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Effects of physical and psychological multimorbidity on the risk of dementia: multinational prospective cohorts and a meta-analysis

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Abstract

Background Previous studies only considered the impact of a single physical or psychological disorder on dementia. Our study investigated the association of physical and psychological multimorbidity with dementia among older adults using two multinational prospective cohorts to supplement the limited joint evidence.

Methods We utilized the Health and Retirement Study (HRS 2012 to 2018) in the United States (US) and the Survey of Health, Ageing and Retirement in Europe (SHARE 2012 to 2018). Physical disorder was defined as any one of seven self-reported physician-diagnosed conditions. Psychological disorder was assessed using the 8-item Center for Epidemiologic Research Depression (CES-D) scale or the EURO-D. Dementia was determined through a combination of self-reported physician diagnosis of dementia or Alzheimer's disease, or the 27-point HRS cognitive scale. Competing risk models were utilized to estimate the hazard ratios (HRs) and 95% confidence intervals (95% CI). DerSimonian-Laird random-effects meta-analyses were conducted to obtain pooled estimates.

Results The prevalence of physical and psychological multimorbidity was 17.29% (1027/5939) in continental Europe and 15.52% (1326/8543) in the US. The incidence of dementia was 6.21 per 1000 person-years in continental Europe and 8.27 per 1000 person-years in the US, respectively. It was highest among participants with physical and psychological multimorbidity in continental Europe (10.46 per 1000 person-years) and the US (14.82 per 1000 person-years), compared with the other three groups. In the univariate model, participants who reported physical and psychological multimorbidity had a higher risk of dementia compared with those who reported no physical and psychological disorders in continental Europe (HR = 2.59; 95% CI: 1.55, 4.33) and the US (HR = 4.11; 95% CI: 2.44, 6.94). After adjusting all covariates, the risk of dementia among participants who reported physical and psychological multimorbidity increased by 86% in continental Europe (aHR = 1.86; 95% CI: 1.08, 3.21) and by 176% in the US (aHR = 2.76; 95% CI: 1.61, 4.72), respectively. After pooling the outcomes, the risk of dementia among participants who reported physical and psychological multimorbidity increased by 115% (aHR = 2.15; 95% CI: 1.27, 3.03).

Conclusions Physical and psychological multimorbidity was prevalent among older adults in the US and continental Europe. Given the consistent associations with dementia, it is imperative to increase awareness of the links and recognize the limitations of single-disorder care. Specific attention should be given to providing care coordination.

Keywords Physical disorders, Psychological disorder, Multimorbidity, Dementia, Cohort

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Background

Dementia, a prevalent health issue of aging, refers to the various challenges in memory, learning, concentration, and decision-making [1]. Rapid population aging has posed a significant challenge for preventing dementia. According to the report from the World Health Organization (WHO), there were nearly 50 million people with dementia and 10 million new cases every year worldwide [2]. In May 2017, the *Global action plan on the public health response to dementia 2017–2025* projected that the number of older adults with dementia would rise to 75 million by 2030 and 132 million by 2050 [1]. Dementia has been recognized as a public health priority. The fifth target of this plan suggests that integrating the reduction and control of modifiable dementia risk factors into national health planning processes and development agendas is essential for the prevention and management of dementia [1].

Previous cohort studies have shown that a physical or psychological disorder such as stroke, diabetes, and depression is risk factor for dementia [1, 3–5]. However, in the context of the globally increasing aging population, physical and psychological multimorbidity is emerging as a common condition among older adults [6, 7]. Ni et al. reported that the prevalence of physical–psychological multimorbidity was 18% in high-income countries and 20% in upper-middle-income countries [6]. Therefore, physical or psychological disorders should not be considered in isolation. However, the associations of physical and psychological multimorbidity with the onset of dementia among older adults are still unknown. In general, there are three reasons supporting the importance of the related research. Firstly, related research suggests that dementia, physical disorders, and psychological disorders may share similar risk factors and all be age-related and inflammatory-associated diseases [8–10]. One cross-sectional study indicated that physical and psychological disorders may have a collective and mutually reinforcing impact on the increased risk of cognitive decline [11]. Physical and psychological health could even impact the associated care of dementia [12]. Secondly, the world is now paying attention to the high prevalence of physical and psychological multimorbidity [6]. Physical and psychological multimorbidity is an emerging concept useful in conceptualizing disease burden. Its impact on dementia provides evidence for managing the dementia epidemic through integrated approaches that target risk factors shared by co-occurring diseases common in older age [7, 13]. Improving common contributing factors of physical and psychological multimorbidity to prevent dementia can help clinicians focus on enhancing overall well-being in care coordination. Furthermore, it also supports the development of accessible and sustainable strategies for populations in various geographical, economic, and cultural contexts [14]. Finally, the control group, consisting of participants who do not have one specific disease, may include individuals with other harmful diseases, leading to an overestimation of the risk associated with this particular disease. Compared to research that may present an overestimated association between a specific disease and dementia, it may be more practical to investigate the influence of multimorbidity on dementia in the context of high multimorbidity burden among the older population.

