Social isolation, loneliness and all-cause mortality: a cohort study of 35, 254 Chinese older adults

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Impact Statement

We certify that this work is confirmatory of recent novel clinical research [1-5]. This study showed evidence of the adverse effect of objective social isolation on mortality of Chinese older adults. The subjective feeling of loneliness was associated with an increased mortality only among subjects aged < 80 years.

Key Points

Among community-dwelling Chinese adults > age 60 years social isolation was associated with mortality over a mean follow-up of 4.8 years.

Loneliness was associated with mortality only for participants with age < 80 years.

Why does this matter?

This study implied that policies and public health interventions aimed at increasing social connectedness may potentially reduce excess mortality among older adults.

ABSTRACT

Background Few studies of social isolation, loneliness and associations with all-cause mortality in older adults have been conducted in non-Western countries. The aim of this study was to conduct such an analysis in a nationally representative sample of Chinese older adults.

Methods This study used eight waves of data from the Chinese Longitudinal Healthy Longevity Survey from 1998 to 2018 and focused on participants aged ⩾ 60 years. A total of 21,570 people died (61.2%) over a median follow-up of 4.8 years. Social isolation, loneliness, demographic, health and lifestyle factors were measured at baseline. The primary outcome was all-cause mortality. *Cox* proportional hazard regression models were used to examine the associations of isolation and loneliness with all-cause mortality.

Results This study included 35,254 participants with mean age of 86.63±11.39 years. Social isolation was significantly associated with an increased mortality (adjusted *HR* 1.22; *95% CI* 1.18–1.25; $P < 0.01$). The association of loneliness with mortality was nonsignificant after adjustment for health indicators and low psychological well-being (*HR* 1.01; *95% CI* 0.98–1.04; $P = 0.69$). However, when stratified by age, there was a significant association of loneliness with mortality among participants aged < 80 years (*HR* 1.15; *95% CI* 1.05-1.26; $P < 0.01$).

Conclusions Social isolation was associated with an increased all-cause mortality among the older Chinese adults. However, loneliness was associated with an increased mortality only among younger participants. Public health interventions aimed at increasing social connectedness may potentially reduce excess mortality among older adults.

KEY WORDS social isolation; loneliness; all-cause mortality; older adults

INTRODUCTION

Impoverished social relationships—including both social isolation or loneliness—have been associated with poor health outcomes in numerous studies.[1] Social isolation refers to the objective lack of social contact with others, and includes factors such as living alone, disengagement from social ties, and limited participation in social activities.[2] In contrast, loneliness is a subjective feeling that describes discrepancy between desired and actual quality of social relationships.[3] Both social isolation[4, 5] and loneliness[6, 7] have been independently associated with an increased all-cause mortality in older adults. Given the distinct nature of social isolation and loneliness, research has increasingly focused on the possible differential effects of these two constructs on mortality.[2] Among the few studies in which both loneliness and social isolation were evaluated the results were mixed. Some studies found a greater association of social isolation with mortality while others found support for a greater association between loneliness and mortality.[8-10]

An important gap in knowledge is the lack of studies on the health consequences of social isolation and loneliness in non-Western countries. Most studies on this topic have been conducted in higher-income countries in North America and Europe.[2] It has not been established whether similar patterns occur in middle and lower income countries. China is expected to experience a rapid population ageing in the next two to three decades. In parallel with this aging profile, the epidemiology of social isolation and loneliness has become more salient among the Chinese older population. It has been suggested that the association of social relationships with health outcomes could be more important in Chinese than Western populations, because cultural traditions emphasize the family system and collectivism.[11] However, little is known about the consequences of isolation and loneliness for the mortality in China. One study investigated the association of loneliness with mortality among Chinese older adults, but social isolation was not fully considered.[7] An additional topic is that most

longitudinal studies of social relationships involve people of younger age at baseline.[1, 2] Therefore, roles of social isolation and loneliness among the oldest-old (people aged >80 years) are not well understood.

We therefore sought to investigate the associations of both subjective and objective deficiencies in social relationships with all-cause mortality in a large sample of Chinese older adults. In this study, we tested the hypotheses that higher levels of social isolation and loneliness are associated with increased mortality among Chinese older adults. We also examined whether the associations of social isolation and loneliness with mortality varied across sex, age, and chronic diseases groups.

METHODS

Participants

The data were derived from all eight waves (1998, 2000, 2002, 2005, 2008–2009, 2011–2012, 2014, and 2018) of the Chinese Longitudinal Healthy Longevity Survey (CLHLS). The CLHLS is the first national longitudinal survey of the oldest-old (mostly aged 80 or over) in China. A multistage stratified cluster sampling design was used to recruit participants from 22 of the 31 provinces in China. A total of 631 cities and counties were then randomly selected. In the sampled counties, village or community was randomly selected as a cluster, in which all eligible subjects were interviewed. Therefore, all participants were community dwelling older adults. A weight variable was calculated based on the estimated numbers of oldest old participants by age, sex, and rural/urban residence. The results indicated that the weight variable was not comparable across different waves and it was therefore not applied to the analysis in this study.[12] More details on sampling design and data quality can be found elsewhere.[13]

The CLHLS initially only included individuals who were aged 80 years or older between wave 1998 and wave 2000, then included individuals aged 65–79 years from 2002 and adult offspring

aged 35-64 years from 2008. Since the mortality rate was high in the oldest-older adults, new participants were recruited in the follow-up surveys to replace the deceased and lost-to-follow-up participants of the same sex and age. All participants aged 60 years or older at each baseline (N = 45,434), consisting of older adults aged 65 years or over and adult offspring aged 60-64 years, were potentially eligible for our analysis. New recruits of the latest wave (2018) were not included in the analysis because no follow-up data were available. In our main analyses, only participants without any missing data were included.[14] Those with missing values on loneliness or isolation (N = 5,996), or any other covariates (N = 4,184) at baseline were excluded. The flow chart for the study participants is shown in Supplemental **Figure S1**. Finally, a total of 35,254 participants [male, 43.9%; mean age (standard deviation (SD)) = 86.63 (11.39) at baseline] were included.

