

Appendix 1. Search strategy, and summary of Included hearing studies (in alphabetical order by first author)

**Databases searched:** PubMed, Ovid Embase, PsycINFO, Web of Science, The Cochrane Library, PROSPERO, and The Centre for Reviews and Dissemination (CRD) from inception to March 20<sup>th</sup>, 2023.

**Keywords and strategy:** We searched “all fields” using the following search terms- "dementia" or "cognitive decline" or "Alzheimer's disease" or "mild cognitive impairment" AND "hearing" or auditory or aural or "presbycusis".

**Inclusion criteria:**

- Incident of dementia only
- Pure-tone assessment
- Years of the follow-up > 5 years
- adjusted cardiovascular factors, cognitive or education at baseline, and age
- HR estimator

**Exclusion criteria:**

- Studies comparing populations with varying severities of hearing loss, but not comparing hearing loss individuals with those with normal hearing.
- Studies that adjusted hearing aids for the risk of dementia
- Other estimators than HR

| Author & year               | N at baseline | Age  | Sex; female% | Education (mean years or N and % with education level) | Hearing assessment | N or percentage with HL  | N % of HA users baseline | Follow-up years | Outcome subtypes | N (%) who develop dementia | Adjustment variables (max)  |
|-----------------------------|---------------|------|--------------|--|--------------------|--|--------------------------|-----------------|------------------|----------------------------|---|
| Brenowitz 2019 <sup>1</sup> | 1810          | 77.4 | 938; 51.8    | 1438, 79.4, completed high school)                     | PTA                | <ul style="list-style-type: none"> <li>▪ mild HI (not defined): 715 (39.5%)</li> <li>▪ moderate to severe HL (&gt;40 dB): 629 (34.8%)</li> </ul> | 237 (17.6)               | 10.0            | dementia         | 336 (18.6)                 | age, race, sex, education, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, smoking status, alcohol use, and physical activity. |

|                             |            |      |               |  |     |  |               |      |                                     |               |   |
|-----------------------------|------------|------|---------------|--|-----|--|---------------|------|-------------------------------------|---------------|---|
| Deal 2017 <sup>2</sup>      | 1889       | 75.5 | 996;<br>52.7  | 920,<br>48.7%,<br>post<br>secondary<br>education)      | PTA | <ul style="list-style-type: none"> <li>▪ mild HI (25-40 dB): 716 (37.9%)</li> <li>▪ moderate (41-70 dB) to severe (&gt;70 dB) HL: 387 (20.5%)</li> </ul>   | 240<br>(21.8) | 6.0  | dementia                            | 229<br>(12.1) | age, sex, race, education, study site and smoking status, hypertension, diabetes, and stroke  |
| Lin 2011 <sup>3</sup>       | 639        | 63.7 | 279;<br>43.7  | 16.5 years   | PTA | <ul style="list-style-type: none"> <li>▪ mild HI (25-40 dB): 125 (19.6%)</li> <li>▪ moderate HL (41-70 dB): 53 (8.3%)</li> <li>▪ severe HL (&gt;70 dB): 6 (0.9%)</li> </ul>                          | 58;<br>(31.5) | 11.9 | dementia                            | 58<br>(9.1)   | age, sex, race, education, diabetes mellitus, smoking, and hypertension   |
| Marinelli 2022 <sup>4</sup> | 1159       | 76.0 | 607;<br>52.4  | 886<br>(76.4%,<br><16 years)                           | PTA | <ul style="list-style-type: none"> <li>▪ mild HI (26-39 dB): 383 (33.0%)</li> <li>▪ moderate HL (40-69 dB): 363 (31.3%)</li> <li>▪ severe (70-89 dB) to profound (90 dB HL) HL: 17 (1.5%)</li> </ul> | 492<br>(64.5) | 6.7  | dementia                            | 207<br>(17.9) | age, sex, years of education, smoking status, diabetes, hypertension, apolipoprotein Eε4 carriership, and hearing rehabilitation (defined as hearing aid or cochlear implant)   |
| Osler 2019 <sup>5</sup>     | 6584<br>65 | 59.1 | 0             | NR   | PTA | <ul style="list-style-type: none"> <li>▪ 59834 (9.1%)</li> </ul>   | NR            | 7.1  | dementia (age > 65 and < 65 groups) | 9114<br>(1.4) | cognitive ability, educational level, depression, diabetes, hypertension, and cerebrovascular disease with age as the underlying time scale   |
| Powell 2022 <sup>6</sup>    | 2408       | 74.0 | 1072;<br>44.5 | 1136<br>(47.2%,<br><br>Post-<br>secondary<br>education | PTA | <ul style="list-style-type: none"> <li>▪ mild or greater HL (&gt;25 dB): 1495 (62.1%)</li> </ul>   | NR            | 8.0  | dementia                            | 223<br>(9.3)  | sex, education (postsecondary vs less than postsecondary), age, race (Black vs. White), smoking (ever vs. never), the presence or absence of hypertension or diabetes, BMI, marital status (never married, married, widowed/ divorced/ separated), and living alone |