At present, the potential influence of a single disease on dementia may overlook the substantial burden of physical and psychological multimorbidity, as well as the interplay between physical and psychological disorders. To address this gap, we utilized data from two prospective cohorts (the United States Health and Retirement Study [HRS] and the Survey of Health, Ageing and Retirement in Europe [SHARE]) to provide comprehensive insights into the relationship between physical and psychological multimorbidity and dementia among older population. Consistent and standardized study protocol can ensure the reliable extrapolation in these two cohorts. Our study aimed to provide a reference for disease surveillance and prevention in clinical practice amidst the high burden of dementia among older adults.

Methods

Study design and participants

Our multinational cohort study utilized individual-level data from two well-characterized cohorts with the same biennial longitudinal design and comparable survey protocols: the HRS and the SHARE. The HRS is a nationally representative longitudinal survey of adults aged 50 years and older in the United States (US) [15, 16]. The SHARE is a longitudinal household survey focusing on retirement and health among the elderly in continental Europe [17]. More information on the sample design and procedures can be found in their cohort profiles [15, 18]. This study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

We used data from the HRS and the SHARE from 2012 to 2018. Baseline data was collected in 2012. The follow-up assessments were conducted until 2018. For HRS and SHARE, we included 30,313 and 39,300 participants aged 60 years or older at baseline. After excluding participants with dementia, Alzheimer's disease, cognitive impairment, or those who lacked the aforementioned information, we included 9926 participants with normal cognitive function in the HRS and 6699 participants with normal cognitive function in the SHARE. Then, we excluded participants who lacked relevant information on physical and psychological multimorbidity and

covariates, and finally included 8543 and 5939 participants in HRS and SHARE, respectively (Fig. 1).

The HRS has received approval from the University of Michigan Institutional Review Board (IRB Protocol: HUM00061128). The SHARE was reviewed and approved by the Ethics Committee of the University of Mannheim and the Ethics Council of the Max Planck Society (IRB: No 723/2009). All participants provided informed consent.

Assessment of physical and psychological multimorbidity

Psychological disorder was identified using the 8-item Center for Epidemiologic Research Depression (CES-D) scale in the HRS. This scale measured the frequency of feelings on eight dichotomous items in the past week, including "depressed," "everything was an effort," "happy," "life was enjoyable," "sad," and "unable to get going" [6, 19, 20]. We reverse-coded the items for "happy" and "life was enjoyable" and then summed all the items. The total scores ranged from 0 to 8, with a cutoff value greater than 3 indicating a psychological disorder. In SHARE, the EURO-D, which comprises 12 items (depressive symptoms, pessimism, death wish, guilt, irritability, crying, fatigue, sleep problems, loss of interest and appetite, reduced ability to concentrate, and capacity to enjoy things over the last month), was used to assess psychological disorder [21]. The cutoff for a clinically relevant psychological disorder is ≥ 4 [21].

Physical disorders included seven self-reported physician-diagnosed conditions: hypertension, diabetes, cancer, lung disease, heart disease, stroke, and arthritis in the HRS and the SHARE [6, 22]. Reported presence of any of the aforementioned seven chronic physical conditions was considered as a physical disorder [6]. Participants were categorized into four groups based on the presence of physical and psychological disorders: none, only physical disorder, only psychological disorder, and physical and psychological multimorbidity.

Assessment of dementia

Referring to previous studies, dementia was determined by a combination of self-reported physician diagnosis of dementia or Alzheimer's disease, or total scores below the cutoff value of 7 on the HRS cognitive scale [23, 24]. This cognitive scale included immediate and delayed 10-noun free recall to assess memory, serial sevens subtraction to evaluate working memory, and counting backwards to measure the speed of mental processing [22, 25, 26]. The total scores ranged from 0 to 27, with a score of 6 or less indicating dementia, while a score of more than 11 indicates normal cognitive function [27, 28]. In the SHARE, cognitive function was assessed using episodic memory and verbal fluency tasks [29]. A memory score of 1.5 standard deviations below the age-specific mean had been considered an indicator of cognitive impairment. If respondents failed to name at least 15 correct words in verbal fluency tasks, they had a verbal fluency problem. Normal cognitive function was defined as having no issues with both episodic memory and verbal fluency [29]. We included participants who reported no dementia and had normal cognitive function at baseline.

