

# The potential for dementia prevention in Brazil: a population attributable fraction calculation for 14 modifiable risk factors



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## Summary

**Background** The Lancet Commission on dementia prevention, intervention, and care 2024 updated the list of modifiable risk factors to include 14 factors. The potential for dementia prevention seems to be greater in low- and middle-income countries (LMIC) due to the higher prevalence of these factors. This study aims to provide the first LMIC figure for the potential for dementia prevention in Brazil attributed to 14 modifiable risk factors.

**Methods** Data was retrieved from 9949 participants aged 50 years or older from the nationally representative second wave of the Brazilian Longitudinal Study of Aging (ELSI-Brazil) conducted between 2019 and 2021. The prevalence of modifiable risk factors was estimated, and principal component analysis was used to account for factor communalities. Overall and individual population attributable fractions (PAF) were calculated using relative risks from the 2024 Lancet Commission report. Stratified analyses by sex, race, and Brazilian macro regions were performed to assess disparities in dementia risk.

**Findings** The overall PAF for the 14 modifiable risk factors was 59.5% (95% CI = 58.5–60.5). The three risk factors with the highest PAFs were less education (9.5%, 95% CI = 8.9–10.1), untreated visual loss (9.2%, 95% CI = 8.6–9.8), and midlife depression (6.3%, 95% CI = 5.8–6.8). The overall PAF was similar across race and region but was higher among women (61.1%, 95% CI = 59.9–62.4) compared to men (58.2%, 95% CI = 56.7–59.8).

**Interpretation** Almost 60% of dementia cases in Brazil could potentially be prevented by addressing 14 modifiable risk factors. Public health strategies could further reduce the dementia burden in Brazil.

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**Keywords:** Dementia; Prevention; Risk factors; Brazil

## Introduction

Globally, dementia prevalence is estimated to increase from 57.4 million individuals in 2019 to 152.8 million individuals in 2050, projected to become one of the

leading causes of disability globally by 2025.<sup>1</sup> This surge underscores the urgent need for effective strategies to mitigate the impact of dementia on individuals, families, societies, and healthcare systems. Prevention is a

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### Research in context

#### Evidence before this study

Before conducting this study, we reviewed the existing literature on the population attributable fraction (PAF) of modifiable risk factors for dementia, with a focus on studies conducted in low- and middle-income countries. We searched PubMed, Scopus, and Web of Science for relevant studies published up to February 2025, using search terms such as dementia, modifiable risk factors, population attributable fraction, and low- and middle-income countries. No language restrictions were applied. We included studies that estimated the PAF of modifiable risk factors for dementia using established methodologies. The overall PAF for dementia was estimated to be around 45%, but studies in Latin America suggest a higher burden, reflecting regional disparities in risk factor prevalence. Previous research highlights the substantial contribution of vascular and psychosocial factors, yet gaps remain in understanding how these risks vary by sociodemographic characteristics.

#### Added value of this study

This study provides a PAF calculation for modifiable dementia risk factors in a large, nationally representative

cohort of adults in Brazil. Additionally, we stratified our analysis by sex, race, and geographic region, offering novel insights into how dementia prevention strategies might be tailored for different subpopulations. Our findings emphasize the distinct contributions of modifiable risk factors in shaping dementia risk in Brazil, highlighting the need for targeted interventions.

#### Implications of all the available evidence

The combined evidence underscores the urgent need for public health strategies addressing key modifiable risk factors for dementia, particularly in low- and middle-income countries with high exposure to these risks. Given the significant PAF observed in Brazil, public health policies promoting cardiovascular health, mental well-being, and lifestyle modifications could substantially reduce dementia incidence. Future research should explore the effectiveness of population-based interventions and consider long-term trends in risk factor prevalence to refine prevention efforts. Additionally, further studies should investigate life course exposures and their cumulative impact on dementia risk in diverse populations.

potential cost-effective approach to addressing this burden, emphasizing the critical importance of identifying and modifying risk factors associated with dementia.

The Lancet Commission on dementia prevention, intervention, and care has been instrumental in addressing the global potential of dementia prevention. In 2020, 12 modifiable risk factors of dementia were reported by this commission, which combined indicated that approximately 40% of dementia cases were attributable to modifiable risk factors worldwide.<sup>2</sup> The most recent update, published in 2024, expanded this list by including two additional factors: untreated visual loss and high LDL cholesterol.<sup>3</sup> In addition, risk factors commonalities and relative risk values were updated and recalculated. Overall, the percentage of dementia cases attributable to the 14 modifiable risk factors rose to 45% globally.

Despite the advances made in identifying modifiable risk factors, the majority of the data have been derived from studies conducted in high-income countries (HIC). The generalizability of these data to other regions requires a regionalized approach to tailor public health interventions. In Latin America, the Population-Attributable Fractions (PAF) of 12 modifiable dementia risk factors were larger than the previously calculated PAF in HIC.<sup>4</sup> Specifically in Brazil, where more than 1.7 million people live with dementia,<sup>5</sup> we conducted studies to estimate the PAF of 12 modifiable dementia risk factors, demonstrating a higher potential for prevention when compared with HIC.<sup>6,7</sup> However, the new

data reported from the 2024 Lancet Commission report was not specifically about any individual country, and therefore as LMICs have less research about such risks, less applicable to LMIC.<sup>3</sup> Therefore, our study aimed to calculate the PAF of the 14 modifiable dementia risk factors using data from the Brazilian Study of Aging (ELSI-Brazil), a nationally representative study of adults aged 50 years and older. This analysis is important for tailoring public health interventions to the specific needs of the Brazilian population and potentially informing broader regional strategies in Latin America.

