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Original Article

Preventing dementia in Italy: Estimations of modifiable risk factors and public health implications

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Background: Dementia is a major global public health challenge, with over 50 million cases in 2020, projected to reach 152 million by 2050. Effective prevention strategies are needed to reduce the impact of modifiable risk factors associated with dementia, particularly in countries with ageing populations like Italy. The Population Attributable Fraction (PAF) and Potential Impact Fraction (PIF) are key metrics for understanding and reducing dementia cases through targeted interventions.
Objectives: This study aimed to revise and expand PAF estimates for dementia in Italy, integrate them with PIF calculations, and assess the alignment of regional health policies with these risk factors. Additionally, the study explored regional variations in PAFs and evaluated the potential for reducing dementia incidence through feasible public health interventions.
Design: A cross-sectional analysis was conducted using data from two national public health surveillance systems, PASSI and PASSI d'Argento (PdA), to estimate PAFs and PIFs for dementia at both national and regional levels. The study used data collected between 2017 and 2019.
Setting: Data were drawn from 19 Italian regions and two autonomous provinces, providing national and subnational estimates of modifiable risk factors for dementia.
Participants: The study population included a nationally representative sample of 86,494 individuals aged 18–64 (PASSI) and 48,516 individuals aged 65 and older (PdA).
Measurements: PAFs were calculated for 11 of the 12 modifiable risk factors identified by the Lancet Commission in 2021, with data from the PASSI and PdA systems. PIFs were calculated to estimate the potential reduction in dementia cases under different intervention scenarios. Regional variations in PAFs were assessed and aligned with health policies outlined in the Regional Prevention Plans.
Results: The national combined PAF for 11 modifiable risk factors was 39.6 % (95 % CI: 20.8–55.9). Midlife hypertension and physical inactivity were the most significant contributors, accounting for 12.3 % of the total PAF. Cardiovascular risk factors collectively explained over 50 % of preventable dementia cases. Regional PAFs ranged from 31.7 % to 47.5 %, with a clear north-south gradient; southern regions exhibited higher PAFs due to cardiovascular factors. Despite broad consistency between national and regional PAFs, significant variability was found in how regions addressed risk factors, particularly air pollution. At the national level, a 10 % reduction in risk factors would prevent 54,495 dementia cases, with subnational PIFs ranging from 3.7 % to 6.0 %.
Conclusions: This study highlights the substantial potential for dementia prevention in Italy through targeted public health interventions. However, significant regional disparities in PAFs and the alignment of health policies underscore the need for a more nuanced, regionally tailored approach. Future strategies should integrate both PAF and PIF to maximize the impact of interventions, particularly in addressing cardiovascular risk factors. These findings can guide the development of evidence-based policies to reduce dementia incidence across Italy.

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1. Introduction

Dementia is a significant and growing public health challenge worldwide. Its prevalence rapidly increases due to longer life expectancy and demographic shifts toward older populations. In 2020, over 50 million people globally were living with dementia, a number projected to triple by 2050, reaching 152 million [1]. The economic burden is substantial, with the global cost of dementia care estimated at about 1.3 trillion US$ in 2019 and expected to reach 2.8 trillion US$ by 2030 [2].. These statistics highlight the urgent need for effective public health strategies to lessen the impact of dementia.

In response to the growing dementia crisis, the World Health Organization (WHO) established the Global Action Plan on the Public Health Response to Dementia 2017–2025 [3]. One of its global targets, the third, emphasizes the importance of reducing risks and enhancing preventive measures to lower the incidence of dementia [3]. This objective is crucial because a significant portion of dementia cases could potentially be prevented through targeted interventions aimed at reducing these risk factors throughout a person's life [4,5].

It also emphasises the link between the prevention of major non-communicable diseases (NCDs) and the relevant global targets defined by the Global Plan of Action for the Prevention and Control of Non-Communicable Diseases 2013–2020, extended to 2030 [3,6].

From a neuroepidemiological perspective, it is important to properly define and understand the impact of different risk factors on the prevalence of dementia. This requires the use of specific metrics, such as the Population Attributable Fraction (PAF) and the Potential Impact Fraction (PIF) [7,8].

The PAF quantifies the percentage of dementia cases that can be attributed to a specific risk factor within a population [7,8]. It allows to estimate how many dementia cases could be avoided by eliminating the contribution of each risk factor [7,8]. On the other hand, PIF looks at the potential decrease in new cases that could be achieved through realistic, partial reductions in exposure to risk factors rather than complete elimination [7,8]. This distinction is crucial for developing practical public health interventions that align with achievable goals in real-world settings.

The PAF for dementia varies significantly across nations and populations due to differences in the prevalence of risk factors, genetic predispositions, and socio-economic contexts [9–16]. For instance, high-income countries may have different PAF values compared to low- and middle-income countries due to variations in lifestyle, healthcare infrastructure, and education levels [9–16]. Cultural factors and health policies also play pivotal roles in influencing these differences.

