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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Appendices

Calculation of Population Attributable Fractions

Definitions

The Population Attributable Fraction (PAF) for a risk factor is defined as the percentage of cases of a disease that would be eliminated if that particular risk factor was eliminated. Its value depends on the prevalence of the risk factor and the strength of its association (relative risk) with the disease.

<u>Analysis</u>

The formula for PAF¹ is:

 $PAF = P_e (RR_e-1) / [1 + P_e (RR_e-1)]$

where P_e is the prevalence of the exposure (e.g. the proportion who smoke) and RR_e is the relative risk of disease (in this case dementia) due to that exposure. We used Relative Risks for risk factors based on previously conducted meta-analyses¹⁻³. Details of how we calculated overall PAF are shown in Box 1 below. People may have several risk factors and individual PAF cannot therefore be summed to get the total PAF therefore it is important to consider overlap between variables and to calculate a weighted PAF taking this into account.

Box 1. Standard method for calculation of population attributable fraction and communality³

Formula for individual Population Attributable Fraction (PAF)

PAF = Pe (RRe-1) / [1 + Pe (RRe-1)]

Pe = prevalence of the exposure

RRe = relative risk of disease due to that exposure

Calculation of communality

- Input data on all 12 risk factors in our model
- Calculate tetrachoric correlation to generate correlation coefficients and a correlation matrix. This calculates the correlation between unobserved/latent variables from observed dichotomous variables.
- Conduct a principal-component analysis on the correlation matrix to generate eigenvectors, which are directions mapped onto the data points and from which variance to the data is measured. These represent unobserved factors underlying all the variables that explain the variance observed.
- Components with eigenvalues ≥1 were retained in the model, as is standard practice, in order to only retain eigenvectors which hold the most information about the data distribution.
- Communality was calculated as the sum of the square of all factor loadings (i.e. how much each unobserved component explained each measured variable).

Calculation of overall Population Attributable Fraction (PAF)

We then calculated overall PAF: PAF = 1-[(1-PAF₁)(1-PAF₂)(1-PAF₃)...]

Each individual risk factor's PAF was weighted according to its communality using the formula:

Weight (w) = 1-communality

Weighting was included in the calculation of overall PAF using the formula:

PAF = 1-[(1-w*PAF₁)(1-w*PAF₂)(1-w*PAF₃)...]

To get individual weighted PAF from the overall PAF, we used the formula below:

Individual weighted PAF = Individual PAF/ Σ (Individual PAF)* Overall PAF.

1. Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *The Lancet* 2017; **390**(10113): 2673-734.

2. Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol* 2011; **10**(9): 819-28.

3. Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *Lancet Neurol* 2014; **13**(8): 788-94.