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Independent and combined associations of depression and cognitive impairment with frailty in oldest-old adults

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Abstract

Background Frailty is one of the most significant issues related to human aging. Although studies have confirmed the association of mental and cognitive disorders with frailty, the association might be influenced by age, since oldest-old adults are more likely to have adverse health outcomes. Thus, this study aimed to examine independent and combined associations of mental health and cognitive function with frailty in oldest-old adults using data from the Chinese Longitudinal Healthy Longevity Survey in 2018.

Methods A sum of 6,891 and 3,171 older adults aged 80 and older were included in this study when analyzing the association of depression and cognitive impairment with frailty, respectively. Frailty was measured by the Study of Osteoporotic Fractures frailty index, depression was assessed by the Center for Epidemiologic Studies Depression Scale, and cognitive impairment was evaluated by the Chinese version of modified Mini-Mental State Examination. Independent sample t-test, Chi-square tests, and logistic regression analyses were used to examine the associations of depression and cognitive impairment with frailty.

Results Older persons with depression or cognitive impairment had a higher chance of frailty. The adjusted odds ratio (OR) of frailty was 1.27 (95% CI: 1.01, 1.59, $p=0.044$) in those with depression, and 1.85 (95% CI: 1.14, 3.01, $p=0.013$) in those with cognitive impairment. Compared to adults who had neither depression nor cognitive impairment, those with either depression or cognitive impairment, and those with both depression and cognitive impairment had a significantly higher likelihood of frailty (adjusted OR: 1.61, 95% CI: 1.07, 2.41; and adjusted OR: 4.03, 95% CI: 2.05, 7.94).

Conclusions The findings suggest that depression and cognitive impairment are associated with frailty. The concurrence of depression and cognitive impairment has an additive effect on frailty in oldest-old population.

Keywords Aging, Cognitive dysfunction, Depression, Frailty, Oldest-old adults

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Introduction

Frailty is one of the most significant issues related to human aging. It is considered a state of decreased multisystem function and physiologic reserve that results in a greater risk of adverse health outcomes such as falls, disabilities, hospitalization, and increased morbidity and mortality [1–3], bringing heavy burden to patients, their families, and society. The term, frailty is used to illustrate why older persons who had the same chronological age vary greatly in physical and mental health. Frailty can also help to identify older adults who have poor health and greater health risk in clinical settings and those who need medical or nursing in the community settings [4, 5]. Therefore, with the increase in the aging population worldwide, frailty has become a medical indicator that needs to be identified, prevented, and treated.

A growing number of studies have suggested that frailty in older adults is associated with mental and cognitive disorders [6–8]. Specifically, a cross-sectional study with 936 Chinese community-dwelling older adults showed that older persons with both depression and poor sleep quality have a greater risk of frailty compared to those with depression or poor sleep quality alone [9]. A systematic review and meta-analysis research was conducted to explore the relationship between frailty and depression [10]. This research discovered a reciprocal interaction between frailty and depression, and suggested that each condition might be a risk factor for the development of another condition in older people. In addition, a cross-sectional study aimed to determine the association between frailty and cognitive impairment in older adults, finding that frail older adults are more likely to develop cognitive impairment when compared to robust or pre-frail older adults [11]. According to a network analysis, cognitive impairment was found to be really central and hence significant within the network in patients with depression [12]. Although previous studies have confirmed the association of mental and cognitive disorders with frailty in older adults, the association might be influenced by age, since oldest-old adults are more likely to report more adverse health outcomes than young-old individuals [13, 14].