Covariates

The baseline covariates included age (<70 years, $70\sim79$ years, ≥ 80 years), gender (female, male), educational level (less than high school, high school or associate degree, college degree or above), marital status (married, unmarried), total wealth income (the lowest quartile, quartile 2, quartile 3, the highest quartile), self-reported body mass index (BMI; underweight, normal, overweight, obesity), physical activity (no, yes), drinking habits (no, yes), and smoking status (no, yes). BMI was classified based on the standard from WHO [30]. The total wealth income (including housing, vehicles, and saving accounts) minus other debts at the household level has been assessed (including secondary residence, if any) in local currencies (HRS: dollars, SHARE: euros), and further divided into four groups based on quartile range [6]. The physical activity was assessed based on the frequency of participating in light, vigorous, or moderate physical activity [6]. Options from any of the activities, including "everyday," "more than once a week," and "once a week," were recoded as "yes," while other options, including "one to three times a month" and "hardly ever or never," were recoded "no." Drinking habits and smoking status were both self-reported based on questions about ever drinking any alcohol or ever smoking.

Statistical analysis

The characteristics of participants were compared using the χ^2 test for categorical variables. We considered mortality as the competing event and utilized univariate and multivariable competing risk models to estimate the crude hazard ratios (cHRs) and adjusted hazard ratios (aHRs), along with their corresponding 95% confidence intervals (95% CIs). For all analyses, we fitted three models: model 1 was a univariate model; model 2 adjusted for age, gender, educational level, marital status, and total wealth income; and model 3 was a full model adding self-reported BMI, physical activity, drinking, and smoking. We conducted subgroup analysis based on age, gender, educational level, marital status, income, BMI, physical activity, drinking habits, and smoking status to assess the robustness of the results. Then, we conducted DerSimonian-Laird random-effects meta-analyses [31] to calculate the pooled HRs and 95% CIs.

