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WITHDRAWN – Social isolation, rather than loneliness, is associated with cognitive decline in older adults: the China Health and **Retirement Longitudinal Study**

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Abstract

Abstract Background. Social isolation and loneliness have each been associated with cognitive decline, but most previous research is limited to Western populations. This study examined the rela-Methods. This study used two waves of data (2011 and 2015) from the China Health and Retirement Longitudinal Study and analyses were restricted to those respondents aged 50 and older. Social isolation, loneliness and cognitive function were measured at baseline. Follow-up measures on cognitive function were obtained for 7761 participants (mean age = 60.07, s.p. = 7.31; male, 50.0%). Lagrad data data and the statement of the 60.97, s.D. = 7.31; male, 50.8%). Lagged dependent variable models adjusted for confounding between baseline isolation, loneliness, and factors were used to evaluate the association cognitive function at follow

Results. Loneliness was significantly associated with the cognitive decline at follow-up (episodic memory: $\beta = -0.03$, p < 0.01; mental status $\beta = -0.03$, p < 0.01) in the partially adjusted models. These associations became insignificant after additional confounding variables (chronic diseases health behaviors, disabilities, and depressive symptoms) were taken into account (all $\rho > 0.05$). By contrast, social isolation was significantly associated with decreases in all cognitive function measures at follow-up (episodic memory: $\beta = -0.05$, p < 0.001; mental status: $\beta = -0.03$, p < 0.01) e en after controlling for loneliness and all confounding variables. Conclusions. Social isolation is associated with cognitive decline in Chinese older adults, and the relationships are independent of loneliness. These findings expand our knowledge about etween so cial relationships and the cognitive function in non-Western populations. the links

Introduction

Population aging is one of the major challenges worldwide. China has the world's largest aging population of older adults. By 2050, the number of Chinese people aged 60 and older is expected to reach 479 million (DESA, 2017). In parallel with this aging profile, the number Chinese older adults with dementia is projected to reach 18 million in 2030 (Chan et al., 2013). Dementia makes a major contribution to disability and health care needs among older people. The much disease burden has made the prevention and treatment of dementia public health priorities for China.

Increasing efforts have been made to identify modifiable factors that may prevent or slow the progression of cognitive decline in older age, and impoverished social relationships defined as social isolation or loneliness - have received considerable attention. Accumulated evidence has shown that both social isolation (Evans, Martyr, Collins, Brayne, & Clare, 2019; Kuiper et al., 2016) and loneliness (Boss, Kang, & Branson, 2015; Cacioppo & Hawkley, 2009) affect cognitive function. Although loneliness and social isolation are sometimes perceived to be synonymous, they are conceptually different. In essence, social isolation refers to the objective aspects of isolation, such as living alone, having few contacts, or little involvement in social activities (Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015). In contrast, loneliness refers to a subjective feeling resulting from a discrepancy between actual and desired social relationships (Peplau & Perlman, 1982). Even socially connected individuals can feel lonely, just as socially isolated individuals can be satisfied with their social relationships. Studies have found that correlations between loneliness and social isolation are generally moderate (Cornwell & Waite, 2009; McHugh, Kenny, Lawlor, Steptoe, & Kee, 2017).

It has been suggested that analyzing both objective and subjective aspect of social relationship in the same study can allow us to better understand how these two social constructs affect



health (Cornwell & Waite, 2009; Holt-Lunstad et al., 2015; Newall & Menec, 2019). However, researchers have mostly examined relationship with cognitive impairment of only one construct, either loneliness, or social isolation (Boss et al., 2015; Evans et al., 2019; Kuiper et al., 2016). Among the few studies in which loneliness and social isolation were examined concurrently, there were mixed results. Some findings support the greater association of loneliness (Holwerda et al., 2014) and some findings support the greater association of social isolation in predicting with cognitive decline (Beller & Wagner, 2018; Griffin, Mezuk, Williams, Perrin, & Rybarczyk, 2020). Synergistic effects of loneliness and social isolation on cognitive function were also found by some researchers. For example, analysis from the Rush Memory and Aging Project found that participants who were lonely and those with limited participation in social activities were more likely to develop Alzheimer's disease (Wilson et al., 2007). A longitudinal study with English older adults also indicated that both social isolation and loneliness were significantly associated with poorer cognitive function (Shankar, Hamer, McMunn, & Steptoe, 2013). More information is needed regarding both the relative and synergistic influences of social isolation and loneliness on cognitive function.