With advancing age, older adults are usually accompanied by a decrease in physical, mental, and cognitive function, and an increased risk of a range of chronic diseases [15–17]. Older people are generally divided into young-old adults (<80 or 75 years old) and oldest-old adults (≥80 or 75 years old). There is evidence to show that compared to the young-old adults, oldest-old individuals are more susceptible to falls and disabilities [15, 16, 18]. According to a previous publication, the rate of frailty has been reported to be higher in oldest-old adults [19]. Specifically, there was nearly 10% of the population aged over 65 years suffering from frailty and the proportion was approximately tripled in those aged more than 85 years [20]. Intrinsic capacity is a critical criterion for healthy aging that includes five parameters: cognition, locomotion, vitality, psychology, and sensory [21]. It has been demonstrated that incident frailty was linked to a reduction in one or more intrinsic capacity parameters during healthy aging [22].

The number of the oldest-old population is rapidly increasing due to advancements in living standards and health services. Understanding how mental health and cognitive function are associated with frailty in oldest-old adults may help to design assessment approaches and intervention strategies to prevent or treat frailty. Therefore, the objective of the study was to assess the association of depression and cognitive impairment with frailty in oldest-old adults. The hypothesis was that oldest-old adults with frailty have a higher rate of depression and cognitive impairment, even adjusting for covariates.

Methods

Data source and sample

This study used data from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) in 2018. The CLHLS is a representative national population-based survey conducted in the majority of provinces (23 out of 31 provinces) in China. The objective of the CLHLS is to find out factors associated with Chinese older adults' healthy longevity. By employing a standardized questionnaire, in total 15,874 face-to-face interviews were completed in the 2018 CLHLS. More details on the 2018 CLHLS and the data quality assessment can be found elsewhere [23, 24]. Each participant had read and signed the written informed consent prior to the survey. The CLHLS research program has been examined and approved by the Research Ethics Committee of Peking University (approval number: IRB00001052-13,074).

A total of 15,874 adults were included in the 2018 CLHLS dataset, 5,455 of whom were excluded due to the age less than 80 years, and 1,309 of whom had to be excluded because of missing or incomplete data for defining frailty. There were 9,110 adults with frailty information. Due to missing or incomplete information for defining depression (n=2,219) and cognitive impairment (n=5,939), there were 6,891 older individuals with complete information of depression and 3,171 older individuals with complete information of cognitive impairment in the final analysis. Figure 1 showed the flowchart of participants involved in this study.

Definition of frailty

Frailty in this study was assessed by the Study of Osteoporotic Fractures (SOF) frailty index according to previous studies of secondary analysis of data on CLHLS [25, 26]. The SOF frailty index was used to identify frailty

