

## Background

- Cardiovascular disease (CVD) is the worldwide leading cause of disability and death, and approximately 85% of CVD deaths are attributable to coronary heart disease (CHD) and stroke.
- Elevated blood pressure (BP) and low muscle strength are major modifiable risk factors for CVD.
- It is currently unclear whether the association between genetic risk of high BP and risk of CVD could be modified by high muscle strength.

## Objectives

To explore the interplay between the associations of genetic susceptibility to high BP and muscle strength in relation to CVD mortality and incident CVD outcomes (CHD and stroke).

## Results

Table 1. Associations between genetic risk of high BP, muscle strength and each CVD outcome

Outcome	Category	CVD mortality	Incident CHD	Incident stroke
Genetic risk of high BP	Low (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
	Medium	1.07 (1.01, 1.13)	1.15 (1.10, 1.20)	1.13 (1.06, 1.20)
	High	1.21(1.13, 1.29)	1.31 (1.25, 1.38)	1.27 (1.19, 1.37)
	P for trend	<0.001	<0.001	<0.001
Muscle strength	High (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
	Low	1.51 (1.43, 1.59)	1.31 (1.25, 1.38)	1.27 (1.19, 1.37)

Models using genetic risk of high BP as the exposure were adjusted for age (as time scale), sex, genetic array type and the first ten principal components of ancestry. Models using muscle strength as the exposure were adjusted for age (as time scale), sex, Townsend deprivation index, highest education qualification, smoking status, alcohol consumption status, resting pulse rate, weekly red meat intake, weekly fish intake, self-rated health, weekly physical activity, **polygenic risk score for high BP**, genetic array type and the first ten principal components of ancestry.

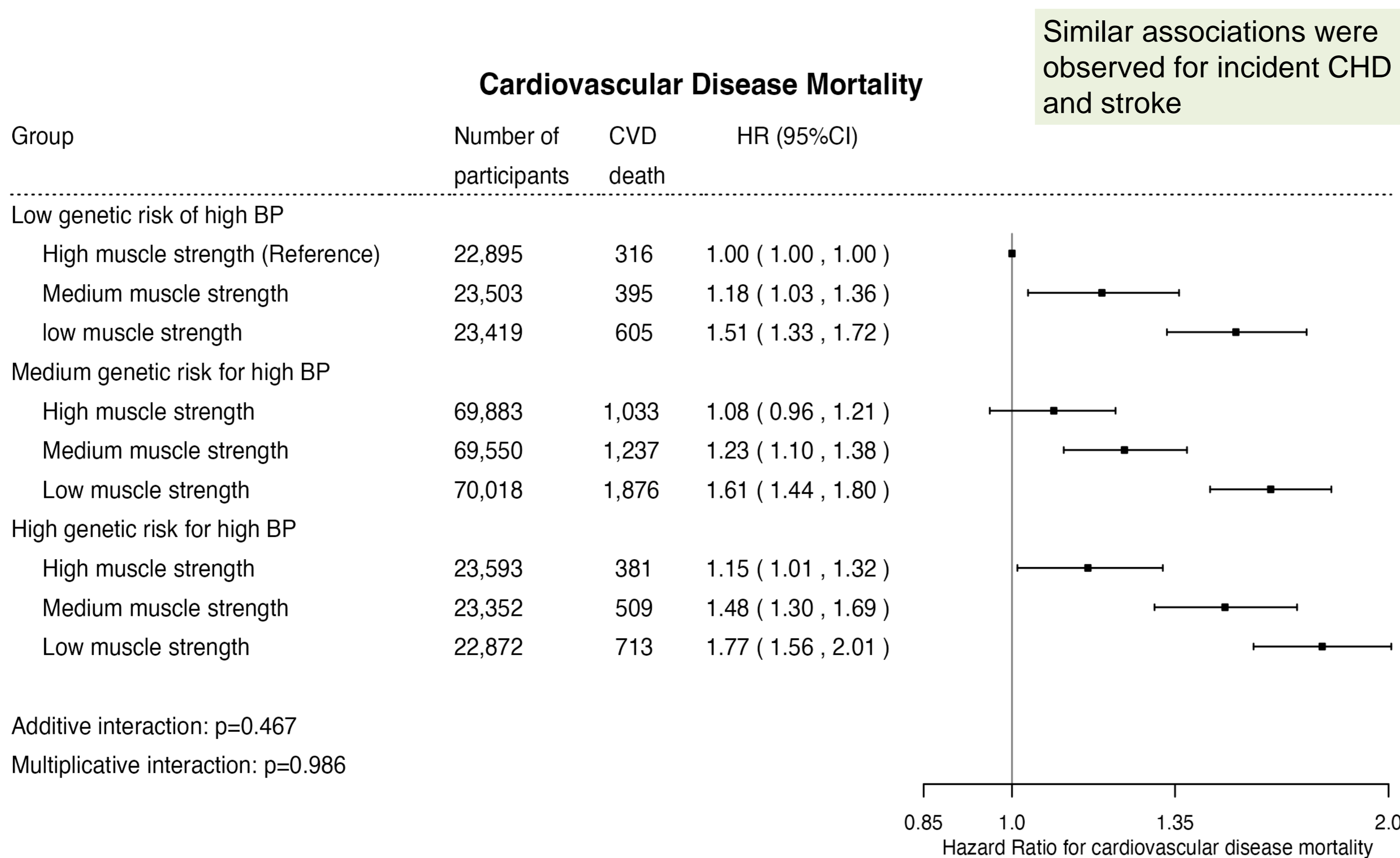


Figure 1. Joint association of combined of genetic risk of high blood pressure and muscle strength with CVD mortality

## Conclusions

- Individuals with higher muscle strength had a lower risk of CVD mortality, and incidence of CHD and stroke, independent of genetic susceptibility to high BP.
- Increased muscle strength may be protective against CVD mortality, CHD and stroke across the population including individuals with high genetic susceptibility to high BP.
- Individuals at high genetic risk of high BP but with high muscle strength may have a lower 10-year absolute risk of CVD mortality, CHD and stroke compared with individuals at low genetic risk of high BP but with low muscle strength.
- Our findings inform clinical trials and policies aimed at modifying BP-related genetic risk of premature CVD death and CVD events through improved muscle strength.

