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RESEARCH ARTICLE

Social determinants of health and risk of dementia among older men and women: A 12-year cohort study in Australia

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Abstract

INTRODUCTION: Social determinants of health (SDH) are recognized as contributing factors to cognitive disorders, but their collective influence on dementia risk remains unclear.

METHODS: A gender-disaggregated analysis was conducted on 12,896 community-dwelling older Australians (mean ± SD age: 75.2 ± 4.3 years; 54% women) without major cognitive impairment upon enrollment. Latent class analysis identified clusters from 72 SDH (70 individual-level and 2 neighborhood-level), while Cox proportional hazards regression estimated dementia risk over 12 years (median: 8.4) follow-up.

RESULTS: Four clusters were identified: least disadvantaged (Class 1: 31.5% men; 30.6% women), most disadvantaged (Class 2: 20.2% men; 19.4% women), high social support with Class 1 features (Class 3: 22.2% men; 24.1% women), and high social support with Class 2 features (Class 4: 26.1% men; 25.7% women). Compared to Class 1, men (HR: 1.49, 95% CI: 1.12–1.98) and women (HR: 1.56, 95% CI: 1.17–2.07) in Class 2, and women in Class 4 (HR: 1.66, 95% CI: 1.28–2.16) had a higher dementia risk.

DISCUSSION: Socioeconomic disadvantage was associated with incident dementia. Despite stronger social support, women's cognitive capacity appeared to be disproportionately impacted by adverse SDH.

KEYWORDS
aged, cluster analysis, cognition, dementia, gender differences, health inequities, healthy aging, latent class analysis, leisure activities, risk factors, social deprivation, social determinants of health, social isolation, social support, socioeconomic disparities in health, structural determinants

Highlights

- Four distinct multidimensional clusters were identified from a wide range of 72 social determinants of health.
- These clusters were associated with dementia risk differently in men and women.
- In both men and women, the most socioeconomically disadvantaged group had a higher risk of dementia.
- Despite stronger interpersonal social support, women had a greater risk of dementia.
- The addition of known dementia risk factors in cluster analysis did not change the findings, suggesting that social determinants of health independently predict dementia risk.

1 | BACKGROUND

Dementia poses a significant and growing public health challenge amidst global demographic shifts toward aging populations. The World Population Prospects 2024 report highlights a rapid increase in the number of older adults, particularly those aged 65 and above, both globally and in Australia.[1] Concurrently, the prevalence of dementia is projected to surge, with an estimated 153 million people worldwide expected to be living with dementia by 2050, and women remain at a greater risk than men.[2, 3] Projections based on Australian data suggest that delaying dementia onset by 5 years through preventive efforts could reduce its prevalence by 44% in 2050.[4]

Numerous systematic reviews provide evidence that socioeconomic and psychosocial conditions throughout the life course influence the risk of developing dementia,[5–10] including less education, low income, neighborhood disadvantages, social isolation, loneliness, and psychosocial stresses, among others. Collectively known as "social determinants of health" (SDH), the World Health Organization (WHO) describes them as non-medical factors that influence health outcomes and constitute the conditions in which people are born, grow, work, live, and age.[11]

The concept of "social gradient" in health explains how individuals positioned lower on the socioeconomic scale tend to experience worse health outcomes compared to those higher up the social hierarchy, thereby contributing to health inequities, with older people being especially vulnerable.[12] The United Nations (UN) has formulated an action plan known as the UN Decade of Healthy Ageing 2021–2030, which aims to reduce inequities related to healthy aging, with particular emphasis on older women who often experience greater socioeconomic disadvantages.[13] Therefore, gaining an in-depth understanding of SDH is necessary to design interventions that will reduce inequities and population burden.

To further contextualize and frame our research, we draw on *Manfred Max-Neef*'s Human Scale Development as the underpinning theory.[14] Unlike hierarchical theories that focus on sequential needs, *Max-Neef*'s theory discusses needs that are complementary, with each being necessary to achieve satisfaction. It argues that fundamental human needs – such as subsistence, protection, affection, understanding, participation, leisure, creation, identity, and freedom – must be viewed as interrelated and interactive components of a broader system. Building on this perspective, SDH are recognized for their systemic, population-based, cyclical, and intergenerational nature.[15] They are interconnected; for example, educational opportunities and achievements influence occupational and employment prospects, which subsequently affect income levels. Income then shapes other SDH conditions, such as access to advantageous neighborhoods, housing, and healthcare. As a result, people often face multiple adverse SDH simultaneously rather than in isolation.

In our prior research,[16] we examined the relationship between clusters of social connections and dementia risk, showing that men with weak social connections and women with social connection pattern characterized by a larger network of friends and relatives had greater dementia risks. Similar to our work, much of the existing literature predominantly focuses on specific subsets of SDH, such as education, income, and social (dis)connectedness, when investigating their association with dementia.[16–21] Another approach involves using composite indices such as the Social Deprivation Index,[22] which is calculated from a set of SDH measures that might oversimplify the interconnected nature of adverse SDH. These approaches, with their focus on limited variables or a single domain of SDH, potentially overlook the co-occurrence or clustering of multidomain adverse SDH within individuals.

Hence, we aimed to fill existing gaps in knowledge with two primary objectives: (1) identifying co-occurring clusters of SDH, and

(2) examining their associations with the risk of dementia in a cohort of relatively healthy community-dwelling adults aged 70+ years. Additionally, we hypothesized that other known risk factors for dementia may cluster with adverse SDH. Therefore, our secondary objectives were: (1) identifying clusters from SDH and other dementia risk factors, and (2) investigating their influence on dementia risk. Given the gender-based disparities in both social determinants and dementia incidence, analyses were gender-disaggregated.

RESEARCH IN CONTEXT

1. **Systematic review**: A literature search was conducted using MEDLINE and Google Scholar databases to identify observational studies examining various social determinants of health (SDH) and their association with the risk of dementia in older adults. While existing research provides insights into the relationship between selective individual and neighborhood-level SDH and dementia risk, there is insufficient investigation into the clustering of multidomain SDH and their collective influence on dementia, especially considering their interconnected nature. This gap is particularly notable in the context of gender-disaggregated analysis. Addressing this area of research is important for understanding how complex and multidimensional factors contribute to dementia risk, which is essential for developing targeted, equitable interventions, and policies to reduce the disease burden.
2. **Interpretation**: Through assessing the interconnected and co-occurring nature of SDH that older Australians experience, we identified four distinct clusters. Our analysis showed how these SDH clusters influence dementia risk differently in men and women.
3. **Future directions**: Interventions and strategies targeting the reduction of multidimensional social deprivation, with particular attention to gender-specific needs, have the potential to mitigate the high prevalence of dementia. Policymakers must prioritize comprehensive strategies that address the root causes of social and economic disadvantages to reduce health inequities and improve cognitive health outcomes. Future research should continue to expand on understanding the link and pathway between multiple adverse SDH and incident dementia across diverse populations.

2 | METHODS

2.1 | Study population

In this prospective cohort study, we conducted a secondary data analysis involving Australian participants from the ASPirin in Reducing Events in the Elderly (ASPREE) trial,[23] its substudy the ASPREE Longitudinal Study of Older Persons (ALSOP),[24] and its extension (ASPREE-XT) observational study.[25] ASPREE was a double-blind, randomized, placebo-controlled trial that examined the effects of daily 100 mg aspirin on various health outcomes. Between March 2010 and December 2014, the trial enrolled 19114 participants, including 16703 (87%) from Australia, through their usual primary healthcare providers. Participants were relatively healthy at baseline, as the inclusion criteria required individuals without major cognitive impairment (defined by a Modified Mini-Mental State Examination [3MS] score < 78/100), clinical diagnosis of dementia, cardiovascular diseases, or independence-limiting physical disability. The intervention phase of the trial concluded in June 2017, and participants were followed prospectively until January 2018, with analysis revealing no evidence supporting the efficacy of aspirin in reducing dementia risk over a median 4.7-year follow-up.[26] Therefore, the present study did not adjust for the intervention arm assignment.

