

Mediation of the association between air pollution and dementia: a UK Biobank study

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Introduction

- The 2024 Lancet Commission on Dementia Prevention, Intervention and Care identified air pollution as one of 14 potentially modifiable risk factors associated with dementia, calculating its population attributable risk fraction to be 3%.
- However, little is known about the causal mechanisms behind the association.
- Existing studies have primarily focused on the potential for cardiovascular health to mediate the association between air pollution and dementia.

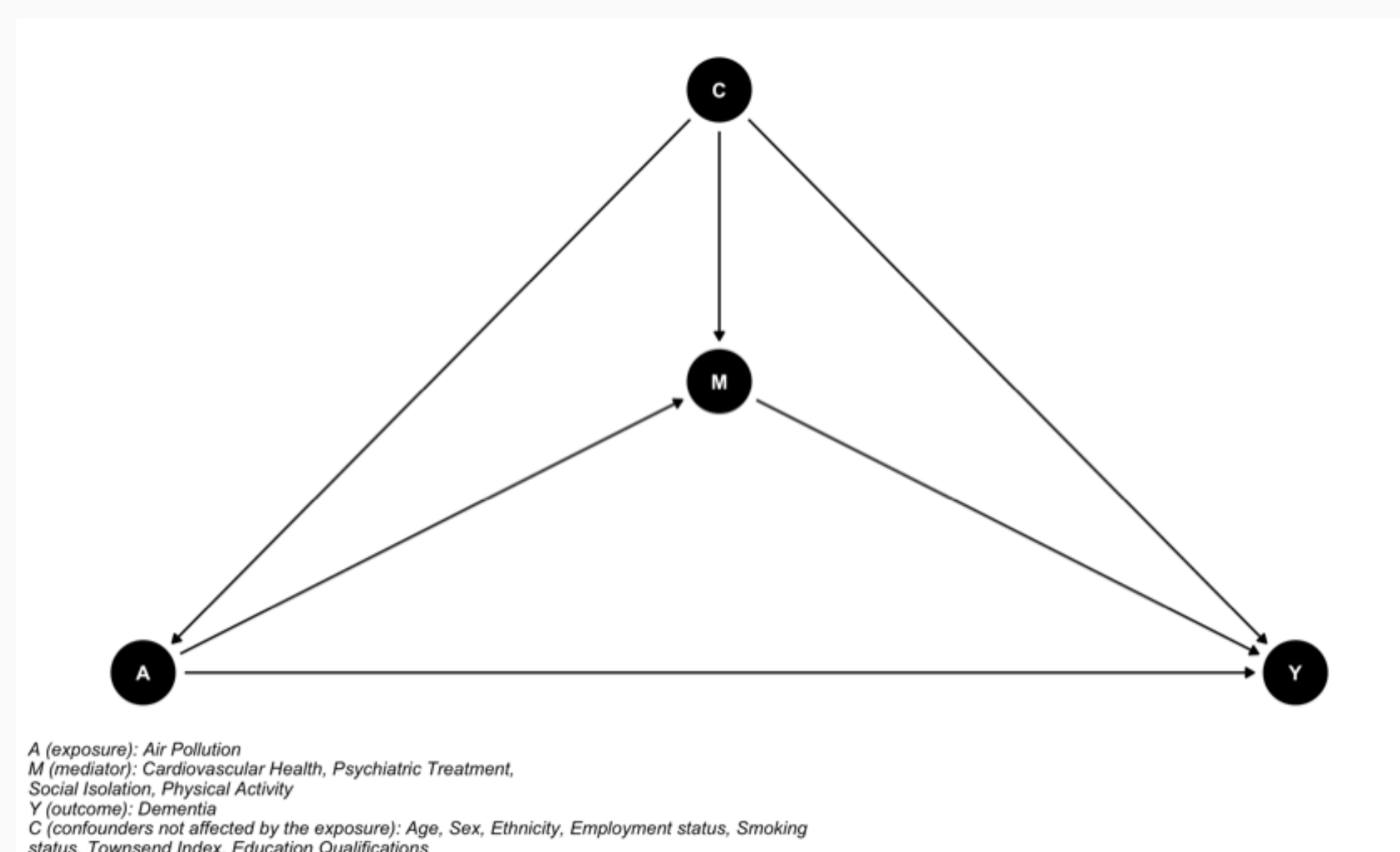


Figure 1. Directional Acyclic Graph of the causal pathway from air pollution to dementia through potentially modifiable mediators.