The CLHLS was approved by the Institutional Review Board, Duke University (Pro00062871), and the Biomedical Ethics Committee, Peking University (IRB00001052–13074). All participants provided written informed consent.

Measures

Social isolation

Five items reflecting different aspects of social network were combined to create an index of social isolation, which was adapted from previous studies.[8, 15] One point was assigned if participants were not married (never married, separated, divorced, widowed), lived alone, had less than monthly contact (including face-to-face or remote contact) with their children, with their siblings, and if they did not participate in either of two social activities (playing chess or cards; attending a religion group) in the past 6 months. This resulted in a scale ranging from 0 to 5. More details about the construct of social isolation can be found in Supplemental File S1. Social isolation scores were positively skewed, so for the purpose of *Cox* regression modeling, participants were categorized into two groups by the top quartile (≥ 3 versus < 3 points) to

indicate isolated (N = 14,945, 42.4%) versus non-isolated (N = 20,309, 57.6%) groups in the main analysis. We did not use score of 2 as cut-off point as previous study [8] because this will result into a relatively high proportion of social isolation (N = 26,108, 74.1%) in our sample.

Loneliness

Loneliness was measured using one single item, asking participants how often they felt lonely. The 5-point response options were 1 = never, 2 = seldom, 3 = sometimes, 4 = often, and 5 = always. This one item measure is strongly correlative with multi-item loneliness scales and has been used in a number of previous studies.[7, 16-18] Loneliness was treated as dichotomous variable (1 = lonely; and 0 = not lonely); participants who responded 'sometimes', 'often', or 'always' were classified as "lonely", participants who responded 'never' or 'seldom' were classified as "not lonely".[18, 19]

Covariates

Several covariates were included in the analyses based on previous research.[8, 10] Age, sex, ethnicity (Han Chinese versus ethnic minorities), education, and area of residence (urban/rural) were measured by self-report. There are 56 ethnic groups in China, all of which except the Han Chinese are called ethnic minorities. Education was categorized into two groups (no formal schooling and elementary school or above). Health habits including smoking and drinking were collected using a standardized questionnaire. Regular exercise was measured using a question "Do you do exercise regularly at present, such as walking, jogging, playing ball, and qigong" and categorized as yes or no. Self-rated health was measured using one item 'how do you rate your health in general?' with five response options: very good, good, fair, poor, and very poor. The options of "very good" and "good" were combined, as were the options "poor" and "very poor" because participants tended not to choose the extreme options. Three categories of self-rated health (good, fair, poor) were then used in the final analyses. Activities of daily living (ADL) disability was defined as self-

reported difficulty with six activities including eating, dressing, transferring, using the toilet, bathing, and continence. A score of 0, 1 or 2 was given if participants needed no, some, or complete assistance with the activity, resulting in the ADL scores with range from 0 to 12. Psychological well-being was measured by five items [20]: (1) Do you always look on the bright side of things? (2) Are you as happy as when you were young? (3) Do you often feel fearful or anxious? (4) Do you feel the older you get, the more useless you are? (5) I can make my own decisions concerning my personal affairs. The 5-point response scale to each item ranged from "never" to "always" (possible range from 0 to 25, with a higher score indicating a lower psychological well-being). Chronic diseases including hypertension, diabetes, and cardiovascular disease (CVD) were obtained by asking participants if a physician had ever told them that they had the condition.

Statistical analysis

Data are presented as means ± SDs for continuous variables and frequencies (percentages) for categorical variables. The differences in the baseline characteristics between isolated and non-isolated groups as well as lonely and non-lonely groups were compared using *t*-tests for continuous variables and *Chi-square* tests for categorical variables. *Cox* proportional hazard regression models were used to examine the associations of baseline isolation and loneliness with all-cause mortality, with survival time measured in months from the first interview date to the recorded death date or last interview date up to 2018. Results were presented as hazard ratios (*HRs*) and 95% confidence intervals (*CIs*) for isolated or lonely individuals, with the non-isolated or non-lonely category as the reference group. We fitted five models for social isolation. Model 1 adjusted for sex and age. Demographic factors (education, urban/rural residence, and ethnicity) were then added to model 2. In model 3, we added health behaviors including smoking, drinking, and exercise. In model 4, health indicators at baseline (self-rated health, ADL disability, psychological well-being, and chronic diseases) were added. Loneliness

was added to model 5. Similar models were fitted for loneliness. The interaction between categorical isolation and loneliness on mortality was also tested. To measure the robustness of these associations, *Cox* regressions were further conducted stratifying by sex, age, and the presence of chronic diseases at baseline.

Four sensitivity analyses were performed. First, isolation and loneliness were analyzed as continuous variables. Second, to prevent the possibility that associations were caused by individuals having become isolated or lonely as a consequence of illness, participants who had died within the first 2 years after baseline were excluded from the analysis. Third, we assessed whether associations varied with the waves of data collection. We therefore carried out a multilevel *Cox* regression to examine the associations, with the waves of entry into the study as the higher level and individuals as the lower level. Fourth, the Multivariate Imputation by Chained Equations (MICE) package in the statistical program R (version 3.5.1) was used to impute missing data of all the variables to investigate the impact of missing data.[21] Analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA) and a two-tailed $P< 0.05$ indicated a statistical significance.