Therefore, a one-size-fits-all approach to dementia prevention is ineffective. Tailored strategies taking into account the national and subnational prevention planning, including local epidemiological data as well as contextual factors, are essential to successfully reduce the risk of dementia at the population level [17].

In Italy, PASSI and PASSI d'Argento (PdA) are two public health surveillance systems that gather information on a broad range of health-related behaviours and the main modifiable risk factors linked to the development of chronic noncommunicable diseases [18,19]. PASSI targets individuals aged 18 to 69, while PdA focuses on those aged 65 and older.

Understanding and updating the PAF and PIF for dementia is particularly critical for Italy, a country with one of the oldest populations globally [20]. A previous study [21] of the entire Italian population focused on the nine potentially modifiable risk factors outlined by the Lancet Commission in 2017 [4]. The study estimated that up to 31.4 % of Alzheimer's disease (AD) dementia and up to 37.8 % of vascular dementia (VaD) cases could potentially be prevented [21].

In 2020, the Lancet expanded the list of potentially modifiable risk factors to 12 [5]. These factors include less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, low social contact, alcohol consumption, traumatic brain injury, and air pollution.

Each factor contributes differently to the overall dementia burden in various settings. Precise and updated calculations of PAF and PIF are necessary for effectively informing and prioritizing preventive strategies in public health policy [17].

This requires continuous research and data collection tailored to the specific national and subnational demographic and socio-economic landscape to ensure that interventions are evidence-based and contextually appropriate.

Our study aims to update and integrate previous PAF estimations with PIFs for all-cause dementia at the national and subnational levels. These estimations are based on the 12 potentially modifiable risk factors identified by the Lancet Commission in 2020. Additionally, we provide context for these estimations to align with Italy's unique epidemiological and health policy environment.

2. Methods

2.1. Sources

Data on the prevalence of modifiable dementia risk factors in Italy's 19 regions and two Autonomous Provinces were sourced from PASSI and PdA, public health surveillance systems modeled on the Behavioural Risk Factor Surveillance (BRFS) [22]. These systems, mandated by the Ministry of Health and National Center for Disease Prevention and Control (CCM), were developed with regional collaboration to monitor, plan, and evaluate policies for preventing chronic noncommunicable diseases as outlined in national and regional prevention plans (PNP and PRP). Both systems are centrally coordinated by the Italian National Institute of Health (ISS) [23].

PASSI and PdA continuously monitor health-related behaviors and risk factors linked to chronic diseases (e.g., cardiovascular, cancer, diabetes) respectively in individuals aged 18–69 and 65+. Both employ cross-sectional surveys, collecting data monthly from random samples drawn from local health unit (LHU) resident lists. Stratified by sex and age, trained LHU personnel conduct phone interviews using standardized questionnaires. Eligible participants include residents contactable by phone, excluding hospitalized individuals, nursing home residents, prisoners, and non-Italian speakers, except in Bolzano, where interviews can be conducted in German. Data are merged, weighted, and analyzed for national and regional estimates. Detailed methodologies are available elsewhere [18,19,24–26].

PASSI and PdA provide age-specific prevalence data for 11 of the 12 modifiable risk factors identified by the 2020 Lancet Commission, excluding traumatic brain injury. Supplementary Table 1 summarizes these risk factors by life phase, per the Lancet Commission's 2020 model.

For this study, we used pre-pandemic data (2017–2019) due to the COVID-19 pandemic's impact on surveillance in 2020. Data were derived from the PASSI sample of 86,494 individuals aged 18–64, and the PdA sample of 48,516 individuals aged 65+. Data for 2017–2019 were available for all regions, except Lombardy, which exited the systems in 2017, and Valle d'Aosta, which did not participate in PdA during this period.

2.2. Statistical analysis

Data on modifiable dementia risk factors for Italy and its regions were obtained from the PASSI and PdA surveillance systems. To calculate the Population Attributable Fraction (PAF), the method outlined by the Lancet Commission was used [5,27]. PAF for each risk factor "i" was estimated using the formula:

$$PAF_i=\left[P_i\left(RR_i-1\right)\right]/\left[1+P_i\left(RR_i-1\right)\right],$$

where P_i is the prevalence of each factor (from PASSI and PdA) and RR_i is its relative risk of dementia (from the Lancet Commission) [5,13]. The total PAF was calculated as:

$PAF_{combined} = 1 - \Pi(1 - PAF_i)$

However, this overestimates the cumulative PAF since it assumes risk factors act independently. To adjust for interdependence, the Lancet Commission's formula was applied:

$PAF_{combinedadjusted} = 1 - \Pi(1 - w_i * PAF_i)$,

where w_i = 1 - Communality. The communality, which measures the interdependence of risk factors, was calculated nationally on the combined and appropriately weighted PASSI and PdA samples using the tetrachoric correlation matrix obtained from a principal component analysis [28]. Individual adjusted PAFs were then calculated using:

$PAF_{individual\ adjusted} = PAF_{combined\ adjusted} * (PAF_i / \Sigma PAF_i)$.