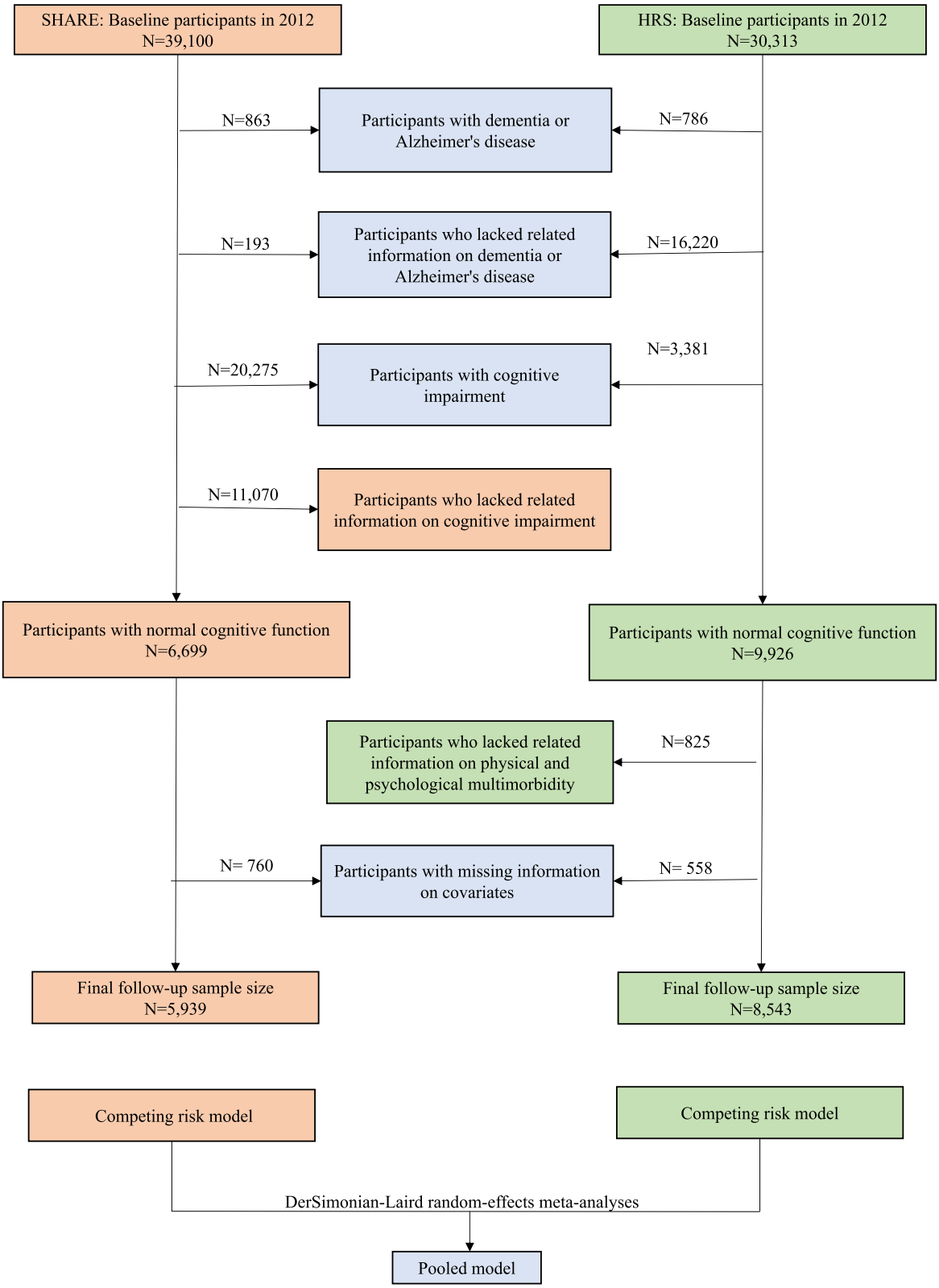

Fig. 1 Study flowchart. HRS, Health and Retirement Study; SHARE, Survey of Health, Ageing and Retirement in Europe

In addition, we conducted three sensitivity analyses to test the robustness of the results: (1) due to discrete follow-up data from the limitations of study design, we utilized robust Poisson regression models instead of competing risk models to observe the risk ratios (RRs) of dementia; (2) after interpolating the missing covariates using the random forest method, we examined the association of physical and psychological multimorbidity with dementia among 9926 in the HRS and 6699 participants in the SHARE, respectively; (3) taking into account the impact of the number of physical and psychological disorders, we reclassified physical and psychological multimorbidity as eight groups (none, only one physical disorder, only two physical disorders, only three or more physical disorders, only psychological disorder, psychological disorder with one physical disorder, psychological disorder with two physical disorders, psychological disorder with three or more physical disorders) and calculate HRs. All analyses were conducted using R software, version 4.2.1 for Windows. The package "cmprsk" was used to fit the competing risk model (Fine-Gray subdistribution hazard model). Two-sided *P* values less than 0.05 were considered statistically significant.

Results

The characteristics of participants

Among 5939 participants from continental Europe, the median age was 71.00 years old (interquartile range [IQR]: 65.00, 78.00), with 2512 (42.3%) being female. Among 8543 participants from US, the median age was 71.00 years old (IQR: 64.00, 77.00), with 4984 (58.34%) being female.

The prevalence of physical and psychological multimorbidity was 17.29% (1027/5939) in continental Europe and 15.52% (1326/8543) in the US. The characteristics of participants, including age, gender, educational level, marital status, total wealth income, BMI, and physical activity, differed among four groups based on various physical and psychological disorders in the US and the continental Europe (all $P<0.05$). The participants who reported physical and psychological multimorbidity were more likely to be older, less educated, obese, and engage in no physical activity in the US and the continental Europe (Table 1).

Associations of physical and psychological multimorbidity with dementia

The incidence of dementia was 6.21 per 1000 person-years in the continental Europe and 8.27 per 1000 person-years in the US, respectively. The incidence of dementia was highest among participants with physical and psychological multimorbidity in the continental Europe (10.46 per 1000 person-years) and the US (14.82 per 1000 person-years) (Table 2).

In the univariate model, we found that participants who reported physical and psychological multimorbidity had a higher risk of dementia compared with those who reported no physical and psychological disorders in the continental Europe (HR = 2.59; 95% CI: 1.55, 4.33) and the US (HR = 4.11; 95% CI: 2.44, 6.94) (Table 2). After adjusting for all covariates, the risk of dementia among individuals with physical and psychological multimorbidity increased by 86% in the continental Europe (HR = 1.86; 95% CI: 1.08, 3.21) and by 176% in the US (HR = 2.76; 95% CI: 1.61, 4.72), respectively (Table 2). However, the associations of only physical disorder and only psychological disorder with dementia were not significant. When the outcomes from continental Europe and the US were pooled, the risk of dementia among individuals with physical and psychological multimorbidity increased by 115% in model 3 (HR = 2.15; 95% CI: 1.27, 3.03) (Table 2). When covariates are accounted for in the model, the goodness of fit of models improves, where the goodness of fit of model 3 is best, following by model 2 and then model 1. The sensitivity analysis 1 and 2 showed that results were relatively stable (Additional file 1: Tables S1–S2). When we reclassified physical and psychological multimorbidity, the pooled outcomes indicted that the risk of dementia among individuals who reported psychological disorder and two physical disorders increased by 134% (Additional file 1: Table S3). Among individuals who reported psychological disorder and three or more physical disorders, the risk increased by 165% (Additional file 1: Table S3). Subgroup analysis revealed that the results were stable (all *P* for interaction > 0.05) (Additional file 1: Tables S4–S5). The pooled outcomes of the results from the subgroup analysis are presented in Additional file 1: Table S6 and Fig. 2.

