Supplement

Risk Factor Data Collection

Most of the data necessary to compute each risk score were regularly collected at clinic appointments. Data on HDL cholesterol was not regularly collected until 1991 and 21% of the patients' index dates are before HDL collection. The missing values were not depended on patients' characteristics and had equal possibilities occurring in both CVD and no CVD patients, hence we assumed the HDL missing were at random. Missing information were imputed using non-missing values in patients with CVD or without CVD. We imputed missing HDL using mean values by whether they had CVD or not separately.

Similar imputations were performed for weight and height for the basis of BMI calculations, which were not regularly collected until 1977 and 1994, respectively.

Information on several risk factors related to QRISK including atrial fibrillation, migraine, RA, atypical antipsychotic use, diagnosis or treatment of erectile dysfunction, and severe mental illness (schizophrenia, bipolar disorder, moderate/severe depression) were not captured in the protocol. Data on the first five aforementioned factors were extracted by chart review using analysis of a subgroup of 224 patients, comprised of both CVD patients and no CVD patients. The proportion of CVD patients and no CVD patients identified with having each risk factor was used to impute the presence of this risk factor for the patients remaining in that subgroup. For severe

mental illness (schizophrenia, bipolar disorder, moderate/severe depression), we used the 36-Item Short Form Survey (SF-36) within one year of the index date, collected since January 4, 1994. In order to capture severe depression, we used modified criteria of both a mental health sub-domain score ≤ 56 and mental component score ≤ 40, rather than just one or the other. Severe mental illness for patients missing the SF-36 (n=360) was imputed from the data on CVD patients and no CVD patients by the same proportion (n=480). Data on family history of CVD and Townsend Score was not gathered and calculated in the QRISK3 score; however, these risk factors have little impact on the final risk score.

Missing data included HDL prior to June 1991 and 21% of the patients' index dates are before HDL collection. The missing values were not depended on patients' characteristics and had equal possibilities occurring in both CVD and no CVD patient, hence we assumed the HDL missing were at random. Missing information were imputed using non-missing values in patients with CVD or without CVD. We imputed missing HDL using mean values by whether they had CVD or not separately.

Anti-hypertensive information was available since 1990's, statins and aspirin since 2000's - the following are the percentages of patients being treated at index date and at CVD events or current visit in the study by decades (N = 1887 patients).

Supplementary Table S1. Treatment with anti-hypertensive, statins and aspirin by decades

	Anti-hypertensive		***Statins***		***Aspirin***	
	At index date	***At CVD event or current visit***	***At index date***	***At CVD event or current visit***	***At index date***	***At CVD event or current visit***
1970's	*/*	*/*	*/*	*/*	*/*	*/*
1980's	*/*	*/*	*/*	*/*	*/*	*/*
1990's	*19.7%*	*36.4%*	*/*		*/*	
2000's	*31.3%*	*45.8%*	*9.6%*	*22.3%*	*8.1%*	*17.5%*
2010's	*25.0%*	*49.6%*	*5.3%*	*25.2%*	*6.0%*	*21.4%*

Supplementary Table S2. Comparison of Cardiovascular Risk Prediction Tools

	Framingham Risk Score	**Modified Framingham Risk Score**	**QRISK 2**	**QRISK3**	**SLE CRE**
Risk factors	Age, sex, treatment for hypertension, diabetes status, smoking status, HDL cholesterol, total cholesterol and systolic blood pressure	Age, sex, treatment for hypertension, diabetes status, smoking status, HDL cholesterol, total cholesterol and systolic blood pressure	Age, sex, ethnicity, Townsend score, smoking status, diabetes status, family history of CVD (angina or heart attack in a first degree relative younger than 60), chronic kidney disease, atrial fibrillation, blood pressure treatment, rheumatoid arthritis, HDL cholesterol, total cholesterol, systolic blood pressure, height and weight	Age, sex, ethnicity, Townsend score (measure of material deprivation within a population), smoking status, diabetes status, family history of CVD (angina or heart attack in a first degree relative younger than 60), chronic kidney disease, atrial fibrillation, blood pressure treatment, rheumatoid arthritis (RA), HDL cholesterol, total cholesterol, systolic blood pressure, height, weight, migraine, SLE, severe mental illness, atypical antipsychotic use, corticosteroid use, diagnosis or treatment of erectile dysfunction, and standard deviation of repeated blood pressure	Age, sex, systolic blood pressure, cholesterol, smoking status, diabetes, mean SLE Disease Activity Index (SLEDAI) of 2 or more, history of lupus anti-coagulant and low mean C3
CVD as defined in each prediction tool	Coronary heart disease (Angina and/or MI), ischemic stroke, hemorrhagic stroke, transient ischemic attack, Peripheral artery disease secondary to atherosclerosis and heart failure secondary to atherosclerosis	Angina, MI, CVD death	Coronary heart disease (Angina and/or MI), ischemic stroke, and transient ischemic attack	Coronary heart disease (Angina and/or MI), ischemic stroke, transient ischemic attack	Stroke or myocardial infarction, angina or coronary procedures, claudication or congestive heart failure
Index date as defined in each prediction tool	Date of study entry	Date closest to 10 years prior to the first CAD event reported for each patient (or last visit for patients without events)	Date of study entry	Date of study entry	Date of enrolment in Hopkins clinic

