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Sex and Socioeconomic Disparities in Dementia Risk: A Population-Attributable Fraction Analysis in Argentina

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Keywords
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Abstract
Introduction: Twelve modifiable risk factors (RFs) account for 40% of dementia cases worldwide. However, limited data exist on such factors in middle- and low-income countries. We aimed to estimate the population-attributable fractions (PAFs) for the 12 RFs in Argentina, assessing changes over a decade and exploring socioeconomic and sex influences. ***Methods:*** We conducted cross-sectional analyses of the 12 RFs from Argentinian surveys conducted in 2009, 2015, and 2018, including 96,321 people. We calculated PAFs and stratified estimates based on sex and income. ***Results:*** We estimated an overall PAF of 59.6% (95% CI = 58.9–60.3%). The largest PAFs were hypertension = 9.3% (8.7–9.9%), physical inactivity = 7.4% (6.8–8.2%), and obesity = 7.4% (6.8–7.9%). Men were more impacted by excessive alcohol, while women by isolation and smoking. Lower income linked to higher PAFs in education, hypertension, and obesity. ***Discussion:*** Argentina has a higher PAF for dementia than the world population, with distinct RF distribution. PAF varied by sex and economic status, advocating tailored prevention strategies.

Background

The rise in dementia prevalence is a global concern. However, the incidence of dementia has changed dramatically in recent years, revealing a complex scenario, with some countries experiencing a decrease, others experiencing stability, and others demonstrating a significant increase [1]. The country's socioeconomic status appears to be associated with these different patterns of dementia incidence, as mostly low- and middle-income countries (LMIC) are showing an increase in dementia incidence, which may be related to increase in the prevalence in individual risk factors (RFs).

One way to change the increasing prevalence of dementia is through prevention strategies. Twelve potentially modifiable RFs have been identified, including less

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education in early life, midlife hearing loss, traumatic brain injury (TBI), hypertension, obesity, excessive alcohol consumption, late-life smoking, depression, social isolation, physical inactivity, diabetes, and air pollution exposure.

In recent years, several population-based studies have estimated the percentage of dementia cases that would be potentially preventable with appropriate management of the aforementioned RF. This measure is known as the population-attributable fraction (PAF). Using the relative risk (RR) of dementia and the prevalence of RF, it is estimated that up to 40% of dementia cases worldwide could be avoided by controlling these 12 factors [2]. It is important to note that most of these data were obtained from studies in high-income countries. While there are some efforts to study LMIC [3–5], there is not sufficient research available to address the magnitude of the problem that these populations will face in the future. LMICs, particularly Latin American countries, are heterogeneous in economic, social, and cultural terms, hence it is expected that the distribution of PAF would not be generalizable from one country to another [6]. Moreover, Latin America is expected to face one of the greatest impacts of dementia prevalence in the coming years [7]. Therefore, studying dementia RF and how they can be modified is a priority for the region [8, 9]. Also, as the Latino population is being targeted by clinical trials to prevent dementia, we need better insight into the distribution of these RF to better design tailored health policies for this region.

Argentina is the second largest country in Latin America and the eighth largest in the world, with a population of 47,327,407, accounting for 6% of all Latino population [10]. Argentina has certain particularities that make previous studies from neighboring countries not extrapolatable. On one hand, it provides free and mandatory education for all since 1884, including free university education since 1949. On the other hand, it has experienced abrupt economic and social changes in the last decade that have had a significant impact on the risk of chronic diseases. There are currently no nationwide studies of dementia RF in the country. Therefore, we aimed to estimate the PAF for the 12 modifiable RFs for dementia. We also aimed to describe the changes that these RFs have shown in the last 10 years and to investigate the impact of socioeconomic status and sex on PAF estimates.

Methods

We conducted cross-sectional data analyses from the National Survey of RF (ENFR) in 2009, 2015, and 2018. This survey is conducted in Argentina every 5 years by the Ministerio de Salud and the Instituto Nacional de Estadística y Censo (INDEC). The aim of this survey was to provide valid, reliable, and timely information on the main noncommunicable diseases in the population aged 18 years and over in Argentina. For this study, we used data from the last three editions of the survey. Surveys were conducted following the same methodology. First, a questionnaire was applied to gather information on housing conditions, the demographics, and educational backgrounds of every member of the household, as well as employment information from the head of the household. An individual questionnaire was additionally applied to a single household member who was at least 18 years old. The second questionnaire was designed to collect data regarding RF for noncommunicable diseases. The selection of the respondent was made through the application of the Kish grid selection method, which ensures that the person most likely to respond to a less invasive survey (such as the general responses requested in the first step) is not different in any specific way from the rest of the population (e.g., older people are more likely to answer about their illnesses than younger populations) [11]. Everyone that met the eligibility criteria, such as being over the age of 18, was included and information on age and sex was collected. Those in the household were placed in a selection grid and the researchers chose a respondent based on their place in the grid, using a random selection process. More explanation of survey methods can be found elsewhere [12].

RF Definition and Prevalence Estimation

Twelve modifiable RF for dementia were previously identified and grouped according to the time in the life course at which the dementia risk was attributable: early life (age <45 years old), midlife (age between 46 and 64 years old), and lat life (age ≥65 years old) [2]. Less education was defined as having 8 years or less of formal education by the age of 25 years old. Hypertension was defined by a previous diagnosis of hypertension by a health professional. To estimate alcohol consumption, participants reported the amount and type of alcohol consumed per week. The result was converted to standard units following the formula suggested by the United Kingdom's National Health System (NHS) [13]. We defined excessive alcohol consumption as consuming more than 21 units per week.