Discussion

Our multinational cohort study found that physical and psychological multimorbidity was prevalent among older adults in the US (15.52%) and continental Europe (17.29%). The incidence of dementia was 6.21 per 1000 person-years in continental Europe and 8.27 per 1000 person-years in the US, respectively. The risk of dementia increased among participants who reported physical and psychological multimorbidity in various cohorts. The consistent and high-risk associations indicate that coordinated management of physical and psychological multimorbidity is essential to prevent dementia and promote healthy aging comprehensively.

The *Global action plan on the public health response to dementia 2017–2025* proposed "dementia risk reduction"

Table 1 The comparison of characteristics between participants with different physical and psychological disorders

Characteristics	Continental Europe					US				
	None, *n* (%)	Only physical disorder, *n* (%)	Only psychological disorder, *n* (%)	Physical and psychological multimorbidity, *n* (%)	*P* value	None, *n* (%)	Only physical disorder, *n* (%)	Only psychological disorder, *n* (%)	Physical and psychological multimorbidity, *n* (%)	*P* value
N	1496 (25.19)	3197 (53.83)	219 (3.69)	1027 (17.29)		794 (9.29)	6354 (74.38)	69 (0.81)	1326 (15.52)	
Age group (years)					< 0.001					< 0.001
< 70	784 (52.41)	1076 (33.66)	99 (45.21)	312 (30.38)		568 (71.54)	2605 (41.00)	51 (73.91)	581 (43.82)	
70 ~ 79	532 (35.56)	1367 (42.76)	78 (35.62)	406 (39.53)		181 (22.80)	2642 (41.58)	11 (15.94)	510 (38.46)	
≥ 80	180 (12.03)	754 (23.58)	42 (19.18)	309 (30.09)		45 (5.67)	1107 (17.42)	7 (10.14)	235 (17.72)	
Gender					< 0.001					< 0.001
Female	823 (55.01)	1720 (53.80)	162 (73.97)	722 (70.30)		427 (53.78)	3603 (56.70)	41 (59.42)	913 (68.85)	
Male	673 (44.99)	1477 (46.20)	57 (26.03)	305 (29.70)		367 (46.22)	2751 (43.30)	28 (40.58)	413 (31.15)	
Educational level					< 0.001					< 0.001
Less than high school	269 (17.98)	804 (25.15)	45 (20.55)	320 (31.16)		70 (8.82)	658 (10.36)	15 (21.74)	259 (19.53)	
High school or associate degree	618 (41.31)	1280 (40.04)	101 (46.12)	418 (40.70)		176 (22.17)	2126 (33.46)	20 (28.99)	442 (33.33)	
College degree or above	609 (40.71)	1113 (34.81)	73 (33.33)	289 (28.14)		548 (69.02)	3570 (56.19)	34 (49.28)	625 (47.13)	
Marital status					< 0.001					< 0.001
Married	1072 (71.66)	2146 (67.13)	153 (69.86)	585 (56.96)		557 (70.15)	4018 (63.24)	21 (30.43)	584 (44.04)	
Unmarried	424 (28.34)	1051 (32.87)	66 (30.14)	442 (43.04)		237 (29.85)	2336 (36.76)	48 (69.57)	742 (55.96)	
Total wealth income					< 0.001					< 0.001
Lowest quartile	215 (14.37)	591 (18.49)	47 (21.46)	297 (28.92)		78 (9.82)	775 (12.20)	20 (28.99)	338 (25.49)	
Quartile 2	283 (18.92)	701 (21.93)	36 (16.44)	233 (22.69)		143 (18.01)	1343 (21.14)	22 (31.88)	348 (26.24)	
Quartile 3	408 (27.27)	953 (29.81)	63 (28.77)	284 (27.65)		225 (28.34)	1834 (28.86)	12 (17.39)	339 (25.57)	
Highest quartile	590 (39.44)	952 (29.78)	73 (33.33)	213 (20.74)		348 (43.83)	2402 (37.80)	15 (21.74)	301 (22.70)	
BMI (kg/m^2)					< 0.001					< 0.001
Normal	782 (52.27)	1113 (34.81)	105 (47.95)	374 (36.42)		339 (42.70)	1696 (26.69)	24 (34.78)	326 (24.59)	
Underweight	21 (1.40)	36 (1.13)	5 (2.28)	15 (1.46)		17 (2.14)	73 (1.15)	4 (5.80)	23 (1.73)	
Overweight	547 (36.56)	1408 (44.04)	88 (40.18)	385 (37.49)		181 (22.80)	1344 (21.15)	18 (26.09)	245 (18.48)	
Obesity	146 (9.76)	640 (20.02)	21 (9.59)	253 (24.63)		257 (32.37)	3241 (51.01)	23 (33.33)	732 (55.20)	
Physical activity					< 0.001					< 0.001
No	63 (4.21)	230 (7.19)	19 (8.68)	172 (16.75)		38 (4.79)	467 (7.35)	6 (8.70)	228 (17.19)	
Yes	1433 (95.79)	2967 (92.81)	200 (91.32)	855 (83.25)		756 (95.21)	5887 (92.65)	63 (91.30)	1098 (82.81)	