**Note.** N=number AD = Alzheimer's disease; CI = cognitive impairment; HA = hearing aids; HI = hearing loss; PTA = Pure-tone assessment; NR = Not reported; Deal JA (2017), We combined risk estimates for subgroups in Osler M (2019) and Powell DS (2022). Marinelli JP (2022)'s unadjusted risk estimate for hearing aid was included in the meta-analysis and meta-regression.

## Appendix 2 Prevalence and relative risk of risk factors

We reviewed evidence from the previous Lancet Commission reports and new evidence to determine which relative risks to use for each risk factor, as well as its worldwide prevalence and which part of the life course the risk factor was relevant for.

### **Less education**

We found no new meta-analyses providing an estimate of relative risk for less education so we have used the previous estimate of RR 1.59 (95% CI 1.35 to 1.86) from a meta-analysis of 13 prospective cohort studies.<sup>7</sup> This relates to early life education. We used global estimates of percentage of people who did not enrol in secondary school to estimate the prevalence of this risk factor. In 2020, 76.8% of children enrolled in secondary school meaning 23.2% did not – we used this as our prevalence figure.<sup>8</sup> We acknowledge that for the current population at risk of dementia, education levels were much lower when they were children. However, we are presenting current prevalence estimates to present current PAF for less education.

### **Hearing loss**

We conducted an updated meta-analysis of the relative risk for dementia associated with hearing loss (in main paper). The updated relative risk is 1.37 (95% CI 1.00-1.87) and mean age of included participants is 59 means this risk factor is now considered more relevant in midlife. We used Global Burden of Disease 2019 estimates for prevalence (<https://vizhub.healthdata.org/gbd-results/>).<sup>9</sup> According to these data, the prevalence of any hearing loss from any cause in those aged 55 and over is 58.98% (95% CI 55.61-62.34)

### **Alcohol excess**

We used an individual participant meta-analysis of 131 415 participants from France, UK, Sweden and Finland which found, after adjusting for confounders, heavier drinking of > 21 units per week in midlife compared to lighter drinking was associated with an increased risk of dementia (HR 1.22, 1.01-1.48).<sup>10</sup> We converted this to RR using published formulae using the formula:  $RR = \frac{1 - e^{HR \ln(1-r)}}{r}$  where  $r$  is the rate of dementia for the reference group, to give RR 1.21, 95% CI 1.01-1.46.<sup>11</sup> Participants had their alcohol consumption measured at baseline (age 18-77). Prevalence - 103 290 were moderate drinkers and 28 125 were heavy drinkers, i.e., 27% of current drinkers but 13.3% overall. We used the latter figure as our prevalence estimate.

### **Smoking**

A meta-analysis found midlife smoking was associated with an increased risk of dementia (RR 1.30 1.18-1.45) in 2015 and similar findings have been found in many other cohorts.<sup>12</sup> We have not found a more up to date meta-analysis so used the existing RR estimate. According to the WHO, 22.3% of the global population used tobacco – over 80% of them in LMIC<sup>13</sup>

### **Physical inactivity**

A new systematic review and meta-analysis of 58 studies studying the link between physical activity and dementia, in adults aged 20 and over, found that higher versus lowest physical activity was associated with a decreased risk of all-cause dementia (RR 0.80, 0.77 to 0.84, n=257 983) so corresponding RR for inactivity would be 1.25, 1.19-1.29.<sup>14</sup> There was an association for dementia subtypes in short and longer follow-ups  $\geq 20$  years, and at all ages. The WHO Global Status Report on Physical Activity 2022 states 27.5% of adults engage in below the recommended amount of daily activity.<sup>15</sup> We have included physical inactivity as a midlife risk factor as most studies (34/48) in the meta-analysis had a baseline age of greater than 40.

