TABLE 1 Baseline characteristics of participants by incident Alzheimer's disease or ischemic stroke developed during the 15-year follow-up period[a]

	No dementia and cerebrovascular disease	Incident AD without cerebrovascular disease[a]		Incident cerebrovascular disease without AD[a]	
	(n = 1738)	(n = 132)	P-value[b]	(n = 260)	P-value[c]
Age (y), mean (SD)	70.40 (10.05)	81.09 (8.19)	<.001	77.03 (9.22)	<.001
Females, n (%)	1083 (62.31)	99 (75.00)	.004	131 (61.92)	.904
Education level, n (%)[d]					
Elementary	217 (12.49)	30 (22.73)		48 (18.46)	
Secondary	834 (47.99)	78 (59.09)		144 (55.38)	
University	686 (39.49)	24 (18.18)	<.001	68 (26.15)	<.001
Occupation, n (%)[d]					
Blue collar	315 (18.25)	42 (32.06)		78 (30.35)	
White collar	1411 (81.75)	89 (67.94)	<.001	179 (69.65)	<.001
Smoking status, n (%)[d]					
Never	789 (45.74)	78 (60.00)		127 (48.85)	
Former	680 (39.42)	34 (26.15)		108 (41.54)	
Current	256 (14.84)	18 (13.85)	.004	25 (9.62)	.079
Heavy drinking, n (%)[d]	331 (19.14)	19 (14.39)	.178	34 (13.23)	.022
Sedentary lifestyle, n (%)	443 (25.49)	49 (37.12)	.003	80 (30.77)	<.001
Diabetes, n (%)	160 (9.21)	5 (3.79)	.034	33 (12.69)	.076
Hypertension, n (%)[d]	1222 (70.64)	98 (74.24)	.379	234 (90.00)	<.001
High cholesterol, n (%)[d]	608 (36.04)	53 (43.09)	.117	111 (43.53)	.021
BMI, n (%)[d]					
<18.5	734 (42.23)	67 (50.76)		98 (11.78)	
18.5–24.9	45 (2.59)	6 (4.55)		1 (0.38)	
≥25	911 (52.42)	43 (32.58)	<.001	147 (56.54)	.009
Heart diseases					
0	1470 (84.58)	98 (74.24)		179 (68.85)	
1	176 (10.13)	22 (16.67)		50 (19.23)	
≥2	92 (5.29)	12 (9.09)	.008	31 (11.92)	<.001
APOE 4 allele, n (%)[d]	460 (26.47)	54 (40.91)	<.001	63 (24.23)	.609
Depression, n (%)[d]	86 (4.95)	9 (6.82)	.358	9 (3.46)	.484
Psychological well-being, mean (SD)[d]	0.07 (0.52)	−0.20 (0.46)	<.001	−0.08 (0.50)	<.001
Leisure activity, mean (SD)[d]	2.58 (1.49)	1.85 (1.35)	<.001	2.25 (1.41)	.002
Social network, mean (SD)[d]	0.09 (0.53)	−0.09 (0.59)	<.001	0.04 (0.52)	.158

Abbreviations: AD, Alzheimer's disease; *APOE*, apolipoprotein gene; BMI, body mass index; IQR, interquartile range; SD, standard deviation.

[a]Participants with incident ischemic stroke in the table did not include those that developed AD, and participants with incident AD did not include those that developed ischemic stroke.

[b]*P*-value was calculated by comparing the baseline characteristics between the non-demented & non-stroke participants and participants who developed AD.

[c]*P*-value was calculated by comparing the baseline characteristics between the non-demented & non-stroke participants and participants who developed ischemic stroke.

[d]Missing values: 1 person for education level, 16 for occupation, 15 for smoking status, 12 for heavy drinking, 8 for hypertension, 65 for high cholesterol, 78 for BMI, 15 for depression, 414 for *APOE* status, 414 for psychological well-being, 327 for leisure activity, and 106 for social network.

