BMJ Open

# Mediating Role of Homebound Status between Depressive Symptoms and Cognitive Impairment among Community-Dwelling Older Adults: A Cross-Sectional Study



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2022-065536 |
| Article Type: | Original research |
| Date Submitted by the Author: | 11-Jun-2022 |
| Complete List of Authors: | Peng, Wenting; Central South University<br>Miyawaki, christina; University of Houston,<br>Okoye, Safiyyah M; Johns Hopkins University<br>Wang, Wenru; National University of Singapore<br>Luo, Yuqian; Central South University<br>Mo, Cen; Central South University<br>Liu, Minhui; Central South University |
| Keywords: | EPIDEMIOLOGY, GERIATRIC MEDICINE, MENTAL HEALTH |
| | |

*I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.*

*The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.*

*Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.*

# Mediating Role of Homebound Status between Depressive Symptoms and Cognitive Impairment among Community-Dwelling Older Adults: A Cross-Sectional Study

**Title:** Mediating Role of Homebound Status between Depressive Symptoms and Cognitive Impairment among Community-Dwelling Older Adults: A Cross-Sectional Study

**Authors:** Wenting Peng, BSN, RN[1]; Christina E Miyawaki, PhD[2]; Safiyyah M Okoye, PhD, RN[3]; Wenru Wang, PhD[4]; Yuqian Luo, BSN, RN[1]; Cen Mo, BSN, RN[1]; Minhui Liu, PhD, RN[1*]

**Affiliations:**
[1] Xiangya School of Nursing, Central South University, Changsha, China
[2] Graduate College of Social Work, University of Houston, Houston, Texas, USA
[3] Johns Hopkins School of Nursing, Baltimore, MD, USA
[4] Alice Lee Centre for Nursing Studies, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

***Correspondence to:**
Minhui Liu, PhD, RN
Associate Professor
Central South University, Xiangya School of Nursing
172 Tongzipo Road of Yuelu District
Changsha, China 410013
Phone: +86 133-7894-9466
Email: mliu62@jhu.edu
Twitter: @MinhuiLiu2

**Article word count:** 2,860
**Abstract:** 291

## Abstract

**Objective:** Depressive symptoms are known predictors of cognitive impairment in older adults. However, the pathway through which depressive symptoms lead to cognitive impairment is not well understood. This study aimed to investigate whether homebound status (defined as usually unable to leave home unassisted) mediates the association between depressive symptoms and cognitive impairment in community-dwelling older adults in the United States.

**Design:** A secondary analysis of cross-sectional data.

**Setting(s):** Communities in the United States.

**Participants:** Community-living older adults (N=7,537) from the 2011 National Health and Aging Trends Study (NHATS), a nationally representative survey of Medicare Beneficiaries in the United States.

**Main outcome measures:** Participants' cognitive impairment status was classified using a composite measure. Depressive symptoms were assessed using Patient Health Questionnaire-2. Homebound status was determined by the frequency, difficulty, and needing help of getting outdoors. We used logistic regression and the Paramed command in STATA to analyze whether homebound mediated the association between depressive symptoms and cognitive impairment.

**Results:** Participants were on average, 77.7 years old, female (58.3%), and non-Hispanic white (68.1%). About 26% of the participants were classified as having cognitive

impairment, 16% reported depressive symptoms, and 25% were homebound. Depressive symptoms (adjusted OR, 1.60; 95% CI, 1.36-1.89) and homebound status (adjusted OR, 1.58; 95% CI, 1.34-1.86) were independently associated with cognitive impairment. Homebound significantly mediated 12.5% of the total effect between depressive symptoms and cognitive impairment, with significant indirect effect (OR, 1.07; 95% CI, 1.04-1.10), direct effect (OR, 1.61; 95% CI, 1.36-1.91) and total effect (OR, 1.72; 95% CI, 1.46-2.03).

**Conclusions:** This study supports a mediating role for homebound status in the relationship between depressive symptoms and cognitive impairment. Interventions to promote outdoor mobility should be studied for their ability to delay cognitive impairment for older adults with depressive symptoms.

***Keywords:*** homebound; depressive symptoms; cognitive impairments; older adults; mediation

## Strengths and limitations of this study

- This study is the first attempt to investigate the mediating role of homebound status in the association between depressive symptoms and cognitive impairments in community-dwelling older adults.
- Homebound status partly mediated the relationship between depressive symptoms and cognitive impairment.
- The strength of the study included a large sample size, the use of nationally representative data and adjustment for potential confounders including demographics and health-related factors.
- The cross-sectional design does not examine causality.
- All indicators were self-reported retrospectively which may cause recall bias and report errors.

## Introduction

Cognitive impairment causes disabilities in older adults' physical and psychological functions and is a major public health concern.[1,2] Cognitive impairment includes mild cognitive impairment and dementia.[3] Approximately 25% of U.S. adults aged 50 and over suffer from cognitive impairment and this rate increases with age,[3] bringing a huge economic burden to families and society.[4] Older adults with cognitive impairments have a high and growing demand for long-term care, which poses a significant challenge for nurse. Thus, it is imperative for nurses and health workers to identify casual pathways and develop effective strategies to prevent and slow the progression of cognitive impairment in older adults.