## Acknowledgements

MW and YK conceptualized this study. MW generated key study variables, performed statistical analyses, and drafted an initial version of the manuscript. All authors have critically reviewed and approved the final version of the manuscript. This research has been conducted using the UK Biobank Resource under Application Number 43528.

## Methods

- 349,085 white British individuals from the UK Biobank study.
- Genetic risk of high BP was estimated using a composite PRS for high BP
  - 136 SNPs for systolic BP
  - 135 SNPs for diastolic BP
- Muscle strength was assessed using a hand dynamometer and expressed relative to fat-free mass.
- A median 13.8-year follow-up
  - 8,275 CVD mortality
  - 14,503 incident CHD
  - 7,518 incident stroke
- Cox regressions with age as the underlying timescale were fit.

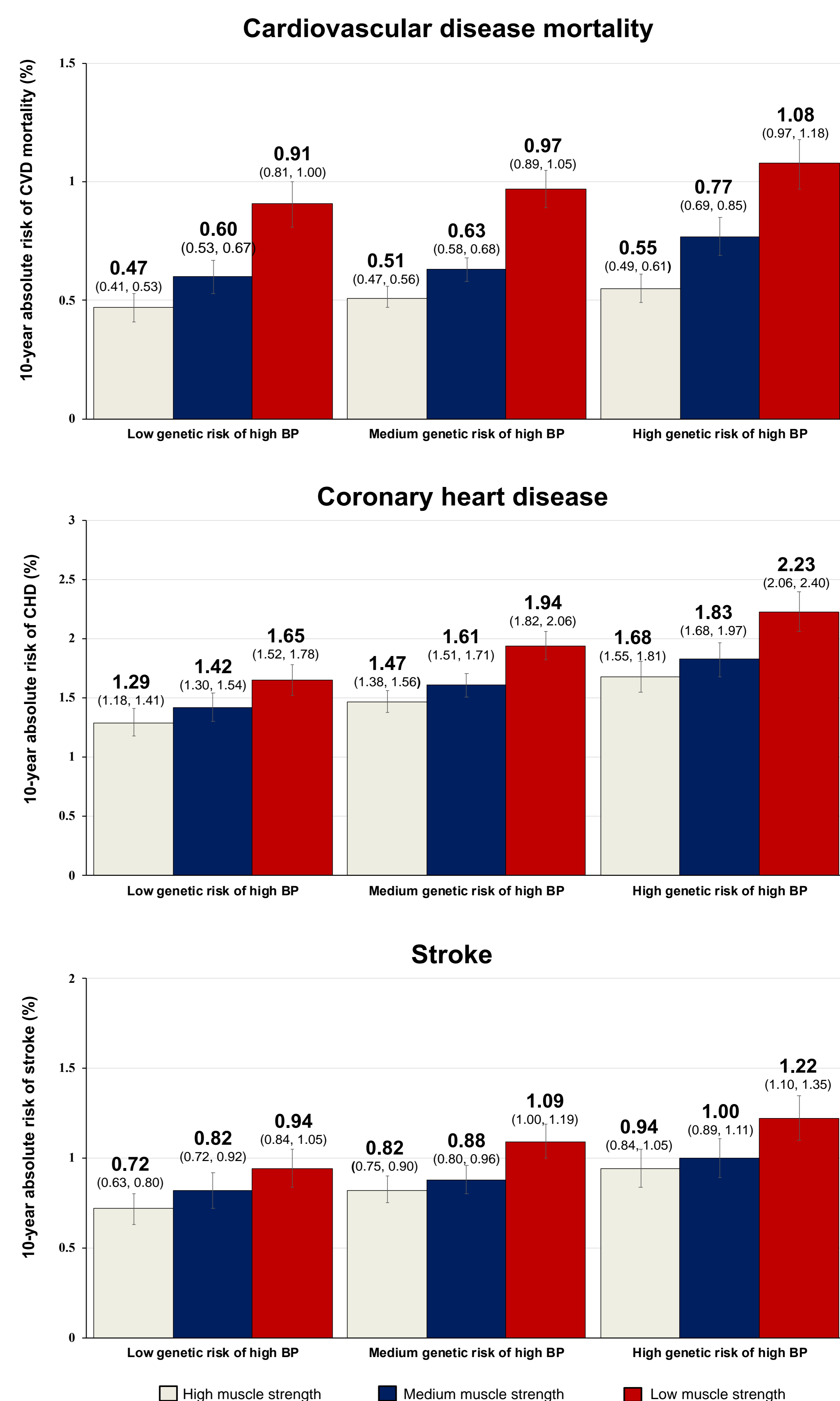


Figure 2. 10-year absolute risk of each CVD outcome stratified by genetic risk for high BP and muscle strength.