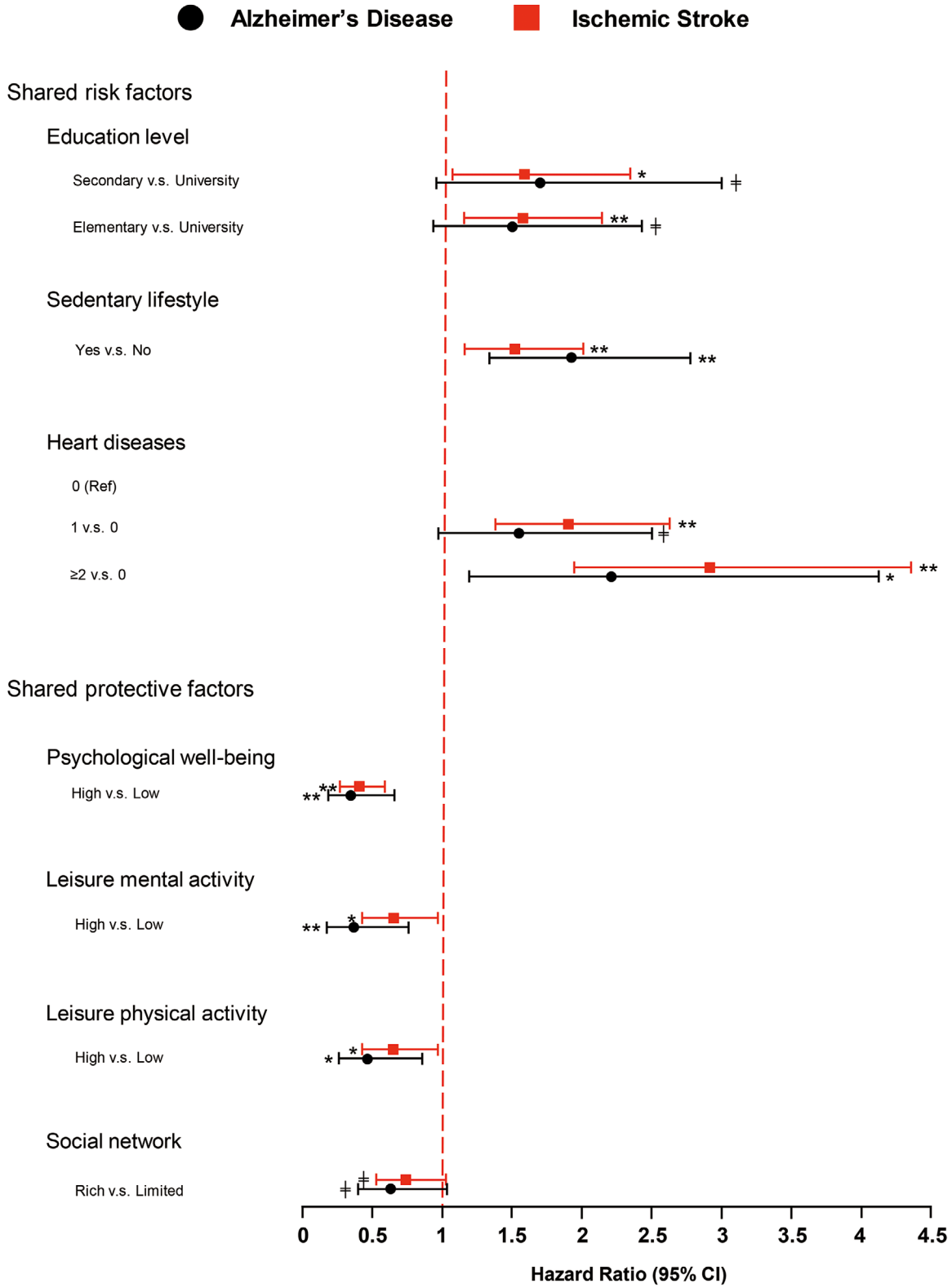

FIGURE 1 Hazard ratio (95% CI) of Alzheimer's disease (AD) and ischemic stroke by shared risk and protective factors. CI, confidence interval; Ref, reference. *Notes*: Models were adjusted for age, sex, and education. Psychological well-being, leisure activity, and social network were divided into three groups, according to their tertiles. High level of psychological well-being or leisure activity refers to the top tertile group, and low level of psychological well-being or leisure activity refers to the bottom tertile group. Rich social network refers to individuals in the top tertile group, and limited social network refers to those in the bottom tertile group. Table S1 and Table S2 provide detailed information related to each risk and protective factor for incident AD and ischemic stroke. $^{\ddagger}.05 < P < .10$, $^{*}.01 < P < .05$, $^{**}P < .01$

TABLE 2 Hazard Ratio (95% CI) of Alzheimer's disease and ischemic stroke by shared risk/protective profiles