Obesity was considered present when the body mass index was ≥30 kg/m^2 based on measured height and weight. Smoking was defined as being a current smoker. Social isolation was present when the respondent reported living alone. The absence of cohabitation was used as a proxy for social isolation as it is much more likely in individuals who live alone than in those who share a household. Physical inactivity was defined as doing vigorous activities for less than 75 min per week, moderate activities or walking for less than 150 min per week, or an equivalent combination of moderate and vigorous [14]. Diabetes was defined by a previous diagnosis by a health care professional. There are no records of air quality and environmental pollution in Argentina. However, small towns have no industrial activity, and the air quality is very good. Therefore, we assigned nonliving in small towns (less than 150,000 inhabitants) as a proxy for air pollution.

The prevalence of depression, TBI, and hearing loss could not be estimated from the ENFR survey. Hearing loss prevalence was determined using the "Estudio Nacional sobre el Perfil de las Personas con Discapacidad" (National Survey on the Profile of Persons with Disabilities), a survey conducted in Argentina in 2018

with a similar methodology aimed at detecting disabilities in the population. We used the depression prevalence estimated by a study conducted in 2018 [15]. There are no national registries for TBIs, so we used the prevalence reported by a previous meta-analysis [2].

PAF Calculation

For the calculation of the overall and individual PAF, we used a four-step approach. First, we calculated the prevalence for each factor considering the life course approach described previously, subsequently, we calculated the communality of the RF and estimated a communality-weighted PAF. Finally, we calculated the total PAF [3].

Individual PAF Calculation

First, PAF for each RF was estimated using the standard method proposed by Norton et al. [16]. This method uses the RR and the prevalence of the RF through the following formula:

$$PAF = P_{RF}\ (RR_{RF} - 1) / (1 + P_{RF}[RR_{RF} - 1])$$

In which P_{RF} is the prevalence of the RF and RR_{RF} is the RR of dementia for that RF. We used the RRs identified by previous high-quality meta-analyses [17, 18].

Communalities Calculation

To accurately calculate the overall PAF, it is important to consider that many RF commonly coexist and some of them represent different manifestations of an underlying latent RF, such as metabolic syndrome. When individual PAFs are simply added together, it can lead to an overestimation of the total PAF. To address this issue, we calculated the communality of the RF. For the calculation of communality, we used the data collected from the Argentinean survey. Subsequently, we conducted tetrachoric correlation calculations to generate a correlation matrix. This matrix depicted the variability of unobserved (latent) variables through the covariance of the observed dichotomous variables. Finally, we performed a principal component analysis on the correlation matrix. This analysis yielded eigenvectors, which are directions mapped onto the data points and measured the variance within the data. These eigenvectors represented the underlying factors that were not directly observed and explained the observed variance across all variables.

Communality was calculated as the sum of the square of all factor loadings (i.e., how much each unobserved component explained each measured variable). Only components with reasonable explanatory power of variance (eigenvalues >1) were considered. It was not possible to calculate communalities for the RF that was not investigated in the survey. In those cases, the average of the other communalities was imputed.

Individual Weighted PAF and Overall PAF Calculation

By presenting the correction factor of each RF (its communality), we could weigh it. We defined the weights as:

$$w_{RF} = 1 - Communality_{RF}$$

The weighting component was added to the sum of the individual PAFs to estimate the overall PAF following the following formula:

$$overall\ PAF = 1 - \prod_{RF}^{n} (1 - w_{RF} * PAF_{RF})$$

In which n is the number of RF (in this case 12), WRF and PAFRF are the weight and individual PAF of each RF, respectively.

Individual PAFs were calculated using the total PAF following the formula:

$$individual\ weigthed\ PAF = \frac{PAF_{RF}}{\sum PAF_{RF}} * overall\ PAF$$

Statistical Analysis

All the analyses were conducted using R version 4.0.5 (2021-03-31) [19] and the packages tidyverse [20], survey [21], and gt [22]. RF prevalence was estimated using the survey package method for proportions in complex survey designs. Confident intervals of proportions were calculated using the Rao-Scott scaled χ^2 distribution for the log-likelihood from a binomial distribution [23].

We analyzed data from the 2018 survey and presented the individual PAF for each RF and the overall PAF. Analyses were stratified by sex and income. To analyze the socioeconomic impact on RF, subjects were classified into quartiles of per capita income informed during the national household survey [24]. Individuals were categorized according to their income per capita into quartiles, where quartile 1 (Q1) represents individuals with the lowest income and quartile 4 (Q4) represents 25% of the sample with the highest income. The same procedure was used to analyze data from the 2009 and 2013 surveys. The overall and individual PAFs for each RF were compared among 2009, 2013, and 2018 surveys to detect changes in PAFs over 10 years. As the comparison among different years could be made with the available data in the surveys, the 2018 PAF was recalculated only with the data from the original surveys. For all comparisons, z tests for independent proportions were used with Yates correction when necessary [25]. The code and source data are publicly available at https://github.com/icalandri/PAF_Argentina_2009-2018.