Australian participants from the ASPREE trial were sent the ALSOP medical and social questionnaires, typically within the first year of their ASPREE study participation, hence referred to as the baseline questionnaires.[24] These questionnaires gathered information on a broad range of general medical, lifestyle, behavioral, psychosocial, economic, and environmental factors. Between June 2017 and January 2018, ASPREE participants were invited to participate in the ongoing ASPREE-XT observational follow-up study, continuing the annual in-person visits, telephone contact, and/or medical record reviews that were part of the clinical trial visits.[25] The present study comprised 12896 Australian ASPREE participants aged 70+ years who completed the ALSOP baseline social questionnaire. The study design and participant flow are illustrated in Figure 1A and B.

2.2 | Measures

The measures used as latent class indicators, assessed at enrollment in the ASPREE and ALSOP studies, were classified into two main groups: social determinants of health, and other modifiable non-social risk factors of dementia. Incident dementia, the study outcome, was longitudinally assessed during follow-ups.

2.2.1 | SDH

The selection of SDH was guided by the conceptual framework developed by the WHO's Commission on Social Determinants of Health.[11] This framework categorizes SDH as follows:

1. *Structural determinants*, which involve an interplay between socioeconomic and political contexts, structural mechanisms generating social stratification, and resulting socioeconomic positions of individuals. Examples of key structural determinants include education, income, race, and gender.

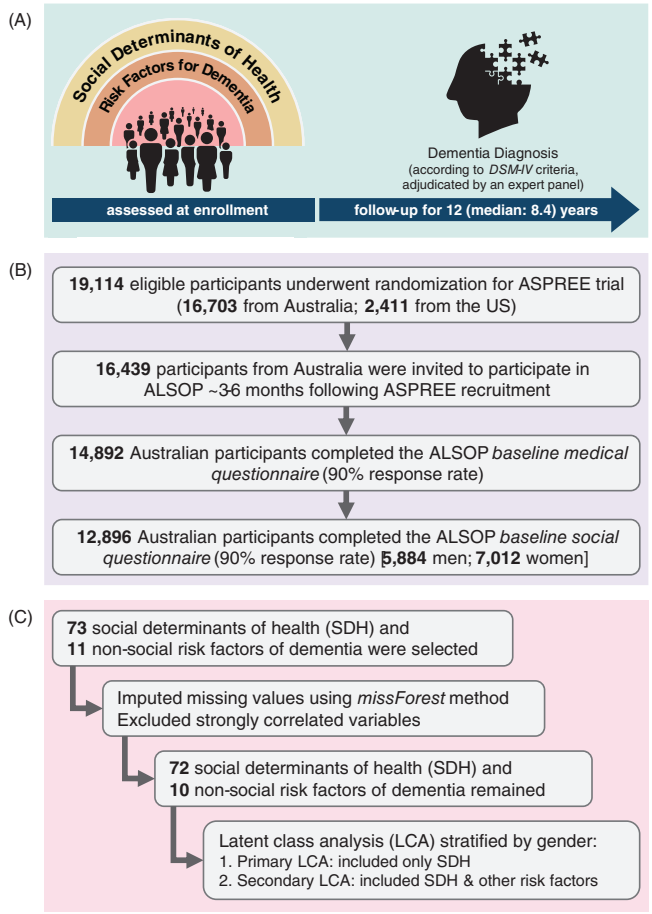

FIGURE 1 An overview of the study illustrating (A) study design, (B) flow diagram of study participants, and (C) analytic strategy.

2. *Intermediary determinants*, which are downstream factors specific to individuals' positions within social hierarchies based on their respective social status. These include material circumstances (e.g., housing characteristics), behaviors and biological factors, and socioenvironmental or psychosocial circumstances (e.g., social connections, adverse life events).

In this study, we initially identified 73 self-reported SDH (the final analysis included 72 SDH; see Subsection 2.3.1 for more details), mostly at the individual level, except for residence remoteness and the Socio-Economic Indexes for Areas – Index of Relative Socio-Economic Advantage and Disadvantage (SEIFA–IRSAD), which were neighborhood-level measures (see Table S1).

2.2.2 | Other modifiable non-social risk factors for dementia

In addition to SDH, we selected potentially modifiable non-social risk factors for dementia outlined in major reviews on dementia prevention, such as the 2020 *Lancet* Commission report[27] and WHO guidelines on risk reduction of cognitive decline and dementia.[28] From the available data, we extracted 11 variables (with the final analysis including 10 variables; see Subsection 2.3.1 for details) representing nine risk factors: hearing impairment, hypertension, excessive alcohol consumption, obesity, smoking, depression, physical inactivity, diabetes, and dyslipidemia. Further details, including measurements and categorizations, are provided in Table S2 and its accompanying footnotes.

2.2.3 | Dementia ascertainment

All participants underwent regular cognitive testing, assessing global cognition, verbal fluency, episodic memory, and psychomotor speed at baseline, years 1, 3, 5, with a final visit in 2017 as part of the ASPREE trial. Annual cognitive assessments have continued during the ASPREE-XT phase, which is ongoing. Although only the global assessment was administered in the first XT-year, the full battery of tests was reinstated thereafter. Individuals suspected of having dementia (based on predefined triggers: a 3MS score < 78/100, a drop in age-education adjusted predicted 3MS score of > 10.15 points from baseline, self-reported cognitive issues, a clinician diagnosis of dementia, or prescription of cholinesterase inhibitors) were referred for further cognitive and functional assessments.[26] An adjudication committee, consisting of neurologists and geriatricians, reviewed these results and diagnosed dementia based on criteria specified in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). Time-to-event was defined as the time from enrollment to the dementia trigger that resulted in a confirmed dementia diagnosis by the adjudication committee.[26]

2.3 | Statistical analysis

Data from the most recently released dataset, collected up to the fourth annual visit of ASPREE-XT (which began on February 1, 2018), were analyzed. Statistical analyses were conducted on a binary gender-disaggregated basis (men vs. women) using Stata/MP v.17 (StataCorp LLC, College Station, Texas, USA) and R v.4.2.0 (R Foundation for Statistical Computing, Vienna, Austria). While a two-tailed $p < 0.05$ was considered the threshold for statistical significance, the quantitative interpretation adheres to the recommendations by the American Statistical Association.[29] The analytic strategy is summarized in Figure 1C.

2.3.1 | Data preprocessing

We evaluated missing data and found it to be low (mostly < 5% in each latent class indicator) (Table S3). To determine whether data were missing completely at random (MCAR), we conducted Little's MCAR test,[30] which showed that the assumption was not met. Therefore, to avoid introducing selection bias from a complete-case analysis, we imputed the missing values using *missForest*,[31] a non-parametric random forest iterative imputation, before clustering analysis.

We then examined the correlation between these variables using Spearman's rank correlation test. Two pairs showed a very strong

correlation (Spearman's $\rho < -0.8$ or > 0.8)[32] in both men and women. One pair from the initial 73 SDH was "living alone" and "currently married/partnered." We retained "living alone" to reflect a more contemporary perspective of an individual's social context, resulting in 72 SDH for further analysis. The second correlated pair among non-social risk factors was "smoking" and "pack-year smoking history." To align with the majority of risk factor studies, we retained "smoking," leaving a total of 10 variables under non-social risk factors.