	Incident Alzheimer's disease (n = 132/N = 1586)			Incident ischemic stroke (n = 260/N = 1998)		
	Rate per 1000 person-years (95% CI)	Model 1[a] HR (95% CI)	Model 2[a] HR (95% CI)	Rate per 1000 person-years (95% CI)	Model 1[a] HR (95% CI)	Model 2[a] HR (95% CI)
Shared risk profile[b]						
Risk factor score, categorical						
0	2.76 (1.64—4.67)	Ref. (1.00)	Ref. (1.00)	8.06 (5.98—10.87)	Ref. (1.00)	Ref. (1.00)
1	7.51 (5.78—9.76)	1.43 (0.79—2.59)	1.69 (0.87—3.29)	13.32 (11.00—16.13)	1.20 (0.83—1.73)	1.12 (0.77—1.63)
≥2	20.75 (16.17—26.61)	2.64 (1.44—4.85)**	3.45 (1.72—6.90)**	34.45 (29.62—41.45)	2.58 (1.77—3.77)**	2.49 (1.66—3.72)**
Risk profile groups						
Low (score 0-1)	5.59 (4.42—7.07)	Ref. (1.00)	Ref. (1.00)	11.20 (9.53—13.16)	Ref. (1.00)	Ref. (1.00)
High (≥2)	20.75 (16.17—26.61)	1.99 (1.39—2.95)**	2.25 (1.50—3.37)**	34.45 (28.62—41.45)	2.26 (1.73—2.96)**	2.29 (1.71—3.07)**
Shared protective profile[b]						
Protective factor score, categorical						
0	17.51 (13.92—22.03)	Ref. (1.00)	Ref. (1.00)	28.20 (23.67—33.61)	Ref. (1.00)	Ref. (1.00)
1	7.26 (5.13—10.27)	0.44 (0.29—0.67)**	0.64 (0.40—1.03)‡	13.96 (10.96—17.76)	0.51 (0.38—0.70)**	0.56 (0.40—0.78)**
≥2	2.61 (1.63—4.21)	0.30 (0.17—0.51)**	0.44 (0.24—0.80)**	8.88 (6.91—11.41)	0.43 (0.31—0.60)**	0.44 (0.30—0.64)**
Protective profile groups						
– (score 0)	17.51 (13.92—22.03)	Ref. (1.00)	Ref. (1.00)	28.20 (23.67—33.61)	Ref. (1.00)	Ref. (1.00)
+ (score ≥1)	4.49 (3.39—5.94)	0.38 (0.26—0.55)**	0.56 (0.36—0.87)*	10.95 (9.20—13.03)	0.47 (0.36—0.62)**	0.51 (0.38—0.68)**

[a]When modeling shared risk factor profile, we adjusted for age and sex in model 1, and additionally for hypertension, diabetes, obesity, high cholesterol, depression, *APOE* status, and number of drugs used in Model 2. In the models in which incident Alzheimer's disease was treated as the outcome, the missing value of covariates was 8 (0.4%) for hypertension, 60 (3.2%) for high cholesterol, 64 (3.4%) for obesity, 98 (5.2%) for *APOE* status, and 6 (0.3%) for number of drugs used. In the models in which incident ischemic stroke was treated as the outcome, the missing value of covariates was 8 (0.4%) for hypertension, 56 (2.8%) for high cholesterol, 62 (3.1%) for obesity, 104 (5.2%) for *APOE* status, and 6 (0.3%) for number of drugs used. When modeling shared protective factor profile, we adjusted for age and sex in model 1, and additionally for social leisure activity in model 2. In the models in which incident Alzheimer's disease was treated as the outcome, the missing value of covariates was 198 (10.6%) for social leisure activity. In the models in which incident ischemic stroke was treated as the outcome, the missing value of covariates was 202 (10.1%) for social leisure activity.

[b]Shared risk factor score was generated by counting the number of following features in an individual: education level below university or college, sedentary lifestyle, and the number of heart diseases. Shared protective score was calculated by counting the numbers of following features in an individual: high level of psychological well-being, intensive leisure-time mental activity, intensive leisure-time physical activity, and rich social network.

*01 < P < .05.

**P < 01.

‡05 < P < .10.

Abbreviations: CI, confidence interval; HR, hazard ratio.

3.4 | Counteracting effect of the shared protective profile on AD/IS in relation to levels of the shared risk profile

There was an interaction between the shared risk score and shared protective score on AD (P = .04), but not on IS (P = .38). A four-category variable of joint exposures was created, by combining the shared risk profile (high vs low) and the shared protective profile (negative vs positive). Figure 2 shows the associations of incident AD and IS with the joint exposures.

Compared to the "high risk and protective (–)" group, only the "low risk and protective (+)" group presented significantly reduced AD risk (Figure 2A), whereas the other three groups all showed substantial reduced IS risk (Figure 2B). The proportion of incident AD cases that could be prevented due to a positive protective profile was 47% (95% CI: 0.22 to 0.64) in participants with a low risk profile and 38% (95% CI: 0.00 to 0.62) in those with a high risk profile. In addition, 28% (95% CI: 0.12 to 0.41) of incident IS cases in participants with a low risk profile and 31% (95% CI: 0.02 to 0.52) of IS cases in participants with a high risk profile were attributable to a positive protective profile. Similar results were obtained when AD and IS were combined (Figure 2C). The protective profile seemed to reduce the risk of AD/IS by 33% (95% CI 0.21 to 0.42) among individuals with a low risk profile and by 28% (95% CI: 0.08 to 0.44) among individuals with a high risk profile.