Results

A total of 96,321 subjects were evaluated in the three surveys. For 2009 and 2013, the sample sizes were 34,732 (28.5% midlife and 16.6% later life) and 32,365 (28.1% midlife and 16.6% later life), respectively. In the 2018 survey, 29,224 participants were interviewed (30.1% of the subjects were between 45 and 65 years old and 19.5% were over 65 years). Table 1 summarizes the demographic data from the three surveys. Eight RF were identified in the survey (less education, hypertension, alcohol consumption, obesity, smoking, social isolation, physical inactivity, and diabetes).

PAF over Time

Using the ENFR data and data available from other sources in 2018, we estimated an overall PAF of 59.6% (95% CI = 58.9–60.3%). The three factors with the largest

Table 1. Demographic characteristics of the sample

	2009				2013				2018			
	total	early life	midlife	later life	total	early life	midlife	later life	total	early life	midlife	later life
n	34,732	19,096	9,885	5,751	32,365	17,898	9,909	5,376	29,224	14,731	8,784	5,709
Women, %	57	55	56	62	56	54	54	62	57	56	56	61
Age, mean (SD)	45 (18)	31 (7)	54 (6)	74 (7)	45 (18)	31 (7)	54 (6)	74 (7)	46 (18)	31 (8)	54 (6)	74 (7)
Education, %												
Incomplete primary education	13	6	16	32	11	5	13	28	9.2	3	10	23
Incomplete secondary education	40	37	42	44	38	35	40	44	35	30	38	43
Complete secondary education and higher	47	57	42	24	51	60	47	28	56	66	52	33
Income quartiles, %												
Q1	25	32	21	10	21	34	22	10	24	33	21	9
Q2	25	26	25	24	25	29	28	25	24	25	25	22
Q3	26	22	26	40	26	17	20	32	26	22	26	37
Q4	24	20	28	27	28	20	29	32	25	20	28	32
Income, mean (SD)[1]	263 (302)	229 (263)	305 (363)	301 (292)	467 (487)	401 (414)	533 (574)	575 (516)	360 (400)	307 (349)	398 (444)	437 (431)

[1]Estimated income in dollars according to the average exchange rate of the Argentine peso in that year 2009: 1 dol = 3.6 peso, 2013: 1 dol = 5.7 peso, and 2018: 1 dol = 28.8 peso.

PAFs were hypertension with 9.3% (95% CI = 8.7–9.9%), physical inactivity with 7.4% (95% CI = 6.8–8.2%), and obesity with 7.4% (95% CI = 6.8–7.9%). Table 2 summarizes the prevalence, the RR, and the overall and individual PAFs.

Using only the survey data, we were able to compare the estimates for 2009, 2013, and 2018. The total PAF in 2018 (48.7%, 95% CI = 47.9–49.4%) was similar to the one in 2013 (47.9%, 95% CI = 47.2–48.6%). Both 2013 and 2018 PAFs were larger than the one in 2009 (46.4%, 95% CI = 45.7–47.0%), $p < 0.001$). Analyzing the change in each factor separately, the factors that changed significantly over time were education, obesity, hypertension, and social isolation. Less education decreased from 3.4% (95% CI = 3.0–4.0%) in 2009 to 1.9% (95% CI = 1.5–2.4%) in 2018 ($p < 0.001$). Hypertension increase from 3.1% (95% CI = 2.8–3.5%) in 2009 to 8.2% (95% CI = 7.6–8.8%) in 2018, as obesity increased from 2.4% (95% CI = 2.1–2.7%) in 2009 to 3.1% (95% CI = 2.8–3.5%) in 2018 ($p = 0.002$) and social isolation increased from 5.1% (95% CI = 4.6–5.8%) in 2009 to 6.6% (95% CI = 6.0–7.3%) in 2018 ($p = 0.003$) (Fig. 1; online suppl. Table 1; for all online suppl. material, see https://doi.org/10.1159/000536524).

Sex Differences

A total of 16,632 (29.6% in midlife and 20.9% in late life) women and 12,592 (30.7% midlife and 17.8% late life) men were evaluated in the 2018 survey. There were no differences in total PAF between women and men (women: 51.3%, 50.4–52.3%; men: 50.8%, 49.7–51.9%; $p = 0.462$). However, we found significant differences in individual RFs, such as smoking, alcohol consumption, and social isolation. Cases attributable to excessive alcohol consumption were higher in men than in women (4.4%, 3.8–5.1% vs. 1.8%, 1.4–2.2 $p < 0.001$). The PAF attributable to smoking was higher in women (6.3%, 5.5–7.1%) than in men (4.6%, 3.8–5.6%, $p = 0.007$). In addition, social isolation PAF was higher in women