## Methods

### Participants

We used data from the second wave of the Brazilian Longitudinal Study on Aging (ELSI-Brazil) collected from 9949 participants from 2019 to 2021. The ELSI-Brazil sample is representative of the Brazilian population aged 50 years or older.<sup>8</sup> A survey was conducted at participants' homes in rural and urban areas and included data on sociodemographic, clinical, and functional variables. Anthropometric measures were taken during the home visit. The mean age of the sample was  $66.3 \pm 10.0$  years, and 59.3% were women. Following the race categories from the Brazilian Census,<sup>9</sup> race was self-reported as Asian ( $n = 27$ ), Indigenous ( $n = 38$ ), Black ( $n = 1052$ ), Pardos (admixed of Black and White races,  $n = 4169$ ), and White ( $n = 4587$ ). Most participants (54.8%) lived in the South and Southeast regions, reflecting the distribution of the Brazilian population.<sup>10</sup>

**Risk factors definitions**

Fourteen modifiable risk factors were selected to estimate the potential for dementia prevention in Brazil following the updated 2024 Lancet Commission report.<sup>3</sup> A life-course perspective was used to reflect the life period when the evidence of associations between each risk factor and dementia was strongest.<sup>3</sup> Less education was considered an early-life factor while hearing loss, high cholesterol, traumatic brain injury, physical inactivity, diabetes, smoking, hypertension, obesity, and excessive alcohol consumption were midlife factors. Social isolation, air pollution, and visual loss were late-life factors. Risk factor definitions and sources of prevalence and communality estimations are described in [Table 1](#) and [Supplementary Methods](#). Risk factor definitions followed the same definitions used in the Lancet Commission 2024 report, whenever possible.<sup>3</sup> LDL-cholesterol was not measured in the second study wave. It was evaluated in 25% of first-wave participants (n = 2226) with an agreement of 86% between self-reported high cholesterol and measured high LDL-cholesterol. Therefore, we used self-reported high cholesterol in the second-wave sample for this risk factor.

**Population-attributable fraction calculation**

Most prevalence and communality estimations were calculated using ELSI-Brazil data. The prevalence of early-life less education was derived from the 2019

National Household Sample Survey (PNAD: *Pesquisa Nacional por Amostras de Domicílios*).<sup>12</sup> Since no information about TBI was collected in the ELSI study, we used the TBI prevalence of 12% reported by the Lancet Commission 2024,<sup>3</sup> which was derived from a previous meta-analysis.<sup>11</sup> The communality for TBI was calculated by averaging the other 13 risk factor communalities. The prevalence of risk factors in the ELSI study was calculated using sample weights to represent risk factor prevalence in the Brazilian population in the age group where the factor was reported (e.g. midlife and late life). PAF calculation requires the relative risks (RR) of dementia for each risk factor. As the ELSI study did not have longitudinal data available that would allow the calculation of RR, we used the RR from the updated Lancet Commission report, which was based on meta-analyses of longitudinal studies.<sup>3</sup> The PAF was calculated according to this formula:

$PAF = Pe (RRe-1) / [1 + Pe (RRe-1)]$ , where Pe is the risk factor prevalence and the RRe is the RR of dementia for each risk factor.

The overall PAF was calculated for the 14 risk factors according to the formula:

$$PAF = 1 - [(1 - PAF_1) (1 - PAF_2) \dots (1 - PAF_{14})]$$

Since risk factors often coexist within individuals, simply summing their individual PAFs would

| Risk factor                   | Definition   | Source for prevalence and communality estimations   |
|-------------------------------|--|---|
| Early-life                    |  |   |
| Less education                | 8 years or less of education   | PNAD (prevalence)/ELSI-Brazil (communality)   |
| Midlife                       |  |   |
| Hearing loss                  | Self-reporting hearing as regular, bad, or very bad  | ELSI-Brazil   |
| High cholesterol              | Previous medical diagnosis   | ELSI-Brazil   |
| Depression                    | Previous medical diagnosis   | ELSI-Brazil   |
| Traumatic brain injury        | Head injury with loss of consciousness OR Hospitalization by head injury   | Frost et al., 2012 <sup>11</sup> (prevalence)/average of the communalities of the other variables (communality) |
| Physical inactivity           | 75 min of vigorous physical activities or 150 min of moderate activities   | ELSI-Brazil   |
| Diabetes                      | Previous medical diagnosis or current use of insulin or hypoglycemic drugs   | ELSI-Brazil   |
| Smoking                       | Current smoking  | ELSI-Brazil   |
| Hypertension                  | Previous medical diagnosis or current use of antihypertensive drugs  | ELSI-Brazil   |
| Obesity                       | BMI $\geq 30$ kg/m <sup>2</sup> calculated using measured weight and height <sup>3</sup>   | ELSI-Brazil   |
| Excessive alcohol consumption | Current alcohol intake of 14 or more units of alcohol per week (1 unit = 10 g of pure alcohol, equivalent to 21 United Kingdom units as in the Lancet Commission) <sup>3</sup> | ELSI-Brazil   |
| Late-life                     |  |   |
| Social isolation              | Seeing family or friends less than once per month  | ELSI-Brazil   |
| Air pollution                 | Living in an urban area, which was defined by IBGE according to the density of inhabitants and built houses per area.  | ELSI-Brazil   |
| Visual loss                   | Self-reporting near or far-sightedness as regular, bad, or very bad  | ELSI-Brazil   |

BMI: body mass index; PNAD: National Household Sample Survey. <sup>3</sup>2% had missing data for measured weight and height, and self-reported weight and height were used to calculate BMI.