Sensitivity analysis results for SLECRE protocol

The following analysis was performed by calculating each risk score at the date of enrolment in the Toronto Lupus Clinic, as designed by the SLE Cardiovascular Risk Equation [data censored at 10 years].

Supplementary Table S3. Descriptive statistics of patients (n=1887) [results for SLECRE protocol]

Variable at index date	Overall (n=1887)	CVD (n = 133)	No CVD (n = 1754)
Age (years)	35 ± 14	47 ± 14	34 ± 14
Female Sex – no. (%)	1653 (88)	108 (81)	1545 (88)
Mean time from SLE clinic enrolment to CVD event (years)	N/A	3.8 ± 3.0	N/A
Number of patients with at least 10 years of follow up from SLE clinic enrolment (%)	768 (41)	64 (48)	704 (40)
Mean time of follow up from SLE clinic enrolment (years) Median (Q1, Q3)	9.5 ± 7.2 7.0 (3.0 – 15.0)	3.8 ± 3.0 3.0 (1.0 – 6.0)	10.0 ± 7.2* 8.0 (3.0 – 15.0)
Ethnicity – no. (%): Caucasian†	1253 (66)	104 (78)	1149 (66)
Asian	252 (13)	9 (7)	243 (14)
Black	250 (13)	15 (11)	235 (13)
Other	120 (6)	5 (4)	115 (7)
Total cholesterol (mmol/L)	4.8 ± 1.1	5.3 ± 1.0	4.8 ± 1.1
HDL (mmol/L)	1.5 ± 0.4	1.6 ± 0.4	1.5 ± 0.4
Systolic blood pressure (mmHg)	121 ± 19	131 ± 23	120 ± 18.1
Hypertension treatment – no. (%)	313 (17)	34 (26)	279 (16)
Smoking – no. (%)	89 (5)	6 (5)	83 (5)
Diabetes – no. (%)	16 (0.8)	2 (2)	14 (0.8)
BMI (kg/m^2)	24.7 ± 4.4	27.0 ± 4.7	24.6 ± 4.3
Lupus anticoagulant – no. (%)	443 ?(23)	42 (32)	401 (23)
Low C3 two years prior to index date – no. (%)	687 (36)	45 (34)	642 (37)
Glucocorticoid treatment – no. (%)	1177 (62)	87 (65)	1090 (62)
Severe mental illness – no. (%)	341 (18)	28 (21)	313 (18)
Migraine – no. (%)	160 (8)	11 (8)	149 (8)

*Patients were censored at 10 years of follow up, therefore data does not reflect follow-up time of patients with greater than 10 years of follow up.

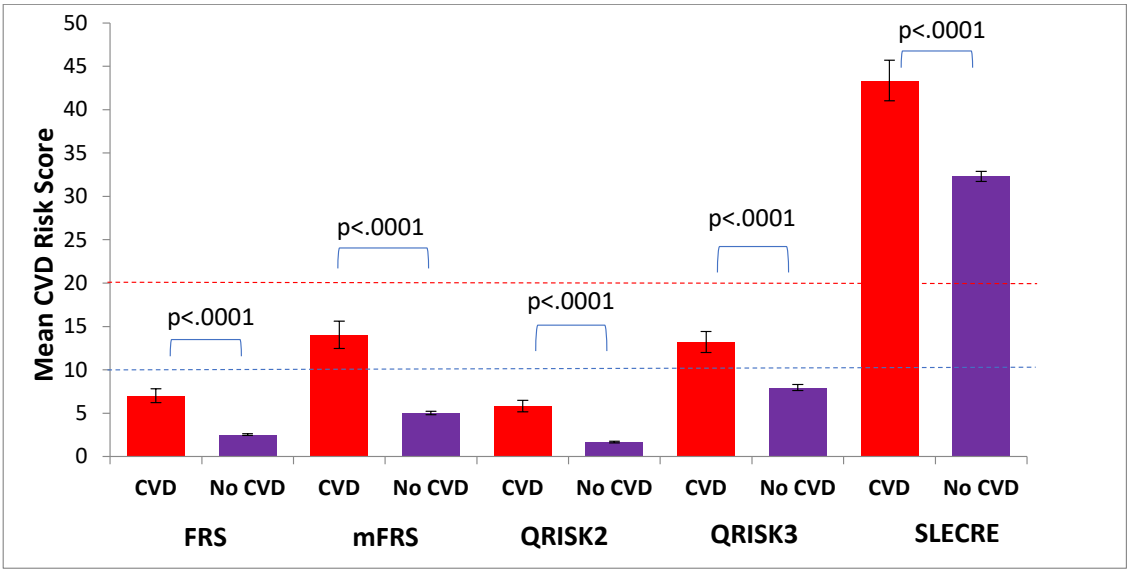
† 12 patients in the No CVD group had missing ethnicity data.