Methods

- 6 measures of air pollution were reported in the UK Biobank (N=432,935): NO₂, NO_x, PM_{2.5-10}, PM_{2.5}, PM_{2.5} absorbance and PM₁₀.
- Four potentially modifiable mediators on the casual pathway from air pollution to dementia were identified: cardiovascular health; mental health; social isolation and physical inactivity.
- We used logistic regression to investigate the associations between 1) Air pollution quintiles and dementia incidence; 2) Air pollution quintiles and mediators and 3) Mediators and dementia incidence.
- Interventional effects for mediation analysis were estimated using the g-formula.

Results

- We found strong evidence for an association between dementia and PM_{2.5}, NO₂ and NO_x.
- PM_{2.5}, NO₂ and NO_x were associated with cardiovascular and mental health. Evidence regarding associations with other mediators was mixed.
- Social isolation, cardiovascular health, mental health and physical inactivity were associated with dementia.
- We found limited evidence that cardiovascular health conditions, mental health, physical inactivity or social isolation mediate associations between PM_{2.5}, NO₂ and NO_x and dementia.
- Among participants exposed to the highest quintile of air pollution, jointly intervening on these mediators was only estimated to reduce their dementia risk by around 1%.

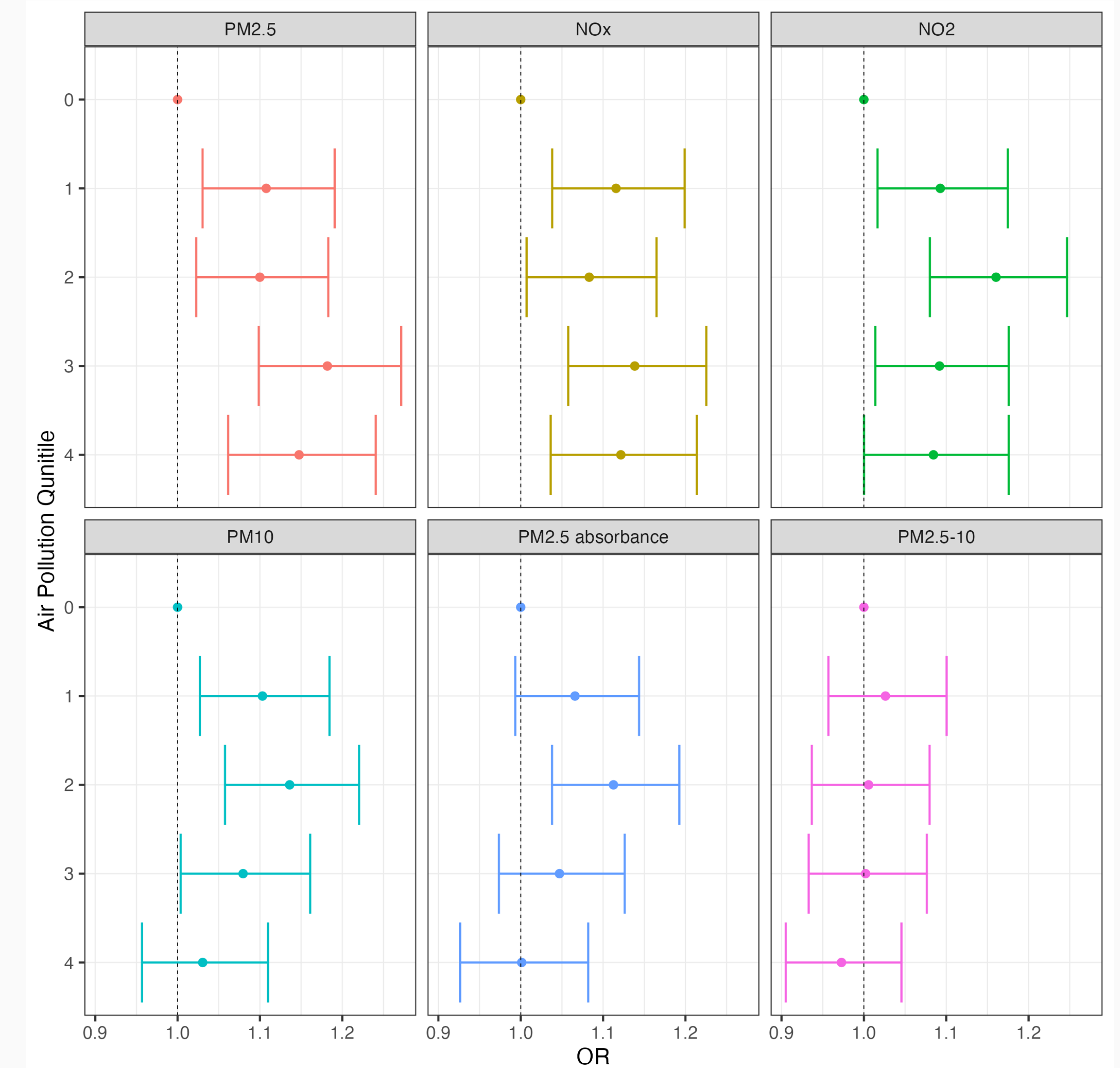


Figure 2. Odds ratio of dementia incidence in association with air pollution quintile.