We also modeled more realistic scenarios by calculating the Potential Impact Fraction (PIF) for a partial reduction in risk factors using Barendregt and Veerman's formula [29]:

$PIF_i = ([P_i - P'_i] * [RR_i - 1]) / [1 + P_i(RR_i - 1)]$.

Confidence intervals for both PAF and PIF were calculated using RR confidence intervals from the Lancet Commission [5]. As with PAF, the PIF was adjusted for communality:

$PIF_{combined\ adjusted} = 1 - \prod (1 - w_i * PIF_i)$.

We then calculated the number of dementia cases that could have been avoided in Italy with a 10 % reduction in each risk factor by applying the PIF to the number of dementia cases estimated in the Italian resident population as of January 1, 2024, using the prevalence data from Bacigalupo et al. [30,31]. Regional analyses used regional prevalence data from PASSI and PdA, and the same communality estimated at national level. The choice to use national estimated communality aims to enable precise comparisons between regions and between regions and the national level. Analyses were performed using STATA version 17.0.

2.3. Evaluation of regional PAFs and health policies

To assess the coherence between the PAF for dementia by risk factor at the regional level and the corresponding health policies implemented for dementia prevention, we analyzed data across Italy's 21 regions. Based on the 95 % confidence interval of the national PAF, three scenarios were defined for regional PAFs in comparison to the national PAF: (1) PAF lower than the national PAF, (2) PAF in line with the national PAF, and (3) PAF higher than the national PAF.

Health policies related to dementia prevention were classified into three categories: (1) policies with direct impact on the risk factor, (2) policies with indirect impact on the risk factor, and (3) absence of policies with either direct or indirect impact on the risk factor. These categories were identified through a document analysis of the 21 Italian Regional Prevention Plans, and a more detailed description of the methodology can be found in our group's previous publication [17].

By combining the three PAF scenarios with the three categories of health policies, we obtained nine distinct categories, allowing for a comprehensive understanding of how well regional policies align with dementia risk reduction strategies.

3. Results

3.1. National and subnational population attributable fractions (PAFs)

In Italy, we estimated that the combined Population Attributable Fraction (PAF) for 11 of the 12 risk factors identified by the Lancet Commission is 39.6 % (95 % CI: 20.8 - 55.9) (see Table 1). The PAF associated with traumatic brain injury (TBI) could not be calculated. We observed significant variability in the contributions of individual potentially modifiable risk factors. Midlife hypertension emerged as the risk factor with the highest weighted PAF (6.5 %, 95 % CI: 2.1 - 10.4), followed by physical inactivity in later life (5.8 %, 95 % CI: 2.8 - 8.3). Diabetes in later life and midlife obesity contributed an additional 4.2 % (95 % CI: 2.9 - 5.3) and 3.4 % (95 % CI: 2.1 - 4.5) to the PAF, respectively. These cardiovascular risk factors collectively accounted for 50.3 % of the combined PAF. Later-life depression was associated with a PAF of 4.5 % (95 % CI: 3.1 - 5.8), and social isolation in later life was linked to a PAF of 4.2 % (95 % CI: 2.7 - 5.4). Hearing loss, assessed in a later-life population (i.e., 65–69 years), was associated with a PAF of 2.3 % (95 % CI: 1.0 - 3.7). Smoking in later life and alcohol consumption in midlife were associated with PAFs of 2.3 % (95 % CI: 0.6 - 4.0) and 0.1 % (95 % CI: 0.0 - 0.1), respectively. Finally, lower education in early life and exposure to air pollution in later life were associated with PAFs of 5.0 % (95 % CI: 2.5 - 7.1) and 1.2 % (95 % CI: 1.0 - 1.4), respectively. Moreover, we estimated combined and individual PAFs for each Italian region (see Fig. 1). Reflecting the significant variability in the prevalence of the 11 risk factors across Italian regions (see Supplementary Table 2), we observed heterogeneous combined and individual PAFs at the sub-national level. The combined PAF ranged from a minimum of 31.7 % to 47.5 %. We observed a noticeable north-south gradient, with lower PAFs in the northern regions and higher PAFs in the southern regions (see Supplementary Figures 1–3). This gradient was mainly due to variations in PAFs linked to cardiovascular risk factors (see Fig. 2). In the southern regions, we observed that PAF associated with midlife hypertension and physical inactivity in later life accounted for up to 8.8 %

Table 1
Population attributable fractions of dementia cases in Italy. Years 2017–2019.