2.3.2 | Latent class analysis

Latent class analysis (LCA) is an unsupervised learning model-based clustering algorithm that enables the identification of relatively homogenous groups within a heterogeneous population based on shared characteristics. We implemented LCA using Marbac and Sedki's approach in the R package *VarSelLCM*.[33, 34] This method allows for the detection of relevant variables for clustering by assuming that only a subset of variables explains the partition. Variable selection was achieved through finite mixture models, facilitating interpretation of results and improving the accuracy of estimators. The relevance of a variable for clustering is determined by its discriminative power, with a higher index indicating greater influence on cluster formation.[34, 35]

Two types of gender-specific latent class analyses were performed. In the primary analysis, 72 SDH served as latent class indicators, while in the secondary analysis, 10 risk factors were added alongside the 72 SDH. Models with one to seven clusters were fitted, with each model undergoing estimation for a maximum of 1000 iterations to achieve stability. The number of clusters was selected based on Bayesian Information Criterion (BIC) values, with lower BIC indicating a better model.[36] Although the 7-class model had the lowest BIC value, it was not optimal for interpretation, public health recommendations, or clinical utility due to the excessive number of classes. Therefore, we applied the elbow method to balance simplicity of interpretation and statistical precision.[37] Graphing BIC values (*y*-axis) against the number of clusters (*x*-axis) revealed a marked flattening at four clusters, prompting the choice of the four-class model (Figure S1). Additional details are given in the Supplementary Methods.

2.3.3 | Summary statistics and regression models

Data were summarized using frequencies and percentages, mean with standard deviation (SD), or median with interquartile range (IQR), as appropriate. Bivariate analyses were performed using Pearson's χ^2 test for categorical variables, and either one-way analysis of variance (ANOVA) or Kruskal-Wallis test for continuous variables. A non-parametric Nelson-Aalen cumulative hazard was estimated and presented graphically to observe differences in event rates over time between the classes.

The association between clusters and dementia risk was examined using Cox proportional hazards models, with estimates presented as hazard ratios (HRs) and 95% confidence intervals (CIs). In the primary analysis, where the classes were derived solely from SDH, two multivariable models were developed. The minimally adjusted model controlled for age, while the full model further controlled for other dementia risk factors, including hearing impairment, hypertension, alcohol consumption, body mass index, waist circumference, smoking, depressive symptoms, physical activity, diabetes, and dyslipidemia. In the secondary analysis, where the classes were derived from both SDH and risk factors, we adjusted only for age, since the risk factors were already accounted for as latent class indicators.

The proportional hazards assumption was checked with a statistical test using scaled Schoenfeld residuals,[38] and no violations were found. Participants were censored at the time of death, withdrawal/loss to follow-up, or upon reaching the data cutoff date if they did not experience the event.

2.3.4 | Sensitivity analysis

We performed two sensitivity analyses by re-running the fully adjusted models. First, we used the Fine-Gray subdistribution hazards models[39] for incident dementia, allowing all-cause death as a competing risk. Second, we excluded individuals diagnosed with dementia during the initial 3 years of follow-up to reduce the potential influence of early subtle dementia symptoms on cognitive scores and SDH such as behaviors and psychosocial factors (i.e., reverse causality).

3 | RESULTS

3.1 | Population characteristics

The study included 12896 Australian participants aged between 70 and 95 years at baseline, comprising 45.6% men ($n = 5884$) and 54.4% women ($n = 7012$) (Figure 1). Figure S2 provides a comparison of SDH between men and women at enrollment. Women, compared to men, had more disadvantageous SDH in structural factors such as lower levels of education, income, and employment, as well as less health insurance coverage and more unfavorable housing characteristics. In terms of socioenvironmental and psychosocial factors, fewer women were currently married/partnered, more women lived alone, felt lonely, and reported experiencing more adverse life events. Men, in contrast, reported less involvement in life enrichment activities, informal caregiving, and volunteering. Regarding other health risk factors (Figure S3), men had a higher prevalence of hearing impairment, smoking, excessive alcohol consumption, and diabetes at enrollment. In contrast, there was a higher prevalence of general obesity (increased body mass index), abdominal obesity (increased waist circumference), dyslipidemia, and depression in women.

3.2 | Class structure

The optimal number of classes was determined to be four for both men and women (see Subsection 2.3.2). Of 72 latent class indicators

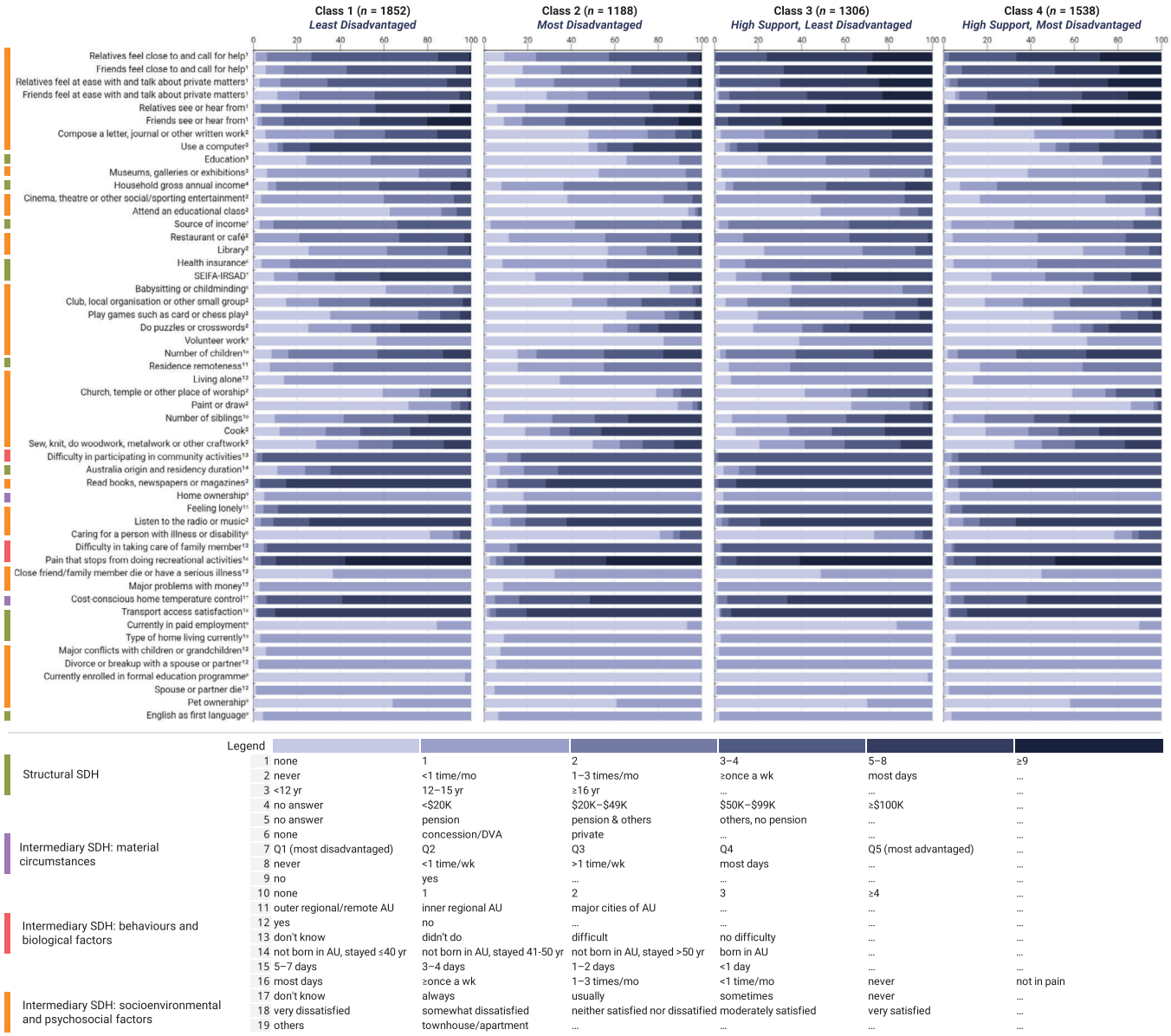

FIGURE 2 Distribution of relevant social determinants of health for clustering in each class among men. *Notes*. The four-class model selected 52 out of 72 latent class indicators. The variables are arranged in order of discriminative power, from highest to lowest (see Figure S4). In general, lighter colors on the graph represent more disadvantaged social determinants of health. Superscript numbers for each variable and color labels are explained in the legend at the bottom of the graph.