Table 1 (continued)

Characteristics	Continental Europe					US				
	None, *n* (%)	Only physical disorder, *n* (%)	Only psychological disorder, *n* (%)	Physical and psychological multimorbidity, *n* (%)	*P* value	None, *n* (%)	Only physical disorder, *n* (%)	Only psychological disorder, *n* (%)	Physical and psychological multimorbidity, *n* (%)	*P* value
Drinking					0.215					< 0.001
No	133 (8.89)	303 (9.48)	27 (12.33)	111 (10.81)		248 (31.23)	2709 (42.63)	28 (40.58)	677 (51.06)	
Yes	1363 (91.11)	2894 (90.52)	192 (87.67)	916 (89.19)		546 (68.77)	3645 (57.37)	41 (59.42)	649 (48.94)	
Smoking					0.084					< 0.001
No	839 (56.08)	1783 (55.77)	134 (61.19)	612 (59.59)		417 (52.52)	2909 (45.78)	26 (37.68)	520 (39.22)	
Yes	657 (43.92)	1414 (44.23)	85 (38.81)	415 (40.41)		377 (47.48)	3445 (54.22)	43 (62.32)	806 (60.78)	

BMI Body mass index

Table 2 The associations of physical and psychological disorders with dementia

	Dementia incidence (per 1000 person-years)/dementia incidence (*n*/*N*)	Model 1	Model 2	Model 3
Continental Europe				
None	3.47/0.01 (22/1496)	1 (reference)		
Only physical disorder	6.46/0.03 (86/3197)	1.75 (1.10, 2.80)	1.22 (0.75, 1.98)	1.23 (0.75, 2.00)
Only psychological disorder	2.10/0.01 (2/219)	0.58 (0.14, 2.44)	0.51 (0.12, 2.15)	0.48 (0.12, 2.01)
Physical and psychological multimorbidity	10.46/0.04 (44/1027)	2.59 (1.55, 4.33)	1.87 (1.09, 3.20)	1.86 (1.08, 3.21)
Pseudo log-likelihood (degrees of freedom) of model		−1190 (3)	−1138 (12)	−1135 (18)
US				
None	3.48/0.02 (16/794)	1 (reference)		
Only physical disorder	7.57/0.04 (272/6354)	2.13 (1.29, 3.52)	1.44 (0.87, 2.40)	1.57 (0.94, 2.62)
Only psychological disorder	10.34/0.06 (4/69)	2.93 (0.98, 8.77)	2.55 (0.85, 7.64)	2.57 (0.85, 7.79)
Physical and psychological multimorbidity	14.82/0.08 (105/1326)	4.11 (2.44, 6.94)	2.66 (1.56, 4.53)	2.76 (1.61, 4.72)
Pseudo log-likelihood (degrees of freedom) of model		−3506 (3)	−3428 (12)	−3405 (18)
Pooled outcome				
None	/	1 (reference)		
Only physical disorder	/	1.89 (1.21, 2.57)	1.31 (0.83, 1.79)	1.35 (0.85, 1.85)
Only psychological disorder	/	0.99 (−0.76, 2.74)	0.87 (−0.66, 2.39)	0.83 (−0.69, 2.36)
Physical and psychological multimorbidity	/	3.08 (1.69, 4.47)	2.13 (1.27, 2.99)	2.15 (1.27, 3.03)

Model 1 was a univariate model; model 2 additionally adjusted for age, gender, educational level, marital status, and total wealth income; and model 3 additionally added self-reported body mass index, physical activity, drinking, and smoking. Data was represented as HR and 95% CI. *HR* Hazard ratio, *95% CI*, 95% confidence interval

