

# Metabolic Mediators of the Effects of Family History and Genetic Risk Score on Coronary Heart Disease—Findings from the Malmö Diet and Cancer Study

## Background

- Family history and genetic predisposition can inform risk assessment for coronary heart disease (CHD). These risk predictors are both independent of established cardiometabolic risk factors.<sup>1</sup>
- Though independent, risk assessment through family history or genetic risk score (GRS) may be partially (directly or indirectly) mediated through cardiometabolic risk factors.
- **Objectives:** The investigators assessed the contribution of established cardiometabolic risk factors to CHD risk assessment by family history or GRS.

## Methods

- The study population included 23,595 men and women between 45 and 73 years old; they were recruited for the Malmö Diet and Cancer study between 1991 and 1996.
  - Of these participants, 2,213 experienced a first CHD event during follow-up (median 14.4 years).
- The GRS was calculated using 50 genetic variants (GRS50).<sup>1</sup>
- Total effects of self-reported family history and of the GRS50 were calculated, as were the effects mediated by:
  - apolipoprotein B (apoB)
  - apolipoprotein A-I (apoA-I)
  - blood pressure
  - diabetes mellitus (DM)

## Results

- Family history and elevated GRS50 were both associated with incident CHD. Hazard ratios (95% confidence intervals) are listed below:
  - Family history (yes vs no): 1.52 (1.39-1.65)
  - GRS50 (highest vs lowest quintile): 2.01 (1.76-2.30)
- Approximately 20% of CHD risk assessed by family history was mediated through the evaluated cardiometabolic risk factors.
- Approximately 13% of CHD risk assessed by GRS50 was mediated through the evaluated cardiometabolic risk factors.
- CHD risk, whether assessed through family history or GRS50, was mediated through ApoB (6.0% to 8.3%) and blood pressure (3.5% to 8.5%); it was not mediated through DM.

## Conclusions

- Only a fraction (13% to 20%) of incident CHD risk as assessed by family history or GRS50 is mediated through established cardiometabolic risk factors. Most of the risk is independent of these factors.
- This study supports assessment of family history and genetic predisposition in addition to established cardiometabolic risk factors.

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### References

1. Tada H, Melander O, Louie JZ, et al. *Eur Heart J*. 2016;37:561–567.