in the primary analysis, 52 for men and 56 for women were selected as relevant for cluster formation. Notably, determinants related to support from relatives and friends, socially and mentally stimulating life enrichment activities, education, and income emerged as the most discriminatory (with a discriminating power of at least 2%) for both genders (Figure S4). In the secondary analysis, which included an additional 10 indicators of dementia risk factors in the model (7 selected for men and 8 for women, all had low discriminating power), the SDH with the highest discriminating power remained relatively consistent (Figure S4). Indicators that were not selected can be discerned by comparing Tables S1 and S2 with Figure S4.

We interpreted the class features by visualizing the probabilities (Figures S5 and S6) and distribution (Figures 2 and 3) of relevant indicators within each cluster. On the surface, the patterns of Class 1 and Class 2 were markedly different, representing the least and most socially disadvantaged groups along the socioeconomic spectrum, respectively. In contrast, Class 3 and Class 4 showed higher levels of social support (i.e., relationships with friends and relatives) which were identified as the key discriminating variables overall (Figure S4). Specifically, most individuals in Class 3 and Class 4 reported having 5+ friends and relatives, which was notably higher compared to both Class 1 and Class 2 (with Class 2 reporting the lowest number of

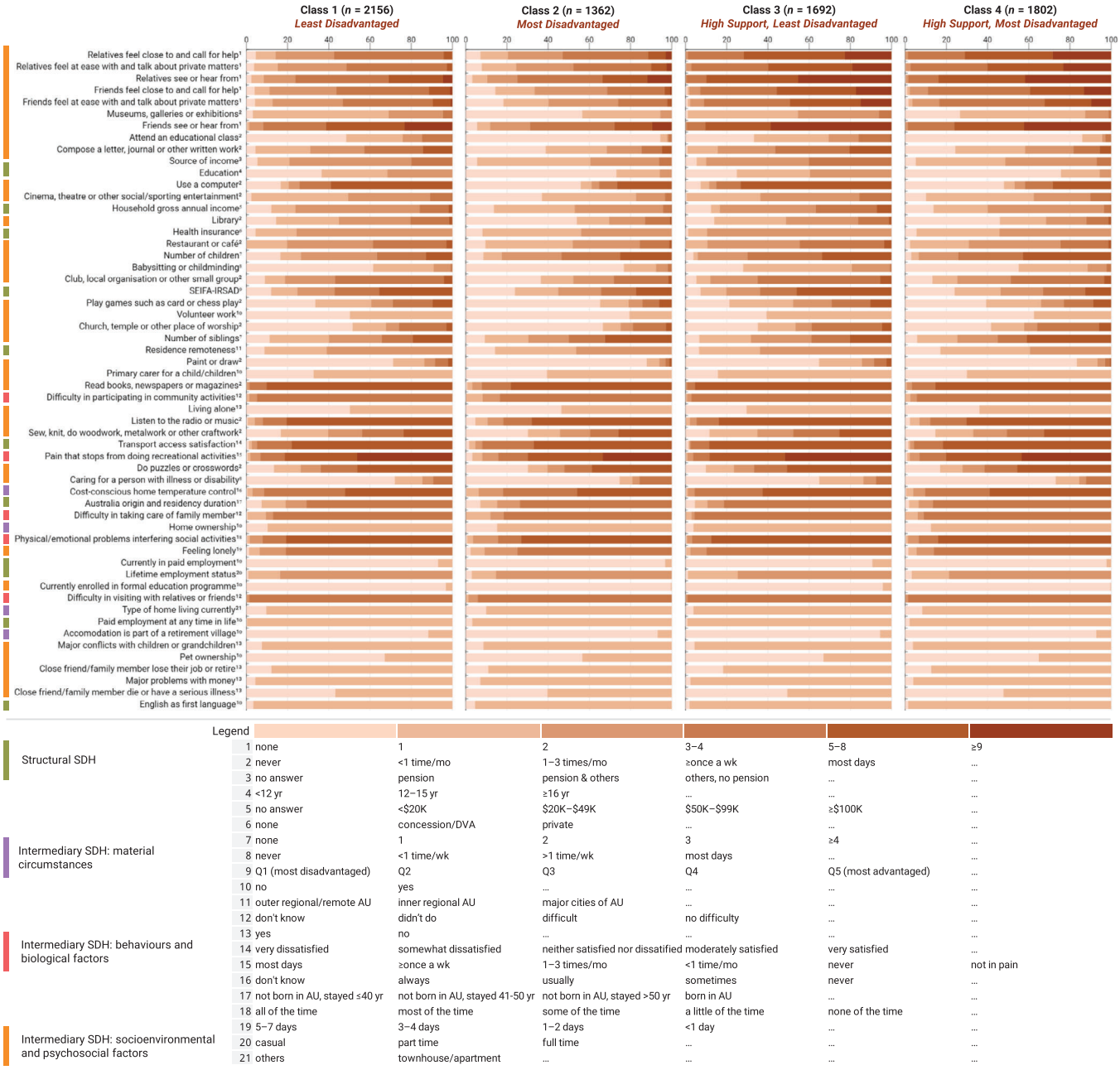

FIGURE 3 Distribution of relevant social determinants of health for clustering in each class among women. *Notes*. The four-class model selected 56 out of 72 latent class indicators. The variables are arranged in order of discriminative power, from highest to lowest (see Figure S4). In general, lighter colors on the graph represent more disadvantaged social determinants of health. Superscript numbers for each variable and color labels are explained in the legend at the bottom of the graph.

friends/relatives for support). When examining other SDH, there was a mix of characteristics, with Class 3 sharing similarities with Class 1, and Class 4 resembling Class 2. Hence, we labeled them as "Class 1: Least Disadvantaged," "Class 2: Most Disadvantaged," "Class 3: High Support and Least Disadvantaged," and "Class 4: High Support and Most Disadvantaged." The labeling of the clusters is intended to facilitate discussion and interpretation, but may oversimplify the cluster patterns and be subject to individual perspectives. For detailed comparison, selected variables with at least 2% discriminative power, as shown in Figures 2 and 3, are again presented in Tables S4 and S5.

Most participants were grouped in Class 1 (31.5% men and 30.6% women), while Class 2 had the lowest representation (20.2% men and 19.4% women). Baseline sociodemographic characteristics and health risk factors are presented in Table 1. When further incorporating dementia risk factors in secondary LCA, the class features remained similar (Figures S7 and S8). Figure 4 shows group composition and changes between the two analyses, demonstrating high agreement (Gwet's AC: men = 0.940, women = 0.927). Figure S9 illustrates a low to negligible probability of misclassification in each cluster.

TABLE 1 Baseline characteristics of study participants.