as the action area 3 [1]. In this area, psychological disorder, diabetes mellitus, and hypertension were considered risk factors for dementia [1]. By preventing and managing chronic diseases and psychological disorder, the risk of developing dementia can be reduced or its progression delayed. Previous studies have mostly only considered the singular effect of one chronic disease or psychological disorder on dementia [1, 3–5]. It is not conducive for healthcare workers to address common risk factors collectively and implement a comprehensive improvement program. Our study is the first study to utilize two cohorts and has found consistent results in different populations. We found that physical and psychological multimorbidity increased the risk of dementia by 86% and 176% among older adults in the Europe and the US, respectively. Only physical disorder and only psychological disorder were not associated with dementia. By pooling estimates, the risk of dementia among participants who reported physical and psychological multimorbidity increased by 115%. The potential mechanisms may be that the co-occurrence of physical and psychological disorders could accelerate vascular pathology changes, such as inflammatory and trophic changes, leading to cognitive impairment [9, 10]. In addition, a decrease in cultural and social engagement due to physical and psychological multimorbidity may further contribute to the progression of dementia among older adults [32]. Considering the accessibility of data and the disease burden, we selected seven self-reported physician-diagnosed conditions. However, it is noted that the scope of included diseases must be considered when interpreting our findings. For example, compared to included diseases, if the incidence of dementia is higher in participants with other diseases, it is possible that this study underestimated the impact of physical and psychological multimorbidity on dementia. The other important thing to note is that there is often a bidirectional relationship between psychological disorder and a preclinical dementia. This means that preclinical dementia and a decline in cognitive abilities may lead to mood disorders rather than the other way around. Therefore, we still need to explore the bidirectional relationship between psychological disorder and dementia using randomized controlled trials (RCT) or time-series studies in the future.

Our study indicates that raising awareness of the associations between physical and psychological multimorbidity and dementia is essential. Patients may postpone addressing their physical health management until their

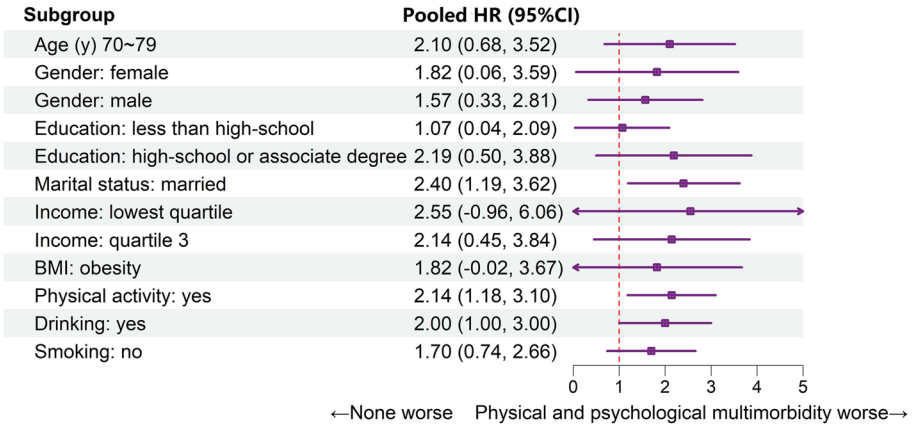

Fig. 2 The subgroup analysis on the associations of physical and psychological multimorbidity with dementia. The reference group was no physical and psychological disorders; model adjusted age, gender, educational level, marital status, total wealth income, self-reported body mass index, physical activity, drinking, and smoking. Data was represented as pooled HR and 95% CI. 95% CI, 95% confidence interval; HR, hazard ratio

psychological health needs are met [33]. Models of integrated elderly healthcare are developing due to the high disease burden of multimorbidity, such as community multidisciplinary teams, joint medical/psychiatry inpatient units, and care home intervention teams [33, 34]. Our findings indicate that joint medical/psychiatry units could be expected to achieve the goal of preventing dementia. However, it is noted that the same model should not be replicated in practice. Care models should consider the local multimorbidity burden, differences in medical resources, and financial support within the scope of team's jurisdiction. Identifying and prioritizing problems, evaluating and selecting cost-effective and efficient models to address the complex and long-term medical needs of older adults before putting them into practice is preferable.

Furthermore, the high prevalence of physical and psychological multimorbidity among older adults poses a significant challenge. In our study, we reported that the prevalence of physical and psychological multimorbidity was higher than 15% among older adults in the US and Europe, which is consistent with previous studies [6, 35], The prevalence of physical and psychological multimorbidity was affected by several factors, such us the number of diseases, population characteristics, and study period [36]. Due to not including more diseases, the prevalence of physical and psychological multimorbidity in the US and Europe may be underestimated. However, more importantly, our study utilized multinational data and identified common characteristics of participants with physical and psychological multimorbidity in the US and Europe, including older age, lower educational level, obesity, and no physical activity. Asante et al. also found that increasing age and lower education were both related to physical or psychological disorders [37]. Increasing awareness and understanding of the at-risk population for experiencing physical and psychological multimorbidity, and creating a medical environment that is friendly to individuals with physical and psychological multimorbidity, will empower people with this condition and their healthcare providers to enhance autonomy by identifying and modifying risk factors early.

