Polygenic scores, risk and cardiovascular disease

Chantal Babb de Villiers, Sowmiya Moorthie, Tanya Brigden, Louise Gaynor, Alison Hall, Emma Johnson, Saskia Sanderson and Mark Kroese

PHG Foundation, Cambridge, UK

Contact: Dr Sowmiya Moorthie: sowmiya.moorthie@phgfoundation.org or
Dr Chantal Babb de Villiers: chantal.babbdevilliers@phgfoundation.org

Introduction

It is widely recognised that common diseases have a genetic component, but for most of the population this information is not being used in preventive approaches.

Recent advances in research on polygenic scores and their application to risk stratification have renewed interest in the use of genetic information for the prevention of cardiovascular disease.

Debate on the utility of such information has strong proponents and critics of the utility of such information. We have been exploring the potential of polygenic scores to contribute to prevention of cardiovascular disease.

Aim

To examine polygenic scores for cardiovascular disease and ascertain their readiness for use in primary and secondary disease prevention.

Methodology

We used mixed methods, including reviewing peer-reviewed and grey literature, interviews with experts and relevant stakeholders. Information was synthesised and analysed to identify gaps in the evidence and assess the considerations around the use of polygenic scores as part of cardiovascular disease prevention programmes.

Overview of polygenic scores for CVD from the literature

Cardiovascular disease polygenic scores

Outcomes investigated

- Incident coronary heart disease
- Prediction of coronary artery disease
- Incidental non-fatal myocardial infarction
- Time to an event
- Acute coronary syndrome
- Composite of coronary heart disease
- Recurrent coronary artery disease

Purpose

- Lifetime risk for coronary heart disease
- Screening tool for primary prevention
- Statin treatment impact
- Risk prediction
- Improvements of risk prediction with
  - Lifestyle
  - Family history
  - Conventional risk factors

Number of SNPs (variants) included in the model

- 13
- 50
- 50,000
- 1.7 million
- 6.6 million

Populations used in model development and testing: primarily European and of a specific age range

Types of models

- Polygenic scores (PGS) only
- PGS adjusted for age +/ sex
- PGS + age +/ sex
- PGS + age +/ sex + family history
- PGS + age +/ sex + other conventional risk factors
- PGS + age +/ sex + other novel risk factors
- PGS + existing risk assessment tools

Key gaps

- Current research is still exploring the different mechanisms to generate a polygenic score and how they improve risk prediction
- There are numerous models for calculating polygenic scores (see left) which, research suggests, could be used to stratify populations
- The implications of stratification using polygenic scores for clinical practice are yet to be fully investigated
- A defined test with an explicit use in a specific population and for a specific purpose is needed
- A defined test would enable fuller assessment of the value of polygenic scores within prevention pathways along with implications for implementation – such as logistical (e.g. collection of genetic data, risk communication) and financial impact

Conclusions

- The application of polygenic scores for cardiovascular disease risk is a promising area of development; a polygenic score for cardiovascular disease can improve stratification, potentially supporting more effective prevention
- Nevertheless, there are still considerable gaps in knowledge, and polygenic scores are unlikely to be ready for clinical use in the next three years

Polygenic scores, risk and cardiovascular disease report is available at www.phgfoundation.org/report/polygenic-scores-cardiovascular