	RR (95 % CI)	Prevalence	Communality	PAF Unweighted	PAF Weighted (CI 95 %)
Early life (age <45 years)					
Less education	1.59 (1.26–2.01)	21 %	50 %	11.7 %	5.0 % (2.5–7.1 %)
Midlife (age 46–65 years)					
Hearing loss[$]	1.94 (1.38–2.73)	6 %	18 %	5.1 %	2.3 % (1.0–3.7 %)
TBI	1.84 (1.54–2.20)	N.A.	N.A.	N.A.	N.A.
Hypertension	1.61 (1.16–2.24)	29 %	26 %	14.8 %	6.5 % (2.1–10.4 %)
Alcohol	1.18 (1.06–1.31)	1 %	75 %	1.8 %	0.1 % (0.0–0.1 %)
Obesity	1.60 (1.34–1.92)	14 %	59 %	7.7 %	3.4 % (2.1–4.5 %)
Later life (age >65 years)					
Smoking	1.59 (1.15–2.20)	9 %	52 %	5.7 %	2.3 % (0.6–4.0 %)
Depression	1.90 (1.55–2.33)	13 %	68 %	10.5 %	4.5 % (3.1–5.8 %)
Social isolation	1.57 (1.32–1.85)	19 %	16 %	10.2 %	4.2 % (2.7–5.4 %)
Physical inactivity	1.39 (1.16–1.67)	40 %	69 %	13.8 %	5.8 % (2.8–8.3 %)
Diabetes	1.54 (1.33–1.79)	20 %	41 %	9.1 %	4.2 % (2.9–5.3 %)
Air pollution[§]	1.09 (1.07–1.11)	33 %	90 %	3.2 %	1.2 % (1.0–1.4 %)
Overall PAF				**62.1 %**	**39.6 % (20.8–55.9 %)**

[$] Estimated using PdA data regarding individuals aged between 65 and 69 (data from Piemonte is unavailable).
[§] Estimated using the urbanization level of the resident municipality as a proxy.

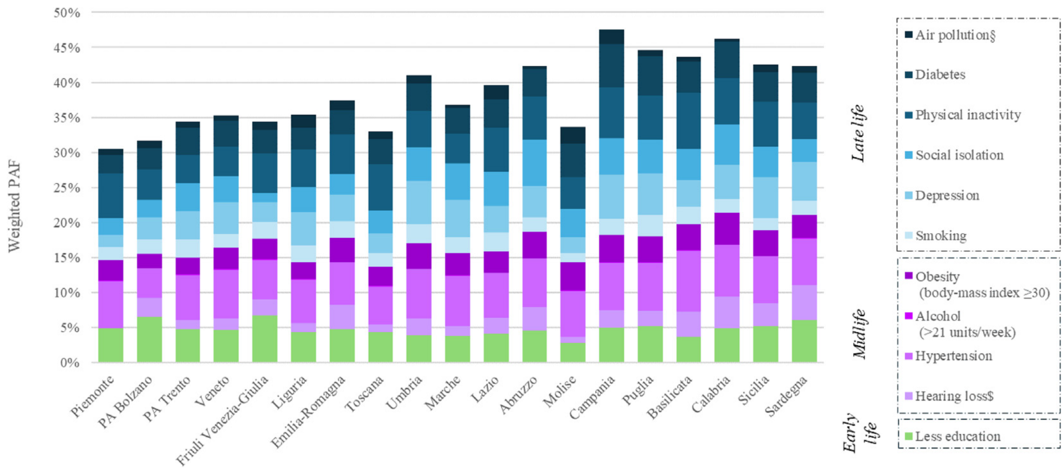

Fig. 1. Regional estimates of weighted Population Attributable Fractions of dementia cases. Years 2017–2019.