Table 2. PAF for dementia RFs – 2018

RF	RF prevalence		RR	Communality	PAF	Weighted PAF	
	prevalence	(95% CI)				individual PAF	(95% CI)
Early life							
Less education	6.6%	(5.4–8.0)	1.6	31.7%	3.8%	1.7%	(1.4–2.2)
Midlife							
Hearing loss[1]	16.7%	(11.8–22.5)	1.9	33.3%	13.1%	5.9%	(5.4–6.4)
TBI[2]	12.1%	–	1.8	33.3%	8.8%	4.0%	(3.6–4.4)
Hypertension	42.7%	(40.9–44.6)	1.6	27.0%	20.4%	9.3%	(8.7–9.9)
Alcohol consumption	33.1%	(31.4–34.9)	1.2	21.4%	6.2%	2.8%	(2.5–3.2)
Obesity	32.2%	(30.5–34.0)	1.6	45.0%	16.2%	7.4%	(6.8–7.9)
Later life							
Smoking	19.9%	(17.4–22.5)	1.6	37.9%	10.7%	4.8%	(4.3–5.4)
Depression[3]	7.6%	(4.9–10.3)	1.9	33.3%	6.4%	2.9%	(2.5–3.4)
Social isolation	25.3%	(23.7–26.8)	1.6	48.2%	13.2%	6.0%	(5.4–6.6)
Physical inactivity	49.0%	(46.8–51.2)	1.4	29.7%	16.4%	7.4%	(6.8–8.2)
Diabetes	21.4%	(19.6–23.3)	1.5	26.1%	9.7%	4.4%	(3.9–5.0)
Air pollution	70.1%	(68.3–71.7)	1.1	33.0%	6.5%	3.0%	(2.6–3.5)
Total PAF					75.6%	59.6%	(58.9–60.3)

[1]Data from "Estudio Nacional sobre el Perfil de las Personas con Discapacidad" 2018. [2]Data from Livingston, 2020 [2]. [3]Data from Cía, 2018 [15].

(7.6%, 6.7–8.5%) than in men (5.2%, 4.3–6.2%, $p < 0.001$) (online suppl. Table 2).

When analyzing change over time, both sexes have a significant decrease ($p < 0.01$) in the overall PAF. Specifically, men declined from a total PAF of 50.8% (49.7–51.9%) in 2009 to 46.8% (45.6–48.0%) in 2018. Similarly, women PAF decreased from 51.3% (50.4–52.3%) in 2009 to 45.5% (44.6–46.4%) in 2018.

In terms of changes over time, in women the PAF for less education levels declined (2009: 3.0% [2.4–3.7%]; 2013: 3.2% [2.6–4.0%]; 2018: 1.6% [1.1–2.3%], $p = 0.001$), whereas smoking PAF increased (2009: 6.0% [5.4–6.7%]; 2013: 6.2% [5.6–6.9%]; 2018: 7.5% [6.8–8.3%], $p = 0.004$). For men RF, there was a decrease in the PAF associated with lower education (2009: 3.9% [95% CI = 3.2–4.7%], 2018: 2.2% [1.6–3.0%], $p < 0.001$). However, there was a significant increase in alcohol consumption (2009: 3.7% [95% CI = 3.1–4.3%], 2018: 4.4% [95% CI = 3.8–5.1%], $p = 0.042$), obesity (2009: 7.0% [95% CI = 6.2–7.8%], 2018: 8.5% [95% CI = 7.7–9.5%], $p = 0.029$), and social isolation (2009: 3.4% [95% CI = 2.7–4.2%], 2018: 5.2% [95% CI = 4.3–6.2%], $p = 0.012$) (online suppl. Table 2). Figure 2 summarizes the distribution of PAFRF between sexes and their PAF changes over time.

Socioeconomic Differences

Total PAF was higher in those with lower income (Q1: 54.5%, 95% CI = 53.0–56.1%; Q2: 50.4%, 95% CI = 48.9–51.9%; Q3: 50.7%, 95% CI = 49.3–52.0%; Q4: 49.7%, 95% CI = 48.2–51.1%; $p < 0.001$). Comparing the distribution of each PAF for each RF by income, we found that people with the lowest income had more cases attributable to less education (3.5%, 95% CI = 2.6–4.5%) than Q3 and Q4 (Q3: 0.9%, 95% CI = 0.4–2.0%; Q4: 0.1%, 95% CI = 0.0–1.1%, $p < 0.001$). Cases attributed to hypertension were significantly ($p = 0.038$) higher in Q1 (11.8%, 95% CI = 10.3–13.3%) than in Q4 (9.1%, 95% CI = 8.0–10.3%). Likewise, obesity is significantly higher in the Q1 group (9.7%, 95% CI = 8.4–11.1%) than in the Q4 group (6.4% 95% CI = 5.5–7.4%, $p = 0.001$). In the opposite direction, the PAF for social isolation increased with income (Q1: 1.5%, 95% CI = 0.7–3.1%; Q2: 3.9%, 95% CI = 2.9–5.2%; Q3: 6.9%, 95% CI = 5.9–8.1%; Q4: 10.5%, 95% CI = 9.1–12.0%; $p < 0.001$) (online suppl. Table 4). When analyzing changes over time, we found that cases attributable to less education increased from 2009 to 2018 in the two lowest quartiles of income (Q1: 2009 = 3.4%, 95% CI = 2.6–4.3%; 2013 = 4.0%, 95% CI = 3.2–5.0%; 2018 = 1.7%, 95% CI = 1.1–2.4%; $p < 0.001$; Q2: 2009 = 2.0%, 95% CI = 1.3–2.9%; 2018 = 0.7%, 95% CI = 0.3–1.5%, $p = 0.024$) (online suppl. Table 5; Fig. 3).