3.5 | Population attributable fraction of shared risk and protective factors for AD/IS

The proportions of either AD or IS cases that would be reduced by controlling the shared risk factors and promoting the shared protective factors are shown in Figure 3. Specifically, 26% (95% CI: 0.10 to 0.38)

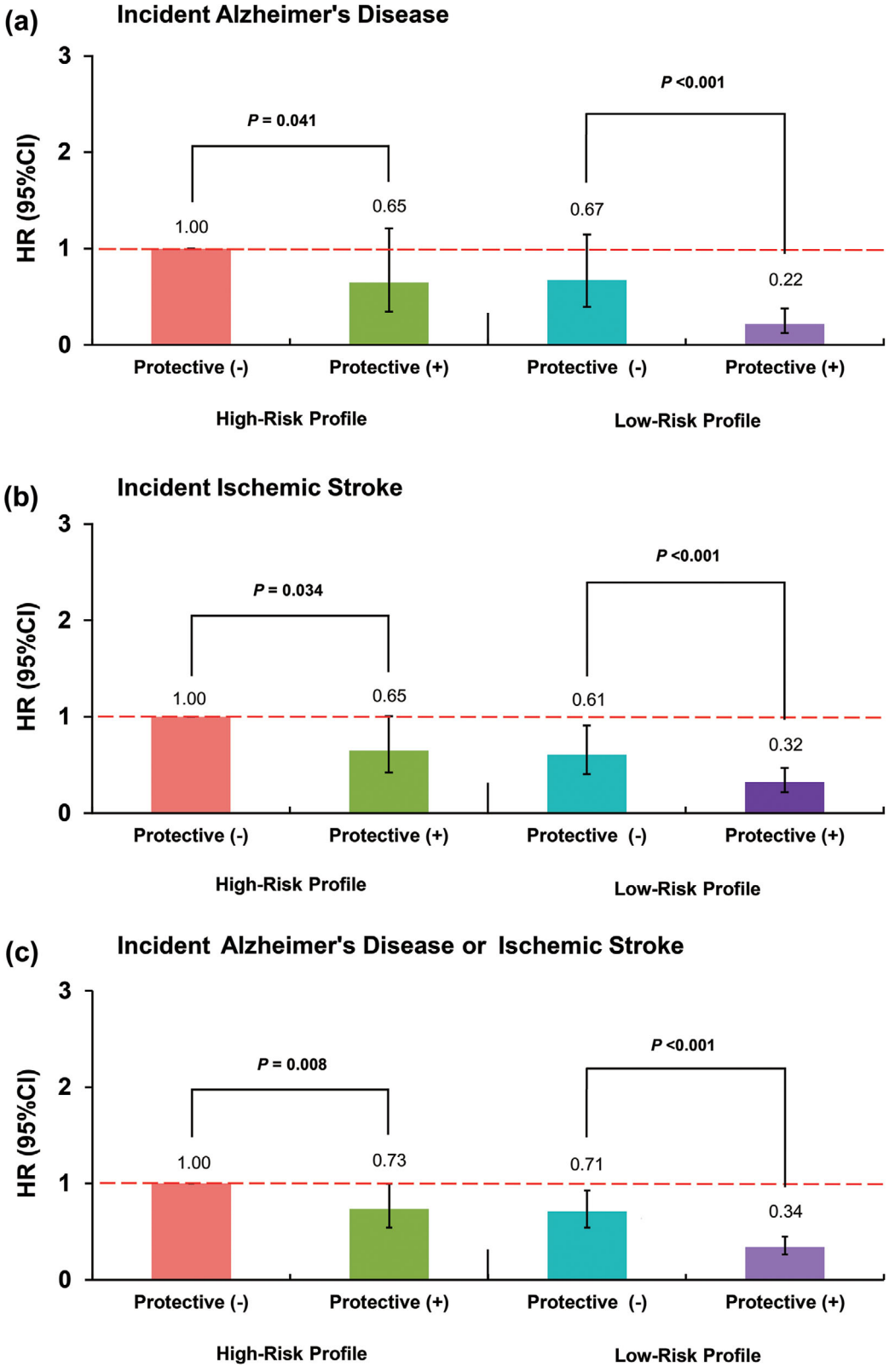

FIGURE 2 Joint effects of shared risk and protective profiles on incident Alzheimer's disease (AD) and ischemic stroke. CI, confidence interval; HR, hazard ratio. *Notes*: *P*-values were obtained by estimating the effect of the protective profile (positive versus negative) on incident AD (a), incident ischemic stroke (b), and incident AD or ischemic stroke (c) by levels of risk profiles