RESULTS

We carried out analyses on 35,254 participants at baseline. The mean number of observations for the same participant was 2.12 (ranging from 1 to 8). The median follow-up period was 4.80 years (range from 1 to 20 years). By the census date, a total of 21,570 people had died (61.2%), of whom 9,282 were men (43.0%). The mean scores (SD) of social isolation and loneliness for this sample were 3.13 (1.11) and 2.11 (0.99) respectively. 42.4% of the participants were categorized as socially isolated and 31.3% as lonely. Social isolation and loneliness were moderately positively correlated ($r= 0.20$, $P< 0.01$).

A total of 10,180 participants were excluded due to missing data at baseline. Compared with those who were excluded, participants in the analytic dataset were more likely to be current

smokers, alcohol consumers, and regular exercisers. They were less likely to have chronic diseases (Supplemental Table S1).

The characteristics of all participants and subgroups based on social isolation and loneliness status are shown in **Table 1**. Overall, 75.4% of participants were aged 80 years or over at baseline, with 45.6% of participants aged over 90 years. There were significant differences in all characteristics between non-isolated and isolated groups. Meanwhile, significant differences between not lonely and lonely groups were observed in all characteristics, except hypertension (P= 0.67), diabetes (P= 0.82), CVD (P= 0.24), and monthly contact with siblings (P= 0.16).

Figure 1 presents the adjusted associations of social isolation with all-cause mortality. After adjustment for age and sex, *HR* for the isolated group was 1.28 [*95% CI* 1.24–1.31; P< 0.01] compared with the non-isolated group. Adjusting for other covariates including demographic factors, health behaviors, and health indicators did not substantially affect the estimates [model 4: *HR* 1.22; *95% CI* 1.18–1.25; P< 0.01]. *HR* also remained unchanged (model 5: *HR* 1.22; *95% CI* 1.18–1.25; P< 0.01) when loneliness was additionally taken into account. The full regression models including all variables are shown in Supplemental Table S2.

The age- and sex-adjusted *HR* for loneliness was also significant (1.14; *95% CI* 1.11–1.18; P< 0.01) as shown in **Figure 2**. Adjustment for demographic and health behaviors slightly reduced the strength of this association (*HR* 1.12; *95% CI* 1.09–1.15; P< 0.01) (model 3). But when health indicators including self-rated health, psychological well-being and chronic diseases were adjusted, the association was attenuated by 79.0% and became nonsignificant (*HR* 1.03; *95% CI* 0.99–1.06; P= 0.12) (model 4).

Supplemental Table S3 shows that the interaction between categorical social isolation and loneliness was statistically significant (P for interaction< 0.01). Further analysis was then conducted by forming four groups combining isolation and loneliness. Compared to the group with both no isolation and no loneliness, groups with isolation but no loneliness or no isolation

but loneliness have a significantly increase of *HR*. However, *HR* for the group with both isolation and loneliness (*HR* 1.21; *95% CI*, 1.13-1.23; *P*< 0.01) was no greater than that for the group with isolation but no loneliness, indicating no synergistic association of social isolation and loneliness with mortality (Supplemental Table S4).

Models including both isolation and loneliness and all other covariates were then conducted stratifying by sex, age, and the presence of chronic diseases at baseline. Results for these three models are shown in **Table 2**. The association for social isolation was consistent across different stratifications, although associations were somewhat weaker among men than women, and in participants aged > 90 years than other age groups. A significant association for loneliness was observed for the youngest subgroup (< 80 years) (*HR* 1.15; *95% CI* 1.05-1.26; *P*< 0.01) but not in older groups. Based on this finding, we further analyzed the interaction between social isolation and loneliness for the subgroup of < 80 years. No significant interaction was found (*P* for interaction= 0.44).

The first sensitivity analysis showed that the results were unchanged from those in the categorical analyses, with an adjusted *HR* for mortality of 1.13 (*95% CI* 1.11–1.15; *P*< 0.01) for every unit increase in social isolation but no significant relationship with loneliness (*HR* 1.01; *95% CI* 0.99–1.02; *P*= 0.53; see Supplemental Table S5). Our second sensitivity analysis suggested that the results of the fully adjusted model were comparable to those in the main analysis (isolation: *HR* 1.22; *95% CI* 1.18-1.27; *P*< 0.01; loneliness: *HR* 1.02; *95% CI* 0.98-1.07; *P*= 0.26). The results of the third sensitivity analysis were consistent with the main analysis (isolation: *HR* 1.17; *95% CI* 1.14-1.21; *P*< 0.01; loneliness: *HR* 1.01; *95% CI* 0.98-1.04; *P*= 0.47; Supplemental Table S6). The results of the fourth sensitivity analysis were essentially unchanged from those of the complete-cases analyses (isolation: *HR* 1.22; *95% CI* 1.20-1.25; *P*< 0.01; loneliness: *HR* 1.01; *95% CI* 0.98-1.04; *P*= 0.46; Supplemental Table S7).

DISCUSSION

In this study of a national sample of older adults in China, we found that social isolation was associated with a higher all-cause mortality in the complete cohort as well as in subgroups of males and females, younger and older, initially healthy and unhealthy participants. The associations were independent of loneliness and other covariates. The association of loneliness with mortality in the total cohort became insignificant when baseline mental and physical health were taken into account, but subgroup analysis indicated a significant relationship with loneliness for the younger individuals (below 80 years old). We did not detect any synergistic association of social isolation and loneliness with mortality.