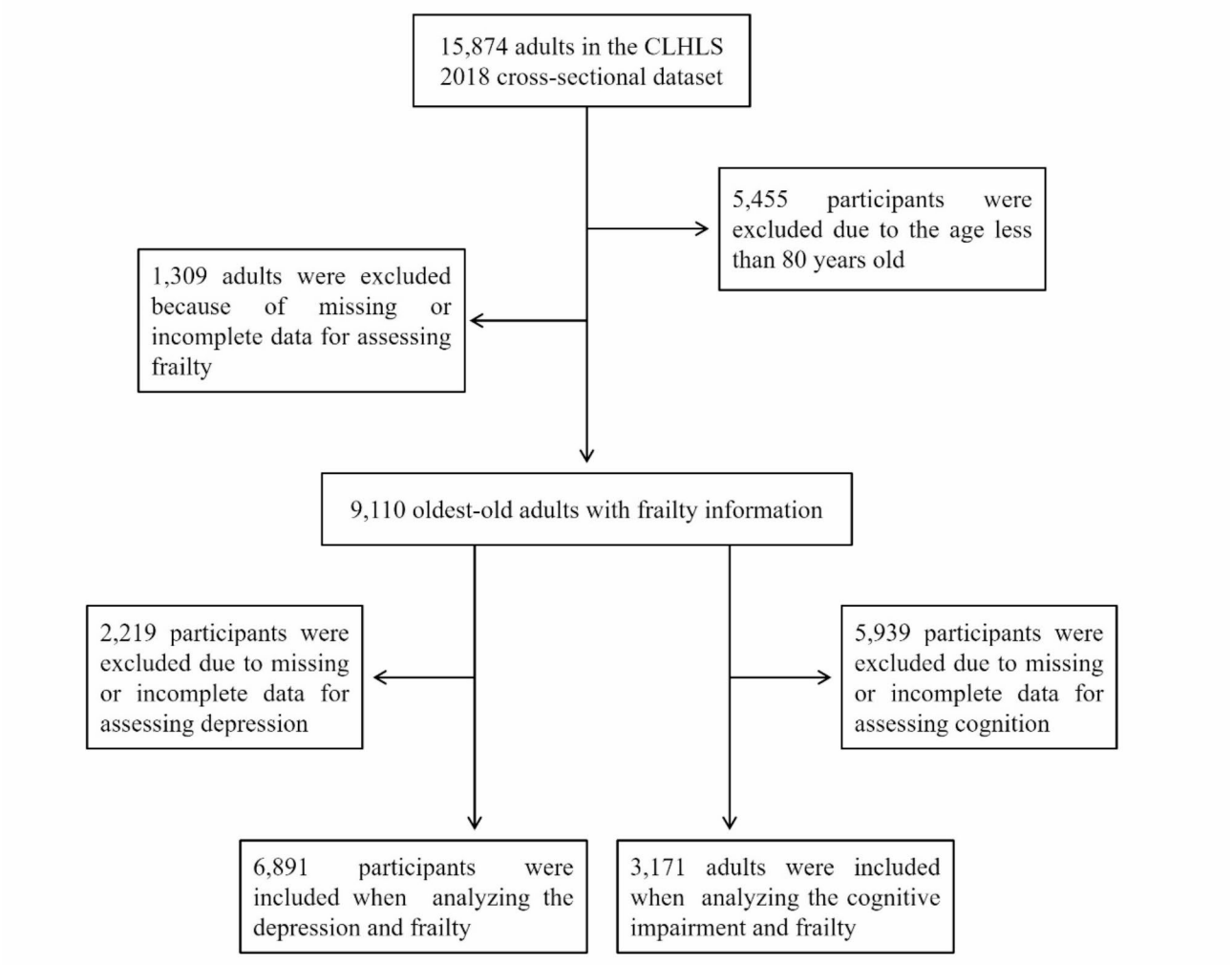

Fig. 1 Flowchart of participants included in this study

since it had a high biological age ability in older Chinese individuals [27]. The SOF frailty index included the following three components: (1) underweight (defined by having a body mass index < 18.5 kg/m^2), (2) low energy level (identified by a positive answer to the question "for the last 6 months, were you limited in activities because of health problems?"), and (3) poor muscle strength (indicated by a negative response to the question "able to stand up from sitting in a chair without the assistance of arms?). As recommended, participants who had at least two of the three components were identified as frail adults [25].

Ascertainment of depression

Depression in this study was assessed by using the Center for Epidemiologic Studies Depression Scale (CES-D-10). Previous studies have used CES-D-10 in Chinese populations and demonstrated its good validity and reliability [28, 29]. The CES-D-10 included ten items and used a four-point metric to score (ranged from 0 for "rarely" to 3 for "most of the time"). The total scores of the CES-D-10 ranged from 0 to 30, and the higher scores represented a greater risk of depression. Participants were identified as having depressive symptoms if they scored more than 10 scores based on previous studies [30, 31]. In our study, the Cronbach alpha coefficient was 0.772 for the CES-D-10.

Assessment of cognitive impairment

The cognitive function of older adults in this study was evaluated by employing a Chinese version of modified Mini-Mental State Examination (MMSE) through a face-to-face interview. The MMSE was modified by the CLHLS research group in order to make older persons to accept and understand easily. The modified MMSE has been frequently used by Chinese scholars and has been proven to have good validity and reliability [32, 33]. The MMSE with 24 items covers seven categories of cognitive function including orientation (ranged from 0 to 5 points), naming (ranged from 0 to 7 points), registration

(ranged from 0 to 3 points), attention and calculation (ranged from 0 to 5 points), copying a Fig. (1 point), recalling (ranged from 0 to 3 points), and language capability (ranged from 0 to 6 points). The total score ranged from 0 to 30 for the MMSE, and a lower score represented poorer cognitive function. According to previous studies [34–36], older adults with MMSE scores less than 24 were defined as having cognitive impairment. In this study, the Cronbach alpha coefficient was 0.805 for the modified MMSE.