### **Traumatic brain injury**

The risk of all-cause dementia following traumatic brain injury (TBI) was calculated in the 2020 commission meta-analysis (RR 1.84, 1.54–2.20).<sup>16</sup> Two subsequent meta-analyses have similar findings, the first, a meta-analysis of 21 studies, with a total sample size of n= 8,684,485 found an OR

1.81 (1.53-2.14) for TBI and risk of dementia.<sup>17</sup> A meta-analysis of 32 studies (n= 7,634,844), which included 17 studies from the other meta-analysis, found a RR for dementia after TBI of 1.66 (1.42-1.93).<sup>18</sup> Both of these studies found that younger age (<65 years), male sex and Asian ethnicity were associated with higher risk of dementia. On this basis we have included this as a midlife risk factor. We used the largest meta-analysis for estimation of relative risk and calculated this from the OR using published methods,<sup>11</sup> giving a RR of 1.72. A meta-analysis of population-based surveys for traumatic brain injury provided an estimate of prevalence of TBI of 12%.<sup>19</sup> This only included surveys from higher income countries and included all adults, not limiting to midlife. However, our attempts to find a global prevalence estimate were unsuccessful. The Global Burden of Disease survey had a very low estimate of prevalence and communication with the authors indicated this was likely to be an under-estimate due to the number of people seen in primary care for these injuries which in many countries and studies are not able to be represented systematically in their figures and subject to poor coding and missed diagnosis.

### **Obesity**

A large and new systematic review and meta-analysis examining the relationship between obesity and dementia included 11 studies and 64,265 participants and found that midlife obesity was associated with subsequent all cause dementia (RR 1.31, 1.02-1.68).<sup>20</sup> WHO Obesity and overweight report 2021 finds that 13% of adults worldwide are obese – we could not find an estimate for midlife obesity specifically.<sup>21</sup>

### **Depression**

For this commission, we performed a new random effects meta-analysis using the seven studies with a 10-to-14-year follow-up in the systematic review by Stafford et al.<sup>22</sup> We found an increased risk of dementia (RR 2.25, 1.69- 2.98  $I^2 = 82.8\%$ ). Mean age from included studies (except one which did not specify mean age) was 63.1 years so we have included depression as a midlife risk factor. We found a meta-analysis including 30 countries which reported community prevalence between 1994 and 2014. The estimates were 7.2% point prevalence and 10.8% lifetime prevalence.<sup>23</sup> We used point prevalence as the RR are from depression at a specified time point, not lifetime exposure.

### **Hypertension**

A new meta-analysis individual participant data meta-analysis found individuals with untreated hypertension had a 42% increased risk of dementia compared with healthy controls (hazard ratio [HR], 1.42; 95% CI 1.15-1.76;  $P = .001$ ).<sup>24</sup> However, this only included older adults and previous evidence has shown the risk of dementia was greater for those with hypertension in midlife. One paper meta-analysed 9 studies to give a RR of dementia associated with midlife hypertension of 1.20 (1.06-1.35).<sup>25</sup> We used this estimate for our PAF calculations.

The best evidence of hypertension prevalence we could find came from a global standardized prevalence from 90 countries and was defined as systolic BP  $\geq 140$  mm Hg, diastolic BP  $\geq 90$  mm Hg, and/or current use of antihypertensive medication and was 31.1% (95% CI 30.0–32.2%).<sup>26</sup>

### **Diabetes**

The global diabetes prevalence in 2019 was estimated to be 9.3% (463 million people aged 20-79).<sup>27</sup> The most up to date meta-analysis on risk for dementia showed a pooled RR of developing dementia in 20 studies of 1.73 (1.65–1.82)  $I^2 = 71.2\%$ .<sup>28</sup> Of these studies, four included only participants who were in midlife at baseline, four included participants from midlife onwards, one did not report mean age and the remaining 11 studies included participants who were in later life at baseline. We therefore include diabetes as a risk factor in later life.