**Table 1: Risk factor definitions and source of prevalence and communality estimations.**

overestimate their total contribution to dementia burden. To account for this overlap, we calculated communality weights to adjust for shared variance among risk factors.<sup>13</sup> First, we assessed the pairwise tetrachoric correlations among the 13 risk factors present in the ELSI-Brazil study. We then performed a principal component analysis on the resulting correlation matrix, determining each risk factor's communality as the sum of squared loadings from all principal components with eigenvalues greater than one. In the ELSI sample, five components with eigenvalues greater than one explained 56% of the total variance among the 13 risk factors. Factor weights were derived as one minus the communality of each risk factor. The weighted overall PAF was then computed using the formula:

$$\text{PAF} = 1 [(1-w_1 * \text{PAF}_1)(1-w_2 * \text{PAF}_2) (1-w_3 * \text{PAF}_3)... (1-w_{14} * \text{PAF}_{14})]$$

In addition, the weighted PAF for each risk factor was estimated using the formula:

$$\text{Individual weighted PAF} = \frac{\text{Individual PAF}}{\sum(\text{Individual PAF})} * \text{Overall PAF}$$

We calculated overall and individual PAF for each modifiable risk factor. Confidence intervals were calculated using the binomial calculation for proportions. We performed stratified analyses by sex, race, and Brazilian macro-regions. For the stratified analyses by race, we excluded participants who did not report their race ( $n = 76$ ), and Asian and Indigenous participants due to small numbers. Black and Pardo races were combined and reported as Black because these individuals face similar racism and adverse health outcomes.<sup>14,15</sup> Brazil has five macro-regions considering their location proximity and sociodemographic development.<sup>10</sup> The Southeast and South regions have the largest socioeconomic development (53% and 17% of the gross domestic product, GDP) and were grouped as rich regions. The North, Northeast, and Central West regions (5%, 14%, and 10% of GDP) were analyzed together and classified as poor regions.<sup>10</sup> Stata 15 (StataCorp, College Station, TX, 2017) was used for statistical analyses.

### Ethics approval

The ethical committee from the Oswaldo Cruz Foundation approved the study (CAAE: 34649814.3.0000.5091), and participants signed an informed consent agreeing to participate.

### Role of the funding source

The funder had no role in the study design, data collection, data analysis, interpretation of the results, and writing this manuscript.

## Results

We estimated that 59.5% of dementia cases in Brazil were attributable to 14 risk factors (95% CI = 58.5–60.5) (Fig. 1, Table 2). When comparing the PAF of each risk factor in Brazil to the global estimates from the Lancet Commission 2024, Brazil presented a larger PAF than global estimates for most risk factors, except for hearing loss (3.6% vs. 7.0%), high cholesterol (2.8% vs. 6.9%), social isolation (0.2% vs. 4.6%) and excessive alcohol consumption (0.4% vs. 1.0%) (Fig. 2). Early-life less education presented the largest PAF (PAF = 9.5%, 95% CI = 8.9–10.1), followed by late-life visual loss (PAF = 9.2%, 95% CI = 8.6–9.8), and midlife depression (PAF = 6.3%, 95% CI = 5.8–6.8). Regarding life stages, the majority of dementia cases were attributable to midlife modifiable factors, summing up 37.1% out of 59.5% of the overall PAF.

### Population attributable fraction by sex

Sex differences were investigated regarding PAF of modifiable risk factors of dementia (Fig. 3, Supplementary Table S2). The overall PAF was larger in women (PAF = 61.1%, 95% CI = 59.9–62.4) than in men (PAF = 58.2%, 95% CI = 56.7–59.8). The three most important risk factors in women were less education (PAF = 9.0%, 95% CI = 8.3–9.8), vision loss (PAF = 9.0%, 95% CI = 8.3–9.7), and depression (PAF = 6.9%, 95% CI = 6.3–7.6), while in men less education (PAF = 10.0%, 95% CI = 9.1–10.9), vision loss (PAF = 9.3%, 95% CI = 8.5–10.2), and physical inactivity (PAF = 6.1%, 95% CI = 5.4–6.8) were the most important risk factors. Women presented larger PAF for high cholesterol and depression than men, while men had larger PAF for smoking and excessive alcohol consumption. Other PAF of modifiable dementia risk factors were similar between men and women.

