Prognostic Value of Clinical and Genomic Data on Predicting Major Adverse Cardiovascular Events (MACE)

Ivy Kar Yin Ho[1], Ify Mordi[2]

[1]School of Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY

[2]Division of Cardiovascular and Diabetes Medicine, Ninewells Hospital and Medical School, Dundee DD1 9SY

Background

- An individual's risk of cardiovascular disease (CVD) is largely influenced by a number of lifestyle and genetic factors.
- CVD risk prediction models are regularly used in clinical practice to assess patients' risk of developing CVD and support primary prevention.
- The Pooled Cohort Equation (PCE) was designed by the American College of Cardiology/American Heart Association (ACA/AHA) to estimate a patient's 10-year risk of ASCVD.
- ASCVD risk score is determined by patient age, sex, ethnicity, total cholesterol, high-density lipoprotein (HDL) cholesterol, blood pressure, use of anti-hypertensive medications, smoking status, and diabetes status (1).
- Although use of these algorithms have been effective in stratifying patients at risk of CVD, it neglects to take into account the patient's genetic susceptibility to atherosclerotic disease.
- Atherosclerotic cardiovascular disease (ASCVD) has an estimated heritability of 40-60% (2,3).
- Application of genomic risk scores (GRS) may provide additional benefit in the identification of patients at high risk of CVD and allow for early intervention (4,5).

Objective

This study aims to determine whether genomic risk prediction of CVD confers prognostic value when compared with conventional clinical risk prediction models.

Methods

1. Patients in the Genetics of Diabetes Audit and Research Tayside Scotland (GoDARTS) database had their clinical risk score for ASCVD calculated using the PCE.
2. The genetic risk of ASCVD for each patient was determined by genome-wide analysis and data provided by Khera et al. (6)
3. Cox Regression and Kaplan-Meier analysis were applied to evaluate the independent association of GRS and PCE risk scores with major adverse cardiovascular events (MACE), comprising non-fatal myocardial infarction (MI), non-fatal stroke, and CV death.
4. Interactions between genetic and clinical risk scores were then evaluated using Cox Regression to determine if there is significant association between the two groups.
5. PCE and GRS models were evaluated using the area under the receiver-operator curve (ROC) to determine it's prognostic value

Results 1: Patient Characteristics

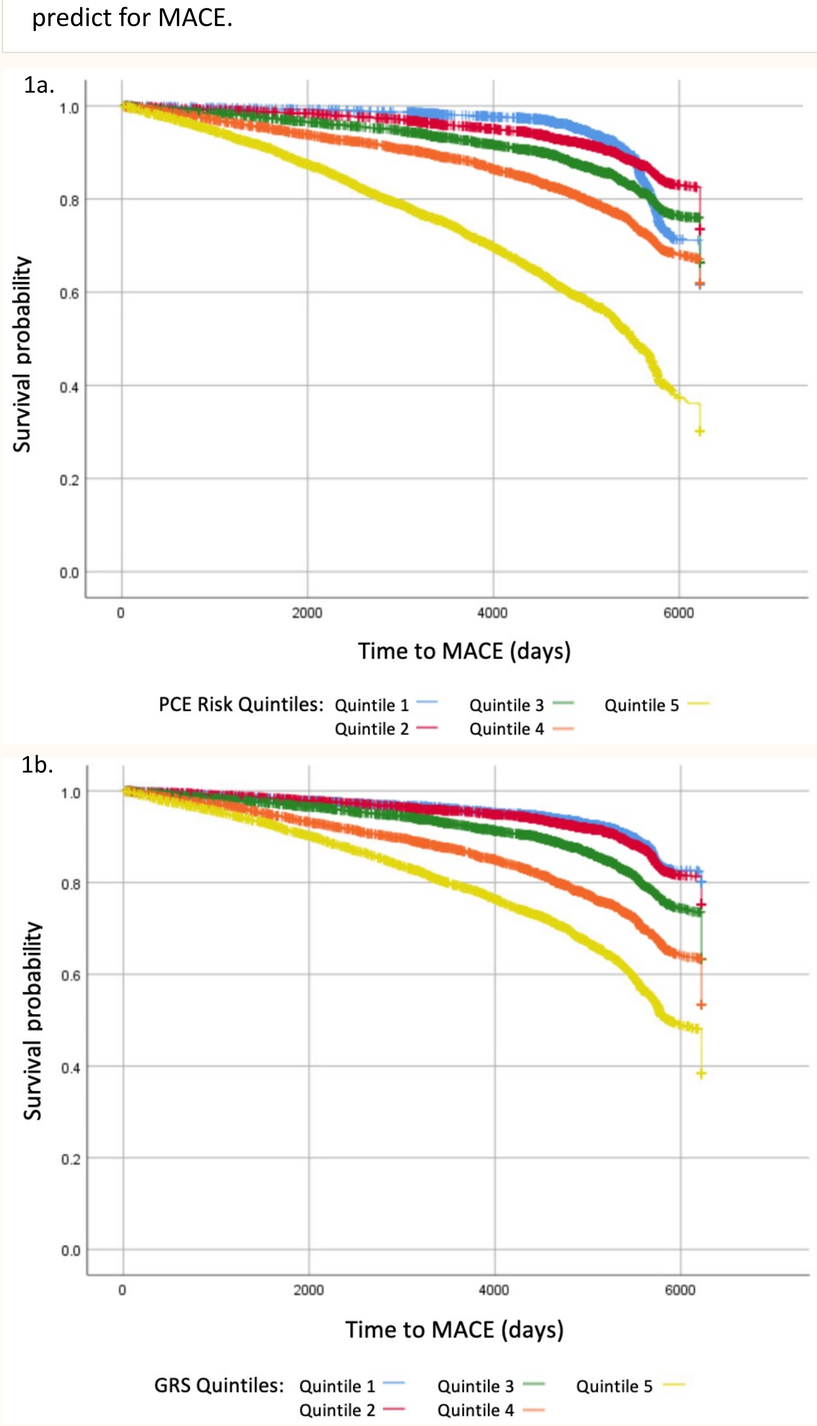
Baseline characteristics	Total number of patients = 19 709
Age (years)	62.8 ± 8.8
Female number (percent)	9257 (47.0)
Total cholesterol (mg/dL)	185.8 ± 31.4
HDL cholesterol (mg/dL)	55.6 ± 14.2
Systolic blood pressure (mm/Hg)	137.2 ± 14.7
Smoking status (percent)	3750 (19.0)
Diabetes (percent)	12761 (64.7)
PCE 10-year ASCVD risk (percent)	22.6 (7.7-30.0)
Genetic risk score (GRS) (percent)	6.6 (6.0-7.1)
MACE (percent)	4502 (22.8)