To our knowledge, this was the first large-scale study to investigate the associations of social isolation and loneliness with mortality in a nationally representative sample of older adults in China. Our research complements findings mainly from Western countries, which reported the associations of social isolation and loneliness with an increased all-cause mortality.[1, 2] Moreover, our study involved a sample with a mean age of over 86 years and over 40% of participants were older than 90 years. Very few studies on this topic have been conducted among samples with this extreme old age.[1, 2, 22]

Several possible pathways have been proposed to explain the adverse effects of social isolation on health and mortality. Social isolation may promote unhealthy behaviors such as poor nutrition and physical inactivity, which can increase risk of death.[23] Moreover, older adults who live alone or lack social contacts may be at an increased risk of death because acute symptoms may develop when they are alone, or because they have smaller networks of individuals who can help them secure prompt medical attention.[24]

Loneliness has been shown to be associated with an increased level of mortality.[6, 7] However, in our study, when examined simultaneously with social isolation, loneliness did not have a significant association with mortality in the fully adjusted models. This is consistent with previous studies conducted in Western countries which showed associations between measures

of social isolation, but not loneliness, with mortality.[6, 8, 9, 25] It is possible that loneliness is associated with other risk factors, so that in multivariate analysis it does not emerge as an independent risk factor. When subgroup analysis was conducted, a significant relationship was found for the younger group of participants. In fact, the results for isolation were also stronger for the younger group. These results are consistent with findings from a meta-analysis, which suggested that younger adults were at a greater risk of mortality when lonely or living alone than older adults in these same circumstances.[2] One plausible explanation is that individuals who do not die at younger ages may have more robust social or health characteristics than those who die earlier. Thus, the observed difference across ages could be confounded with preexisting health status. It might also be the case that impoverished social relationships of younger individuals are associated with more harmful effects on health-related outcomes.[26]

Significant correlations were found between social isolation and loneliness in our study, which was also consistent with previous findings in Western countries.[4, 9, 27] One could conjecture that mortality risk would escalate for those who are lonely and isolated at the same time. However, no synergistic interaction between loneliness and social isolation was detected by further analysis in our study, which was consistent with a previous study with Finnish sample.[25] This result supports the idea that objective and subjective perspectives of social relationships have their own separate effects on mortality.[2] It might also be possible that effect of social isolation in our study was too strong, which diminished the effect of loneliness.

The strengths of this study include the large sample size, long follow-up, and adjustment of multiple demographic and health factors. Our study also had limitations. First, loneliness was assessed with only one direct question regarding the perception of loneliness. 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. Moreover, using a single item to directly measure loneliness might be more prone to social

desirability bias since people may reluctant to admit feeling "lonely". [28] This could be especially true for samples from China, where values interdependence, mutual support, and common goals. Therefore, future research should establish whether our results can be replicated using a more comprehensive measure of loneliness. Second, although we adjusted for a broad set of variables, our study did not prove that social isolation contributed directly to mortality. There were other possible confounding variables which were not assessed, such as personality and coping styles. Third, a large number of participants were excluded from the final analysis. Included participants were healthier (e.g., more likely to be regular exercisers and less likely to have chronic diseases) than those excluded, which might limit the generalizability of the results. It must also be acknowledged that our findings possibly underestimated the true associations of social isolation and loneliness with mortality. Fourth, due to the high proportion of oldest-old in this study, there was a high mortality rate of 61.0%, which might also limit the generalizability of the results.

In conclusion, this study showed evidence of the adverse effect of objective social isolation on mortality among Chinese older adults. The subjective feeling of loneliness, in contrast, was only associated with an increased mortality among the younger subgroup of samples.

These results could be important for the design of health promotion interventions in older Chinese adults and perhaps those in Western countries. Further intervention studies should be conducted to see if increasing social connections can lead to health benefits for general populations.[3] The development of interventions aimed at tackling loneliness in the younger group of older adults might contribute to mortality risk reduction.

ACKNOWLEDGMENTS

Conflict of Interest

The authors have no conflicts.

Author Contributions

Bin Yu contributed to data interpretation and writing the original draft. Andrew Steptoe contributed to review and editing the draft. Yongjie Chen contributed to data curation, formal analysis, and study design. All authors read and approved the final manuscript.

Sponsor's Role

The sponsor has no role in the design, methods, subject recruitment, data collections, analysis and preparation of paper.

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LEGENDS

Figure 1 The associations of social isolation with all-cause mortality.

Notation: Hazard ratio plots with a logarithmic scale.

Model 1: Adjusting for age and sex; Model 2: Additionally adjusting for education, living areas, and ethnicity. Model 3: Additionally adjusting for smoking, drinking, and exercise. Model 4: Additionally adjusting for self-rated health, psychological well-being, hypertension, diabetes, cardiovascular disease, and activities of daily living; and Model 5: Additionally adjusting for loneliness.

Figure 2 The associations of loneliness with all-cause mortality.

Notation: Hazard ratio plots with a logarithmic scale.

Model 1: Adjusting for age and sex; Model 2: Additionally adjusting for education, living areas, and ethnicity. Model 3: Additionally adjusting for smoking, drinking, and exercise. Model 4: Additionally adjusting for self-rated health, psychological well-being, hypertension, diabetes, cardiovascular disease, and activities of daily living; and Model 5: Additionally adjusting for social isolation.

Supplemental Figure S1 The flow chart of study participants.

Table 1. Characteristics of participants at baseline according to categories of social isolation and loneliness