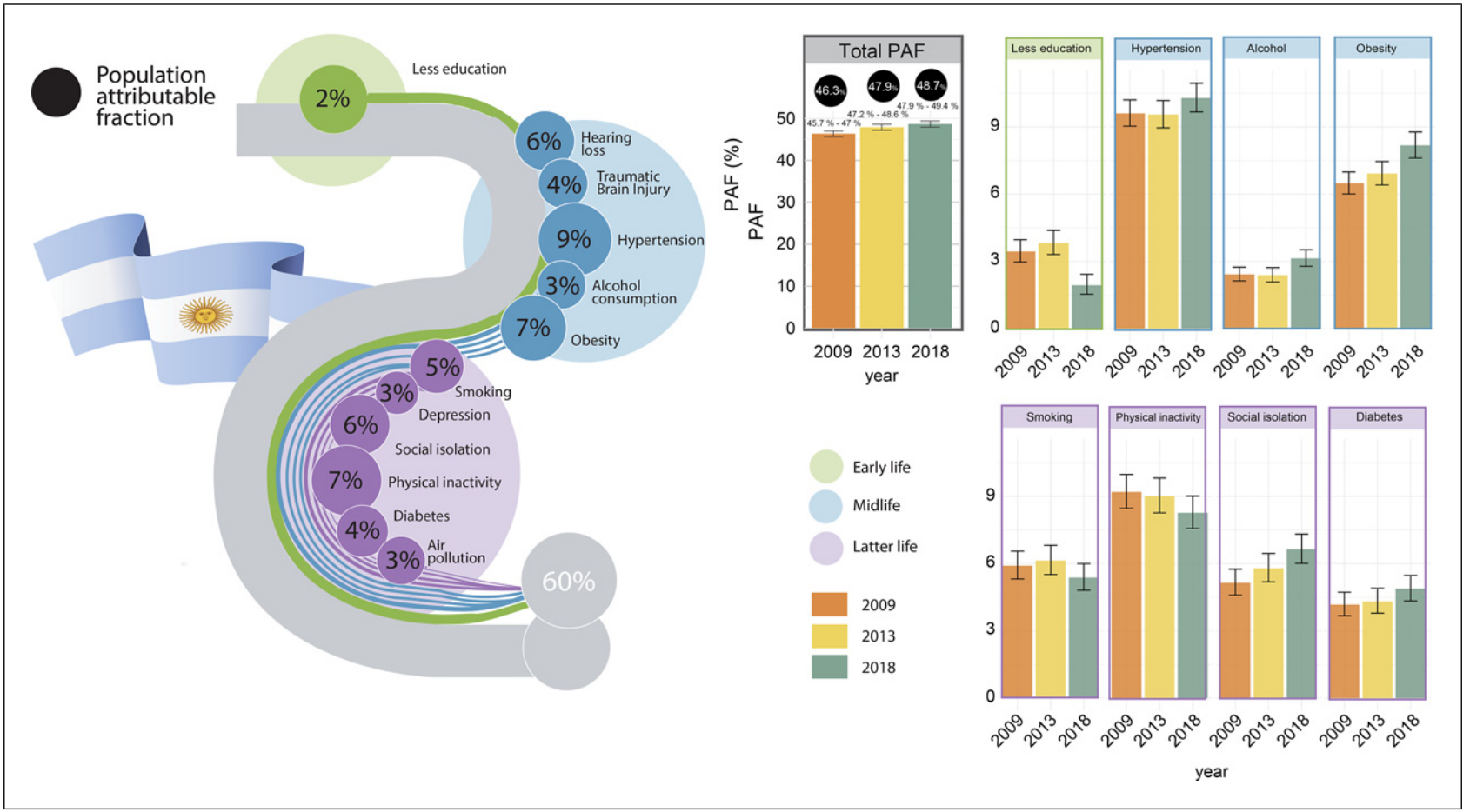

Fig. 1. PAF of potentially modifiable RFs for dementia in Argentina. On the left, the individual PAF for each RF in Argentina in 2018. In the middle, the comparable total PAF between 2018, 2013, and 2009. On the right, the individual PAF of each factor over the years.