### Population attributable fraction by Brazilian regions

PAFs were similar among poor (PAF = 58.7%, 95% CI = 57.3–60.2) and rich regions (PAF = 59.9%, 95% CI = 58.6–61.2) (Fig. 3, Supplementary Table S3). In poor regions, less education (PAF = 10.0%, 95% CI = 9.1–10.9), untreated visual loss (PAF = 9.6%, 95% CI = 8.8–10.5), and physical inactivity (PAF = 6.0%, 95% CI = 5.3–6.7) were the most important modifiable risk factors. In rich regions, less education (PAF = 8.8%, 95% CI = 8.1–9.6), untreated visual loss (PAF = 8.6%, 95% CI = 7.9–9.4), and depression (PAF = 6.6%, 95% CI = 5.9–7.2) were the most important factors. Regarding weighted PAF for each risk factor, poor regions exhibited larger PAF of hearing loss (PAF = 4.2%, 95% CI = 3.6–4.8) than rich regions (PAF = 3.1%, 95% CI = 2.6–3.5), while PAF for depression was larger PAF in rich than in poor regions (PAF = 3.8%, 95% CI = 3.24.4).

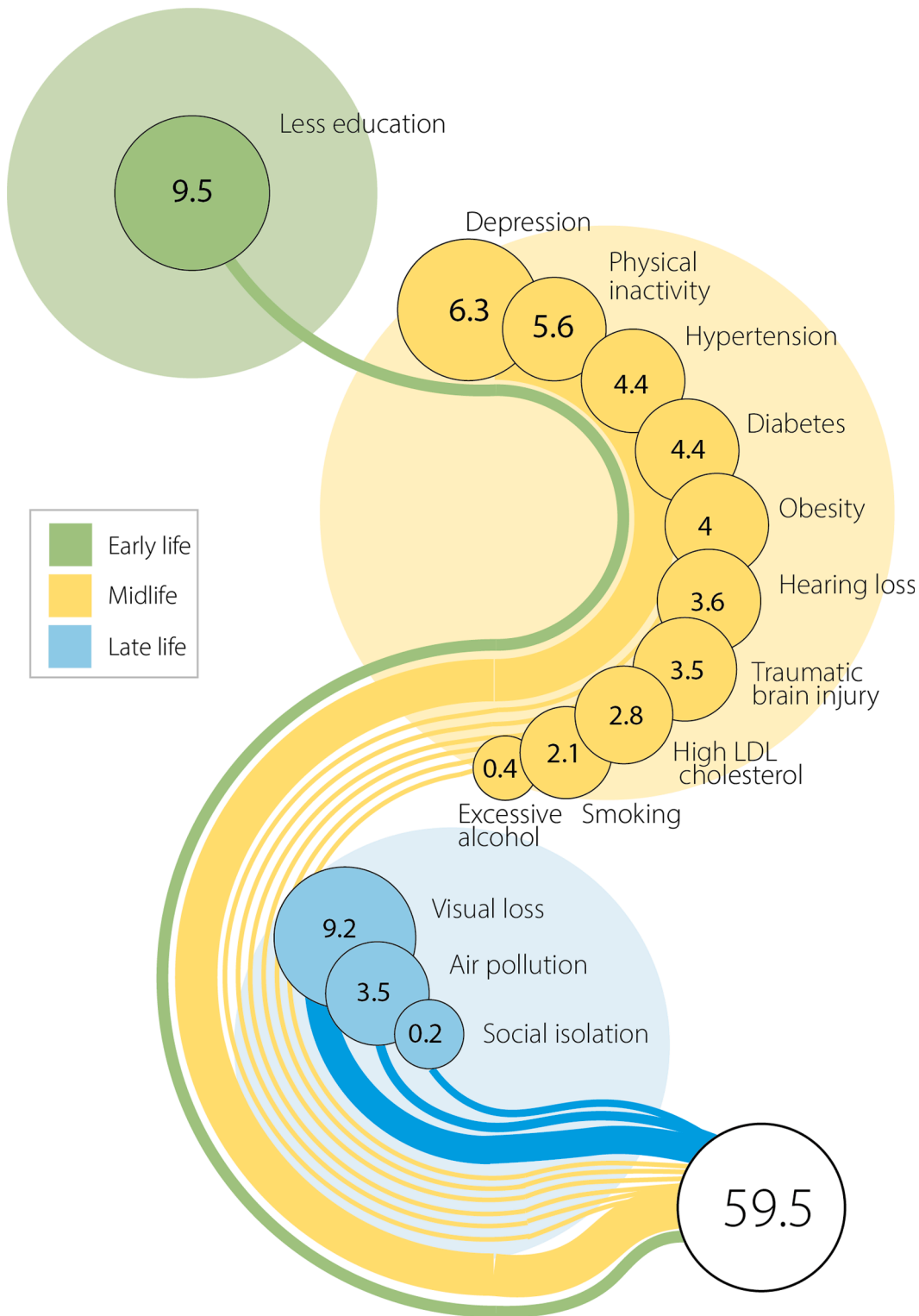


Fig. 1: Population attributable fractions for 14 modifiable risk factors for dementia prevention in Brazil.