### **Cholesterol**

A meta-analysis of LDL-C in adults < age 65 years followed up for > 12 months, found 3 cohort studies with 1,138,488 participants, all from UK, reported each 1mmol/l increase in LDL-C was associated with increased incidence of all-cause dementia (ES = 1.08; 1.03 - 1.14;  $I^2 = 0.3\%$ ).<sup>29</sup> We considered a study of 1,189,090 participants which found high LDL (>3mmol/l) was associated with

an increased risk of dementia – HR 1.33, 95% CI 1.26-1.40. (46) We converted this to RR using published formulae<sup>11</sup> using the formula:  $RR = \frac{1 - e^{HR \ln(1-r)}}{r}$  where  $r$  is the rate of dementia for the reference group, to give RR 1.32, 95% CI 1.25-1.38. As all participants were under the age of 65 at baseline, and evidence is that treatment of those under 65 reduces dementia we have included this as a midlife risk factor.

We could find no global prevalence estimates for high LDL cholesterol, so we considered using the UK nationally representative study used for the RR as an estimate. However many people had not had LDL-C measured and therefore the prevalence data was inaccurate.<sup>30</sup> We therefore extracted data from HUNT study which has little missing data and found the prevalence of high LDL-C was 76.5% when we dichotomized at 3.36 mmol/l or 130mg/dl) and used this figure. This is in line with UK biobank with a healthy population which gave data in quintiles so we could not extract an exact figure, but it was nearly 80%.<sup>31</sup>

### **Air pollution**

We found several studies showing an increase in dementia risk with a variety of air pollutants. All reported risk increases per standard deviation or per  $\mu\text{g}/\text{m}^3$  which means we were not able to dichotomise for higher versus lower levels of pollution. We therefore used our previous method of calculating the RR of dementia for those in the three highest quartiles compared to the lowest from a cohort study including 2,066,639 people, with a mean baseline age of 67 year.<sup>32</sup> The RR was 1.09 (1.07–1.11) and prevalence of higher levels of pollution was 75%. As baseline age was >65, we have included pollution as a risk factor in later life.

### **Vision**

The associated RR= 1.47 (1.36-1.60) from the Shang et al 2021 metanalysis and we have included in as a late life risk factor.<sup>33</sup> This is the largest meta-analysis of 14 prospective cohort studies with 6 204 827 participants and 171 888 dementia patients. Follow up was 3.7 – 14.5 years (but 8/14 studies had fu <7 years). 8 of 14 studies had age as > 65 years, 5 studies listed age as > 50 and one range 40-69, so we have categorised it as late life, which is in keeping with mechanisms. The paper also estimated a PAR of 4.7% (2.3-7.5) based on the prevalence of vision impairment in 2015 estimated by the Global Burden of Disease Study and the pooled relative risk for incident dementia associated with vision impairment in their meta-analysis.<sup>34</sup> A 2020 meta-analysis of population based surveys of eye disease gave a global prevalence of avoidable vision impairment and blindness including uncorrected cataracts and refractive error in adults aged >50 years of 12.65%.<sup>35</sup> We did not find a prevalence estimate for later life visual impairment so this may be an underestimate.

### **Social isolation**

We have continued to use the meta-analysis of relative risk used in our previous commission as it is the only such paper we could find which considers frequency of contacts and dementia (RR 1.57, 1.32-1.85).<sup>36</sup> Mean age of all except one paper in this meta-analysis was over 65 (mostly over 70) with only one paper stating mean age was 60+, so we have included it as a late life risk factor. We used a systematic review and meta-analysis of the global prevalence social isolation among community-dwelling older adults, including 41 studies from databases and reference lists. The pooled prevalence excluding covid studies was 24% (95% CI: 20.0-29.0)<sup>37</sup>

### Appendix 3: calculation of population attributable fractions

We included all participants in the HUNT2 study, aged 45 years or older (<https://www.ntnu.edu/hunt/hunt2>).

### *Dichotomization*

For all the risk factors the **value 0** means not exposed to the risk factor and the **value 1** exposed to the risk factor.