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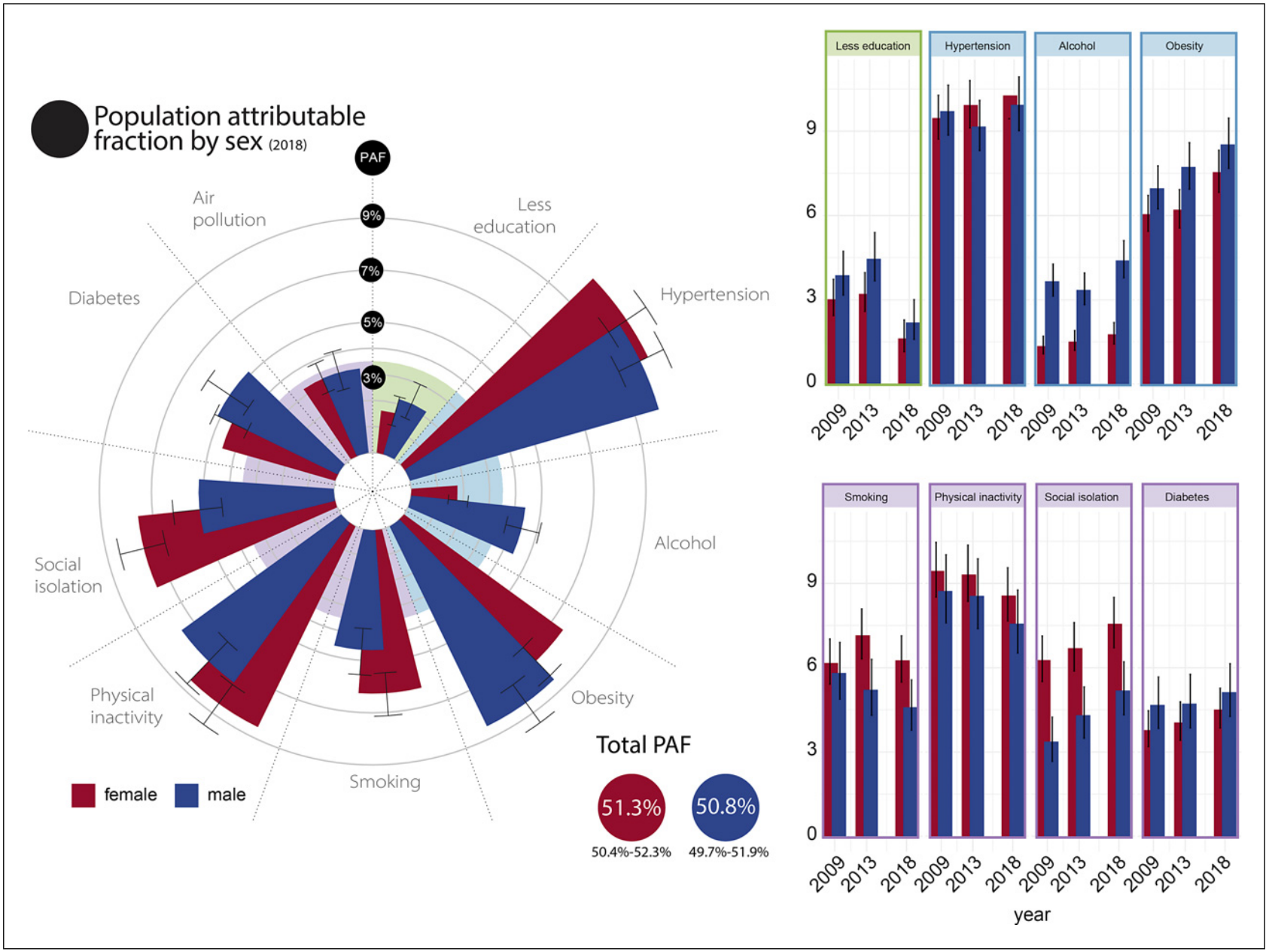

Fig. 2. PAF of potentially modifiable RFs for dementia by sex. On the left, circular bar chart with the individual PAF for each RF in men and women. Below, the total PAF for both groups with its 95% confidence interval. On the right, the individual PAF value for each RF by sex and year.

Discussion

We found that the total PAF for Argentina is significantly higher than that reported for the world population. This represents a great potential for dementia prevention. Almost 60% of dementia cases in Argentina were attributable to 12 modifiable RFs. It is important to highlight that this elevated PAF is particularly related to a few RFs. While less education seems to have a smaller impact compared with global estimation, factors related to metabolic syndromes such as obesity, hypertension, and physical inactivity were important contributors to the overall PAF in Argentina. When we examined changes over time, we observed a small but significant increase in the total PAF. By focusing on individual factors, sustained increases in hypertension, obesity, and sedentary lifestyle-attributable fractions were found. Trying to explain these complex processes is challenging; however, it is undeniable that socio-demographic changes must be analyzed in terms of the increasing industrialization of Argentinean society, the rise in sedentary lifestyle, and dietary changes. However, education seems to be an important asset. The cases attributable to low educational attainment are lower than those reported globally, and there is even a noticeable trend toward improvement. Moreover, education has the potential to influence other RF control, as prevention policies seem to be better implemented in a highly educated population, and it is a key tool to achieve social and gender equity.

When we compared other regional PAF calculations to the one in Argentina, the PAFs for dementia considering the 12 RFs have been calculated for some countries, such as the USA (41%) [26], New Zealand (47%) [27], Australia (40.6%) [28], and Brazil (48%). In addition to a marked difference in the total PAF, the distributions of some factors are different. For example, less education in the USA showed an individual PAF of 11%, 14% in India, and 11% in China [3], while in Argentina it was only 2%.

It could be argued that these experiences describe populations very dissimilar in both culture and genetics, which is why it is necessary to compare with different Latin American populations. A study with data from Cuba, Dominican Republic, Mexico, Peru, Puerto Rico, and Venezuela calculated a similar overall PAF for Latin America (56%) with less education as the main factor (11% PAF) [3]. This study only assesses nine factors, which may underestimate the total PAF, and presents an overrepresentation of Caribbean countries (with which Argentina shares fewer similarities). Even when we compared our findings with similar countries in terms of ethnicity, economy, and culture, such as those in the southern region of Latin America, we found that Argentina had marked differences in overall RF and the distribution of RF. In Chile [5], the total PAF was lower (47%) but analyzing only nine of the 12 factors. Education had a higher PAF (up to 11% depending on the age group), but excessive alcohol consumption, was up to twenty times lower (0.1%) compared to the Argentinean estimates. In Brazil [4], the total PAF was 48% with higher individual PAF for less education (8%) and hearing loss (7%), and a lower PAF for excessive alcohol consumption (0.3%). These findings underscore the need to estimate the proportion of attributable cases of dementia for each country in Latin America to design effective strategies for dementia prevention. As mentioned earlier, these differences arise from the cultural and economic heterogeneity inherent in a vast territory, encompassing 13% of the habitable surface of the planet, such as Latin America. While this study highlights variations in RFs, it also underscores the imperative to investigate the socioeconomic and cultural differences that give rise to them. It is reasonable to anticipate that a national survey may not fully address this complexity. Therefore, multinational studies are essential to explore the interactions between social factors and these RFs.