Note: No patients found to have atrial fibrillation, atypical antipsychotic medication, rheumatoid arthritis or diagnosis/treatment of erectile dysfunction.

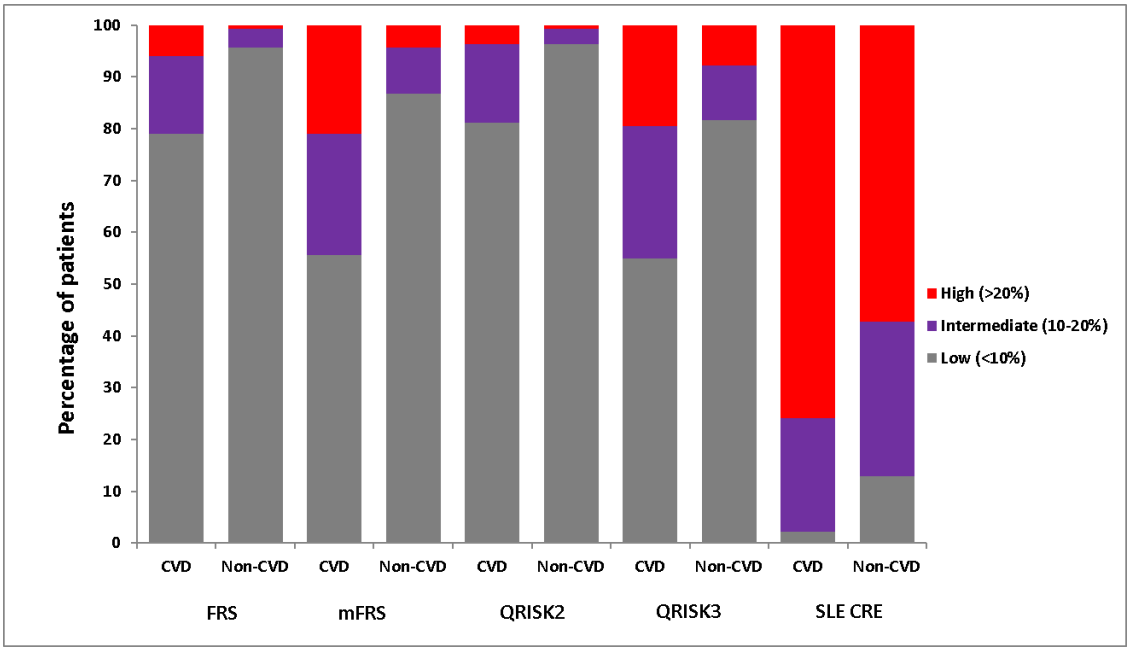
Supplementary Table S4. Breakdown of cardiovascular events seen in the cases [results for SLECRE protocol]

Cardiovascular event	**Number of Patients (%)**
Angina	43 (32)
Myocardial infarction	31 (23)
Congestive heart failure	30 (23)
CVD death	8 (6)
Transient ischemic attack	12 (9)
Pacemaker insertion	5 (4)
Cerebrovascular accident	4 (3)
Total	133

Supplementary Figure S1. Sensitivity Analyses: Mean CVD Risk Score (% ± SD) for the FRS, mFRS, QRISK2, QRISK3 and SLECRE, stratified according to cases (n=133) and controls (n=1754) [results for SLECRE protocol]