Covariates

Covariates were obtained by a structured questionnaire. Covariates in our study included sex, age, residence, co-residence, body mass index, drinking, smoking, exercise, marital status, education level, taking medicines, and taking nutrient supplements. Age, body mass index and education were three of the most frequent confounders and were presented as continuous variables. Body mass index was calculated by dividing weight by the square of body height. Education level was collected by asking people their years of schooling. The residence was classified as "urban" or "rural", and co-residence was categorized as "with household member(s)", "living alone", or "in an institution". Current smokers, drinkers, and exercisers were categorized into "yes" or "no" by the question "do you smoke/drink/exercise or not at present?". Marital status was classified as "married and living with spouse", "widowed", or "others". Taking medicines and taking nutrient supplements were classified into "yes" or "no" by the question "are you taking medicines/nutrient supplements?".

Table 1 The characteristics of participants stratified by frailty

	Frailty (*n* = 1,389)	Non-frailty (*n* = 7,721)	*p* value
Age (yrs)	96.58 ± 6.73	91.00 ± 7.55	< 0.001
Height (cm)	151.35 ± 10.77	153.26 ± 10.80	< 0.001
Weight (kg)	41.77 ± 9.69	52.27 ± 11.97	< 0.001
Body mass index (kg/m^2)	18.17 ± 3.50	22.14 ± 3.97	< 0.001
Education level (yrs)	2.08 ± 7.32	2.52 ± 5.09	0.010
Sex, n (%)			< 0.001
Men	381 (27.4)	3,410 (44.2)	
Women	1,008 (72.6)	4,311 (55.8)	
Residence, n (%)			0.348
Urban	756 (54.4)	4,310 (55.8)	
Rural	633 (45.6)	3,411 (44.2)	
Co-residence, n (%)			< 0.001
With household member(s)	1,140 (83.6)	5,844 (76.7)	
Living alone	158 (11.6)	1,495 (19.6)	
In an institution	65 (4.8)	284 (3.7)	
Current smokers, n (%)			< 0.001
Yes	116 (8.4)	1,018 (13.3)	
No	1,259 (91.6)	6,625 (86.7)	
Current drinkers, n (%)			< 0.001
Yes	115 (8.5)	978 (12.9)	
No	1,245 (91.5)	6,622 (87.1)	
Current exercisers, n (%)			< 0.001
Yes	113 (8.3)	2,189 (28.7)	
No	1,245 (91.6)	5,425 (71.2)	
Marital status, n (%)			< 0.001
Married and living with spouse	162 (11.8)	2,022 (26.4)	
Widowed	1,186 (86.4)	5,455 (71.3)	
Others	25 (1.8)	173 (2.3)	
Taking medicines			< 0.001
Yes	458 (33.6)	3,164 (42.0)	
No	907 (66.4)	4,363 (58.0)	
Taking nutrient supplements			0.290
Yes	146 (10.6)	907 (11.9)	
No	1,229 (89.4)	6,699 (88.1)	

Statistical analysis

The characteristics of participants were stratified by frailty. Variables were described as means with standard deviations for numerical variables and represented as numbers with percentages for categorical variables. The Shapiro-Wilks test was performed to investigate the normality of the distribution, and the results revealed that the variables obey a normal distribution. We used an independent sample t-test for continuous data and Chi-square tests for categorical data to analyze the differences between frailty and non-frailty groups. We employed logistic regression analyses to determine the association of depression and cognitive impairment with frailty with and without adjusting for covariates. We used the "No" in depression and cognitive impairment as the reference. The odds ratios (OR) with 95% confidential intervals (95% CI) for frailty were obtained in all the logistic regression analyses. The combined effects of depression and cognitive impairment on frailty was also examined using the logistic regression analyses. In the combined analysis, older adults who had neither depression nor cognitive impairment were selected as the reference. All the analyses were performed by using SPSS Statistics for Windows (Version 25.0, IBM Corp, Armonk, NY), and a two-tailed $p < 0.05$ was regarded to be statistically significant.