With women having had a greater prevalence of dementia, a closer look at gender differences in the modifiable risk for dementia is warranted. While excessive alcohol consumption accounts for a higher percentage of attributable cases in men, social isolation and smoking had a larger PAF in women. However, as we used living alone as a proxy for social isolation, the large PAF for social isolation may be an overestimation since living alone does not necessarily mean not having enough social contact. Although excessive alcohol consumption is expected to occur more in men than in women, the high PAF for smoking in women is intriguing. Prevention strategies that are directed toward women may be more effective in reducing the impact of smoking. It is possible that the higher prevalence of dementia in women is partly the result of a failure to understand sex differences in RF and the need to address them with gender-specific health policies.

Our results also showed that income was related to overall PAF mainly driven by differences in the PAF for less education. This is particularly interesting in the context of Argentina, where education (including college degrees) is free for all citizens. Individuals with low income are still likely to

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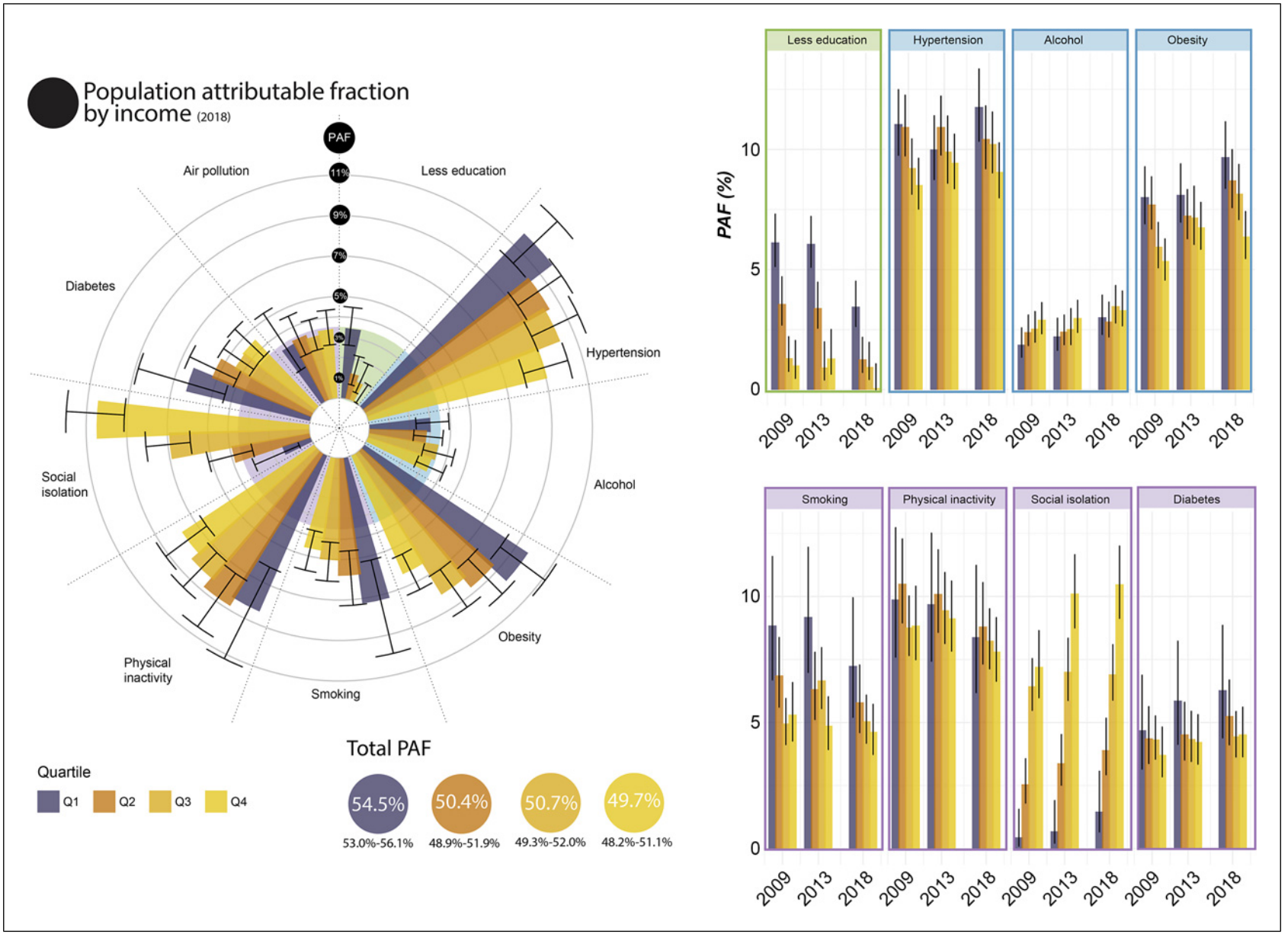