Depressive symptoms are common in older adults and are associated with physical disability,[5] social isolation,[6] and cardiovascular diseases,[7] all of which have been identified as contributors to declines in cognition.[8,9] A systematic review concluded that depressive symptoms are an independent risk factor for dementia.[10] In addition, multiple systematic reviews found that depressive symptoms are associated with the progression of mild cognitive impairment to dementia.[11–13] Despite these well-established associations between depressive symptoms and cognitive impairment, the mediating mechanisms of the association remain unclear.

In this paper we examined homebound status as a potential mediator between depressive symptoms and cognitive impairment. Being homebound, defined as limited at home, is closely related to depression and cognitive impairment. Homebound older adults

have consistently been found to experience depression in high numbers; in one population-based study 59% of older adults who had not left their homes in the previous month had positive depressive symptoms.[14–17] Prior research have also found cognitive impairment more prevalent in the homebound population than the non-homebound population.[18,19] The confluence of mental health, physical, and social impairments that result in homebound status,[20] may lead to cognitive impairment and should be better understood as a potential target of intervention. For example, previous studies have shown that older adults with depressive symptoms were more likely to have physical impairments and loss of interest or energy in social participation,[5,21] resulting in homebound status.[19,20] Rates of physical activity and social participation, well-known protective factors against cognitive impairment,[22] are low in homebound older adults and may contribute to the higher rates of cognitive impairment in this population.[20]

Homebound status can be improved using assistive devices, modifying the home environment, and accessing transportation.[15] It is therefore important to investigate the potential of homebound status as a target of interventions to improve cognitive function. However, to the best of our knowledge, no study has attempted to investigate whether homebound status mediates the association between depressive symptoms and cognitive impairment. The purpose of this study was to examine whether homebound status mediates the association between depressive symptoms and cognitive impairment in a nationally representative sample of community-dwelling older adults in the U.S. We hypothesized that

homebound status is a significant mediator between depressive symptoms and cognitive impairment in community-dwelling older adults.

## Methods

### Design and Sample

We used the first round (2011) of data from the National Health and Aging Trends Study (NHATS), a nationally representative longitudinal cohort study of older adults in the United States who are Medicare beneficiaries aged 65 and older.[23] The NHATS study began in 2011 and aimed to understand the disability trends of older adults in late life. In the initial round, a total of 7,609 participants who lived in the community completed the sample person interview. We excluded 72 participants who had incomplete data on depressive symptoms, homebound or cognitive function, for a resulting analysis sample size of 7,537. These excluded participants were older, living alone with less education, were less likely to perform vigorous activities, had stroke, and tended to have more activities of daily living (ADL) impairments, visual impairment, and auditory impairment, compared to those who had complete data. The NHATS was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board, and the NHATS investigators obtained informed consent form NHATS participants. The current analyses were deemed exempt from review by the Xiangya School of Nursing Ethic Committee of Central South University.

### Measurement

#### *Dependent variables*

Cognitive function was determined by a previously modified validated algorithm including a diagnosis from physicians (self-reported) and assessment of cognitive function in 3 domains (memory, orientation, and executive function).[24] Participants were classified into three groups as follows: participants with a diagnosis of dementia, a score on the AD8 Dementia Screening Interview provided by proxy respondents, or scores ≤ 1.5 Standard Deviation (SDs) below the mean in at least 2 of 3 cognitive performance tests were classified as having *probable dementia*; participants were classified as *possible dementia* if they scored ≤ 1.5 SDs below the mean in 1 cognitive performance test; all other participants were classified as having *no dementia*. We considered participants with a classification of probable dementia or possible dementia as having cognitive impairment; we considered participants with a classification of no dementia as without cognitive impairment. The NHATS dementia definition (defined as probable or possible dementia) has shown high sensitivity (85.7%) and specificity (83.7%) compared to a structured in-home clinical measurement in the landmark Aging, Demographics, and Memory Study.[24] For the purposes of terminology consistent with the cognitive impairment instrument, the term "cognitive impairment" was used throughout this article to replace dementia.

***Independent variable***

Depressive symptoms were measured using the Patient Health Questionnaire-2 (PHQ-2), a well-validated screening instrument for depression status.[25] Participants were asked: "Over the last month, how often have you: 1) had little interest or pleasure in doing

things; 2) felt down, depressed, or hopeless." Responses were recorded on a 4-point Likert scale (scored 0-3) with total scores ranging from 0 to 6. A higher score suggested more depressive symptoms. Following the recommendation from previous studies, we used a cut-off of 3 and higher to determine depressive symptoms. The cut-off of 3 has a sensitivity of 0.79 and a specificity of 0.86 for any type of depressive disorder.[25]

***Mediator***

Based on the measurement developed by Ornstein and colleagues, homebound status was measured using four questions based on the reported frequency of outdoor mobility.[15] First, participants were asked about the frequency of going outside, and response options were on a 5-point Likert scale: never; rarely (≤ 1 day per week); some days (2-4 days per week); most days (5-6 days per week); and every day. Participants reporting going outside at least 2 days per week were asked whether they needed help from others to go outside. Those who reported needing help were also asked about the frequency of going outside independently. Those who reported ever going outside by themselves were asked whether they had any difficulties leaving home independently. Participants were classified as homebound if they never left home, or left home with any difficulties and assistance. All other participants were classified as non-homebound.