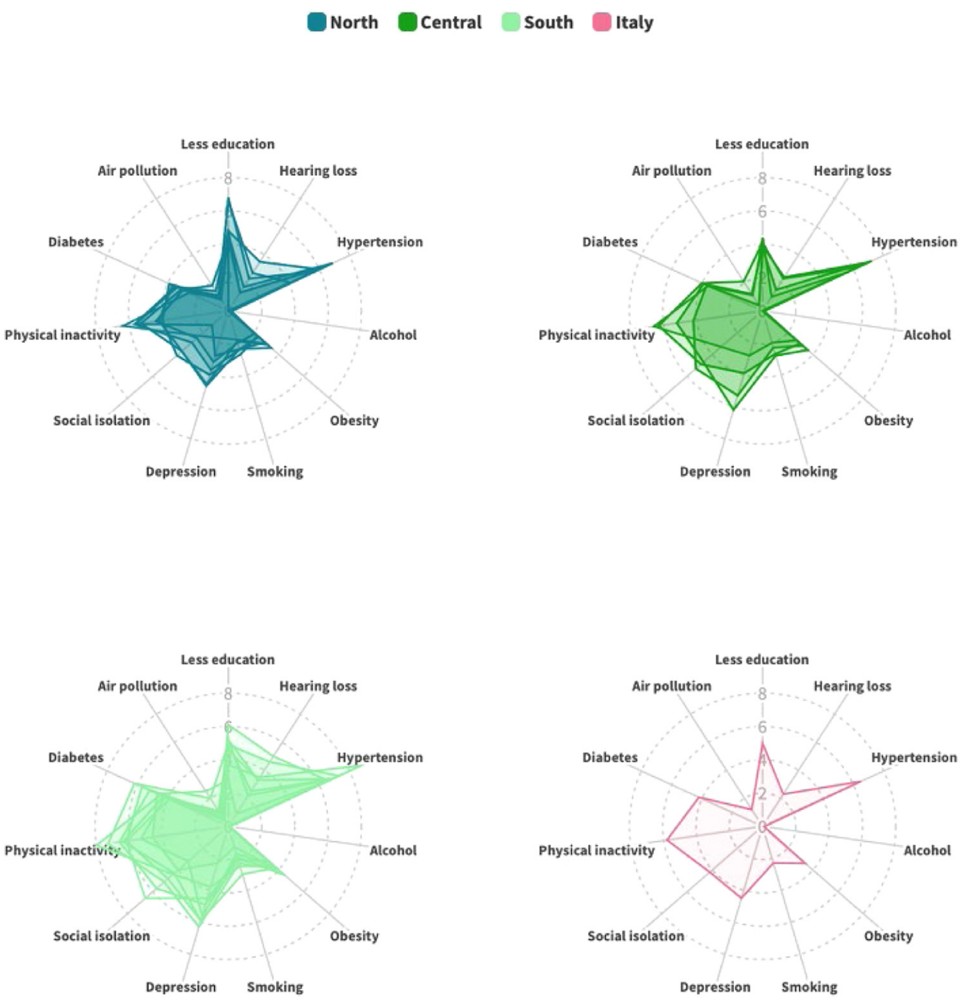

Fig. 2. Regional estimates of weighted Population Attributable Fractions of dementia cases by macroarea. Years 2017–2019.

(95 % CI: 2.9 % - 13.2 %) and 8.0 % (95 % CI: 4.0 % - 10.9 %) respectively; the highest PAF for diabetes in later life was found to be 6.2 % (95 % CI: 4.4 % - 7.5 %), and the highest PAF for midlife obesity was observed to be 4.5 % (95 % CI: 3.0 % - 5.8 %). In the northern regions, we observed the lowest PAFs for depression and diabetes in later life, at 1.7 % (95 % CI: 1.1 % - 2.3 %) and 2.5 % (95 % CI: 1.7 % - 3.5 %), respectively. In this area, we also observed the lowest PAFs for midlife hypertension and obesity, at 4.1 % (95 % CI: 1.2 % - 7.1 %) and 2.1 % (95 % CI: 1.3 % - 2.9 %), respectively. Finally, PAFs associated with air pollution, hearing loss, and social isolation in later life exhibited the highest variability across different regions, with the highest PAFs more than five times greater than the lowest PAFs.

3.2. Population-level interventions alignment with subnational PAFs

At the subnational level, PAFs were broadly consistent with the national estimates across most regions and APs. Despite this overall homogeneity in PAFs, we identified significant heterogeneity in the align-