Meanwhile, another gap in knowledge is the lack of studies on the cognitive consequences of social isolation and loneliness in non-Western countries. Most studies on this topic have been conducted in North America and European countries (Courtin & Knapp, 2017; Evans et al., 2019; Kuiper et al., 2016), and it it not established whether similar patterns occur in other cultures. The importance of such research is underscored by the fact that isolation and loneliness are equally prevalent in non-W estern a in Western countries. The proportion of empty-nest families (refers to those older people with no children or whose children have already left home) in China is estimated to reach 90% by 2030 (Rafnsson, Orrell, d'Orsi, Hogervorst, & Steptoe, 2020). It has been suggested that the association between social relati ships and health could be more salient in Chinese populations, for whom cultural tradition emphasizes the family system and collectivism (Yang & Victor, 2008). However, only a few studies have investigated the impact of social relationships on cognitive function among older adults and most were limited by small sample size or cross-sectional design (Fung, Lee, Cheng, & Lam, 2019; Wang et al., 2012). Two recent publications based on the Chinese Longitudinal Healthy Longevity Survey using relatively large sample size have reported the negative impact of poor social relation-ships on cognitive function. However, both of these studies mainly focused on loneliness rather than social isolation (Zhong, Chen, & Conwell, 2016, Zhong, Chen, Tu, & Conwell, 2017). Given that very few studies examined loneliness and social isola-

Given that very tew studies examined loneliness and social isolation simultaneously in relation to cognition in non-Western populations, and the inconclusive findings in this area, we used data from the China Health and Retirement Longitudinal Study (CHARLS) to examine the impact of social isolation and loneliness, individually and simultaneously, on cognitive function among Chinese older adults. We hypothesize that both social isolation and loneliness would be significantly associated with cognitive decline over 4 years. However, we made no specific assumption about which of these two factors might play a stronger role in light of existing mixed results. Regarding previous evidence indicating possible gender differences in the association between social relationship factors and health (Shumaker & Hill, 1991; Shye, Mullooly, Freeborn, & Pope, 1995), we also tested the interaction of gender with social isolation and loneliness on cognitive function for our sample.

Methods

Participants

Data are from the CHARLS, a nationally representative longitudinal survey sampled residents from 150 counties across 28 provinces in China, with a response rate of 80.5% (Zhao, Hu, Smith, Strauss, & Yang, 2012). The CHARLS is one of the most up-to-date longitudinal data sets collected in China to study the health and well-being of older adults. The survey assigned 23 422 dwelling units to interviewers at baseline in 2011. After excluding empty or non-resident dwellings, 12 740 were age-eligible for CHARLS data from two (Zhao et al., 2012). In the current study, we waves of the CHARLS collected in 2011 and 2015. The baseline sample included 17 708 respondents. Our analytic sample was restricted to those respondents aged 50 and older (n = 13649). We excluded those respondents who had missing values on any predictor or cognitive test at baseline (n = 3506) or cognitive test at follow-up (n = 2382), which resulted in a final sample size of 7761 respondents (mean age = 60,97, s.D. = 7.31; male, 50.8%).

Measures

Loneliness

mess was measured with one single item In our study, lo cluded in the Centre for Epidemiological Studies Depression scale (CESD): 'In the last week, how often did you feel lonely?'. The respondent chose among four ordinal responses scored 1-4: arely or none of the time (<1 day), some or a little of the time (1-2 days), occasionally or a moderate amount of the time (3–4 days), most or all of the time (5–7 days). This one item measre correlates highly with multi-item loneliness scales and has en used in a number of previous studies (Gow, Corley, Starr, & ary, 2013; Holwerda et al., 2014; Luo & Waite, 2014; ummela, Seppanen, & Uutela, 2011; Tilvis, Pitkala, Jolkkonen, & Strandberg, 2000). Loneliness was dichotomized into two categories [0 (not lonely) = those who reported feeling lonely rarely or none of the time, and 1 (lonely) = those who felt lonely sometimes, occasionally or most of the time] (Teguo et al., 2016).

Social isolation

Three items were combined to create an index of social isolation, which was adapted from previous research (Glei, Goldman, Ryff, Lin, & Weinstein, 2012; Steptoe, Shankar, Demakakos, & Wardle, 2013). One point was assigned if participants were not married; had less than weekly contact (by phone, in person, or by e-mail) with children, not participating in any social activities over the last month (e.g. interacted with friends; played chess or cards; going to the community club; went to a sport, social, or other club; did voluntary or charity work). Scores of social isolation ranged from 0 to 3, with higher scores indicating greater isolation.