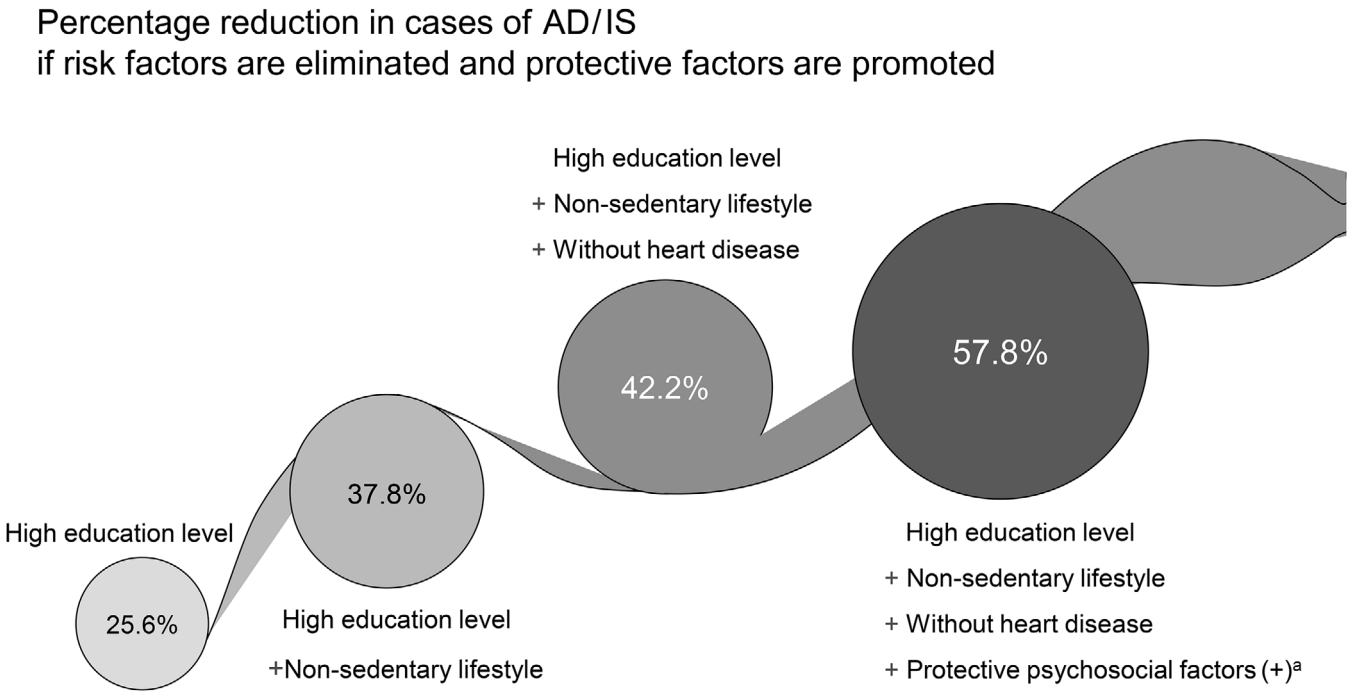

FIGURE 3 Population attributable fraction of shared risk and protective factors for either incident Alzheimer's disease (AD) or incident ischemic stroke (IS). [a]Protective psychosocial factors are the shared protective factors between AD and IS, including high levels of psychological well-being, intensive mental leisure activity, intensive physical leisure activity, and a rich social network. Protective psychosocial factors (+) indicates that an individual has at least one of the shared protective factors. *Notes*: The figures in the circles represent the percentage reduction of cases of either AD or IS if one risk factor (low education level), two risk factors (low education level and sedentary lifestyle), three risk factors (low education level, sedentary lifestyle, and heart diseases) were eliminated, and at least one protective factor was additionally promoted

of AD/IS cases could be prevented if all individuals in a population had a high level of education, and 42% (95% CI: 0.26 to 0.55) of AD/IS cases could be prevented if all individuals in a population were free from any of the shared risk factors (ie, low level of education, sedentary lifestyle, and heart diseases). In total, 58% (95% CI: 0.42 to 0.69) of AD/IS cases could be prevented by promoting a positive protective profile in individuals free from any of the shared risk factors.