Characteristics	All participants Mean (SD) or N (%)	Non-isolated Mean (SD) or N (%)	Isolated Mean (SD) or N (%)	*P*	Not lonely Mean (SD) or N (%)	Lonely Mean (SD) or N (%)	*P*
N	35,254	20,309 (57.6)	14,945 (42.4)		24,233 (68.7)	11,021 (31.3)	
Sex				<0.01			<0.01
Females	19,768(56.1)	9,826(48.4)	9,942(66.5)		12,967(53.5)	6,801(61.7)	
Males	15,486(43.9)	10,483(51.6)	5,003(33.5)		11,266(46.5)	4,220(38.3)	
Age, (years, %)				<0.01			<0.01
<80	8,673(24.6)	7,050(34.7)	1,623(10.9)		6,593(27.2)	2,080(18.9)	
80-90	10,507(29.8)	6,334(31.2)	4,173(27.9)		7,285(30.1)	3,222(29.2)	
90+	16,074(45.6)	6,925(34.1)	9,149(61.2)		10,355(42.7)	5,719(51.9)	
Living area				<0.01			<0.01
Urban	24,359(69.1)	15,030(74.0)	9,329(62.4)		16,455(46.7)	7,904(71.7)	
Rural	10,895(30.9)	5,279(26.0)	5,616(37.6)		7,778(22.1)	3,117(28.3)	
Education				<0.01			<0.01
< Primary	21,775(61.8)	10,944(53.9)	10,831(72.5)		14,174(58.5)	7,601(69.0)	
Primary school	13,479(38.2)	9,365(46.1)	4,114(27.5)		10,059(41.5)	3,420(31.0)	
Ethnicity (Han)	33,092(93.9)	19,139(94.2)	13,953(93.4)	<0.01	22,802(94.1)	10,290(93.4)	0.01
Current smoker	6,815(19.3)	4,539(22.4)	2,276(15.2)	<0.01	5,017(20.7)	1,798(16.3)	<0.01
Current alcohol	7,394(21.0)	4,565(22.5)	2,829(18.9)	<0.01	5,467(22. 6)	1,927(17.5)	<0.01
Exercise (yes)	10,789(30.6)	7,006(34.5)	3,783(25.3)	<0.01	8,229(34.0)	2,560(23.2)	<0.01
Self-rated health				<0.01			<0.01
Poor	4,239(12.0)	2,370(11.7)	1,869(12.5)		2,176(9.00)	2,063(18.7)	
Fair	11,806(33.5)	6,552(32.3)	5,254(35.2)		7,230(29.8)	4,576(41.5)	
Good	19,209(54.5)	11,387(56.1)	7,822(52.3)		14,827(61.2)	4,382(39.8)	
Psychological well-	12.2±3.3	11.9±3.3	12.7±3.3	<0.01	11.3±3.1	14.2±3.0	<0.01
Activities of daily	0.8±2.0	0.6±1.6	1.1±2.3	<0.01	0.7±1.7	1.1±2.3	<0.01
Chronic diseases							

Hypertension	21,082(59.8)	12,236(60.3)	8,846(59.2)	0.05	14,473(59.7)	6,609(60.0)	0.67
Diabetes	732(2.1)	528(2.6)	204(1.4)	<0.01	506(2.1)	226(2.1)	0.82
CVD	1,523(4.3)	1,007(5.0)	516(3.5)	<0.01	1,026(4.2)	497(4.5)	0.24
Loneliness	11,021(31.3)	5,245(25.8)	5,776(38.7)	<0.01	-	-	
Social isolation	14,945(42.4)	-	-		9,169(37.8)	5,776(52.4)	<0.01
Married (no)	24,728(70.1)	9,835(48.4)	14,893(99.7)	<0.01	8,659(35.7)	1,867(16.9)	<0.01
Living alone	5,978(17.0)	1,196(5.9)	4,782(32.0)	<0.01	3,237(13.4)	2,741(24.9)	<0.01
Monthly contact	29,866(84.7)	15,017(73.9)	14,849(99.4)	<0.01	20,330(83.9)	9,536(86.5)	<0.01
Monthly contact	23,298(66.1)	9,404(46.3)	13,894(93.0)	<0.01	15,957(65.9)	7,341(66.6)	0.16
Social	26,367(74.8)	12,546(61.8)	13,821(92.5)	<0.01	17,613(72.7)	8,754(79.4)	<0.01

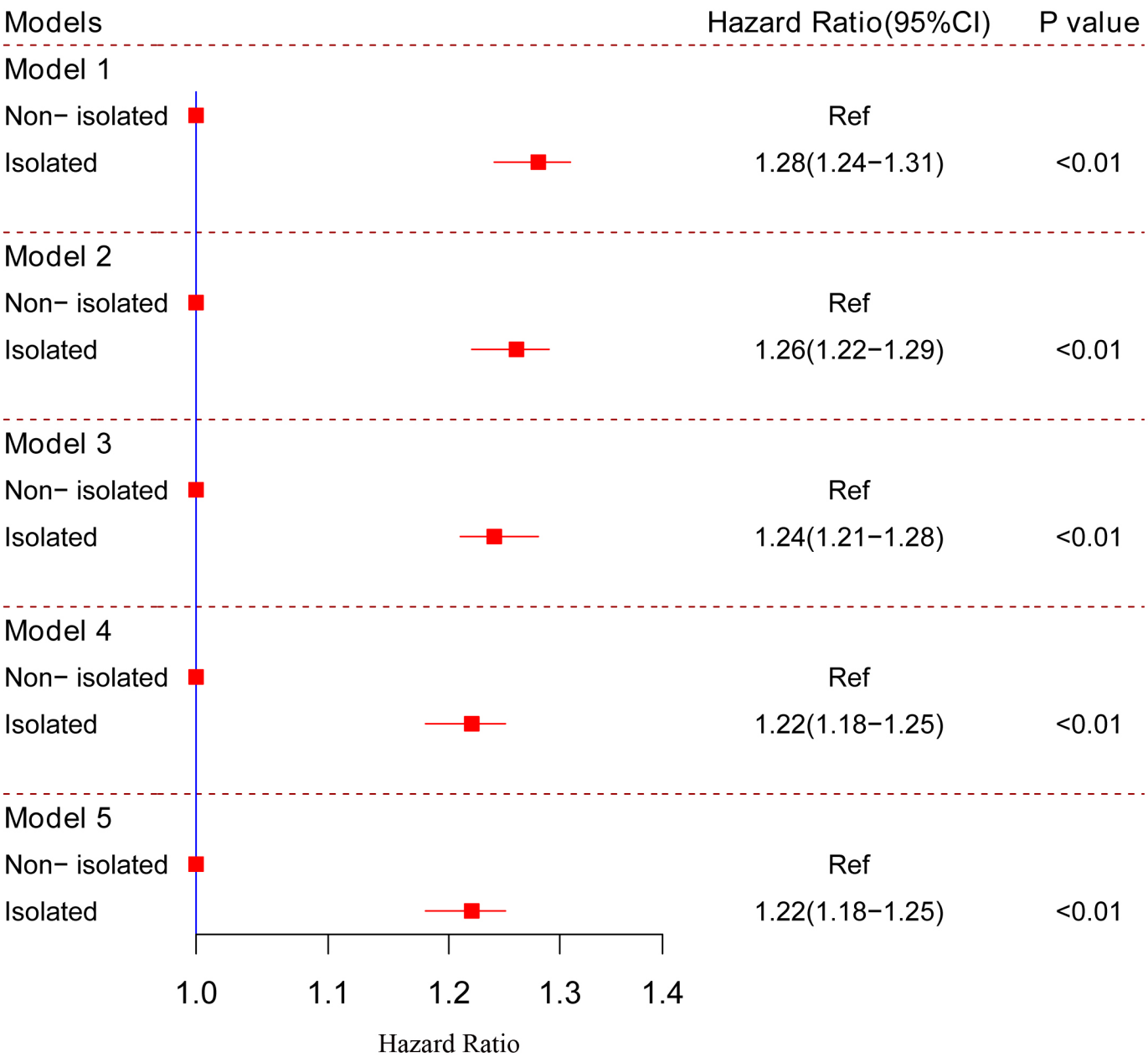
Table 2. Hazard ratios for the associations of social isolation and loneliness with all-cause mortality stratified by sex, age groups, and chronic disease status