Cognitive assessment

CHARLS included similar items for cognitive function as those used in the American Health and Retirement Study (HRS), which were components of the Telephone Interview for Cognitive Status (TICS) (Crimmins, Kim, Langa, & Weir, 2011). McArdle, Fisher, and Kadlec's (2007) study of the HRS data suggested two factors to adequately capture cognitive function (McArdle et al., 2007). Following McArdle et al. and based upon previous studies using the CHARLS data (Lei, Hu, McArdle, Smith, & Zhao, 2012; Pan, Luo, & Roberts, 2018), we constructed two measures of cognitive function. The first is an episodic memory measurement. In CHARLS, memory was assessed through an immediate word recall based on respondents' capacity to immediately repeat in any order a list of 10 Chinese nouns just read to them, followed by a delayed recall that tests respondents' ability to repeat the same list of words 4 to 10 min later (Crimmins et al., 2011). The episodic memory measure was created by averaging the immediate and delayed recall scores, and scores ranged from 0 to 10. The second cognitive measure is based on components of the mental status questions of the TICS established to capture the intactness or mental status of individuals. Orientation was assessed by asking respondents to name today's date (month, day, year), and identify the correct day of the week. Visuospatial ability was assessed by asking respondents to accurately re-draw a previously shown picture. Numeric ability was assessed through the serial subtraction of 7 from 100 (up to five times). Scores on these items were aggregated into a single score that ranged from 0 to 10 and was labeled as mental status, as recommended by McArdle et al. (2007). For both measures, higher scores indicate better cognitive function.

Control variables in the baseline survey

The analyses were adjusted for several demographic variables and behavioral, psychological, and clinical risk factors. Age, gender, education, and area of residence (urban/rural) were measured by self-report. Education was dichotomized as lower than secondary school and secondary school or above. Health habits including drinking and smoking, were collected using a standardized ques tionnaire (Zhao et al., 2012). Respondents were asked whether they were current smokers and whether they consumed alcohol in the past 12 months. Two measures of functional limitation were considered. CHARLS asked respondents if they required assistance with any of six activities of daily living (ADLs: walking, dressing, bathing, eating, getting into and out of bed, and toileting) or five instrumental ADLs (IADLs: preparing a hot meal, shopping for groceries, making telephone calls, taking medic and managing money) (Lei et al., 2014). Both ADLs and IADLs were treated as binary predictors (1 - functional limitations present; 0 = no functional limitations present) due to most respondents (ADL: 83.8%; IADL: 80%) denying any limitations. Chronic diseases including hypertension, diabetes, and heart diseases were obtained by asking respondents if a physician had ever told them that they had the condition. Depressive symptoms were measured with the 10-item Center for Epidemiological Studies Depression Scale (CESD-10). Modified CESD scoring was used to exclude the loneliness question in order to derive a separate depression score that was calculated as the sum of the remaining nine questions (CESD-9 range 0–27).

Statistical analysis

Characteristics of the overall sample at baseline were described using means and standard deviations for continuous data and percentages for categorical data. Rank order correlations were used to assess correlations between key predictors including loneliness (continuous scores ranged from 1 to 4 were used) and social isolation and other variables included in the analyses. To examine the association between isolation, loneliness, and cognitive function, we used lagged dependent variable regression models with ordinary least squares estimation. The lagged dependent variables model is superior for analyzing the effects of predictor variables on an outcome with two-wave panel data while controlling for the influence of time-invariant variables (Johnson, 2005). Seven models were fitted for both cognitive measurements. Model 1A was constructed to examine the associations between loneliness at baseline and cognitive function at follow-up by partially adjusting for control variables including age, gender, education, area of residence, and baseline cognitive function. Other control variables including chronic diseases, smoking and drinking status, ADL and IADL disabilities were then added in model 1B. Model 1C added CESD-9 scores in the fully adjusted model. Three similar models were fitted to test the independent associations of isolation with cognitive function (models 2A, B, and C). Model 3 added both isolation and loneliness into the fully adjusted ion effect between model. We tested whether there was an inter isolation and loneliness on cognitive function by including appropriate interaction terms into the fully adjusted model. The interactions between isolation loneliness, and gender were also assessed. For all regression unalyses, standardized regression coefficients (β) were reported as variables under study were measured on different scales. Analyses carried out using SPSS version 20.0.