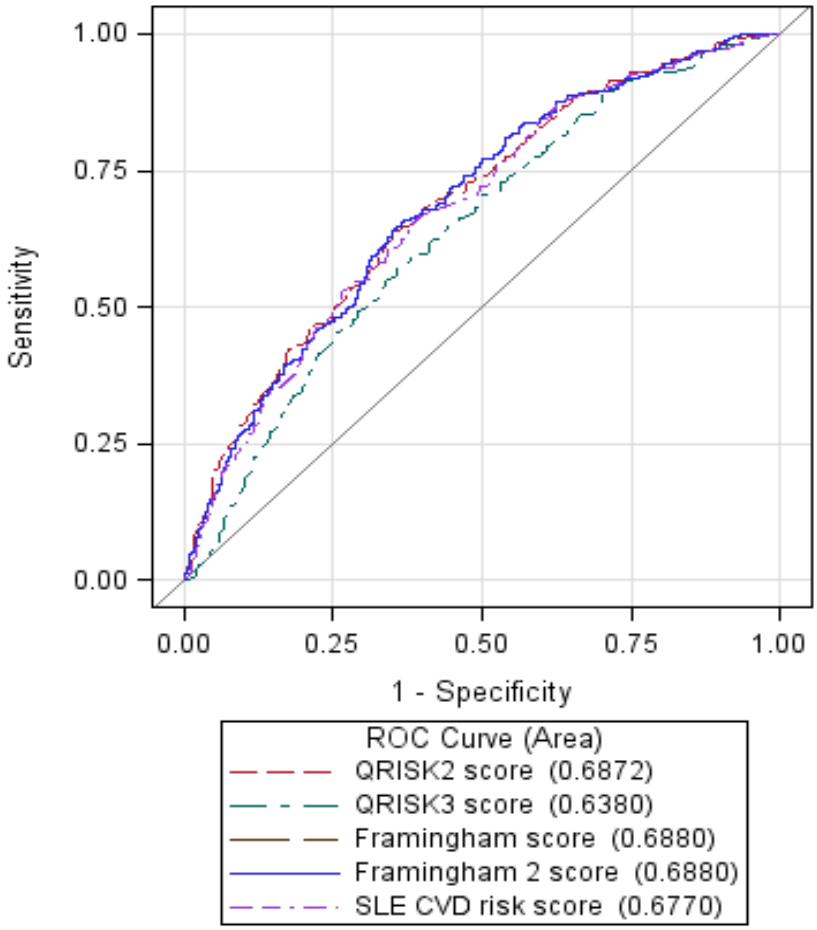
Supplementary Figure S2. Sensitivity Analyses: Percentage of patients considered low (<10%), intermediate (10-20%) and high risk (>20%) between cases (CVD, n=133) and controls (no-CVD, n=1754) according to the FRS, mFRS, QRISK2, QRISK3 and SLECRE [results for SLECRE protocol]



Supplementary Table S5. Sensitivity Analyses*:* Sensitivity, specificity, PPV, NPV and c-statistic of the FRS, mFRS, QRISK 2, QRISK 3 and SLECRE. Dichotimized risk scores using a cutoff of 10% 10-year CVD risk [results for SLECRE protocol].

	Sensitivity (%)	**Specificity (%)**	**Positive Predictive Value (%)**	**Negative Predictive Value (%)**	**c-statistic**
FRS	21.1	95.7	26.9	94.1	0.76
mFRS	44.4	86.8	20.3	95.4	0.76
QRISK2	18.8	96.4	28.1	94.0	0.78
QRISK3	45.1	81.6	15.7	95.1	0.70
SLECRE	97.7	12.8	7.8	98.7	0.63

Supplementary Figure S3. Sensitivity Analyses: Receiver operating curve (ROC) for the FRS, mFRS, QRISK2, QRISK3 and SLECRE. FRS and mFRS have the same ROC curve [results for SLECRE protocol]



Supplementary Table S6. Sensitivity Analyses: Kappa coefficient (lower and upper 95% confidence interval) demonstrating agreement between the QRISK3, QRISK2, FRS, mFRS and SLECRE.

	QRISK3	QRISK2	FRS	mFRS	SLECRE
QRISK3	1	0.24 (0.19, 0.29)	0.37 (0.51, 0.41)	0.53 (0.48, 0.58)	0.04 (0.03, 0.05)
QRISK2		1	0.51 (0.41, 0.60)	0.31 (0.25, 0.37)	0.009 (0.007, 0.012)
FRS			1	0.48 (0.42, 0.54)	0.015 (0.012, 0.019)
mFRS				1	0.039 (0.30, 0.049)
SLECRE					1