Fig. 3. PAF of potentially modifiable RFs for dementia by income. On the left, circular bar chart with the individual PAF for each RF in each income quartile. Below, the total PAF for quartile groups with its 95% confidence interval. On the right, the individual PAF value for each RF by income and year.

face barriers other than the cost of education, such as access to transport, study materials, and protected time to study. Moreover, adolescents from low-income families may need to abandon school to help with their household income. When analyzing school dropout after primary education, the most frequent reasons were working (20%), financial difficulties (14%), and care duties (14%), all reasons linked to family income [29]. In fact, there is a negative relationship between participation in the labor market and school attendance: 45% of adolescents who left school were involved in economically productive activities [30]. Hypertension and obesity were two other factors that were inversely related to income. The complexity of RF sources undoubtedly needs to take into account socioeconomic factors.

The interaction between socioeconomic variables and RFs is a key aspect when discussing Argentina. The country exhibits a highly dynamic economic scenario. These data are derived from the latest available survey (2018); however, Argentina has been undergoing an economic crisis since 2017, which escalated rapidly with the COVID-19 pandemic and events triggering inflationary economies worldwide since 2020. Despite having a poverty rate of 25.7% in 2017, Argentina concludes 2022 with a rate of 39.2%. This surge in poverty undoubtedly determines an increase in RFs.

While the available data up to date suggest that metabolic syndrome may be the most efficient target for intervention, it is anticipated that education will assume a new role. Additionally, a contemplation is warranted; there may be a temporal interval between a variation in a socioeconomic condition strongly linked to a RF and the emergence of that RF, a timeframe that can vary based on the inherent resilience of that factor to change. For instance, an increase in obesity may be expected a few months after a dietary change, while deficiencies in education may take decades to manifest.

From this perspective, our current results represent a snapshot of the past. Hence, we aim to showcase two aspects: the trend over the last 10 years and the interaction with socioeconomic levels. We believe that a thorough analysis of these variables can enable us to be prepared for the new scenario posed by the economic crisis [31].

An accurate understanding of the distribution of RFs may exceed primary prevention. RF profiles should also be considered in the implementation of novel disease-modifying therapies for conditions like Alzheimer's disease. We tend to think of neurodegenerative diseases as the result of consecutive events, where one process is inevitably linked to the next [32, 33]. Nevertheless, we now recognize the existence of forces capable of modifying the onset of symptoms or the speed at which they progress. RFs directly affect these forces, for example, education is an important component of cognitive reserve, and cardiovascular RFs are associated with cerebrovascular damage and thus lower brain resistance in adapting to neurodegenerative diseases. The differential distribution of these factors between men and women could potentially explain why new therapies, such as Lecanemab [33], exhibit varying effectiveness between the sexes in sub-analyses. Therefore, it is important to consider regional variations in modifiable RF, as they can alter treatment response. Therefore, in addition to observational studies, clinical trials targeting RF control are crucial, such as the trial of lifestyle changes to prevent cognitive impairment in Latin America (LatAm-FINGERS), which is investigating a multidomain intervention in 12 Latin American countries [9].

Our work has some limitations. Some RF (e.g., social isolation and air pollution) was not fully harmonized with previous studies [2, 17]. In addition, data on depression, hearing loss, and TBI had to be extracted from other sources. This may have led to certain biases that can lead to overestimating the PAF, especially when interpreting the absence of cohabitation as social isolation. As poverty is associated with a higher incidence of cohabitation due to limited housing opportunities, our approach tends to overestimate the effect of social isolation in the higher economic strata. It is to be expected that these data may be tainted with information biases. In this discussion, we encourage the reader to take this into consideration, not as the best evidence, but as the best available.

We found that Argentina has enormous potential for prevention, as it exhibits a markedly higher total PAF compared to other high-income countries. Although it has a free education system, metabolic syndrome control seems to be the most important challenge for dementia risk reduction in Argentina. Furthermore, notable sex differences were found as men should be targeted to reduce excessive alcohol consumption, while programs to reduce social isolation and smoking should be implemented for women. Our findings suggest that evaluation of the risk profile by gender and socioeconomic status can contribute to the design of tailored interventions to reduce dementia risk.

Statement of Ethics

This study protocol was reviewed and approved by local Fleni IRB (Comite de etica e investigacion, Fleni, Buenos Aires, Argentina), approval number 340. The study received an exemption due to the nature of the research using census data.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

I.L.C. was responsible for data curation, design, statistical analysis, and manuscript preparation. G.L. took charge of design, contextualization of the results, result review, and manuscript work. R.P. handled the review of statistical analysis and data curation, reviewed, and approved the manuscript. R.O. was responsible for the design and contextualization of information and manuscript review. L.C. was involved in contextualizing the results and manuscript review. C.K.S. managed the research design, contextualization, execution planning, statistical analysis supervision, manuscript preparation, and final review.

Data Availability Statement

The data utilized in this study is publicly accessible and can be located at the web address referenced in the methodology section of the text. Furthermore, the analysis and the code employed in this study are also publicly available and can be found on the author's website, as indicated in the text.

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