3.6 | Additional analyses

Similar results were observed in the old-old group (>75 years) and the young-old group (<75 years) regarding the association of shared risk/protective factors with AD/IS (Tables S3 and S4 in supporting information). Furthermore, the findings were similar when we applied different cut-offs for cardiovascular risk factors (Table S5 in supporting information), when we removed the incident AD and IS cases detected in the first 3-year follow-up period or those who had died within 3-years from baseline (Table S6 in supporting information), when covariates were adjusted for as either 3 levels of categorical variables or as continuous variables, and when we conducted multiple imputation to replace the missing covariates in the models. Finally, change in psychosocial well-being was not significantly associated with either AD (HR [95% CI] = 0.78 [0.46 to 1.34]) or IS (HR 0.82, 95% CI: 0.60 to 1.13) in our additional analyses.

4 | DISCUSSION

In this population-based long-term follow-up study of Swedish older adults aged 60 years and above, we found that: (1) low level of education, a sedentary lifestyle, and heart diseases are the shared risk factors for AD and IS. High levels of psychological well-being, leisure-time mental and physical activity, and a rich social network are the shared protective factors for AD and IS; (2) a protective profile may decrease 47% of AD and 28% of IS risk among older adults with a low risk profile, and 38% of AD and 31% of IS risk in those with a high risk profile; and (3) more than half of the cases with either AD or IS could be theoretically preventable by controlling the risk profile and promoting the protective profile.

Previous population-based studies have demonstrated that certain risk and protective factors are related to both AD and stroke, including vascular risk factor burden, depression, and social networks.[8,9,29–31] When investigating the association of these factors with AD or IS, previous researchers focused exclusively on one of the outcomes, or treated stroke and dementia as a combined outcome. In the current study, we examined AD and IS cases in a mutually exclusive manner, and the shared risk factors identified accordingly may suggest shared pathophysiologies between AD and IS. To the best of our knowledge, this is the first study attempting to detect shared risk/protective factors for AD and IS, involving a large range of demographic, genetic, vascular, mental, and psychosocial factors.

Several studies have developed scores or indices to predict the risk of stroke or dementia, based on the expected accumulated synergistic effect of multiple risk factors.[30,32,33] The Framingham Stroke Risk Score (FSRS) and the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) dementia risk score are two recognized examples.[34] The only overlapping modifiable risk factor between the two scores is high systolic blood pressure. However, the Whitehall II study has revealed that the FSRS is associated with accelerated cognitive decline over 10 years,[35] and another study showed that the FSRS score might even perform better than the CAIDE score in predicting cognitive decline.[34] These findings indicate that the stroke risk–related factors, may play a potential role, either independently or synergistically, in the development of dementia or AD.

Female sex is a well-established risk factor for AD, but sex was not associated with AD in our analyses. The population in the current study consists of a random sample (63.6% females) from central Stockholm (Kungsholmen) during the years 2001 to 2003. Interestingly, females in our sample were more likely to drop out either at baseline or during the follow-up period. Specifically, among those who refused to participate in follow-up interviews, 64.36% were female, and among those who died before the first follow-up interview, 57.39% were female. A lower education level and a higher burden of multimorbidity in females than in males may contribute to the higher attrition rates in females, which may further influence the association between female sex and the risk of AD. The associations of cardiovascular risk factors (eg, high blood pressure, and high total cholesterol level) with AD and IS may vary by age, the presence of frailty, multimorbidities, and treatments. Guidelines for the diagnosis and management of certain cardiovascular risk factors (eg, hypertension and high cholesterol) have been updated recently.[36,37] In our additional analysis, we have applied multiple cutoffs to cardiovascular measurements in the additional analyses, and the results are consistent with our main findings—cardiovascular measurements (eg, blood pressure and BMI) showed a tendency of protective effect on AD but a risk effect on IS. The reduced hazard of AD associated with cardiovascular measurements may be driven partially by reverse causality.

In the current study, three major heart diseases (ie, coronary heart disease, atrial fibrillation, and heart failure) were involved in the analysis, and we counted the numbers of heart diseases in each participant as a proxy of aggregation. Yet, future studies need to pay attention when the AD/IS risk was estimated in relation to a distinct combination of two heart diseases, especially when treatments were taken into account. For example, heart failure or atrial fibrillation alone was associated with a higher risk of mortality than coronary heart disease.[38] Coexistince of atrial fibrillation and heart failure may worsen the disease progression and complicate treatments. Subtypes of heart failure (eg, heart failure with preserved ejection fraction and heart failure reduced ejection fraction) are linked to variations in treatments, survival rates, and subsequent stroke risk. In addition, treatments for heart disease (eg, anticoagulant therapy, antiplatelet agents, and statins), could modify the association between burden of heart diseases and AD/IS. Anticoagulation medication in particular may significantly reduce the stroke risk in atrial fibrillation patients; however, there is still debate regarding whether warfarin anticoagulation may increase the risk of all dementia types in atrial fibrillation patients.[39] Therefore, the diverse cardiovascular pathologies, specific aggregations of heart diseases, and treatments are vital factors to consider for future studies when investigating the association of AD/IS with heart diseases.