Results

Table 1 displayed the characteristics of 9,110 older adults stratified by frailty. There were 1,389 and 7,721 older people assigned to the frailty and non- frailty group respectively. The prevalence of frailty in the oldest-old adults was 15.2%. Older adults with frailty were more likely to be older (96.58 ± 6.73 vs. 91.00 ± 7.55 years), have lower body mass index (18.17 ± 3.50 vs. 22. 14 ± 3.97 kg/m^2), and received less education (2.08 ± 7.32 vs. 2.52 ± 5.09 years) when compared to those without frailty. Older persons in the frailty group had a decreased prevalence of living

with household member(s) (12.7% vs. 65.0%), married and living with spouse (1.8% vs. 22.4%), taking medicines (5.1% vs. 35.6%), and taking nutrient supplements (1.6% vs. 10.1%) than those in the non- frailty group.

Statistical comparisons of depression and cognitive impairment with frailty were shown in Table 2. There were 283 (37.1%) participants with and 480 (62.9%) participants without depression in the frailty group, and 1,339 (21.9%) adults with and 4,789 (78.1%) adults without depression in the non-frailty group. A chi-square test showed that a significant difference was observed between depression and frailty ($p<0.001$). There were 136 (28.4%) participants with and 343 (71.6%) participants without cognitive impairment in the frailty group, and 317 (11.8%) adults with and 2,375 (88.2%) adults without cognitive impairment in the non-frailty group. A chi-square test showed a statistical significance between cognitive impairment and frailty ($p<0.001$).

Table 3 presented the independent association of depression and cognitive impairment with frailty in older adults. Compared to participants without depression, those with depression had a higher risk of frailty, and the OR was 2.11 (95% CI: 1.80, 2.47, $p<0.001$) and the adjusted OR was 1.27 (95% CI: 1.01, 1.59, $p=0.044$), respectively. Compared to adults without cognitive impairment, those with cognitive impairment had a higher risk of frailty, and the OR was 2.12 (95% CI: 1.45, 3.12, $p<0.001$) and adjusted OR was 1.85 (95% CI: 1.14, 3.01, $p=0.013$), respectively.

The combined association of depression and cognitive impairment with frailty in older adults was listed in Table 4. Compared to older adults who had neither depression nor cognitive impairment, those with either depression or cognitive impairment had a significantly higher risk of frailty, and the OR was 1.97 (95% CI: 1.39, 2.80) and the adjusted OR was 1.61 (95% CI: 1.07, 2.41), and those with both depression and cognitive impairment had a much higher risk of frailty, and the OR was 6.03 (95% CI: 3.40, 10.70) and the adjusted OR was 4.03 (95% CI: 2.05, 7.94), respectively.

Table 2 Statistical comparisons of depression and cognitive impairment with frailty

Variables	Frailty		Chi-square	*p* value
	Yes	No		
Depression ($n=6,891$)				<0.001
No	480 (62.9)	4,789 (78.1)	87.56	
Yes	283 (37.1)	1,339 (21.9)		
Cognitive impairment ($n=3,171$)				<0.001
No	343 (71.6)	2,375 (88.2)	45.46	
Yes	136 (28.4)	317 (11.8)		

Table 3 The independent association of depression and cognitive impairment with frailty