Characteristics	Men ($n = 5884$)[a]					Women ($n = 7012$)[a]				
	Class 1	Class 2	Class 3	Class 4	p_1	Class 1	Class 2	Class 3	Class 4	p_2
Number (row %)	1852 (31.5)	1188 (20.2)	1306 (22.2)	1538 (26.1)	–	2156 (30.6)	1362 (19.4)	1692 (24.1)	1802 (25.7)	–
Age, years										
Mean ± SD	74.6 ± 4.0	76.3 ± 5.0	74.4 ± 3.9	75.4 ± 4.4	<0.001	75.1 ± 4.3	76.5 ± 4.8	74.1 ± 3.6	75.8 ± 4.4	<0.001
Median (IQR)	73.4 (71.4–76.6)	75.1 (72.3–79.4)	73.2 (71.5–76.4)	74.2 (71.9–77.6)	<0.001	73.9 (71.7–77.6)	75.4 (72.4–79.7)	73.1 (71.4–75.8)	74.8 (72.2–78.6)	
Race										
White participants	1826 (98.6)	1161 (97.7)	1285 (98.4)	1523 (99.0)	0.053	2130 (98.8)	1342 (98.5)	1677 (99.1)	1785 (99.1)	0.397
All other groups[b]	26 (1.4)	27 (2.3)	21 (1.6)	15 (1.0)		26 (1.2)	20 (1.5)	15 (0.9)	17 (0.9)	
Education										
<12 years	450 (24.3)	777 (65.4)	314 (24.0)	1121 (72.9)	<0.001	786 (36.5)	996 (73.1)	421 (24.9)	1362 (75.6)	<0.001
12–15 years	546 (29.5)	286 (24.1)	354 (27.1)	341 (22.2)		688 (31.9)	287 (21.1)	601 (35.5)	339 (18.8)	
≥ 16 years	856 (46.2)	125 (10.5)	638 (48.9)	76 (4.9)		682 (31.6)	79 (5.8)	670 (39.6)	101 (5.6)	
CES-D-10 score										
<8	1721 (92.9)	1027 (86.4)	1257 (96.2)	1445 (93.9)	<0.001	1911 (88.6)	1146 (84.1)	1590 (94.0)	1657 (92.0)	<0.001
≥ 8	131 (7.1)	161 (13.6)	49 (3.8)	93 (6.1)		245 (11.4)	216 (15.9)	102 (6.0)	145 (8.0)	
Hearing impairment										
Don't know	41 (2.2)	18 (1.5)	33 (2.5)	19 (1.2)	<0.001	70 (3.3)	40 (2.9)	47 (2.8)	48 (2.7)	0.011
Not impaired	778 (42.0)	476 (40.1)	583 (44.6)	585 (38.0)		1217 (56.5)	758 (55.7)	1044 (61.7)	1070 (59.4)	
Impaired	1033 (55.8)	694 (58.4)	690 (52.8)	934 (60.7)		869 (40.3)	564 (41.4)	601 (35.5)	684 (38.0)	
Hypertension[c]										
No	486 (26.2)	235 (19.8)	370 (28.3)	350 (22.8)	<0.001	622 (28.9)	284 (20.9)	553 (32.7)	409 (22.7)	<0.001
Yes	1366 (73.8)	953 (80.2)	936 (71.7)	1188 (77.2)		1534 (71.1)	1078 (79.1)	1139 (67.3)	1393 (77.3)	
Alcohol consumption[d]										
Never	116 (6.3)	128 (10.8)	101 (7.7)	162 (10.5)	<0.001	283 (13.1)	461 (33.9)	239 (14.1)	522 (29.0)	<0.001
Former	77 (4.2)	115 (9.7)	33 (2.5)	98 (6.4)		73 (3.4)	91 (6.7)	46 (2.7)	64 (3.6)	
Current, low risk	1007 (54.4)	536 (45.1)	723 (55.4)	710 (46.2)		1379 (64.0)	605 (44.4)	1080 (63.8)	963 (53.4)	
Current, high risk	652 (35.2)	409 (34.4)	449 (34.4)	568 (36.9)		421 (19.5)	205 (15.1)	327 (19.3)	253 (14.0)	
Body mass index, kg/m^2										
<18.5	<5	<5	<5	<5	<0.001	20 (0.9)	17 (1.3)	12 (0.7)	7 (0.4)	<0.001
18.5-24.9	443 (23.9)	265 (22.1)	276 (20.9)	273 (17.6)		672 (31.2)	345 (25.3)	544 (32.2)	470 (26.1)	
25.0-29.9	1008 (54.4)	582 (49.0)	714 (54.7)	846 (55.0)		848 (39.3)	483 (35.5)	714 (42.2)	726 (40.3)	
≥ 30.0	401 (21.7)	341 (28.7)	316 (24.2)	419 (27.2)		616 (28.6)	517 (38.0)	422 (24.9)	599 (33.2)	

(Continues)

TABLE 1 (Continued)

Characteristics	Men ($n = 5884$)[a]					Women ($n = 7012$)[a]				
	Class 1	Class 2	Class 3	Class 4	p_1	Class 1	Class 2	Class 3	Class 4	p_2
Waist circumference, cm										
<94 (M) or < 80 (W)	432 (23.3)	232 (19.5)	279 (21.4)	258 (16.8)	<0.001	343 (15.9)	175 (12.9)	265 (15.7)	229 (12.7)	<0.001
94-101 (M) or 80-87 (W)	618 (33.4)	339 (28.5)	414 (31.7)	476 (31.0)		451 (20.9)	239 (17.5)	392 (23.2)	367 (20.4)	
≥ 102 (M) or ≥ 88 (W)	802 (43.3)	617 (51.9)	613 (46.9)	804 (52.3)		1362 (63.2)	948 (69.6)	1035 (61.2)	1206 (66.9)	
Smoking										
Never	853 (46.1)	417 (35.1)	650 (49.8)	621 (40.4)	<0.001	1343 (62.3)	839 (61.6)	1176 (69.5)	1323 (73.4)	<0.001
Former	960 (51.8)	696 (58.6)	635 (48.6)	853 (55.5)		763 (35.4)	467 (34.3)	503 (29.7)	437 (24.3)	
Current	39 (2.1)	75 (6.3)	21 (1.6)	64 (4.2)		50 (2.3)	56 (4.1)	13 (0.8)	42 (2.3)	
Physical activity in a week (self-reported)										
Never/Rarely	12 (0.6)	39 (3.3)	< 5	17 (1.1)	<0.001	15 (0.7)	72 (5.3)	7 (0.4)	20 (1.1)	<0.001
No more than light	431 (23.3)	430 (36.2)	222 (17.0)	405 (26.3)		806 (37.4)	685 (50.3)	478 (28.3)	724 (40.2)	
No more than moderate	1016 (54.9)	552 (46.5)	774 (59.3)	842 (54.8)		1096 (50.8)	491 (36.1)	928 (54.9)	840 (46.6)	
Regular vigorous	393 (21.2)	167 (14.1)	310 (23.7)	274 (17.8)		239 (11.1)	114 (8.4)	279 (16.5)	218 (12.1)	
Diabetes[e]										
No	1663 (89.8)	991 (83.4)	1196 (91.6)	1347 (87.6)	<0.001	2021 (93.7)	1217 (89.4)	1597 (94.4)	1632 (90.6)	<0.001
Yes	189 (10.2)	197 (16.6)	110 (8.4)	191 (12.4)		135 (6.3)	145 (10.6)	95 (5.6)	170 (9.4)	
Dyslipidemia[f]										
No	828 (44.7)	517 (43.5)	561 (43.0)	677 (44.0)	0.791	489 (22.7)	336 (24.7)	397 (23.5)	397 (22.0)	0.336
Yes	1024 (55.3)	671 (56.5)	745 (57.0)	861 (56.0)		1667 (77.3)	1026 (75.3)	1295 (76.5)	1405 (78.0)	

Note: Values are expressed in number (column %) unless otherwise indicated. Counts and percentages are suppressed when the number is less than 5 and are combined with adjacent group for reporting. Class 1: Least Disadvantaged, Class 2: Most Disadvantaged, Class 3: High Support and Least Disadvantaged, and Class 4: High Support and Most Disadvantaged.