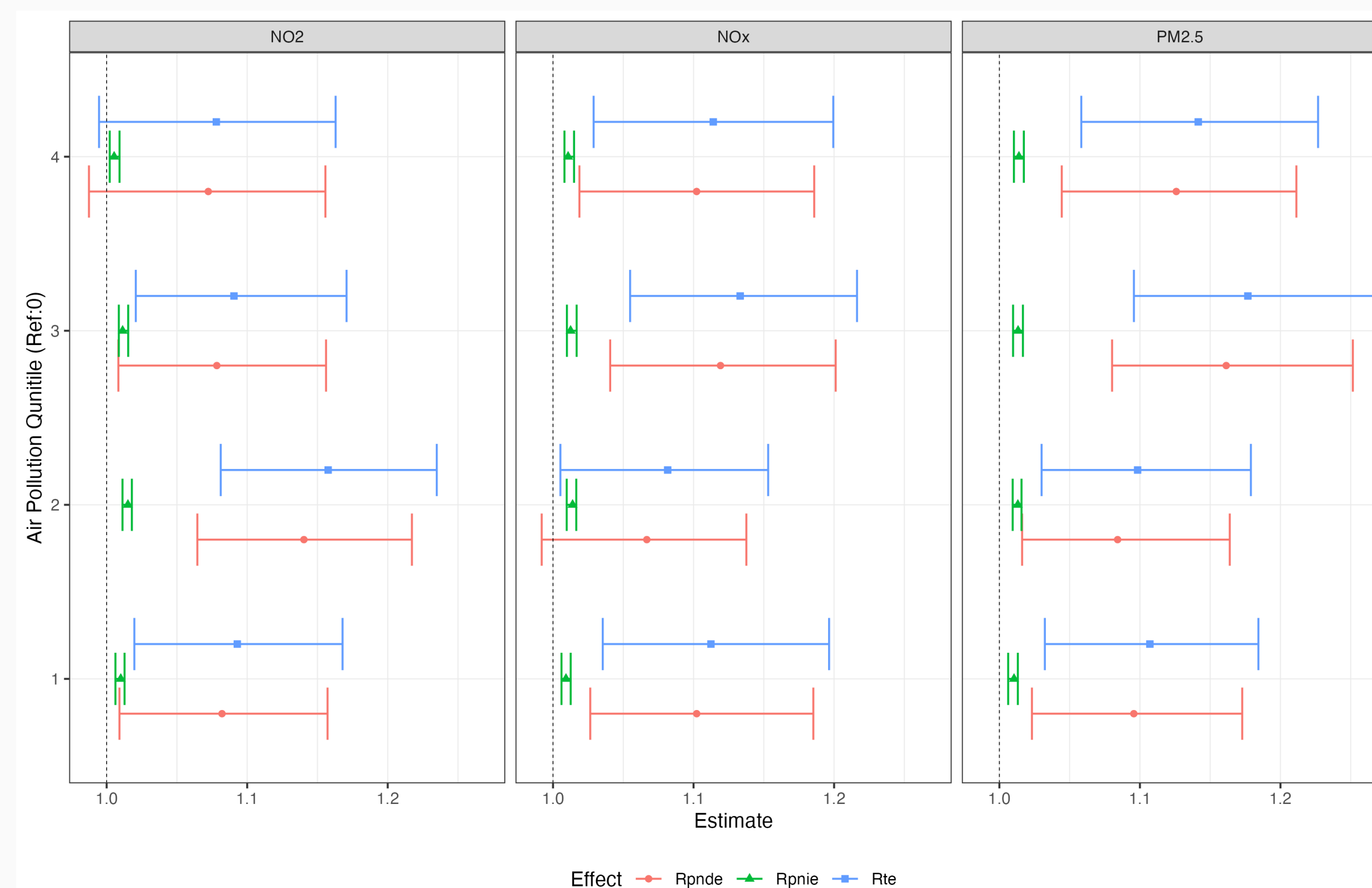


Figure 3. Joint mediation effects of cardiovascular health conditions, mental health, social isolation and physical inactivity on the association between air pollution quintile and dementia. Rpnpe: Randomised pure natural direct effect. Rpnie: Randomised pure natural indirect effect. Rte: Randomised total effect.

Conclusions

- The association between air pollution and dementia is largely driven by the direct effect of air pollution or through pathways not captured by our considered mediators.
- Interventions targeting downstream risk factors may not substantially reduce the dementia risk associated with air pollution exposure.
- Public health strategies should prioritise reducing air pollution exposure, or preventing inhalation, to lower dementia incidence.

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