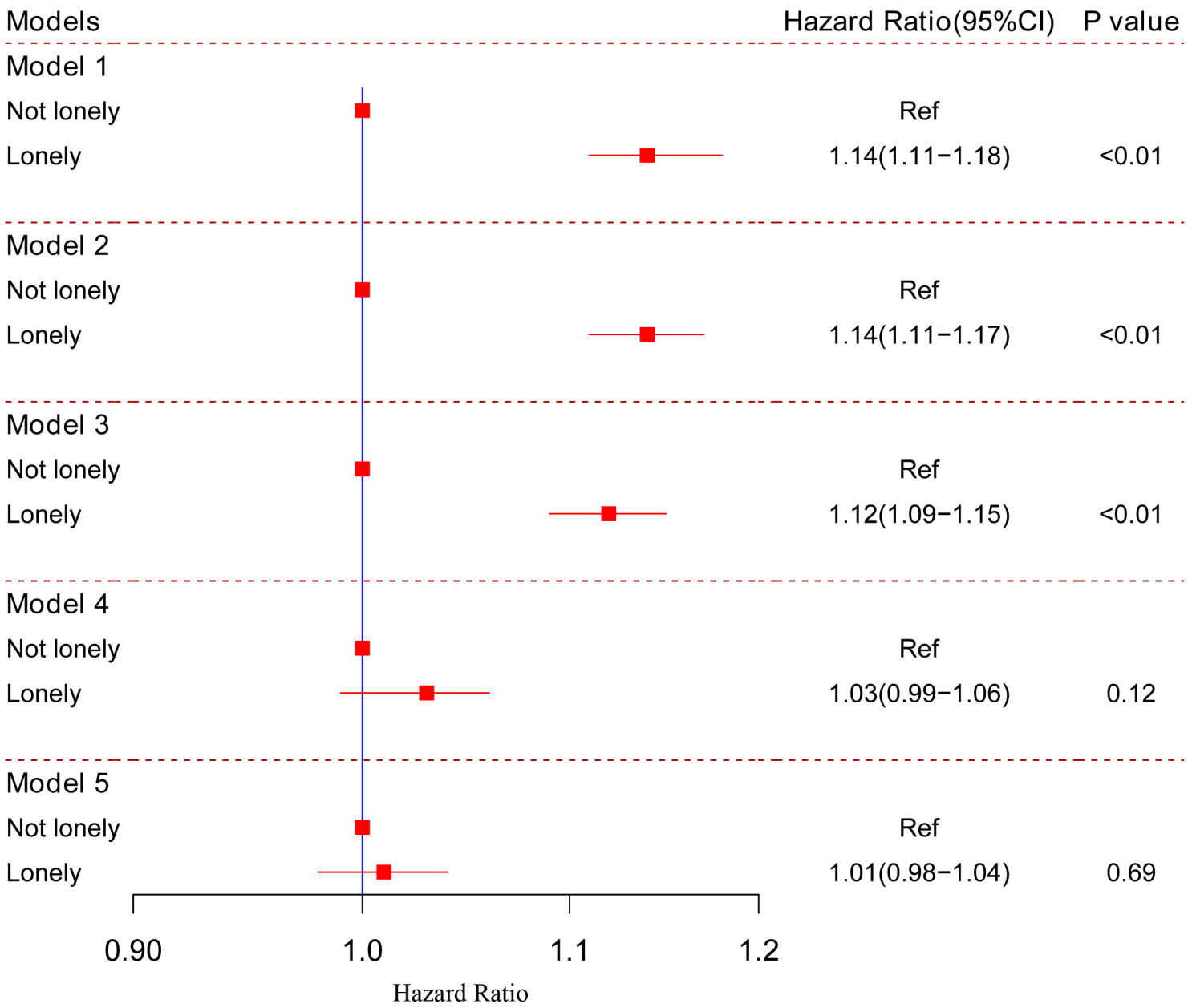
Models	Social isolation		Loneliness	
	HRs (95% CI)	*P*	*HRs (95% CI)*	*P*
Models stratified by sex [a]				
Males (N=19,768)	1.19(1.14-1.23)	<0.01	1.01(0.97-1.05)	0.66
Females (N=15,486)	1.27(1.22-1.33)	<0.01	1.01(0.96-1.06)	0.71
Models stratified by age groups [b]				
< 80 years (N=8,673)	1.41(1.29-1.54)	<0.01	1.15(1.05-1.26)	<0.01
80-90 years (N=10,507)	1.31(1.24-1.38)	<0.01	1.05(0.99-1.11)	0.12
＞90 years (N=16,074)	1.13(1.09-1.17)	<0.01	0.97(0.93-1.01)	0.14
Models stratified by chronic disease status [c]				
Present (N=21,683)	1.22(1.18-1.27)	<0.01	0.98(0.94-1.02)	0.34
Absent (N=13,571)	1.21(1.16-1.27)	<0.01	1.05(1.00-1.10)	0.05