Variables	Frailty	
	OR (95% CI)	Adjusted OR† (95% CI)
Depression		
No	Ref.	Ref.
Yes	2.11 (1.80, 2.47)	1.27 (1.01, 1.59)
p value	<0.001	0.044
Cognitive impairment		
No	Ref.	Ref.
Yes	2.12 (1.45, 3.12)	1.85 (1.14, 3.01)
p value	<0.001	0.013

Note: OR, odds ratio; CI, confidential intervals

† Adjusted for potential confounders including sex, age, residence, co-residence, body mass index, drinking, smoking, exercise, marital status, education level, taking medicines, and taking nutrient supplements

Table 4 The combined association of depression and cognitive impairment with frailty

Variables	Frailty	
	OR (95% CI)	Adjusted OR† (95% CI)
Neither depression nor cognitive impairment	Ref.	Ref.
Either depression or cognitive impairment	1.97 (1.39, 2.80)	1.61 (1.07, 2.41)
Both depression and cognitive impairment	6.03 (3.40, 10.70)	4.03 (2.05, 7.94)
p value	<0.001	<0.001

Note: OR, odds ratio; CI, confidential intervals

† Adjusted for potential confounders including sex, age, residence, co-residence, body mass index, drinking, smoking, exercise, marital status, education level, taking medicines, and taking nutrient supplements

Discussion

The prevalence of frailty has been increasing worldwide due to the rapidly growing aging population. This study was conducted to examine the association of mental health and cognitive function with frailty in older adults. To the best of our knowledge, this is the first study to assess whether depression and cognitive impairment were associated with frailty in oldest-old adults in China. We adjusted for several confounders such as age, sex, residence, co-residence, body mass index, drinking, smoking, exercise, marital status, education level, taking medicines, and taking nutrient supplements.

The current study showed that the prevalence of frailty was 15.2% in adults aged 80 years and over in China. Based on data from the World Health Organization Study on global AGEing and adult health China Wave 1, Ruan et al. [37] reported that the prevalence of frailty was 14.7%, which was nearly similar to that was shown in our study. However, other comparable studies observed a much greater prevalence of frailty, and the prevalence was 58.5% [38] and 67.6% [39]. Differences between studies may be because of the difference in the

age of participants as well as the assessment methods for frailty. In the current study, we also observed that the mean body mass index was 18.17±3.50 kg/m^2 in older adults with frailty, which is significantly lower than that in older persons without frailty (22.14±3.97 kg/m^2). The result is consistent with that of other researchers and emphasizes the significance of a greater body mass index for preventing and controlling frailty in older adults [40, 41]. Additionally, our study showed a low prevalence of taking medicines and nutrient supplements in both frail and non-frail older adults. A possible explanation is that nearly all the participants were from communities rather than hospitals or health care facilities, and the majority of them might be in healthy condition.

Depression is a common mental problem in older adults. It has been reported to be associated with a series of adverse clinical outcomes such as decreased health-related quality of life, increased morbidity and mortality [42–44]. Our study discovered a significant association between depression and the occurrence of frailty in older adults. Specifically, older adults with depression were 1.27 times more likely to have frailty than those without depression. The finding is consistent with a previous study in which researchers found that frailty and late-life depression are associated in a dose-dependent manner in geriatric outpatients, regardless of the used definitions [45]. Moreover, Ribeiro and colleagues [46] used data from two Portuguese Centenarian Studies to explore the relationship between depressive symptoms and the frailty syndrome, finding that depression is a clinical comorbid independent disorder that is frequent in pre-frail and frail centenarians. Based on the above studies, it can be found that depression is one of the most important factors associated with frailty in older adults.