Abbreviations: CES-D-10, 10-Item Center for Epidemiologic Studies Depression Scale; IQR, interquartile range; SD, standard deviation.

p_1, statistical test between four classes in men; p_2, statistical test between four classes in women.

[a]Gender was conceptualized based on self-reported data collected during enrollment. The original data collection focused on binary gender categories (men and women), and no data were collected for individuals identifying outside of these categories.

[b]All other groups included Aboriginal/Torres Strait Islanders ($n = 9$), Native Hawaiian/Pacific Islander/Māori ($n = 6$), Asian ($n = 91$), American Indian ($n < 5$), Black ($n < 5$), more than one race ($n = 47$), and those whose race could not be determined ($n = 11$). The racial categories used in this study reflect those established in the ASPREE study, which included participants from both the US and Australia. Although this analysis is restricted to the Australian population (drawn from ALSOP substudy), these categories were retained to maintain consistency with the original ASPREE framework and to provide a comprehensive overview of diversity within the sample.

[c]Hypertension was defined as one or more of the following: prescription of antihypertensive medications, systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg.

[d]Current alcohol drinkers were classified according to Australia's National Health and Medical Research Council (NHMRC) guidelines. Current (low risk) alcohol consumption comprises those who drink no more than 10 standard drinks a week AND no more than 4 standard drinks on any day. If these limits are exceeded, it is classified as current (high risk) alcohol consumption.

[e]Diabetes was defined as one or more of the following: self-reported diabetes, prescription of glucose-lowering medications, or afasting blood sugar of ≥7.0 mmol/L (126 mg/dL).

[f]Dyslipidemia was defined as one or more of the following: prescription of cholesterol lowering medications, total serum cholesterol ≥5.5 mmol/L (212 mg/dL), or LDL-cholesterol > 4.1 mmol/L (160 mg/dL).

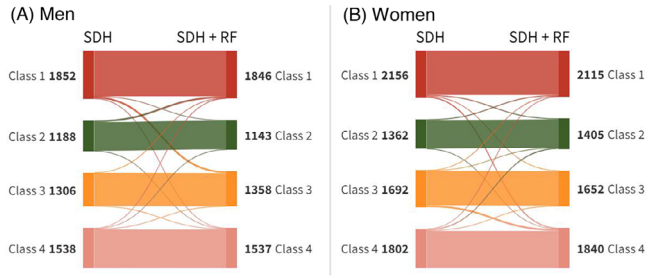

FIGURE 4 Changes in group composition between two types of latent class analyses in (A) men and (B) women. *Notes*. "SDH" denotes latent class analysis using social determinants of health as indicators. "SDH + RF" denotes latent class analysis incorporating both social determinants of health and other risk factors for dementia. Each band of the alluvial plot represents the number of participants classified using either SDH or SDH with RF. High agreement was observed between the two analyses (Men: 95.5% agreement, Gwet's AC = 0.940; Women: 94.5% agreement, Gwet's AC = 0.927).

3.3 | Risk of dementia

Over a median follow-up of 8.4 years (IQR: 7.3–9.5; range: 0.2–11.9), dementia was diagnosed in 6.4% (n = 374) of men with an incidence rate of 7.9 per 1000 person-years (95% CI: 7.1–8.7), and in 6.1% (n = 426) of women with an incidence rate of 7.3 per 1000 person-years (95% CI: 6.7–8.0). The cumulative hazard of dementia was highest in Class 2 for men and in both Class 2 and Class 4 for women, whereas Class 1 and Class 3 were similar in both genders (Figures 5 and S10).

In multivariable analysis (Figure 6), after adjusting for potential confounders and using Class 1 as the reference, in men, Class 2 was associated with a higher dementia risk (HR: 1.49, 95% CI: 1.12–1.98), whereas Class 3 showed no significant association (HR: 0.90, 95% CI: 0.66–1.23). Class 4 was modestly associated with dementia (HR: 1.20, 95% CI: 0.91–1.59), although the data were statistically consistent with parameter values ranging from little or no effect to a considerable increase in risk. In women, both Class 2 (HR: 1.56, 95% CI: 1.17–2.07) and Class 4 (HR: 1.66, 95% CI: 1.28–2.16) were associated with a greater risk of dementia.

The secondary analysis, in which classes were determined through SDH and other risk factors (Figure S11), and the sensitivity analyses using the Fine-Gray hazards model for competing risk (Figure S12) and excluding dementia cases diagnosed in the first 3 years of follow-up (Figure S13), aligned with the main findings.

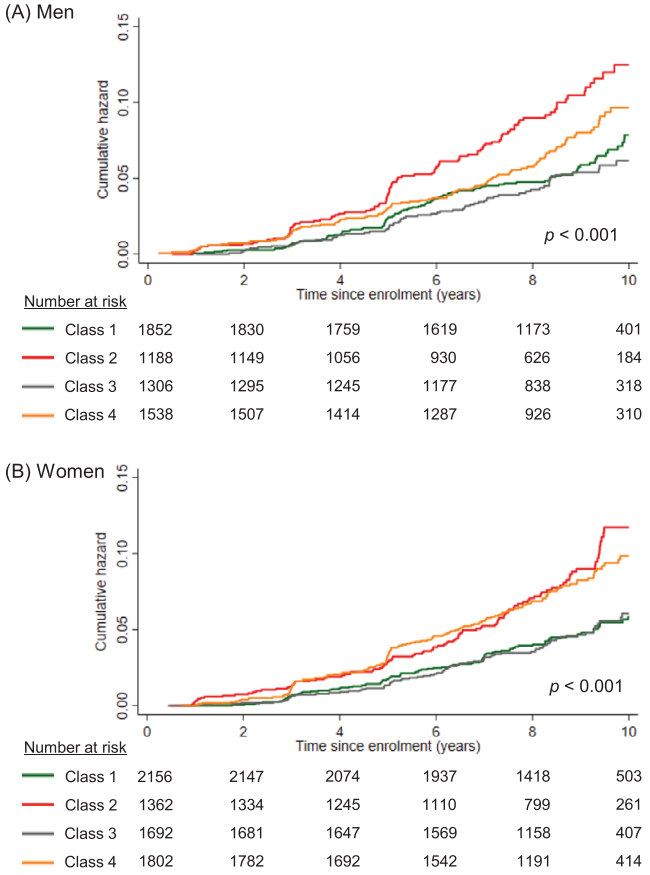

FIGURE 5 Cumulative hazard plots for dementia, estimated using the Nelson–Aalen estimator, across four classes in (A) men and (B) women. *Notes*. These classes were identified through latent class analysis, using social determinants of health as indicators. p-values were calculated from the Tarone–Ware test for equality of survival distributions. Class 1: Least Disadvantaged, Class 2: Most Disadvantaged, Class 3: High Support and Least Disadvantaged, and Class 4: High Support and Most Disadvantaged.