Moreover, psychosocial factors, such as an active and socially integrated lifestyle, have been suggested to protect older adults from both stroke and dementia/AD.[12,40] A dose-response association of psychosocial factors with AD has been reported when such factors were aggregated together into a cognitive reserve score,[41] as was the case in our study. We moreover found that a positive protective profile can offset the risk of AD or IS due to shared risk profiles. This is encouraging because, even in older adults with a high risk profile with a low level of education, a sedentary lifestyle, and multiple heart diseases, approximately one third of AD and IS risk, could be counteracted through promoting psychological well-being, leisure activity, and social network.

The Lancet Commission life-course model has demonstrated that up to 35% of dementia cases were potentially preventable if nine life-long factors were diminished, including early life low education, mid-life risk factors (hearing loss, hypertension, and obesity), and late-life risk factors (smoking, depression, physical inactivity, social isolation, and diabetes).[42] The INTERSTROKE study, a world-wide study including 32 countries and focusing on 10 potentially modifiable risk factors (ie, blood pressure, physical activity, apolipoprotein B-to-apolipoprotein A ratio, diet, waist-to-hip ratio, psychological factors, smoking, cardiac events, alcohol consumption, and diabetes), has presented that the 10 factors were collectively linked to about 90% of PAF of IS. In addition, 90% of the PAF of IS was independent with regions, ethnic groups, sex, and age. In the current study, we found that shared risk and protective factors were associated with nearly 60% of PAF of AD/IS. The varied PAF between our study and others may be due to the different age, diversity in the combination of risk/protective factors, and inclusion/exclusion criteria of outcomes.

Vascular dysfunction, atherosclerosis, and deposition of amyloid in cerebral vessels may partially explain the common underlying mechanism between AD and IS.[44,45] The hypoperfusion and hypoxia caused by atherosclerosis may boost the production of Aβ. The Aβ, in turn, may accelerate the formation of atherosclerotic lesions through endothelial dysfunction or vascular oxidative stress, leading to further vascular damage in the brain.[40,41] Mitochondrial dysfunction with epigenetic impairment in oxidative respiration appears to be the earliest mechanism in the progression of AD and IS, and they are closely linked to the age-related energy deficits.[46] Certain risk factors, such as peripheral insulin resistance, could largely contribute to this energy deficit and exacerbate Aβ/tau accumulation. Life-long risk factors (eg, low education, sedentary lifestyle, and heart diseases), in theory, may act in different cascades of IS and AD pathologies. For example, one factor may cause oxidative stress and trigger atherosclerosis in middle age, and another factor may lead to the thickening of vascular basement membranes and hypoperfusion in older age. Other pathologies or clinical profiles that are captured by neuroimaging or molecular levels, such as microbleeds and cerebrovascular reactivity, may play an essential role in connecting AD and IS, and may easily be

influenced by shared risk factors as well.[47] However, it is difficult to speculate the direct causality from the shared risk factors to the common mechanisms, due to lacking neuroimaging and biomarker confirmation, and unmeasured confounding. Moreover, mixed pathologies are frequently observed in AD patients or the aging brain.[48] Specifically, cerebral amyloid angiopathy and small vessel disease are the common vascular pathologies in the aging brain and in AD cases. Certain risk factors, such as heart diseases and cardiovascular risk factors, may give rise to cerebral small vessel disease and consequently, a higher AD or IS risk.[49,50] The mechanisms in which positive psychosocial factors may lower or compensate the risk of AD and IS are not fully understood. Nevertheless it is plausible to assume that the reduction in AD risk could be achieved through vascular mechanisms that are in part independent of AD pathology. This hypothesis is supported by a recent study displaying that midlife physical activity is associated with a lower incidence of vascular dementia, but not AD.[51] The cognitive reserve concept assumes that individuals with certain lifestyles and psychosocial factors could cope better with increasing brain lesions (eg, AD pathology), reflecting a more flexible or adaptive cognitive network.[40,41] In the current study, the findings suggest that individuals with more positive psychological profiles tend to have better self-perceptions of aging, which may impact their values, health behaviors, health-care use, and access to instrumental and emotional support.[52] These factors may reduce and/or make people more resilient to psychosocial stress, and therefore improve cardiovascular health by enhancing the immune system or reducing systemic inflammation.[40]