### 1. Education

- a. Variable: Educ@NT2BLQ1 (What is your educational background? Only specify highest level achieved.)

|  |   |
|--|---|
| 7-10 years of education, primary school, continuation school, folk high school | 1 |
| High school, intermediate school, vocational school, 1-2 years high school     | 0 |
| University qualifying examination, junior college, A level                     | 0 |
| University or other post-secondary education, less than 4 years                | 0 |
| University/college, 4 years or more  | 0 |

### 2. Smoking

- a. Variable: SmoStat@NT2BLQ1 (Smoking status) in HUNT2 and corrected using answers in HUNT1 and HUNT3.

|                      |   |
|----------------------|---|
| Current smoker daily | 1 |
| Ex-smoker daily      | 0 |
| Never smoked daily   | 0 |

### 3. Alcohol use

- a. Variable: AlcTotUnitW@NT2BLQ1 (Total alcohol units per week)

|                             |   |
|-----------------------------|---|
| ≥ 21 units (=168 g) pr week | 1 |
| <21 units (=168 g) pr week  | 0 |

### 4. Traumatic brain injury

- a. Variable: HospHeadInju@NT2Hear1Q (Have you ever been hospitalised for a head injury?)

|                   |   |         |
|-------------------|---|---------|
| Yes               | 1 |         |
| No                | 0 |         |
| Don't know, maybe | x | missing |

### 5. Depression

- a. Variable: HADSDepr@NT2BLQ1 (We used respondents who answered all seven questions in HADS-D or those who had answered at least five questions and use the mean for the 1-2 missing questions.)

|     |   |
|-----|---|
| < 8 | 0 |
|-----|---|

|     |   |
|-----|---|
| ≥ 8 | 1 |
|-----|---|

## 6. Diabetes

a. Variable: DiaEv@NT2BLQ1 (Have you had, or do you have diabetes (Do you have, or have you ever had?)). Or non-fasting blood glucose ≥11.1 mmol/l at HUNT2.

|   |   |
|---|---|
| No  | 0 |
| Yes   | 1 |
| Non-fasting blood glucose ≥11.1 mmol/l at HUNT2 | 1 |

## 7. Obesity

a. Variable: Bmi@NT2BLM

|          |   |
|----------|---|
| BMI < 30 | 0 |
| BMI ≥ 30 | 1 |

## 8. Social isolation

a. Variable: CohNo@NT2BLQ2

The variable differs between age group 20-69 and 70+.

The question in both cases is “Who do you live with?”

In the group 20-69 the responses are yes/no for spouse/partner, other people over the age of 18, people below the age of 18. Those who answer no in all these three categories live alone. The others are unexposed.

In the group 70+ the categories are Spouse/partner, Children/children-in-law, Live alone, Sister/brother, other family/relatives, Other. I suggest that those who tick off the category “Live alone” as exposed. The others are unexposed.

|                  |   |
|------------------|---|
| Not living alone | 0 |
| Live alone       | 1 |

## 9. Vision

a. Variable: VisImp@NT2BLQ1 (Vision impairment (If Yes [longstanding illness that impairs your functioning] Would you describe your impairment as slight, moderate, or severe?)).

|                      |   |
|----------------------|---|
| No vision impairment | 0 |
| Slight               | 1 |
| Moderate             | 1 |
| Severe               | 1 |

### 10. Air pollution (variable not in dataset)

Those who live in a municipality with a mean level of particle pollution  $\geq 1.5$  in 2016 are exposed. These are Namsos, Steinkjer, Stjørdal, Frosta, Levanger, Verdal, Overhalla, Flatanger, Nærøysund, Leka, Inderøy, Leksvik.

People living in a municipality with a mean level of particle pollution  $< 1,5$  in 2016 are unexposed. These municipalities are Meråker, Snåsa, Lierne, Røyrvik, Namsskogan, Grong, Høylandet.

|  |   |
|--|---|
| Namsos, Steinkjer, Stjørdal, Frosta, Levanger, Verdal, Overhalla, Flatanger, Nærøysund, Leka, Inderøy, Leksvik | 1 |
| Meråker, Snåsa, Lierne, Røyrvik, Namsskogan, Grong, Høylandet  | 0 |

### 11. Hypertension

a. Variables: BPSystMn23@NT2BLM, BPDiasMn23@NT2BLM

|   |   |
|---|---|
| BPSystMn23@NT2BLM $< 140$ and BPDiasMn23@NT2BLM $< 90$      | 0 |
| BPSystMn23@NT2BLM $\geq 140$ or BPDiasMn23@NT2BLM $\geq 90$ | 1 |

### 12. Cholesterol

a. Variables: SeHDLChol@NT2BLM, SeTrig@NT2BLM, SeChol@NT2BLM.