Results

Table 1 shows the characteristics of the participants under study at baseline and their correlation with isolation and loneliness. The of participants was just over 60 years, and more than ean a half were men. When compared with those who were excluded from the original sample (n = 5888), participants included in the tudy sample (n = 7661) were more likely to be male (50.8% v. %; p = 0.001), younger (mean age in years: 60.97 v. 64.05, (1), and living in rural area (62.3% v. 56.8%; p < 0.001). p < They were more likely to be current smoker (32.9% v. 25.4%; < 0.001) and drinker (34.1% v. 30.2%; p < 0.001), were less likely have hypertension (28.4% v. 31.5%; p = 0.001), ADL disabilities 16.2% v. 24.1%; p < 0.001) and IADL disabilities (20.0% v. 30.3%; p < 0.001). In addition, individuals who were included into the study sample were more likely to feel lonely (35.7% v. 28.1%, p < 0.001), had a lower level of depressive symptoms (mean CESD-9 score: 6.80 v. 7.71, p < 0.001), lower level of isolation (mean score: 0.76 v. 0.90; p < 0.001), and both their episodic memory (mean score: 3.50 v. 3.09; p < 0.001) and mental status (mean score: 6.57 v. 5.50; p < 0.001) were better than those who were excluded from the analysis.

Of all the participants, the mean scores (s.D.) for loneliness and social isolation was 1.52 (0.94) and 0.76 (0.67), respectively, with 28.1% reported that they felt lonely sometimes, occasionally or most of the time. A total of 15.3% of participants were unmarried. Unadjusted correlations between baseline control variables included in the analyses and isolation and loneliness were evaluated (Table 1). Being more socially isolated or lonelier was associated with being females, older, less educated, living in rural area, being a drinker, having more ADL and IADL disabilities, and a higher level of depressive symptoms. Diagnosed hypertension was positively associated with loneliness but negatively associated with isolation, as was diagnosed heart diseases. Diagnosed diabetes was only negatively associated with isolation. Loneliness was positively associated with every sub-dimension of isolation and moderately correlated with the total score of isolation ($\rho = 0.17$, p < 0.001). After 4 years, the mean scores on both episodic memory (from 3.50 to 3.12) and mental status (from 6.57 to 6.11) were significantly lower (t = 18.07, p < 0.001 for memory; t = 14.93, p < 0.001 for mental status).

Table 1. Baseline characteristics of the participants (n = 7761)

| Characteristic | Mean (s.d.), or % | Correlation with loneliness | Correlation with social isolation | |
|--|-------------------|-----------------------------|-----------------------------------|--|
| Age, M (s.p.), years | 60.97 (7.31) | 0.060*** | 0.106*** | |
| Gender (male, %) | 50.8 | -0.100*** | -0.060*** | |
| Education (less than lower secondary education, %) | 88.7 | -0.080*** | -0.131*** | |
| Residence (live in the urban area, %) | 37.7 | 0.102*** | 0.095*** | |
| Hypertension, % | 28.4 | 0.048*** | -0.002 | |
| Diabetes, % | 6.8 | 0.005 | -0.042*** | |
| Heart diseases, % | 14.0 | 0.058*** | -0.029* | |
| Smoking, % | 32.9 | -0.022 | -0.024* | |
| Drinking, % | 34.1 | -0.047*** | -0.061*** | |
| ADL disability, % | 16.2 | 0.190*** | 0.102*** | |
| IADL disability, % | 20.0 | 0.175*** | 0.102*** | |
| CESD-9, <i>M</i> (s.d.) | 6.80 (5.79) | 0.454*** | 0.152*** | |
| Baseline cognitive function | | | | |
| Episodic memory, M (s.p.) | 3.50 (1.63) | -0.118*** | -0.143*** | |
| Mental Status, M (s.d.) | 6.57 (2.84) | -0.184*** | -0.172*** | |
| Loneliness, M (s.d.) | 1.52 (0.94) | | 0.165*** | |
| Social isolation, M (s.d.) | 0.76 (0.67) | 0.187*** | - | |
| Not married, % | 15.3 | 0.225*** | 0.487*** | |
| Less than weekly contact with children, % | 8.2 | 0.048*** | 0.379*** | |
| Not participate in social activities, % | 52.5 | 0.044*** | 0.768*** | |

M, mean; s.b., standard deviation; ADL, activities of daily living; IADL, instrumental activities of daily living, CESD, Center for Epidemiologic Studies Depression scale. **p* < 0.05, ***p* < 0.01.