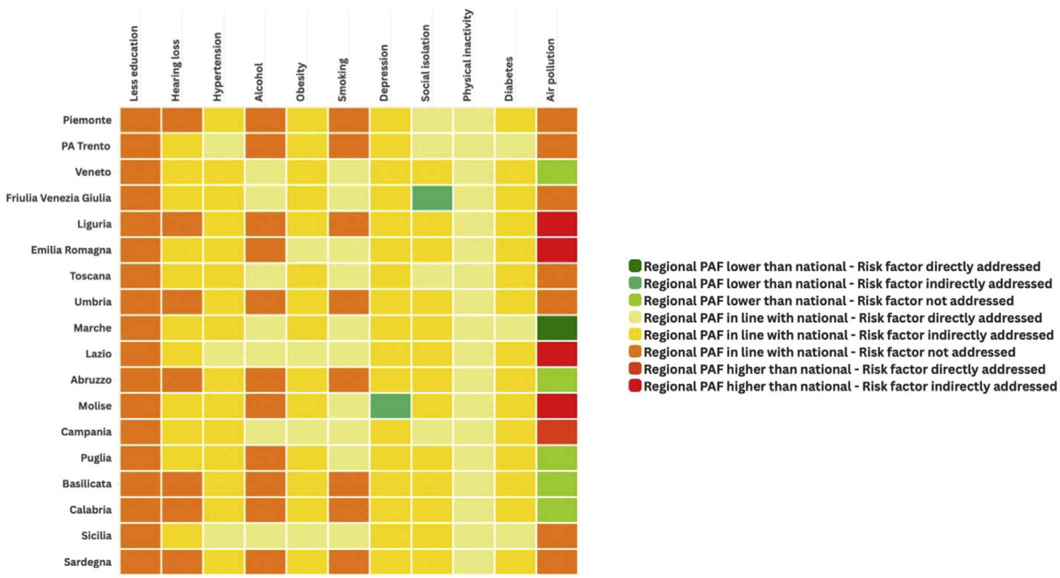

Fig. 3. Coherence between regional PAFs for dementia and population-level interventions by risk factor
Notes: a) the scenario "Regional PAF higher than national – Risk factor not addressed" was not found in our data; b) the Autonomous Province of Bolzano is excluded as its Regional Prevention Plan's organisation did not allow for the analysis of dementia-specific preventive interventions.

ment between the PAFs of specific risk factors and the corresponding subnational health policies aimed at dementia prevention (see Fig. 3). In the two regions where PAFs associated with depression and social isolation were lower than the national average (Molise and Friuli Venezia Giulia, respectively), these risk factors are addressed indirectly through broader population-level interventions. Among the five regions with PAFs for air pollution higher than the national average, only one region (Molise) has implemented direct interventions targeting air pollution as part of their population-level dementia prevention strategies. In comparison, the remaining four Italian regions do not address this risk factor, either directly or indirectly, in their dementia prevention policies.

In regions where PAFs aligned with the national data, the most common scenario was "PAF in line with national - Risk factor indirectly addressed" (n = 85). This was followed by "PAF in line with national - Risk factor not addressed" (n = 51) and "PAF in line with national - Risk factor directly addressed" (n = 49), indicating variability in the approach to risk factor management across different regions. Among the five regions where PAFs associated with air pollution were higher than the national average, only Campania includes air pollution as a specific target in its population-based dementia prevention interventions. In contrast, the remaining four Italian regions address air pollution risk factors indirectly through other dementia prevention strategies.

3.3. National and subnational potential impact fractions (PIFs)

In Italy, we estimated 142,445 dementia cases by applying age- and gender-specific prevalence data from Bacigalupo et al. [30] to the resident population as of January 1, 2024 [31]. A 10 % reduction in the 11 potentially modifiable risk factors would have resulted in a 4.8 % (95 % CI: 2.3 % - 7.5 %) reduction in the prevalence of dementia at the national level during the reference period, corresponding to 54,495 (95 % CI: 26,011 - 85,420) preventable cases during the period 2017–2019 in Italy (see Table 2).

At the subnational level, PIFs ranged from 3.7 % (95 % CI: 1.7 % - 6.3 %), corresponding to 325 avoidable dementia cases that could be avoided in the AP of Bolzano, to 6.0 % (95 % CI: 3.0 % - 9.2 %) in the Campania region, corresponding to 4911 avoidable dementia cases (see Table 2).

4. Discussion

Our study provides a comprehensive update and expansion of previous estimations of the Population Attributed Fraction for dementia in Italy [21]. We integrate these findings with the Potential Impact Fraction to offer a more nuanced understanding of the potential for reducing dementia incidence through clinical and public health interventions.

We estimated that 39.6 % of dementia cases in Italy could be attributed to 11 modifiable risk factors, with midlife hypertension and physical inactivity in later life being the most significant contributors. Regional variations were notable, with higher PAFs observed in southern regions, driven by cardiovascular factors, while northern regions had lower PAFs for factors like depression, diabetes and physical inactivity. Despite overall consistency between regional and national PAFs, there was significant heterogeneity in how regions addressed these risk factors in their dementia prevention strategies. At the national level, a 10 % reduction in risk factors could have prevent 4.8 % of dementia cases, equivalent to 54,495 cases.

Our study has several strengths. One of the primary strengths is using data from two national surveillance systems that share the same methodology regarding selection criteria, sampling, data collection, analysis instruments, and operational protocols [18,19]. The robustness of our findings is supported using two national surveillance systems, PASSI and PdA, which follow a standardized methodology across selection criteria, sampling, data collection, and analysis. Another strength is the calculation of prevalence estimates from a large, gender- and age-representative sample of the Italian population aged 18 and over [18,19]. The congruence of these systems ensured precise PAF and communality calculations among the investigated risk factors in Italy. This extensive coverage ensures that our results reflect the broader population, enhancing the generalizability of our findings. Finally, data from the PASSI and PdA surveillance systems are publicly accessible and practically actionable, allowing decision-makers to translate our findings for evidence-based policy planning and interventions easily. It is, however, important to mention that recent findings from the Lancet Commission introduced high cholesterol and vision loss as new risk factors, highlighting areas for future research [32]. Although these risk factors are not part of the study carried out within the Italian Fund for Alzheimer's and other Dementias 2021–2023 [33], they offer opportunities to enhance our analysis and deepen our understanding of dementia's complex risk

Table 2
Potential impact fractions and estimated reductions in Italian dementia cases with 10 % risk factor reductions.