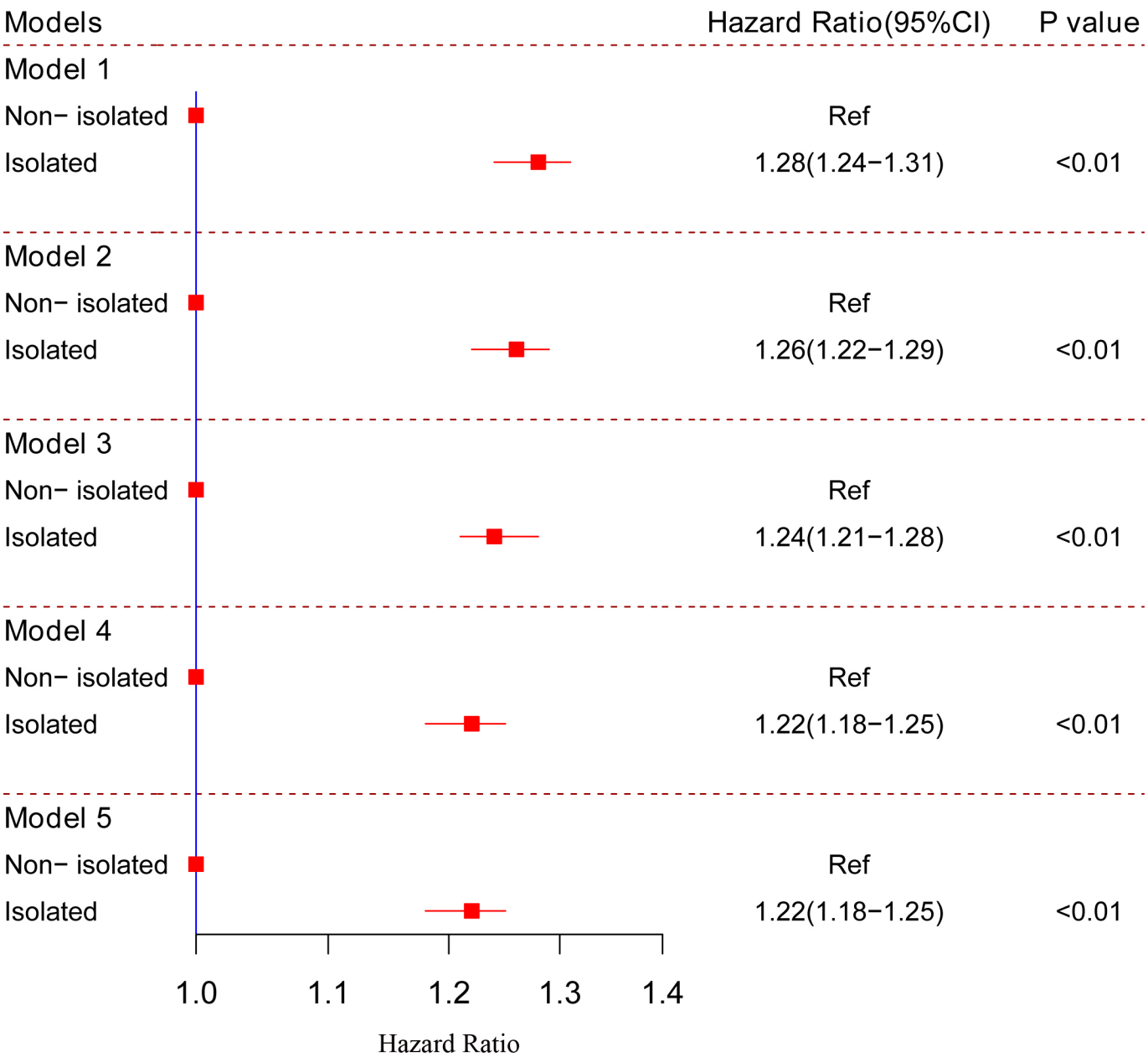
[a] Age, education, living areas, and ethnicity, smoking, drinking, exercise, self-rated health, psychological well-being, hypertension, diabetes, cardiovascular disease, and activities of daily living were adjusted.