Tables 2 and 3 show the results of lagged regression on epis memory and mental status respectively. Loneliness was significantly associated with cognitive decline (episodic memory: β = -0.03. p = 0.002; mental status: $\beta = -0.03$, p = 0.002 after 4 years when five control variables including age, gender, education, area of residence, and baseline episodic memory or mental status score were adjusted (model 1A). These associations remain significant when other covariates suchas chronic disease, health behaviors, and disabilities were included in the models (model 1B). However, these associations were no longer significant (episodic memory: $\beta = -0.02$, p = 0.179; mental status: $\beta = -0.02$, p = 0.088) when CESD-9 were adjusted (model 10). In contrast, greater isolation was significantly associated with lower scores on episodic memory ($\beta = -0.04$, p < 0.001) and mental status ($\beta = -0.03$, p = 0.003) 4 years later even after all the covariates including CESD-9 scores were taken into account (model 2C). Adding loneliness to the model did not reduce the association with isolation (model 3). The interaction terms between isolation and loneliness were not statistically significant for episodic memory (p for interaction = 0.690) or mental status (p for interaction = 0.050), indicating that there was no synergistic effect between isolation and loneliness on cognitive decline. Isolation × gender interaction was tested by adding the terms into the fully adjusted model including isolation and loneliness. This interaction term was neither significant for episodic memory (p for interaction = 0.934) nor for mental status (p for interaction = 0.224). No significant interaction between gender and loneliness was found for either cognitive measure (all p for interaction >0.5).

To reduce the risk of reverse causation in analyses, we reran model 3 after excluding the respondents with very low cognition scores at the baseline survey (bottom 10%), on the grounds that people with very impaired cognition may find it difficult to engage socially with others. The results were unchanged [for episodic memory: isolation ($\beta = -0.04$, p = 0.001); loneliness ($\beta = -0.02$, p = 0.064); for mental status: isolation ($\beta = -0.03$, p = 0.013); loneliness ($\beta = -0.02$, p = 0.111)].

Discussion

In this study, a large representative sample of Chinese older adults was selected to examine simultaneously the associations of social isolation and loneliness with cognitive decline over a 4-year follow-up period. In accordance with our hypotheses, both loneliness and social isolation showed association with decreases in episodic memory and mental status. However, this association becomes less significant for loneliness when all the other confounding variables, especially depressive symptoms, were taken into account. However, the association for social isolation seems independent of loneliness and other confounding variables. Our results seem to indicate a stronger negative relationship between social isolation than loneliness and cognitive function, which is consistent with two recent studies. For instance, Griffin et al. found that social isolation was longitudinally associated with worse cognitive performance in older Americans whereas loneliness only cross-sectionally correlated with lower cognitive function (Griffin et al., 2020). Another longitudinal study

Table 2. Predicting episodic memory at follow-up

| | Model 1 | | | Model 2 | | | Model 3 |
|-----------------|----------|----------|----------|----------|----------|----------|----------|
| | Α (β) | В (β) | C (β) | Α (β) | В (β) | C (β) | (β) |
| Age | -0.22*** | -0.22*** | -0.22*** | -0.22*** | -0.22*** | -0.22*** | -0.22*** |
| Gender | 0.01 | 0.02 | 0.02 | 0.01 | 0.02 | 0.02 | 0.02 |
| Education | 0.13*** | 0.13*** | 0.13*** | 0.13*** | 0.13*** | 0.12*** | 0.12*** |
| Residence | -0.11*** | -0.10*** | -0.10*** | -0.11*** | -0.10*** | -0.10*** | -0.10*** |
| Baseline EM | 0.33*** | 0.32*** | 0.32*** | 0.33*** | 0.32*** | 0.32*** | 0.32*** |
| Loneliness | -0.03** | -0.03* | -0.02 | - | - | | -0.01 |
| Isolation | | - | - | -0.05*** | -0.04*** | -0.04*** | -0.04*** |
| Hypertension | | -0.00 | -0.00 | | -0.00 | -0.00 | -0.00 |
| Diabetes | | -0.00 | -0.00 | | -0.01 | -0.00 | -0.00 |
| Heart diseases | | 0.05*** | 0.05*** | | 0.05*** | 0.05*** | 0.05*** |
| Smoking | | -0.03* | -0.03* | | -0.03* | -0.03* | -0.03* |
| Drinking | | 0.01 | 0.01 | | 0.01 | 0.01 | 0.01 |
| ADL disability | | 0.00 | 0.01 | | 0.00 | 0.01 | 0.01 |
| IADL disability | | -0.06*** | -0.06*** | | -0.06*** | -0.06*** | -0.06*** |
| CESD-9 | | | -0.03* | | | -0.03* | -0.03* |