|                                  |   |
|----------------------------------|---|
| LDL cholesterol $< 130$ mg/dL    | 0 |
| LDL cholesterol $\geq 130$ mg/dL | 1 |

LDL-calculation is based on the Sampson equation:

$$\text{LDL-C} = \text{SeChol@NT2BLM}/0.948 - \text{SeHDLChol@NT2BLM}/0.971 - (\text{SeTrig@NT2BLM}/8.56 + \text{SeTrig@NT2BLM} \times (\text{SeChol@NT2BLM} - \text{SeHDLChol@NT2BLM})/2140 - \text{SeTrig@NT2BLM}^2/16100) - 9.44.$$

HUNT databank uses mmol/L. We used the Sampson equation(591) which is based on mg/dL to convert to mg/dl. This meant we dichotomized at 3.36 mmol/l).

### 13. Hearing impairment



a. variables: nt2htl54l nt2htl54r nt2htl54best

This was measured using a combination of questionnaire, otoscopy, and pure-tone audiometry.

|                                 |   |
|---------------------------------|---|
| Hearing threshold level < 25 dB | 0 |
| Hearing threshold level ≥ 25 dB | 1 |

#### 14. Physical inactivity

a. Variables: ExeLigDuLY@NT2BLQ1 (Average of hours of low physical activity per week in the last year? (How has your physical activity in leisure time been during the last year?)) and ExeHarDuLY@NT2BLQ1 (Average of hours of vigorous physical activity per week in the last year? (Abbreviated question) (How has your physical activity in leisure time been during the last year?))

We use Moholdt et al 2020<sup>38</sup> definition of recommended or below recommended level of physical activity.

|                  | ExeLigDuLY@NT2BLQ1 | ExeHarDuLY@NT2BLQ1 |
|------------------|--------------------|--------------------|
| None             | A                  | A                  |
| Less than 1 hour | B                  | B                  |
| 1-2 hours        | C                  | C                  |
| 3 hours or more  | D                  | D                  |

The following combinations are unexposed (value 0): AC, AD, BC, BD, CC, CD, DA, DB, DC, DD.

The following combinations are exposed (value 1): AA, AB, BA, BB, CA, CB.

In addition, we include among unexposed (value 0) those who have:

- 3 hours or more on ExeLigDuLY@NT2BLQ1 and missing on ExeHarDuLY@NT2BLQ1
- 1-2 hours on ExeHarDuLY@NT2BLQ1 and missing on ExeLigDuLY@NT2BLQ1
- 3 hours or more on ExeHarDuLY@NT2BLQ1 and missing on ExeLigDuLY@NT2BLQ1

#### **Set up of risk factors.**

Step 1: Use Stata command 'tetrachoric' to create tetrachoric correlation matrix of fourteen risk factors.

Step 2: Use Stata command 'pcamat C, n(###) forcepsd mineigen (1)', followed by the postestimation command 'estat loadings, cnorm eigen' to conduct principal components analysis of the matrix.

- This generates three tables. The first table contains components and their respective eigenvalues. The third table contains component loadings scaled to their respective eigenvalues.

Step 3: Retain eigenvalues ≥1.

Step 4: Calculate communality as the sum of the square of all component loadings in the third table.

- The component loadings that are scaled to eigenvalues should be used for communality.

### **Calculation of individual risk factor PAF**

The formula for PAF1 is:  $PAF = Pe (RRe-1) / [1 + Pe (RRe-1)]$  where Pe is the prevalence of the exposure (e.g., the proportion who smoke) and RRe is the relative risk of disease (in this case dementia) due to that exposure.

### **Calculation of overall Population Attributable Fraction (PAF)**

The formula for overall PAF:

$PAF = 1 - [(1-PAF1) (1-PAF2) (1-PAF3) \dots]$  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:  $PAF = 1 - [(1-w*PAF1) (1-w*PAF2) (1-w*PAF3) \dots]$

### **Weighted PAF for individual risk factors**

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

Individual doi: 10.1016/S2666-7568(22)00241-0  
 $\text{weighted PAF} = \text{Individual unweighted PAF} / \sum (\text{Individual unweighted PAF}) * \text{Overall PAF}$

