**Title** Genetic risks in early-onset cardiovascular diseases

**Aim:**

Genetic information may improve the accuracy of cardiovascular risk assessment, particularly for individuals with strong family histories. We aimed to investigate genetic risk factors for early-onset cardiovascular disease (CVD) in NZ.

**Method:**

The Family Heart Study (FHS) recruited 28 participants meeting strict criteria for documented personal and family history of early-onset CVD (≤50 years for men, ≤60 years for women) from 2011-2014. Cardiovascular events were recorded over a median of 9 years. Genotyping was performed using CardioMetabochips (Illumina). Polygenic risk scores (PRS) for coronary heart disease were compared with heart-healthy volunteers (n=101) and CVD patients without a premature onset (‘No pCVD’, n=1391), and tested for association with cardiovascular outcomes.

**Results:**

FHS participants were predominantly NZ European (89%, 11% Māori), with a mean CVD onset age of 46.6 years (75% myocardial infarction) and an average of 2.4 affected first-degree relatives. Eleven participants experienced a cardiovascular event over follow-up. Compared with the FHS, the PRS was 1.07-fold lower in the No pCVD group (p=0.030), and 1.11-fold lower in healthy volunteers (p<0.001). The PRS was not associated with subsequent cardiovascular events in the FHS (p=0.775).

**Conclusion:**

Individuals with a personal and family history of premature CVD have a higher burden of common CVD genetic risk variants than patients without a personal and/or family history of premature CVD and heart-healthy controls. The FHS may provide a valuable resource for the discovery of genetic risk factors in NZ families with strong inherited susceptibility to CVD.