equivalent

Supplementary Figure 3. Association between Retinal Risk Score and Major Adverse Cardiovascular Events.

Kaplan-Meier curve showing the association between tertiles of retinal risk score and time to first MACE incidence.