## References

1. Brenowitz WD, Kaup AR, Lin FR, et al. Multiple Sensory Impairment Is Associated With Increased Risk of Dementia Among Black and White Older Adults. *J Gerontol a-Biol* 2019;74(6):890-96. doi: 10.1093/gerona/gly264
2. Deal JA, Betz J, Yaffe K, et al. Hearing Impairment and Incident Dementia and Cognitive Decline in Older Adults: The Health ABC Study. *J Gerontol a-Biol* 2017;72(5):703-09. doi: 10.1093/gerona/glw069
3. Lin FR, Metter EJ, O'Brien RJ, et al. Hearing Loss and Incident Dementia. *Arch Neurol-Chicago* 2011;68(2):214-20. doi: DOI 10.1001/archneurol.2010.362
4. Marinelli JP, Lohse CM, Fussell WL, et al. Association between hearing loss and development of dementia using formal behavioural audiometric testing within the Mayo Clinic Study of a prospective population-based study. *Lancet Health Longev* 2022;3(12):E817-E24. doi: 10.1016/S2666-7568(22)00241-0
5. Osler M, Christensen GT, Mortensen EL, et al. Hearing loss, cognitive ability, and dementia in men age 19-78 years. *Eur J Epidemiol* 2019;34(2):125-30. doi: 10.1007/s10654-018-0452-2 [published Online First: 20181010]
6. Powell DS, Brenowitz WD, Yaffe K, et al. Examining the Combined Estimated Effects of Hearing Loss and Depressive Symptoms on Risk of Cognitive Decline and Incident Dementia. *J Gerontol B Psychol Sci Soc Sci* 2022;77(5):839-49. doi: 10.1093/geronb/gbab194
7. Caamaño-Isorna F, Corral M, Montes-Martínez A, et al. Education and dementia: a meta-analytic study. *Neuroepidemiology* 2006;26(4):226-32. doi: 10.1159/000093378 [published Online First: 20060516]
8. Roser M. Global Education 2016 [accessed 21/10/2023].

9. Global Burden of Disease 2019 estimates for prevalence (<https://vizhub.healthdata.org/gbd-results/>).
10. Kivimaki M, Singh-Manoux A, Batty GD, et al. Association of Alcohol-Induced Loss of Consciousness and Overall Alcohol Consumption With Risk for Dementia. *Jama Netw Open* 2020;3(9):e2016084. doi: 10.1001/jamanetworkopen.2020.16084
11. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *Jama* 1998;280(19):1690-1. doi: 10.1001/jama.280.19.1690
12. Zhong G, Wang Y, Zhang Y, et al. Smoking is associated with an increased risk of dementia: a meta-analysis of prospective cohort studies with investigation of potential effect modifiers. *PLoS One* 2015;10(3):e0118333. doi: 10.1371/journal.pone.0118333
13. World Health Organisation. WHO global report on trends in prevalence of tobacco use 2000-2025. Third ed. Geneva, 2019.
14. Iso-Markku P, Kujala UM, Knittle K, et al. Physical activity as a protective factor for dementia and Alzheimer's disease: systematic review, meta-analysis and quality assessment of cohort and case-control studies. *Brit J Sport Med* 2022;56(12) doi: 10.1136/bjsports-2021-104981
15. Guthold R, Stevens GA, Riley LM, et al. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1.9 million participants. *Lancet Global Health* 2018;6(10):E1077-E86. doi: 10.1016/S2214-109x(18)30357-7
16. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet* 2020;396(10248):413-46. doi: 10.1016/S0140-6736(20)30367-6
17. Gu D, Ou S, Liu G. Traumatic Brain Injury and Risk of Dementia and Alzheimer's Disease: A Systematic Review and Meta-Analysis. *Neuroepidemiology* 2022;56(1):4-16. doi: 10.1159/000520966 [published Online First: 20211124]
18. Gardner RC, Bahorik A, Kornblith ES, et al. Systematic Review, Meta-Analysis, and Population Attributable Risk of Dementia Associated with Traumatic Brain Injury in Civilians and Veterans. *J Neurotrauma* 2022 doi: 10.1089/neu.2022.0041
19. Frost RB, Farrer TJ, Primosch M, et al. Prevalence of traumatic brain injury in the general adult population: a meta-analysis. *Neuroepidemiology* 2013;40(3):154-9. doi: 10.1159/000343275 [published Online First: 20121218]
20. Qu Y, Hu H-Y, Ou Y-N, et al. Association of body mass index with risk of cognitive impairment and dementia: a systematic review and meta-analysis of prospective studies. *Neuroscience & Biobehavioral Reviews* 2020; 115:189-98.
21. World Health Organisation. Obesity and overweight 2021 [Available from: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight> accessed 22/10/2023].
22. Stafford J, Chung WT, Sommerlad A, et al. Psychiatric disorders and risk of subsequent dementia: Systematic review and meta-analysis of longitudinal studies. *Int J Geriatr Psychiatry* 2022;37(5) doi: 10.1002/gps.5711
23. Lim GY, Tam WW, Lu YX, et al. Prevalence of Depression in the Community from 30 Countries between 1994 and 2014 (vol 8, 2861, 2018). *Scientific Reports* 2022;12(1) doi: 10.1038/s41598-022-19021-x
24. Lennon MJ, Lam BCP, Lipnicki DM, et al. Use of Antihypertensives, Blood Pressure, and Estimated Risk of Dementia in Late Life: An Individual Participant Data Meta-Analysis. *Jama Netw Open* 2023;6(9):e2333353. doi: 10.1001/jamanetworkopen.2023.33353
25. Ou Y-N, Tan C-C, Shen X-N, et al. Blood Pressure and Risks of Cognitive Impairment and Dementia. *Hypertension* 2020;76(1):217-25. doi: doi:10.1161/HYPERTENSIONAHA.120.14993
26. Mills KT, Bundy JD, Kelly TN, et al. Global Disparities of Hypertension Prevalence and Control A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation* 2016;134(6):441-+. doi: 10.1161/Circulationaha.115.018912

27. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pr* 2019;157 doi: 0.1016/j.diabres.2019.107843
28. Gudala K, Bansal D, Schifano F, et al. Diabetes mellitus and risk of dementia: A meta-analysis of prospective observational studies. *J Diabetes Invest* 2013;4(6):640-50. doi: 10.1111/jdi.12087
29. Wee J, Sukudom S, Bhat S, et al. The relationship between midlife dyslipidemia and lifetime incidence of dementia: A systematic review and meta-analysis of cohort studies. *Alzh Dement-Dad* 2023;15(1) doi: 10.1002/dad2.12395
30. Mukadam N, Marston L, Lewis G, et al. South Asian, Black and White ethnicity and the effect of potentially modifiable risk factors for dementia: A study in English electronic health records. *PLoS One* 2023;18(10):e0289893. doi: 10.1371/journal.pone.0289893
31. Welsh C, Celis-Morales CA, Brown R, et al. Comparison of Conventional Lipoprotein Tests and Apolipoproteins in the Prediction of Cardiovascular Disease Data From UK Biobank. *Circulation* 2019;140(7):542-52. doi: 10.1161/Circulationaha.119.041149
32. Chen H, Kwong JC, Copes R, et al. Exposure to ambient air pollution and the incidence of dementia: A population-based cohort study. *Environment international* 2017;108:271-77. doi: 10.1016/j.envint.2017.08.020
33. Shang XW, Zhu ZT, Wei W, et al. The Association between Vision Impairment and Incidence of Dementia and Cognitive Impairment. *Ophthalmology* 2021;128(8):1135-49. doi: 10.1016/j.ophtha.2020.12.029
34. Steinmetz JD. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study (vol 2, pg 144, 2021). *Lancet Global Health* 2021;9(4):E408-E08. doi: 10.1016/S2214-109x(21)00054-1
35. Steinmetz JD. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study (vol 2, pg 144, 2021). *Lancet Global Health* 2021;9(4):E408-E08. doi: 10.1016/S2214-109x(21)00054-1
36. Kuiper JS, Zuidersma M, Oude Voshaar RC, et al. Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. *Ageing Research Reviews* 2015;22(pp 39-57):July-57
37. Teo RH, Cheng WH, Cheng LJ, et al. Global prevalence of social isolation among community-dwelling older adults: A systematic review and meta-analysis. *Arch Gerontol Geriat* 2023;107 doi: 10.1016/j.archger.2022.104904
38. Moholdt T, Skarpsno ES, Moe B, et al. It is never too late to start: adherence to physical activity recommendations for 11-22 years and risk of all-cause and cardiovascular disease mortality. The HUNT Study. *Br J Sports Med* 2020 doi: 10.1136/bjsports-2020-102350