			Base case: 10 % reduction in the prevalence of the 11 potentially modifiable risk factors	
	Population[$], N°	Dementia cases[§], N°	Weighted PIF, (95 % CI)	Avoidable cases, N° (95 % CI)
Italy	**14,357,928**	**1,142,445**	**4.8 % (2.3–7.5 %)**	**54,495 (26,011–85,420)**
Piemonte	1,131,007	93,432	3.9 % (1.7–6.3 %)	3,676 (1602–5876)
AP Bolzano	110,599	8,893	3.7 % (1.7–5.9 %)	325 (152–523)
AP Trento	128,631	10,289	4.0 % (1.9–6.4 %)	414 (193–657)
Veneto	1,186,333	94,959	4.1 % (1.9–6.6 %)	3,936 (1843–6233)
Friulia Venezia Giulia	324,357	27,181	4.0 % (1.8–6.5 %)	1,100 (500–1764)
Liguria	437,058	38,693	4.2 % (1.9–6.6 %)	1,606 (753–2543)
Emilia-Romagna	1,098,680	92,197	4.5 % (2.1–7.1 %)	4,106 (1902–6545)
Toscana	967,750	81,434	3.8 % (1.8–6.1 %)	3,119 (1459–4951)
Umbria	230,358	19,727	5.0 % (2.4–7.8 %)	984 (471–1536)
Marche	388,515	32,872	4.3 % (2.1–6.8 %)	1,426 (679–2237)
Lazio	1,341,439	106,079	4.8 % (2.3–7.5 %)	5,066 (2415–7944)
Abruzzo	324,828	26,020	5.2 % (2.5–8.0 %)	1,345 (652–2088)
Molise	77,275	6,303	3.9 % (1.9–6.1 %)	246 (119–386)
Campania	1,169,476	81,630	6.0 % (3.0–9.2 %)	4,911 (2463–7470)
Puglia	942,120	71,298	5.5 % (2.7–8.5 %)	3,955 (1938–6094)
Basilicata	135,107	10,705	5.4 % (2.5–8.4 %)	575 (269–896)
Calabria	439,617	33,136	5.8 % (2.8–8.9 %)	1,922 (940–2961)
Sicilia	1,113,466	81,795	5.2 % (2.5–8.1 %)	4,275 (2068–6643)
Sardegna	420,835	32,069	5.2 % (2.5–8.1 %)	1,661 (786–2608)

[$] Resident population aged 65+ on 1st January 2024. Downloaded at www.demo.istat.it on April 11 2024.
[§] Estimated using the urbanization level of the resident municipality as a proxy.

profile. Additionally, it will be essential for future studies to investigate how the COVID-19 pandemic has impacted the distribution of risk factors, particularly social isolation, which may have further influenced dementia risk trajectories. A further limitation stems from the self-reported nature of data collection. Self-reported data can introduce biases, as they cannot be validated with objective measures, potentially leading to underestimations or overestimations of certain risk factors. Nevertheless, it is essential to note that self-reported data have demonstrated robust consistency and sensitivity in previous research, making them valuable for monitoring trends and changes over time [34]. While this limitation is inherent in many large-scale epidemiological studies, the strengths of our study design, particularly the use of consistent methodologies and large, representative samples, help to mitigate these potential biases and ensure the reliability of our findings.

4.1. PAFs, PIFs and the Italian health policy environment

In line with data published from a few other European countries [35], the national combined PAF for the 11 modifiable risk factors was estimated at 39.6 %, underscoring the significant potential for dementia prevention in Italy. Our study identified midlife hypertension and physical inactivity in later life as the most influential factors, collectively contributing to more than 12 % of the combined PAF. This finding is consistent with previous studies from both the European region and globally [35]. Nearly half of the preventable dementia cases were associated with cardiovascular risk factors, such as hypertension, obesity, diabetes and physical inactivity, reinforcing the importance of shared dementia prevention strategies that leverage resources dedicated to heart and brain health initiatives [36]. For purposes of discussion, it is essential to contextualize the national-level data within the framework of the Lancet Commission findings [5]. While the overall national PAF closely aligns with the figures reported in the 2020 Lancet Commission - the reference report for this study, notable discrepancies emerge in the contribution of individual risk factors (see Table 1). The Lancet report attributes 2 % of dementia cases to hypertension, with a PAF of 2.2 % [5]. In contrast, data derived from the Italian national surveillance systems indicate a substantially higher proportion, with a PAF of 6.5 %. Similarly, alcohol consumption represents another notable example: in our study, it was associated with a PAF 10 times lower than that reported by the Lancet Commission [5]. Moreover, we found that only 2.3 % of dementia cases in Italy can be linked to hearing loss, which is lower than global estimates [5]. This lower percentage may be due to differences in the definition of hearing loss or how the survey was conducted. Since the survey was performed by phone, it might have indirectly excluded a proportion of individuals with hearing loss. These discrepancies emphasize the importance of analyzing national-level data to complement and refine global estimates. They also highlight the critical need for collaborative efforts in designing and implementing harmonized and sustainable prevention models that account for contextual characteristics and regional differences.