| Risk factor                      | RR for dementia (95% CI) | Risk factor prevalence (%) | Communality (%) | PAF (%) <sup>a</sup> | Weighted PAF (%) <sup>b</sup> |
|----------------------------------|--------------------------|----------------------------|-----------------|----------------------|-------------------------------|
| <b>Early life (&lt;45 years)</b> |                          |                            |                 |                      |                               |
| Less education                   | 1.6 (1.3–2.0)            | 45.2                       | 26.6            | 21.3                 | 9.5 (8.9–10.1)                |
| <b>Midlife (45–65 years)</b>     |                          |                            |                 |                      |                               |
| Hypertension                     | 1.2 (1.1–1.4)            | 55.3                       | 33.6            | 10.0                 | 4.4 (4.0–4.8)                 |
| Obesity                          | 1.3 (1.0–1.7)            | 32.8                       | 31.7            | 9.0                  | 4.0 (3.6–4.4)                 |
| Hearing loss                     | 1.4 (1.0–1.9)            | 22.1                       | 30.3            | 8.1                  | 3.6 (3.3–4.0)                 |
| High cholesterol                 | 1.3 (1.3–1.4)            | 22.0                       | 32.2            | 6.2                  | 2.8 (2.4–3.1)                 |
| Depression                       | 2.2 (1.7–3.0)            | 13.7                       | 41.4            | 14.1                 | 6.3 (5.8–6.8)                 |
| Physical inactivity              | 1.2 (1.2–1.3)            | 71.1                       | 49.9            | 12.4                 | 5.6 (5.1–6.0)                 |
| Diabetes                         | 1.7 (1.6–1.8)            | 15.5                       | 29.4            | 9.8                  | 4.4 (4.0–4.8)                 |
| Smoking                          | 1.3 (1.2–1.4)            | 16.3                       | 52.4            | 4.7                  | 2.1 (1.8–2.4)                 |
| TBI                              | 1.7 (1.4–1.9)            | 12.1                       | 38.5            | 7.8                  | 3.5 (3.1–3.8)                 |
| Excessive alcohol                | 1.2 (1.0–1.5)            | 4.9                        | 47.5            | 1.0                  | 0.4 (0.3–0.6)                 |
| <b>Late-life (&gt;65 years)</b>  |                          |                            |                 |                      |                               |
| Social isolation                 | 1.6 (1.3–1.8)            | 0.9                        | 46.5            | 0.5                  | 0.2 (0.1–0.3)                 |
| Air pollution                    | 1.1 (1.1–1.1)            | 84.7                       | 49.7            | 7.8                  | 3.5 (3.1–3.8)                 |
| Vision loss                      | 1.5 (1.4–1.6)            | 52.0                       | 28.9            | 20.6                 | 9.2 (8.6–9.8)                 |
| <b>Overall</b>                   |                          |                            |                 | <b>76.1</b>          | <b>59.5 (58.5–60.5)</b>       |

TBI: traumatic brain injury. <sup>a</sup>PAF =  $Pe (RRe - 1) / [1 + Pe (RRe - 1)]$ , where Pe is the risk factor prevalence and the RRe is the RR of dementia for each risk factor. For example, for education: PAF =  $0.452 * (1.6 - 1) / [1 + 0.452 * (1.6 - 1)] = 0.213$ . <sup>b</sup>Weighted PAF =  $\frac{Individual\ PAF}{\sum(Individual\ PAF)}$  \* Overall weighted PAF. For example, for education: Weighted PAF =  $\frac{0.213}{1.33} * 0.595 = 0.095$ .

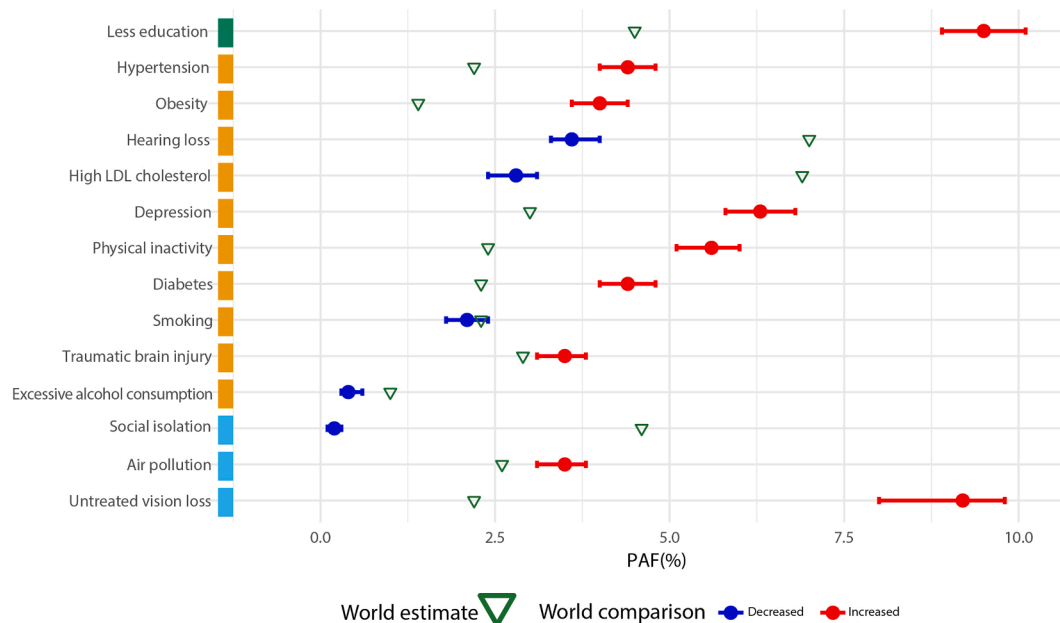
**Table 2: Population attributable fraction (PAF) for 14 dementia risk factors in Brazil (n = 9949).**