4 | DISCUSSION

4.1 | Key results and interpretation

Our study is among the first to provide gender-disaggregated evidence of the association between SDH clusters and dementia risk over a median 8.4-year follow-up in a cohort of community-dwelling Australians aged 70+. Using an unsupervised latent class modeling, we identified four classes from 72 SDH indicators. In our sample, "least disadvantaged" was the most prevalent (~1 in 3), whereas the "most disadvantaged" was the least frequent (~1 in 5). The remaining two classes, distinguished by their notably higher interpersonal social support, are referred to as the "least disadvantaged with high social support" (~1 in 4) and "most disadvantaged with high social support" (~1 in 4). Compared to the "least disadvantaged," we found that the "most disadvantaged" class was associated with a 49% higher dementia risk in men and a 56% higher risk in women. Additionally, the "most disadvantaged with high social support" had a 66% higher risk in women. In contrast, the "least disadvantaged with high social support" showed no significant association with dementia for either gender.

This study advances the literature by highlighting co-occurring life-course SDH and their collective influence on dementia risk. Using extensive SDH data, it builds upon our previous research,[16] which focused solely on social connection, offering in-depth understanding. While prior research has explored the clustering of behavioral and metabolic risk factors for dementia risk,[40–42] SDH clustering remains underexplored, often relying on a limited set of socioeco-

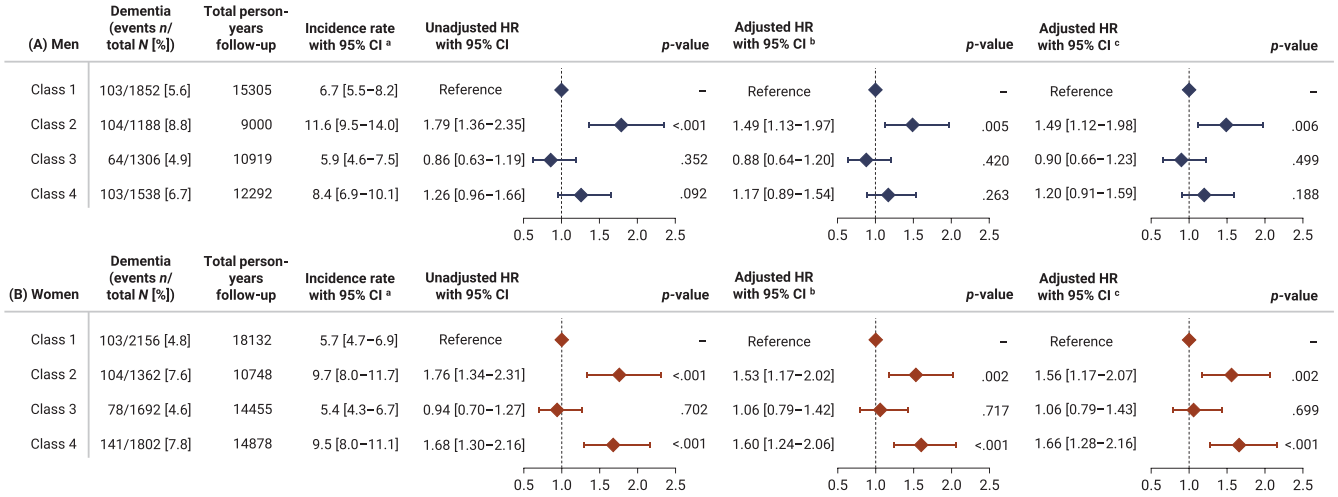

FIGURE 6 Association between class membership and risk of dementia in (A) men and (B) women. *Notes*. These classes were identified through latent class analysis, using social determinants of health as indicators. Class 1: Least Disadvantaged, Class 2: Most Disadvantaged, Class 3: High Support and Least Disadvantaged, and Class 4: High Support and Most Disadvantaged. CI, confidence interval; HR, hazard ratio. [a] Incidence rates per 1000 person-years. [b] Adjusted for age (continuous). [c] Adjusted for age (continuous), hearing impairment (don't know, not impaired, impaired), hypertension (no, yes), alcohol consumption (never, former, current–low risk, current–high risk), body mass index (< 18.5 kg/m^2, 18.5–24.9 kg/m^2, 25.0–29.9 kg/m^2, ≥ 30 kg/m^2), waist circumference (men: < 94 cm, 94–101 cm, ≥ 102 cm; women: < 80 cm, 80–87 cm, ≥ 88 cm), smoking (never, former, current), depressive symptoms (10-Item Center for Epidemiologic Studies Depression Scale [CES-D-10] score: < 8, ≥ 8), physical activity (never/rarely, no more than light, no more than moderate, regular vigorous), diabetes (no, yes), and dyslipidemia (no, yes).

nomic variables.[43–45] For example, a UK study identified three classes based on selected SDH (income, education, employment).[43] Compared to low socioeconomic status (SES) group, both medium and high-SES groups showed a lower risk of dementia over 8-year follow-up.[43] Our findings align, showing a 33%–40% lower dementia risk in the least disadvantaged groups compared to the most disadvantaged. However, our study goes further by incorporating a broader range of SDH, demonstrating that later-life social connections and engagement in socially and mentally stimulating life enrichment activities are stronger discriminators of cluster formation than conventional socioeconomic factors. These results reinforce the importance of support and socializing in later life alongside other socioeconomic factors in delaying dementia onset.

Furthermore, the most disadvantaged cluster had a higher prevalence of modifiable dementia risk factors, aligning with previous reports.[27,46] This may reflect the adverse effects of unfavorable SDH already affecting this group. In the general Australian population, the estimated population attributable fraction (PAF) for dementia from 12 modifiable risk factors was 40.6%.[47] The PAF could be higher in more disadvantaged groups, such as lower-income individuals, as noted in the Argentinian population,[48] indicating that interventions would benefit socioeconomically disadvantaged groups most.

Interestingly, the cluster characterized by the most socioeconomically disadvantaged group with stronger social support had a higher dementia risk in women, but not in men. We have two possible explanations for this gender disparity. First, the disproportionate impact of adverse SDH on women may contribute to this difference. In our sample, women faced more disadvantageous SDH across structural factors, including lower education, income, and employment, as well as a greater variety of socioenvironmental and psychosocial challenges. This cumulative burden of various socioeconomic and psychosocial disadvantages may exacerbate the risk. These challenges also contribute to chronic stress and social isolation, both well-documented dementia risk factors.[19,49,50] Therefore, the stress of managing multiple co-existing adverse SDH may outweigh the protective effects of social support. Second, gender differences in support-seeking behavior and quality of support may play a role.[51–55] Women tend to seek out more emotional support, while men typically are more receptive to instrumental support. However, our study lacks specific data to substantiate this. It is plausible that men's greater receipt of instrumental support may partially mitigate the impact of adverse SDH. Conversely, women, despite potentially receiving more emotional support, may also contend with greater emotional demands and frequent negative interactions with their network members, consistent with the "social complexity hypothesis."[56] This could result in chronic psychological distress,[51,52] potentially negating the protective effects of social support against dementia.