At the subnational level, the PAFs for most regions aligned with national data. However, notable exceptions emerged, especially concerning air pollution, where difficulties in defining indicators – such as the urbanisation level of the municipality – led to significant variations in PAFs among regions. Additionally, our analysis uncovered a complicated landscape of regional health policy responses throughout Italy. Among the five regions where PAFs for air pollution surpassed the national average, only Campania initiated direct population-level interventions aimed at this risk factor within dementia prevention strategies, underscoring a crucial gap in public health policy. In regions like Molise and Friuli Venezia Giulia, where PAFs for depression and social isolation were below the national average, these risk factors were addressed through structured interventions targeting other established dementia risk factors, indirectly impacting both depression and social isolation. For the remaining risk factors, the most frequently observed scenario across regions was that PAFs matched national data, while population-level interventions targeting dementia either neglected or indirectly addressed these risk factors. This pattern reveals the variability in how regions handle dementia risk factors, indicating that national guidelines may not be fully suited to regional contexts.

Integrating PAFs with PIFs adds an important dimension to the assessment of dementia prevention strategies. A 10 % reduction in the prevalence of the 11 modifiable risk factors would have prevented approximately 54,495 dementia cases in Italy. At the subnational level, PIFs ranged from 3.7 % in the Autonomous Province of Bolzano to 6.0 % in Campania, indicating that even regions with lower PAFs could significantly reduce dementia cases through targeted interventions. This further emphasises the importance of tailored, region-specific strategies in reducing dementia incidence across Italy.

4.2. Implications for future policy and research

The findings from our study highlight the need for a coordinated and contextually informed approach to dementia prevention in Italy. National-level strategies must account for regional variations in risk factor prevalence and PAFs to ensure practical and equitable interventions. Additionally, integrating PAFs with PIFs provides policymakers with a valuable tool to evaluate and prioritize interventions that balance significant benefits for dementia-specific risk factors with broader effects on noncommunicable diseases. Special attention should also be dedicated to monitoring prevention activities, addressing context-specific limitations and opportunities, and building on evaluations of past initiatives to guide future strategies. These efforts are critical for creating adaptable and practical prevention models that allow for adjusting ongoing interventions and planning new measures.

As demonstrated by this study, national-level analyses of dementia risk factor prevalence offer a comprehensive perspective while revealing regional variations in modifiable risk factors, resulting in diverse scenarios for avoidable dementia cases. This underscores the importance of targeted public health interventions tailored to local needs and supported by robust evaluations of the effectiveness of current strategies, particularly in regions where policy responses remain indirect or inconsistent. International partnerships should build on national experiences to foster harmonized prevention models that address variations in data collection methodologies, socio-cultural norms, healthcare infrastructure, and geographic determinants. By leveraging such collaborations and facilitating the exchange of best practices, it is possible to reduce the global burden of dementia while ensuring that all regions benefit from the latest evidence-based strategies.

Ethical standards

The article does not contain studies involving human participants or animals. This study was approved by the Ethics Committee of the Istituto Superiore di Sanità (the protocol number of the final opinion is CE-ISS 06/158—8 March 2007 for PASSI and AOO-ISS—11 July 2023—0,032,688 for PASSI d'Argento).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data presented in this study are available upon request from the corresponding author. The data are not publicly available due to privacy restrictions.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors used AI tools (Grammarly) solely for grammar checking and text editing. AI tools were not used for the production, analysis, or interpretation of the data reported in the study.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Guido Bellomo reports technical and financial support was provided by Italian Ministry of Health. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Federica Asta: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Formal analysis, Data curation. **Guido Bellomo:** Writing – review & editing, Writing – original draft. **Benedetta Contoli:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation. **Flavia L Lombardo:** Writing – review & editing, Writing – original draft, Visualization, Software, Formal analysis, Data curation. **Valentina Minardi:** Writing – review & editing, Writing – original draft, Visualization, Software, Formal analysis, Data curation. **Simone Salemme:** Writing – review & editing, Writing – original draft. **Nicola Vanacore:** Writing – review & editing, Supervision, Conceptualization. **Maria Masocco:** Writing – review & editing, Supervision, Methodology, Data curation, Conceptualization.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjpad.2024.100055.

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