**Population attributable factor by race**

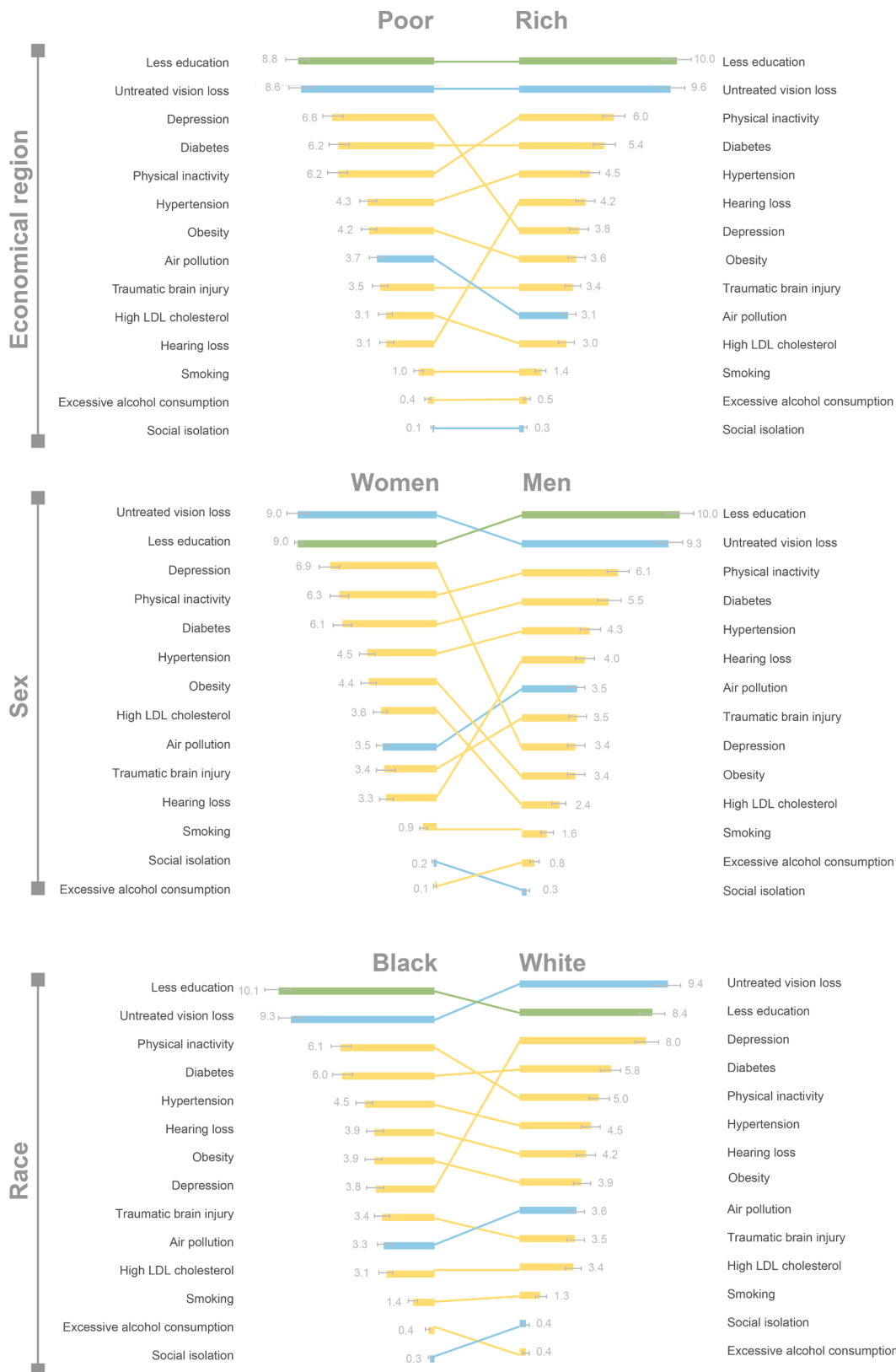
Overall PAFs were similar between Black (PAF = 59.5%, 95% CI = 58.2–60.9) and White participants (PAF = 61.9%, 95% CI = 60.5–63.3) (Fig. 3, Supplementary Table S4). Less education PAF was larger in Black (PAF = 10.1%, 95% CI = 9.3–11.0) than White participants (PAF = 8.4%, 95% CI = 7.6–9.2), while the PAF for depression was larger in White individuals (PAF = 8.0%, 95% CI = 7.3–8.8) than in Black individuals (PAF = 3.8%, 95% CI = 3.4–4.4). In Black individuals, less education, untreated visual loss (PAF = 9.3%, 95% CI = 8.5–10.1), and physical inactivity (PAF = 6.1%, 95% CI = 5.4–6.7) were the three most impactful risk factors. In White individuals, untreated visual loss was the factor with the largest PAF (PAF = 9.4%, 95% CI = 8.5–10.2), followed by less education, and depression.