The major strength of this study was its design, which utilized two cohorts from different regions to investigate the association between physical and psychological multimorbidity with dementia, ensuring robust extrapolation. In recent years, multi-cohort analysis for complex health outcomes, such as cognitive impairment and dementia, has been advocating [38–40]. Regional differences in economic and medical care may affect the progression of dementia. Analysis of related mental health issues from multi-cohort analysis is generalizable due to participants from various socioeconomic backgrounds [38–41]. However, several limitations and future research directions should be discussed. Firstly, self-reported information may have been a recall bias in our study. In addition, the diagnostic criteria for specific diseases (i.e., hypertension) may vary over time and across different geographic regions with the development of clinical practice. We used baseline data from the same year to minimize the impact on results. In addition, we excluded older adults with unavailable information on dementia or cognitive impairment at baseline to observe the subsequent risk of dementia among older adults with normal cognition. Some participants with unavailable information may do not have dementia but be excluded,

which may lead us to overestimate the risk of developing dementia. Secondly, follow-up is commonly limited by the discrete nature of large-sample epidemiological design [42, 43]. Utilizing discrete-time data may overlook events that occur between each discrete-time point and significant number of ties (events that were recorded to have happened at the same time). However, for the 2-year follow-up interval, the number of ignored events may be relatively lower. In addition, the time-varying risk (i.e., some participants might have developed additional psychological diseases during the follow-up) was not considered in our study due to the decreasing sample size with low statistical power and the minimal variations in the observed exposure variables across the four waves. Future research should consider the time-varying risk of physical and psychological multimorbidity on dementia. Finally, there is a consolidated trend towards multi-component interventions for the progression of dementia, especially evident in the World-Wide Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (WW-FINGERS) [44]. The WW-FINGERS, launched in 2017 and spanning over 25 countries, is the first global network of multidomain lifestyle intervention trials aimed at reducing the risk of dementia. Our results further provide evidence of the associations between complex multimorbidity and dementia, supporting the aim of WW-FINGERS. The results from the FINGER trial highlighted the importance of addressing multiple dementia risk factors as a strategy to protect brain health, promote overall health and functioning, and reduce the risk of developing new chronic diseases [14, 44, 45]. The WW-FINGERS study points that the focus is on individual-based preventive approaches in persons with increased risk of dementia [44]. The WW-FINGERS proposed that the impact on the occurrence of dementia by risk factor modifications in public health interventions can be expected [44]. Public health interventions focus not only on the integrated preventive measures, but also on its cost-effectiveness. Therefore, RCTs should provide more information, such as health economics and the completion rate of behavior change, specific intervention methods (health education at individual-level or community empowerment) to assist researchers in exploring the cost-effectiveness in cross-cultural and different socioeconomic settings in the future.

Conclusions

In conclusion, our results suggest that physical and psychological multimorbidity was prevalent among older adults in the US and continental Europe. Considering its consistent associations with dementia, it is urgent to raise awareness of the links, improve the capacity of health and social care professionals, and recognize the limitations of single-disorder care. Meanwhile, specific components of care for patients with dementia include providing care coordination for common modifiable risk factors of physical and psychological disorders, which may be more economical and feasible. Improving the contributing factors of physical and psychological multimorbidity to prevent dementia can assist clinicians in avoiding the cumulative implementation of a risky single-disease approach. Meanwhile, they can focus on the enhancing overall well-being by optimizing medication management and improving care coordination.

Abbreviations

BMI	Body mass index
CES-D	Center for Epidemiology Depression Scale
CI	Confidence interval
HR	Hazard ratios
HRS	Health and Retirement Study
IQR	Interquartile range
RR	Risk ratio
SHARE	Survey of Health, Ageing and Retirement in Europe
WHO	World Health Organization
WW-FINGERS	World-Wide Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-024-03642-2.

Additional file 1: Table S1. The associations of physical and psychological disorders with dementia using Poisson models. Table S2. The associations of physical and psychological disorders with dementia using random forest interpolation. Table S3. The associations of physical and psychological disorders (eight groups) with dementia. Table S4. The subgroup analysis on the associations of physical and psychological disorders with dementia in continental Europe. Table S5. The subgroup analysis on the associations of physical and psychological disorders with dementia in the US. Table S6. The pooled outcomes of the results from subgroup analysis on the associations of physical and psychological disorders with dementia in continental Europe and the US.

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Authors' contributions

JL conceptualized and designed the study. JL did data acquisition. MD did data curation, formal analysis, writing the original draft. MD, ML and JL did writing- reviewing and editing. All authors read and approved the final manuscript.

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Availability of data and materials

The HRS and SHARE datasets are openly available fromhttps://g2aging.org/survey-overview (accessed on 10 May 2023)

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The HRS has received approval from the University of Michigan Institutional Review Board (IRB Protocol: HUM00061128). The SHARE was reviewed and approved by the Ethics Committee of the University of Mannheim and the Ethics Council of the Max Planck Society (IRB: No 723/2009). All participants provided informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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