EM, episodic memory; ADL, activities of daily living; IADL, instrumental activities of daily g, CESD, Cent for Epidemi gic Studies Depression scale.

 β = standardized regression coefficient. *p < 0.05, **p < 0.01, ***p < 0.001.

| Table 3. Predicting m | nental status at follow | r-up | | | | | |
|-----------------------|-------------------------|----------|----------------|----------|----------|----------|----------|
| | Model 1 | | | Model 2 | | | Model 3 |
| | Α (β) | В (β) | C (<i>β</i>) | Α (β) | В (β) | C (β) | (β) |
| Age | -0.11*** | -0.11*** | -0.11*** | -0.11*** | -0.11*** | -0.11*** | -0.11*** |
| Gender | 0.12*** | 0,14*** | 0.13*** | 0.12*** | 0.14*** | 0.14*** | 0.13*** |
| Education | 0.08*** | 0.08*** | 0.08*** | 0.08*** | 0.08*** | 0.08*** | 0.08*** |
| Residence | -0.08*** | -0.08*** | -0.07*** | -0.08*** | -0.08*** | -0.08*** | -0.07*** |
| Baseline MS | 0.49*** | 0.49*** | 0.48*** | 0.49*** | 0.48*** | 0.48*** | 0.48*** |
| Loneliness | -0.03** | -0.03** | -0.02 | - | - | - | -0.02 |
| Isolation | | _ | - | -0.03** | -0.03** | -0.03** | -0.02** |
| Hypertension | | 0.02 | 0.02 | | 0.01 | 0.01 | 0.01 |
| Diabetes | | -0.00 | -0.00 | | -0.00 | -0.00 | -0.00 |
| Heart diseases | | 0.02* | 0.03** | | 0.02* | 0.02* | 0.02* |
| Smoking | | -0.03* | -0.03* | | -0.03** | -0.03** | -0.03* |
| Drinking | | 0.01 | 0.01 | | 0.00 | 0.00 | 0.00 |
| ADL disability | | 0.01 | 0.01 | | 0.01 | 0.01 | 0.01 |
| IADL disability | | -0.03** | -0.03** | | -0.04*** | -0.03** | -0.03*** |
| CESD-9 | | | -0.03* | | | -0.03** | -0.02* |

MS, mental status; ADL, activities of daily living; IADL, instrumental activities of daily living; CESD, Center for Epidemiologic Studies Depression scale.

 β = standardized regression coefficient. *p < 0.05, **p < 0.01, ***p < 0.001.

with German older adults also found that social isolation rather than loneliness can predict cognitive health (Beller & Wagner, 2018).

Substantial evidence indicated that loneliness is associated with a higher risk of cognitive decline at older ages (Boss et al., 2015), and may contribute to the development of dementia (Rafnsson et al., 2020; Wilson et al., 2007). However, contradictory evidence also exists that indicates no independent association between loneliness and cognitive decline (Okely & Deary, 2019; Rawtaer et al., 2017). Two studies with Chinese older adults found a significant association between loneliness and cognitive decline. Although loneliness was measured with one single item in these two studies as ours, depressive symptoms were not controlled in their models (Zhong et al., 2016, 2017). Our study does indicate negative associations between loneliness and cognitive function. However, these relationships become non-significant when all the confounding variables including depressive symptoms were controlled. It is notable that in our study, the associations between loneliness and baseline poor health was stronger than the associations between social isolation and the same health index, especially for cardiovascular health and depressive symptoms. Therefore, our finding that loneliness no longer was associated with cognitive decline after these confounding variables had been controlled may reflect its association with baseline health. Accounting for depressive symptoms did more to reduce the association between cognitive function than accounting for the clinical and behavioral covariates. Loneliness was measured by one item from CESD in our study, and the two are significantly correlated ($\rho = 0.45$, p < 0.001). Thus, it is not a surprise that controlling for depressive symptoms would reduce the size of the association. Such a result is consistent with previous studies. In a longitudinal study of Scottish aging adults, the associations between loneliness and cognitive ability were no longer significant when the mode included depressive symptoms as covariates (Gow et al., 2013). Similar results were also found for studies of mortality (Steptoe et al., 2013; Teguo et al., 2016). In a cohort study adopted the same measurement of loneliness as ours, the association between loneliness and mortality also became insignificant when depressive symptoms (CESD scores excluding londiness item) were adjusted (Teguo et al., 2016). These results may not imply that loneliness is not important but rather indicate that the experie of loneliness may be characteristic of people who already have mental health problems. Future studies with more independent measurements of loneliness and depressive symptoms are warranted to clarify this issue.