**Discussion**

Almost 60% of dementia cases in Brazil were attributable to 14 modifiable risk factors. Early-life less education, late-life visual loss, and midlife depression were the three factors with the largest PAF in Brazil. In addition, the potential for dementia prevention was larger in women than in men. High cholesterol and depression had larger PAFs in women, while smoking and excessive alcohol consumption had larger PAFs in men. We did not find differences in the overall PAF by region and race. PAF for hearing loss was larger in poor regions compared to rich ones, while PAF for



**Fig. 2: Comparison between population attributable fractions (PAF) for the 14 modifiable risk factors in Brazil and global estimates calculated by the 2024 Lancet Commission on dementia.<sup>3</sup> Red bars represent worse PAFs in Brazil than in global estimates, while blue bars represent better PAFs in Brazil than in global estimates. Green triangles represent the worldwide PAF estimates according to the 2024 report of the Lancet Standing Commission.<sup>3</sup>**



**Fig. 3:** Stratified analyses of population-attributable fractions for 14 modifiable risk factors by Brazilian regions, sex, and race. Colors represent the period in the life course when the risk factor is likely associated with dementia according to the 2024 Lancet Commission. Blue: early-life; yellow: midlife; and green: late life.

depression was larger in rich regions compared to poor regions. Black participants had higher PAF for less education than White participants. On the other hand, depression PAF was larger in White than Black individuals.

In 2024, the Lancet Commission updated the PAF calculation from 2020 by adding two new modifiable risk factors (high LDL-cholesterol and visual loss), moving some risk factors from the late-life to the midlife window, changing RR and prevalence based on newer meta-analyses, and using a new dataset to calculate communalities.<sup>2,3</sup> The overall worldwide PAF increased from 40% in 2020 to 45% in 2024 report.<sup>2,3</sup> We previously calculated the overall PAF based on the 2020 Lancet Commission and produced similar results.<sup>6,7</sup> In line with worldwide estimations, the potential for dementia prevention in Brazil increased from 48 to 50% based on the Lancet Commission 2020–60% when we applied the updated 2024 framework in the most recent available wave of the ELSI-Brazil study.

Most risk factors had higher prevalence and therefore PAFs than global estimates. For example, PAFs for less education (9.5% vs. 4.4%) and depression (6.3% vs. 3.0%) in Brazil were higher than the global averages reported by the 2024 Lancet Commission.<sup>3</sup> These highlight how socioeconomic disparities and inadequate access to education and mental health care can contribute to dementia risk.<sup>16–19</sup> Brazil's history of unequal access to formal education, especially among older people,<sup>20</sup> exacerbates the vulnerability to cognitive decline through lower cognitive reserve and socioeconomic profile that leads to lower access to healthcare and poor health literacy.<sup>21,22</sup> The significantly higher PAF for untreated visual loss in Brazil (9.0%) compared to the global estimate (2.2%) reflects systemic gaps in ophthalmological care, particularly in underserved areas.<sup>23</sup> In a study of 14 Latin American countries, inequalities in the distribution and level of training of ophthalmologists were found with better service available in more developed and socially advantaged areas.<sup>23</sup> Although Brazil has universal health coverage, access to eye care is limited. The ophthalmologic training of primary care physicians or universal availability of ophthalmic care is essential to reduce this gap.<sup>24</sup> Previous studies have shown that initiatives like cataract surgery and corrective lenses can mitigate visual loss and improve cognitive outcomes.<sup>25</sup> The fact that depression PAF in Brazil was higher than worldwide is consistent with the growing importance of mental health as a key dementia risk factor in LMIC. Midlife depression has been recognized as a risk factor for dementia with the new meta-analysis in the 2024 Lancet Commission finding a 2.2 times increase in the risk of dementia among people with midlife depression.<sup>3</sup> Conversely, Brazil's lower PAFs for high cholesterol, excessive alcohol consumption, social isolation, and hearing loss suggest cultural differences, as well as access

to healthcare. For example, although social isolation and loneliness were also related to poor cognitive performance in the ELSI-Brazil study,<sup>26</sup> strong familial networks and community ties in Brazil likely mean that social isolation is less common and so less important as a dementia risk factor. However, urbanization, decreasing fertility rates, and increasing internal migration rates could erode these protective social structures over time,<sup>27</sup> underscoring the need for proactive interventions to maintain connectivity among older adults. In addition, the self-reported cholesterol and hearing loss, and depression diagnosed from doctor visits may systematically underestimate the risk in people with less resources who are not as likely to visit a doctor or self-report.

Brazil is a continental country and can offer useful insights about differences in the potential for dementia prevention by sex, race, and geographic regions with different socioeconomic development levels.<sup>10</sup> The estimated overall PAF was slightly higher for women than men (61% vs. 58%), which is consistent with evidence suggesting that women may face unique dementia risks, particularly for Alzheimer's disease, due to a combination of biological, social, and behavioral factors.<sup>28</sup> However, given the close estimates, caution is needed when interpreting sex differences in PAF. In Brazil, women had higher PAFs for high cholesterol and depression, which could indicate a need for targeted interventions addressing these conditions. Metabolic syndrome, which includes dyslipidemia, has been suggested to have a stronger association with dementia in women, but further research is needed to clarify these relationships.<sup>28</sup> Depression is more common in women and the sex difference in depression prevalence may be related to hormonal changes from puberty to menopause and environmental exposures, such as lower socioeconomic status, gender differences in socialization, and different coping styles.<sup>28</sup> Conversely, men had higher PAFs for smoking and excessive alcohol consumption, reflecting culturally ingrained lifestyle behaviors. A similar pattern was observed in Argentina for excessive alcohol consumption.<sup>29</sup> Programs targeting excessive alcohol use and smoking cessation, particularly among men, could potentially reduce this risk.<sup>30</sup> Policy initiatives, such as minimum legal drinking age, decreasing the acceptable legal limits for blood alcohol for driving, and limiting alcohol access for underage individuals are effective interventions.<sup>31</sup>