Cognitive impairment is another common psychological disorder in older persons. Previous studies have shown that cognitive impairment is correlated with a range of adverse health outcomes including frailty, disability, and decreased health-related quality of life [47–49]. For instance, Yuan et al. [50] reported that older adults with moderate cognitive impairment had 35% more likely (adjusted OR: 1.35; 95% CI: 1.33, 1.37) and those with severe impairment had 74% more likely (adjusted OR: 1.74; 95% CI: 1.72, 1.77) to be frail than robust and pre-frail, compared to those with none and mild impairment. The results are consistent with our observation, and we found that older adults with cognitive impairment were 1.85 times more likely to have frailty than those without cognitive impairment. There is a significant association between cognitive impairment and frailty in older adults aged 80 years and older. Moreover, we also observed that the concurrence of depression and cognitive impairment has an additive effect on frailty in oldest-old adults.

Studying the association of mental health and cognitive function with frailty is of great public health significance for preventing or treating frailty, especially for oldest-old adults [51, 52]. In the present study, we showed that there is an association between depression, cognitive impairment and frailty in Chinese oldest-old adults. According to the findings, it may be helpful to improve mental health and cognitive function for preventing or treating frailty in the elderly. For instance, Kvæl and colleagues [53] have reported that less depressive symptoms are associated with higher walking speed, and better muscle strength and balance in nursing home residents. On the other hand, Givan et al. [54] have shown that older Mexican Americans with cognitive impairment are more likely to decrease in physical function (assessed by Short Physical Performance Battery) over 20 years of follow-up. Already it is known that physical function is one of the most important components to assess frailty. Therefore, the indirect evidence suggests that improving mental health and cognitive function may be beneficial to prevent or treat frailty in older people. Future work is needed to explore the relationship between depression, cognitive impairment and frailty.

Older adults, especially oldest-old adults, are more vulnerable to a range of adverse health outcomes such as frailty, falls, and disabilities [15–17]. Frailty is considered one of the most important issues associated with aging. Our findings suggest that depression and cognitive impairment are associated with frailty, and the concurrence of depression and cognitive impairment has an additive effect on frailty in the oldest-old population. The findings have implications for identifying older adults with a greater risk of frailty and may be useful for providing corresponding strategies to prevent or treat frailty in older adults. Therefore, community health workers and clinicians should pay more attention to both mental health and cognitive function for the management and prevention of frailty and their consequences in oldest-old adults.

The major advantages of our study are the use of a sample of the oldest-old adults and the use of many covariates in the analyses. But this study still had several limitations. First, this study was a cross-sectional design, and we could not draw a cause-and-effect relationship between depression, cognitive impairment and frailty. Second, this study might have a recall bias because the depression and cognitive impairment were assessed by questionnaires. Third, there was a relatively small sample size when we analyzed the combined effect of depression and cognitive impairment with frailty, which might lead to a decrease in statistical power. Last, our study did not measure and control several potential covariates such as dietary status and physical activity that may be associated with frailty in older adults.

Conclusion

This is the first study that determined the relationship between depression, cognitive impairment and frailty in oldest-old adults in China. The findings suggest that depression and cognitive impairment are associated with frailty in the Chinese oldest-old population (aged ≥ 80 years). Moreover, the concurrence of depression and cognitive impairment has an additive effect on frailty in oldest-old adults. A future study is needed to carry out a comparative analysis of cognitive impairment and depression levels between frail and non-frail adults. This is because conducting such a study helps provide deeper insights into the psychological and cognitive differences in frail and non-frail adults, thus contributing to more targeted interventions for improving the quality of life in older adults.

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Author contributions
X. Z. contributed to the conception, design, prepared the first draft and revised the final draft of manuscript. X. D. and S. S. did the data analysis, manuscript editing and interpretation of data. J. W. contributed to the acquisition, analysis, interpretation of data and manuscript editing. All Authors have read and approved the final manuscript.

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Data availability
The data that support the findings of this study are available in Peking University Open Research Data at https://opendata.pku.edu.cn/dataverse/CHADS.

Declarations

Ethics approval and consent to participate
The participants provided written, informed consent before the start of the study. The study was conducted in accordance with the Declaration of Helsinki and was approved by the research committee at Peking University (approval number: IRB00001052-13,074).

Consent to publish
Not applicable.

Competing interests
The authors declare no competing interests.

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