This study has several strengths, including the relatively large study sample with a long follow-up period, the high rate of participation, and the comprehensive diagnoses using multiple resources (eg, physical examination, patient and death registers). The structured SNAC-K interviews provide a wide range of information on demographics, clinical, lifestyle, psychosocial, and behavioral factors. Yet, several limitations need to be pointed out. First, using self-reported questionnaire data on psychosocial factors may introduce measurement bias. This is especially true among older adults who may have cognitive impairment or memory complaints. Second, selection bias may have been introduced by excluding those subjects who did not have any follow-up information or who refused to participate in follow-up interviews, although the proportion of those people was rather small (10.3%). A few factors need to be taken into accounts in future validation studies, such as heart diseases, cancer, and COVID-19. Specifically, when a world pandemic that is associated with elevated mortality in older populations occurs, such as COVID-19, survival bias might be introduced to a study to affect the link of shared risk/protective factors to AD/IS. Third, similar to most observational studies, bias that may be caused by unmeasured confounding factors remains (eg, low-density lipoprotein), even though multiple sensitivity analyses have been carried out in the current study. The factors that we included in this study were from baseline. With a rather long follow-up period in the current study, certain risk or protective factors may vary with time, for instance, the increasing number of heart diseases and reduction in social networks. Furthermore, certain factors, such as the use of medications, treatment of heart diseases, or psychosocial factors, may interact with shared risk factors to influence the AD/IS risk over time. Future studies should further verify the time-varying effect of those factors in relation to both AD and IS. High education is often treated as one of the important cognitive reserve proxies, and showed a protective effect on both AD and IS. The risk factors in our study have been predefined as being either pathogenic or as negative exposures in early life, hence, both low education and sedentary lifestyles are identified as risk factors. However, it is worth investigating the underlying mechanisms of resilience and reserve between AD and IS with respect to the cognitive reserve proxies. Fourth, IS includes a wide range of subtypes, and it can be subdivided into several categories including cardioembolism, small-vessel occlusion, large-artery atherosclerosis, and stroke of undetermined etiology. For example, cardioembolic stroke (embolic events occur in the valve or chambers of the heart) and lacunar stroke (blood vessel occlusion in a perforating artery) are two subtypes of IS. The diverse etiologies and treatments of the two IS categories may display different risk factors; disease burden; comorbidity; and eventually, influence the connection with AD. In the current study, we focused only on general IS without specifying subcategories. Fifth, the AD and IS cases in the current study were based on the clinical diagnosis, which do not represent "pure" AD or "pure" ischemic damage. The advent of molecular neuroimaging techniques enables us to identify the often-combined cerebrovascular disease and AD pathologies in vivo, and more evidence has accumulatively suggested that mixed pathologies are common in aging and important in lowering the threshold for cognitive impairment and dementia.[53] Lack of neuroimaging and biomarkers in this study makes it difficult to relate the shared factors to a "pure" specific pathology. Sixth, although our results display a sufficient reduction in AD/IS risk at the population level by targeting both shared risk and protective factors, proper interpretation is needed at the individual level because PAF does not allow the designation of affected individuals. Finally, our study participants live in central Stockholm and have a relatively higher socioeconomic status and education level than the general older population. Caution is therefore needed when generalizing our findings to other populations.

In conclusion, several shared risk and protective factors between AD and IS were identified among adults aged 60 years and above. Late-life AD and IS risk may be mitigated by targeting multiple lifelong risk/protective factors, including (1) early-life education; (2) midlife lifestyles and risk factors of heart diseases; and (3) late-life psychosocial well-being, social network, and leisure time activity. Moreover, late-life psychosocial factors may even counteract the harmful effect of risk factors that occurred earlier in life on both AD and IS. Our findings support the notion that AD and IS may share pathophysiological mechanisms or mixed pathologies (eg, neurodegenerative and vascular pathologies), which may be the dominant etiology for AD. We, therefore, provide evidence for the implementation of common preventive strategies for both disorders. Future studies are essential to better understand the compensatory mechanisms in AD and IS pathology. Clinical trials may consider using multifactor interventions, such as targeting heart diseases and psychosocial factors, to prevent AD and stroke.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

R.W. and W.X. conceptualized and designed the study, R.W. performed the data analysis and drafted the manuscript. C.Q., H.-X. W., C.S.D., Y.S., and A.C.-L. contributed to the data interpretation and revision of the manuscript and approved the final draft. R.W. has the full access to all the data in this study, and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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SUPPORTING INFORMATION

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

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