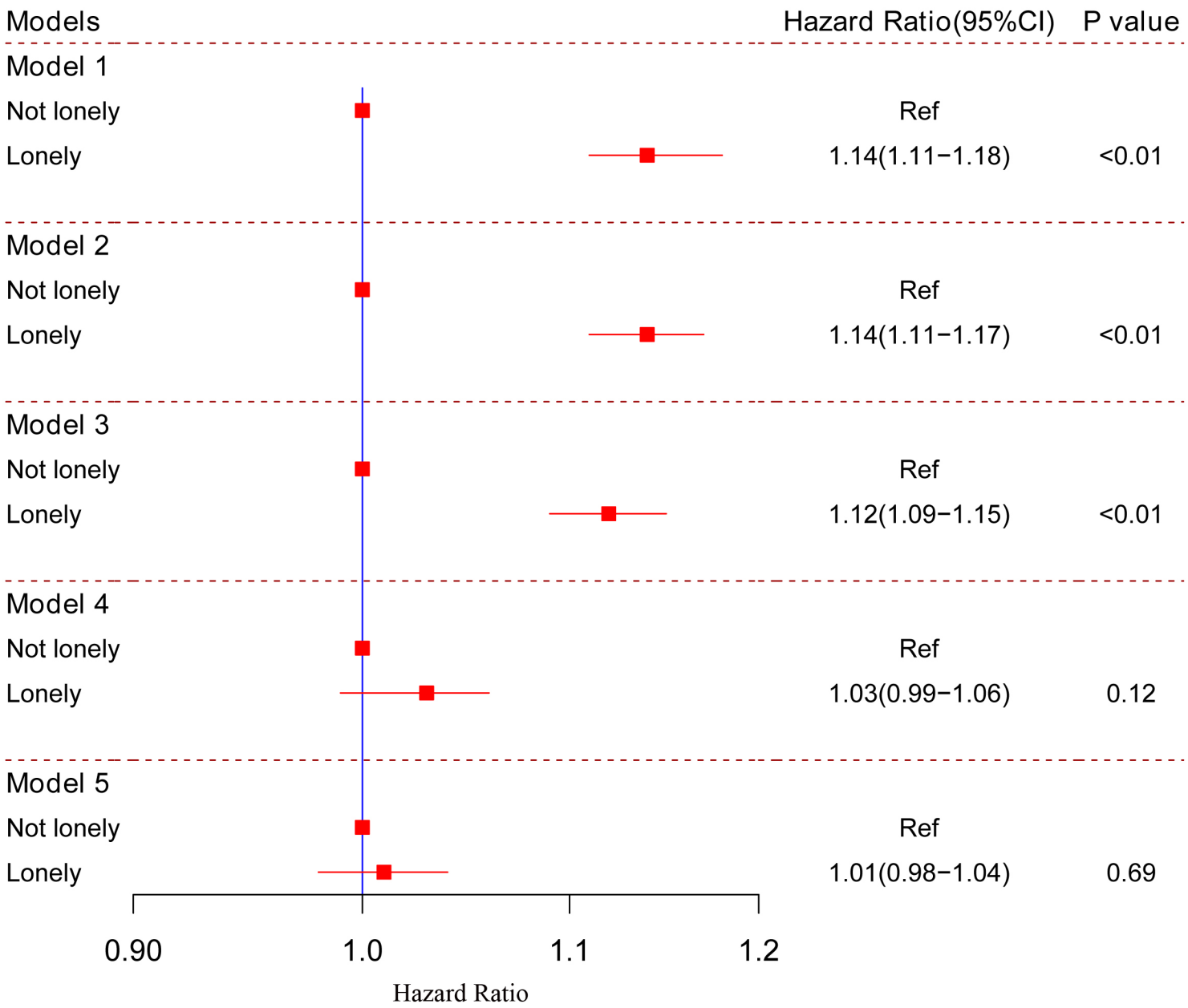
[b] Sex, education, living areas, and ethnicity, smoking, drinking, exercise, self-rated health, psychological well-being, hypertension, diabetes, cardiovascular disease, and activities of daily living were adjusted.

[c] Age, sex, education, living areas, and ethnicity, smoking, drinking, exercise, self-rated health, psychological well-being, and activities of daily living were adjusted.


Models
Hazard Ratio(95%CI)
P value
Model 1
Non− isolated
Ref
Isolated
1.28(1.24−1.31)
<0.01
Model 2
Non− isolated
Ref
Isolated
1.26(1.22−1.29)
<0.01
Model 3
Non− isolated
Ref
Isolated
1.24(1.21−1.28)
<0.01
Model 4
Non− isolated
Ref
Isolated
1.22(1.18−1.25)
<0.01
Model 5
Non− isolated
Ref
Isolated
1.22(1.18−1.25)
<0.01
1.0
1.1
1.2
1.3
1.4
Hazard Ratio


Models
Hazard Ratio(95%CI)
P value
Model 1
Not lonely
Ref
Lonely
1.14(1.11−1.18)
<0.01
Model 2
Not lonely
Ref
Lonely
1.14(1.11−1.17)
<0.01
Model 3
Not lonely
Ref
Lonely
1.12(1.09−1.15)
<0.01
Model 4
Not lonely
Ref
Lonely
1.03(0.99−1.06)
0.12
Model 5
Not lonely
Ref
Lonely
1.01(0.98−1.04)
0.69
0.90
1.0
1.1
1.2
Hazard Ratio


Models
Hazard Ratio(95%CI)
P value
Model 1
Non− isolated
Ref
Isolated
1.28(1.24−1.31)
<0.01
Model 2
Non− isolated
Ref
Isolated
1.26(1.22−1.29)
<0.01
Model 3
Non− isolated
Ref
Isolated
1.24(1.21−1.28)
<0.01
Model 4
Non− isolated
Ref
Isolated
1.22(1.18−1.25)
<0.01
Model 5
Non− isolated
Ref
Isolated
1.22(1.18−1.25)
<0.01
1.0
1.1
1.2
1.3
1.4
Hazard Ratio


Models
Hazard Ratio(95%CI)
P value
Model 1
Not lonely
Ref
Lonely
1.14(1.11−1.18)
<0.01
Model 2
Not lonely
Ref
Lonely
1.14(1.11−1.17)
<0.01
Model 3
Not lonely
Ref
Lonely
1.12(1.09−1.15)
<0.01
Model 4
Not lonely
Ref
Lonely
1.03(0.99−1.06)
0.12
Model 5
Not lonely
Ref
Lonely
1.01(0.98−1.04)
0.69
0.90
1.0
1.1
1.2
Hazard Ratio