4.2 | Implications

Our findings reveal significant social gradient and health inequity in dementia risk, even among relatively healthy, economically advantaged older individuals with access to primary healthcare. Consistent with the Marmot review,[12] our results indicate that dementia-related health disparities stem from socioeconomic conditions. Reducing health inequity requires multifaceted interventions addressing adverse SDH at individual, community and national levels. While

individual-level interventions are effective, systemic approaches are essential to address root causes. System-level changes, such as developing community-based supports, peer networks, and improving access to preventive resources, can empower individuals, particularly those with adverse SDH, to adopt lasting lifestyle changes. Tailoring multidomain interventions to local socioeconomic contexts increases their relevance and effectiveness in achieving equitable health outcomes. Recently, social prescribing has emerged as a promising strategy,[57–59] linking individuals with non-medical community resources by providing holistic support across social, emotional, and material needs. These strategies are especially advantageous as they minimize the risks associated with hospital environments while supporting wellbeing in non-clinical settings.[60–64]

Furthermore, policymakers must recognize the importance of early and continuous intervention to attenuate long-term health disparities. Improving socioeconomic conditions from an early age can promote more equitable health opportunities and reduce the likelihood of adverse health outcomes later in life by minimizing exposure to risk factors over the life course.[65] Our study's gender-specific findings also suggest that socioeconomic adversity disproportionately affects women's cognitive capacity. This information is particularly valuable for policy developers as a foundational resource. For example, in 2024, the Australian Government mandated gender analysis in all Cabinet Submissions and New Policy Proposals, using gender-disaggregated evidence to design policies that advance gender equality and achieve intended outcomes.[66]

We advocate for applying the principle of "proportionate universalism,"[12] which suggests delivering universal interventions/actions at a scale and intensity proportionate to the level of disadvantage, ensuring that those who need more support receive it. Implementing such interventions can lower socioeconomic disadvantages, flatten the social gradient, narrow health inequities, and improve overall population health.[67]

4.3 | Strengths and limitations

One strength is the prospective follow-up of a large cohort of older adults without major cognitive impairment at baseline, with standardized measurements by trained staff. Dementia events were adjudicated by an expert panel, reducing misclassification and information biases. Our analytic approach examines the clustering of multidimensional SDH, recognizing their interconnected nature, which goes beyond the limited SDH typically studied. We also conducted a gender-disaggregated analysis to identify gender-based differences, discussed further in Section 4.2.

There are several limitations. First, the sample comprised relatively healthy, predominantly White, and economically advantaged older Australians recruited through primary healthcare providers, which may limit generalizability. We acknowledge that certain SDH may have already influenced the health and survival of some individuals in the community, affecting their eligibility to participate in this study. However, given the observed social gradient in health inequities, our findings are likely conservative and could be more pronounced in a more diverse population. Second, transitioning from a clinical trial to an observational study might introduce self-selection bias and a healthy cohort effect, potentially explaining the low discriminative power of behavioral and medical risk factors in cluster formation. Third, the LCA results depend on the population characteristics and selected indicators, which may affect generalizability. To support comparison in future studies, we provided the probability of each item response. Fourth, excluding participants diagnosed with dementia in the initial 3 years would not completely eliminate reverse causality, as the preclinical stage may precede disease manifestation by over a decade.[68] Fifth, while extensive individual-level SDH data were used, data on structural/neighborhood-level SDH and commercial determinants, were limited. Lastly, latent classes were constructed using baseline data. Some individuals might experience social mobility during follow-up, such as changes in income or housing, warranting further investigations.

4.4 | Future research directions

Individuals from socially disadvantaged backgrounds are often underrepresented in longitudinal research due to barriers such as limited healthcare access and financial constraints. Therefore, strategies that prioritize the recruitment and retention of these groups are essential. Australia's demographic shift toward greater ethnic diversity, with an increase in Asia-born and a decline in the Europe-born older adults since the dismantling of the discriminatory White Australia Policy in the 1970s,[69] presents an opportunity to include more culturally and linguistically diverse participants in future research. At this stage, complementing our findings with qualitative methods, such as in-depth interviews and focus groups, could provide insights into the needs of these populations and address recruitment challenges. Participatory action research, engaging people with lived experience of social disadvantage, could facilitate co-design of studies and interventions to better address health inequities.

5 | CONCLUSIONS

This study identified four distinct groups among community-dwelling older Australians using a wide range of (nearly all) individual-level SDH. Dementia risk was higher in the most socioeconomically disadvantaged group, regardless of gender. The most disadvantaged socioeconomic group but with stronger interpersonal social support was also associated with an elevated risk of dementia specifically in women. These findings carry significant public health and policy implications, revealing the significant role of multiple coexisting adverse SDH in the onset of dementia, with a disproportionate impact on older women. Addressing multidimensional deprivation at individual, community, and national levels throughout the life course should be a central focus of both new and existing interventions and policies as we strive toward achieving health equity.

AUTHOR CONTRIBUTIONS

Htet Lin Htun: Conceptualization; Methodology; Validation; Formal analysis; Writing—Original Draft; Writing—Review & Editing; Visualization; Project administration. **Achamyeleh Birhanu Teshale**: Methodology; Writing—Review & Editing. **Joanne Ryan**: Methodology; Validation; Investigation; Data Curation; Writing—Review & Editing; Supervision. **Alice J.Owen**: Methodology; Validation; Investigation; Resources; Data Curation; Writing—Review & Editing; Supervision. **Trevor T.-J. Chong**: Data Curation; Writing—Review & Editing. **Suzanne G. Orchard**: Investigation; Writing—Review & Editing. **Anne M. Murray**: Data Curation; Writing—Review & Editing. **Raj C. Shah**: Data Curation; Writing—Review & Editing. **Robyn L.Woods**: Validation; Investigation; Resources; Writing—Review & Editing. **Rosanne Freak-Poli**: Conceptualization; Methodology; Validation; Writing—Review & Editing; Supervision.

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CONFLICT OF INTEREST STATEMENT

Htet Lin Htun and *Achamyeleh Birhanu Teshale* reported receiving the Monash Graduate Scholarship and Monash International Tuition Scholarship. *Joanne Ryan* and *Robyn L. Woods* disclosed receiving grant and fellowship support from the National Health & Medical Research Council, Australia, as well as grant funding from the National Institute on Aging. *Suzanne G. Orchard* and *Anne Murray* reported serving as site principal investigators or sub-investigators for the ASPREE study, supported by grants from the National Institute on Aging and the National Cancer Institute at the U.S. National Institutes of Health. *Trevor T-J Chong* reported receiving honoraria for lectures from Roche. *Raj C Shah* reported being the site principal investigator or sub-investigator for Alzheimer's disease clinical trials for which his institution (Rush University Medical Center) is compensated [Amylyx Pharmaceuticals, Inc., Athira Pharma, Inc., Edgewater NEXT, Eli Lilly & Co., Inc., and Genentech, Inc.]. Other authors declare no competing interests. Author disclosures are available in the supporting information.

CONSENT STATEMENT

All human participants of the ASPREE clinical trial and ALSOP substudy provided informed consent on participation. ASPREE trial and ALSOP substudy were conducted in accordance with the Declaration of Helsinki 1964 as revised in 2008, the NHMRC Guidelines on Human Experimentation, the federal patient privacy (HIPAA) law and ICH-GCP guidelines and the International Conference of Harmonization Guidelines for Good Clinical Practice. ASPREE and ALSOP also follow the Code of Federal Regulations as it relates to areas of clinical research. The data of the present secondary data-analysis study were from a 5-year ASPREE clinical trial and ALSOP substudy [Trial Registration: International Standard Randomized Controlled Trial Number Register (ISRCTN83772183) and ClinicalTrials.gov (NCT01038583)]. The ASPREE trial was approved by multiple Institutional Review Boards in Australia and the U.S. (https://aspree.org). ALSOP has been reviewed and approved by the Monash University Human Research Ethics Committee (Social ALSOP: CF11/1935-2011001094). The present study was approved by the Monash University Human Research Ethics Committee to conduct secondary data analysis (ID: 24743).

DATA AVAILABILITY STATEMENT

All individual participant data underlying the results reported in this manuscript are available upon request to qualified researchers, subject to approval of the analyses by the Principal Investigators and adherence to a standard data sharing agreement. The data will be accessible through a secure Web-based data portal. Information regarding requests for data access is provided on the website (https://aspree.org).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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