We did not find differences in the overall PAF by region and race. When we investigated the PAF using the risk factors from the 2020 Lancet report, we found a larger potential for dementia prevention in poor regions compared to rich ones.<sup>6</sup> The updated PAF framework with two new risk factors, mostly midlife factors, and different relative risks may explain the differences in overall PAF by region. However, we found a similar pattern regarding the PAF for less education being the

most important risk factor among Black participants and individuals in poor regions compared to White participants and wealthier regions. These findings are consistent with studies showing that historical legacies of racism and unequal resource allocation have disproportionately affected educational opportunities for underserved populations in Brazil.<sup>14,32</sup> The higher PAF for depression in wealthier regions might reflect better healthcare access with greater recognition and diagnosis of mental health issues in these areas. However, this also underscores the importance of improving mental health literacy and access to mental and physical care in poor regions, where underdiagnosis might be more prevalent.

We used nationally representative data and provided a nuanced understanding of dementia risk in Brazil. However, some limitations should be considered. First, we used relative risks from meta-analyses based on worldwide data. Future longitudinal studies in Brazil and other LMICs are essential to refine these estimates and inform public health interventions. Second, we did not have information on TBI and LDL-cholesterol. We used the TBI prevalence of a meta-analysis conducted with studies mainly from the United States<sup>31</sup> and imputed the average communality of the other risk factors for TBI. Since less than 25% of the ELSI sample had LDL-cholesterol measurements, we opted to use self-reported high cholesterol. Although we found a high agreement between these LDL-cholesterol measurements and previous medical diagnoses of high cholesterol, some measurement error is expected. While the 2024 Lancet Commission used data from the Norwegian HUNT study, which reported a prevalence of 77% of high LDL-cholesterol; the prevalence of midlife high cholesterol according to previous medical diagnosis in the ELSI-Brazil was 31%. A recent study reporting nationally representative data found a lower prevalence of 18% among Brazilian adults aged 40–64 years old.<sup>33</sup>

Our study highlights the significant potential for dementia prevention in Brazil by addressing modifiable risk factors such as less education, untreated visual loss, and depression. Public health strategies may lead to more substantial and equitable reductions in disease prevalence and incidence and should be prioritized, focusing particularly on early-life educational access, affordable vision care, and expanded mental health services, particularly for underserved populations. In addition, women may have a higher potential for dementia prevention than men with a distinct risk profile. By adopting regionally designed and equity-focused interventions, Brazil can lead the way in reducing the dementia burden across LMICs.

#### Contributors

CKS: literature search, study design, access to raw data, verified the raw data, data analysis, data interpretation, writing-original draft, read and approve the final version, had the final responsibility for the decision to submit the manuscript.

WVB: study design, access to raw data, verified the raw data, data analysis, data interpretation, writing-review&editing, read and approve the final version.

ILC: study design, access to raw data, verified the raw data, data analysis, data interpretation, writing-review&editing, read and approve the final version.

LB: data interpretation, writing-review&editing, read and approve the final version.

RMC: study design, writing-review&editing, read and approve the final version.

PC: study design, writing-review&editing, read and approve the final version.

RN: writing-review&editing, read and approve the final version.

SMDB: writing-review&editing, read and approve the final version.

JL: writing-review&editing, read and approve the final version.

NM: study design, data interpretation, writing-review&editing, read and approve the final version.

GL: study design, data interpretation, writing-review&editing, read and approve the final version.

CPF: study design, data interpretation, supervision, writing-review&editing, read and approve the final version.

#### Data sharing statement

The data that support the findings of this study are available on the ELSI-Brazil website after registration at: <https://elsi.cpqrr.fiocruz.br/en/home-english/en-data-access/>.

#### Declaration of interests

CKS, WVB, PC, JL, NM, GL, RN, and CPF received support from the Alzheimer's Association. CKS also received support from the São Paulo Research Foundation (FAPESP). SB received support from the National Council for Scientific and Technological Development (CNPq) and consulting fees and payment for lectures from Biogen, Lilly, and Novo Nordisk. GL received funding from UCL Hospitals NIHR Biomedical Research Centre, NIHR Senior Investigator (NIHR201321), North Thames NIHR Applied Research Collaboration (ID1861414), Brain Canada (ARCOM-22-875327), the Norwegian Research Council (ES637280), Wellcome Trust (UNS114095 and 00222932/Z/21/Z), NIHR PGfAR (NIHR202345 and NIHR203670), Geller Foundation, UKRI ES/Y011139/1, Fondazione Prada for presentations, GECC travel support. GL had unpaid activities, such as being part of the data safety monitoring board (NIHR131157), participation in the Trustee of Nightingale Hammerson, Chair of Alzheimer's society grant committee, and the Global Council for Brain Health governance committee.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lana.2025.101209>.

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