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Cardiometabolic multimorbidity, genetic risk and dementia

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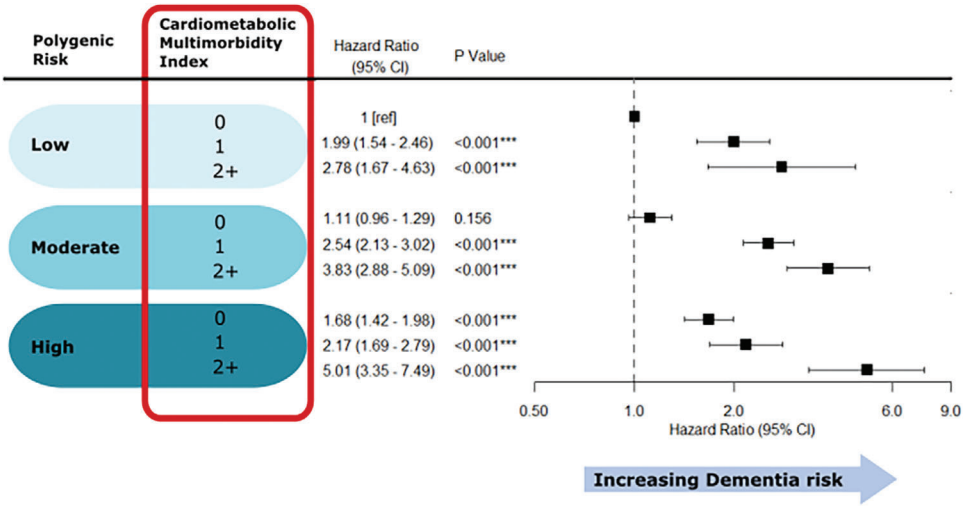
Abstract

Background: The extent to which multiple cardiovascular and metabolic co-morbidity and genetic factors combine or interact to increase dementia risk is unknown.

Method: We analysed 435 105 participants from the UK Biobank prospective cohort of European ancestry, aged 40 to 72 years, without dementia at baseline (2006-2010), followed until 2021. A cardiometabolic multimorbidity index with a point given for co-morbid stroke, diabetes and heart disease (myocardial infarction, atrial fibrillation or heart failure) was calculated for each participant along with a polygenic risk score for dementia with low (lowest quintile), intermediate (quintiles 2 to 4) and high (highest quintile) risk categories. The primary outcome was incident all-cause dementia during follow-up.

Result: Participants with both a high genetic risk and a cardiometabolic multimorbidity index of two or greater had an increased risk of developing dementia, hazard ratio of 5.01(95% confidence interval 3.35 - 7.49), compared to those with a low genetic risk and no cardiometabolic conditions. The risk of developing dementia increased monotonically with increasing cardiometabolic morbidity. Crucially, there was no interaction between cardiometabolic multimorbidity and polygenic risk ($P = 0.11$).

Conclusion: Cardiometabolic multimorbidity was independently associated with higher dementia risk, compared with genetic dementia risk. Addressing cardiometabolic multimorbidity may help to reduce dementia risk regardless of genetic risk.


Polygenic Risk
Cardiometabolic Multimorbidity Index
Hazard Ratio (95% CI)
P Value
Low
0
1
2+
1 [ref]
1.99 (1.54 - 2.46)
2.78 (1.67 - 4.63)
<0.001***
<0.001***
Moderate
0
1
2+
1.11 (0.96 - 1.29)
2.54 (2.13 - 3.02)
3.83 (2.88 - 5.09)
0.156
<0.001***
<0.001***
High
0
1
2+
1.68 (1.42 - 1.98)
2.17 (1.69 - 2.79)
5.01 (3.35 - 7.49)
<0.001***
<0.001***
<0.001***
0.50
1.0
2.0
6.0
9.0
Hazard Ratio (95% CI)
Increasing Dementia risk