Nevertheless, convincing evidence, including the current study, highlights the associations between social isolation and cognitive decline (Kuiper et al., 2016). Several theories have been proposed to explain the association of social isolation and cognitive function. One is the 'use it or lose it' theory (Hultsch, Hertzog, Small, & Dixon, 1999), which argues that engagement in intellectual, physical and social activities stimulates the brain. Decrease in engagement in social activities may result in the lack of use of mental faculties that may in turn lead to a decline or cognitive ability. Another theory is stress-buffering, proposing that social relationships are beneficial in stressful situations (Fratiglioni, Pailard-Borg, & Winblad, 2004). Stress has been associated with cognitive decline due to structural changes in the hippocampus (Wilson et al., 2003). Social relationships may prevent or modulate responses to stressful events that are damaging to health.

Although previous studies provide evidence for the negative associations between social relationships and cognitive function, it should be noted that most findings are based on Western sample and hence a limited cultural context (Courtin & Knapp, 2017; Evans et al., 2019; Kuiper et al., 2016). Westerners tend to have higher objective social isolation compared with non-Western populations. Taking the USA as an example, the percentage of single-person households within the same historical period is almost three times that of China (Hu & Peng, 2015). Furthermore, Western countries tend to be more individualistic from a cultural viewpoint (Hofstede, Hofstede, & Minkov, 2005). Thus, our study expands knowledge about the role of social relationships in a more collectivistic culture.

Strengths of our study include the large sample size and the fact that CHARLS is designed to be representative of the community-dwelling Chinese population aged >50. Cognitive function was assessed with a series of objective tests, and the study benefited from detailed measures of potential confounders. The study also has limitations. First, loneliness was assessed with only one direct question regarding the perception of loneliness in the last week. Despite wide use in the literature and strong correlations with several established multiple-item scales, this measure may be less reliable than a composite measure that taps multiple aspects of loneliness (Holwerda et al., 2014; Petersen et al., 2016; Victor, Grenade, & Boldy, 2005) The effects of loneliness became insignificant when depressive symptoms were adjusted, which may also because the lonelines sitem is derived from the CESD-10. However, another study using a more complex and independent measure of loneliness has reported similar findings as ours (Griffin et al. 2020). Second, the current study investigated the consequences of loneliness and social isolation longitunally with a relative short-term of 4 years. This prevents us from examining long-term association of social relationships with cog-nitive function, and whether certain aspects of social relationships ecome more or less important over time. Future study could test relationship using longer-term panel data of Chinese populat tion. Third, CHARLS does not give full neuropsychological testng for the large sample at baseline, and thus cannot provide mal diagnoses of mild cognitive impairment or dementia. owever, we have applied a widely used way to exclude the espondents with very low cognition scores (bottom 10%) at the baseline survey (Ganguli et al., 1993; Weuve et al., 2004). A sensitivity analysis after the exclusion yielded similar results as the primary analysis. Finally, this is an observational study, and causal conclusions cannot be drawn. Although we took multiple covariates into account, there may be other unmeasured factors responsible for the associations recorded here.

Conclusion

In this prospective study, high levels of social isolation were associated with an increased risk of cognitive decline. By contrast, loneliness was not linked with the cognitive decline when other confounding variables were controlled. These findings expand our knowledge about the association of social relationships with cognitive function in non-Western populations. Cognitive decline is a strong risk factor for development of dementia (Bennett et al., 2002). Efforts to reduce isolation may therefore have substantial benefits in terms of preventing dementia among older adults in China.

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Conflict of interest. None.

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