Table 1: Baseline cohort characteristics. 19709 patients from the goDARTS database were included in the study. Continuous variables are presented as mean ± standard deviation. Non-continuous variables are expressed as medians with interquartile ranges (IQR). Parameters were based on the PCE.

Results 2: Incidence of MACE

	Adjusted Hazard Ratio (95% CI)	p-value
PCE risk score	1.02 (1.02-1.02)	<0.001
GRS	1.67 (1.46-1.90)	<0.001

Table 2: Association of PCE and genomic risk scores with incidence of MACE. Both clinical and genomic risk models independently predict for MACE.



Figures 1a and 1b: Patients with higher clinical and genomic risk scores are more likely to have a MACE. Patients in the highest quintiles of risk are at significantly increased likelihood of MACE compared with those in the lowest quintiles:

PCE: HR 0.93 [95% CI 0.83-1.04] vs HR 4.05 [95% CI 3.66-4.48]

GRS: HR 1.26 [95% CI 1.11-1.43] vs HR 3.91 [95% CI 3.53-4.35]

Results 3: PCE and GRS Risk Scores

Interaction	Adjusted Hazard Ratio (95% CI)	p-value
PCEquin (1)*GRSquin (1)	0.71 (0.58-0.87)	<0.001
PCEquin (1)*GRSquin (4)	2.13 (1.81-2.50)	<0.001
PCEquin (4)*GRSquin (1)	2.09 (1.71-2.56)	<0.001
PCEquin (4)*GRSquin (4)	3.81 (3.27-4.45)	<0.001

Table 3: Interaction between PCE and genomic risk scores. Patients who have low clinical risk but high genomic risk are more likely to have a MACE than those with high clinical risk and low genomic risk (p<0.001).

Results 4: PCE vs GRS Risk Scores

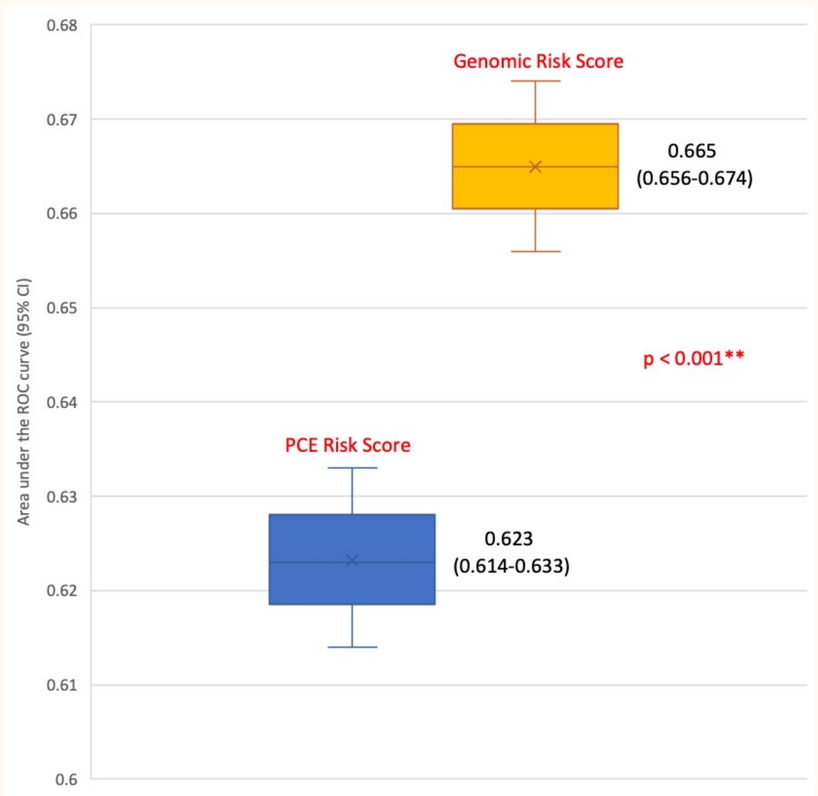


Figure 2: Predictive value of clinical and genetic risk scores assessed and compared using area under the ROC curve. GRS is a better predictor of MACE compared with the PCE risk score (p<0.001).

Conclusion

- Both PCE and genomic risk scores independently predict for MACE
- Patients at high clinical and genomic risk have a greater likelihood of experiencing a MACE
- Genomic factors contribute more to the incidence of MACE than patients' clinical characteristics
- Genomic risk scores are better predictors of MACE compared with assessing clinical risk using the PCE
- Risk stratification based on patients' GRS may allow for earlier detection and management of CVD.

References

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