***Covariates***

Demographic and health-related characteristics that are common risk factors for depression, homebound status, and cognitive impairment were included as covariates in

analyses.

Demographic characteristics included age,[3] sex (male/female),[26] race/ethnicity (non-Hispanic white, non-Hispanic Black, Hispanic, and other),[27] education (less than high school, high school, college or vocational school and bachelor or higher),[28] and living arrangement (alone, with spouse/partner only, with others only, with spouse/partner and with others).[29]

Health-related characteristics included smoking status (never smoker and current/former smoker);[8] whether they performed vigorous activities last month (yes/no);[30] body mass index (BMI) (normal/obesity [≥30 kg/m$^2$]);[8] visual impairment (yes/no);[31] auditory impairment (yes/no);[32] diagnoses of hypertension (yes/no),[8] diabetes (yes/no),[8] and stroke (yes/no);[33] number of activities of daily living impairments;[34] whether the subjects were hospitalized in the last 12 months (yes/no).[35]

**Statistical Analysis**

Demographic and health-related characteristics were described using frequencies, proportions, means, and standard deviations (SDs). Chi-square test and two sample t-test were used to test the differences between groups with and without cognitive impairment for categorical and continuous variables, respectively. Using Baron and Kenny's method for mediation,[36] we assessed the associations among depressive symptoms, homebound status, and cognitive impairment in four logistic regression models. The first model assessed the direct relationship between the independent variable depressive symptoms and the dependent variable cognitive impairment. The second model examined whether depressive symptoms

were associated with the hypothesized mediator homebound status. The third model evaluated the association between the hypothesized mediator homebound status and cognitive impairment. The fourth model estimated the association between the independent variable depressive symptoms and the dependent variable cognitive impairment upon inclusion of the hypothesized mediator homebound status to the model. All models were adjusted for demographics and health-related factors.

Because all the associations in the above models were significant, we were able to further test homebound status as a mediator following Baron and Kenny's approach and using the Paramed command in Stata.[36] This procedure estimates the natural direct effects, natural indirect effects, and marginal total effects in the presence of exposure-mediator interaction. The product of direct and indirect effects was expressed as the total effect. We estimated direct and indirect effects using logistic regression models and performed a bootstrapping analysis with 1000 replications both with and without adjusting for covariates. The proportion of effect mediated by homebound status was calculated as the log of the indirect effect divided by the log of the total effect.

Sensitivity analyses were performed to test the robustness of the findings. We excluded any data provided by proxy respondents (n=583) and reran the analysis (see supplementary table 1, 2 & 3). Odds ratio (ORs) and 95% confidence intervals (CI) were reported. Missing values on covariates ranged from 0.1% (stroke) to 3.5% (BMI). Given the large sample size, no particular technique was used to handle missing data. *P* values less than

0.05 indicated statistical significance. All analyses were performed in Stata version 15.0.[37]

**Patient and public involvement**

No patients were involved in the development of the question, design or data interpretation.

## Results

Characteristics of all participants and their comparisons by cognitive status are presented in Table 1 (N = 7,537). The mean age of the participants was 77.7 years old. Fifty-eight percent were female and 68% were non-Hispanic white. About 26% of the participants had cognitive impairment, 16% reported depressive symptoms and 25% were homebound. Compared to participants with no cognitive impairment, those with cognitive impairment were more likely to be older and less educated, have ADL, visual and auditory impairments, and have comorbidities of diabetes and stroke, and have been hospitalized (*P*<.001 for all comparisons). The prevalence of depressive symptoms and homebound status were significantly higher for those with cognitive impairment than those without (27.4% vs. 12.0% for depression status, and 48.1% vs. 16.7% for homebound).

**Table 1**. Characteristics of community-dwelling older adults, stratified by cognitive impairment status

| Characteristics | Total (N=7,270-7,537)[a] | Cognitive impairment (n=1,849-1,988) | No cognitive impairment (n=5,421-5,549) | *P* values |
|---|---|---|---|---|
| Age, M ± SD | 77.7 ± 7.9 | 81.8 ± 7.8 | 76.2 ± 7.3 | <.001 |
| Sex, n (%) | | | | .800 |
| Female | 4397 (58.3) | 1155 (58.1) | 3242 (58.4) | |
| Male | 3140 (41.7) | 833 (41.9) | 2307 (41.6) | |
| Race/ethnicity, n (%) | | | | <.001 |

| | | | | |
|---|---|---|---|---|
| White, non-Hispanic | 5137 (68.1) | 1119 (56.3) | 4018 (72.4) | |
| Black, non-Hispanic | 1648 (21.9) | 563 (28.3) | 1085 (19.5) | |
| Hispanic | 449 (6.0) | 191 (9.6) | 258 (4.7) | |
| Other | 303 (4.0) | 115 (5.8) | 188 (3.4) | |
| Education, n (%) | | | | <.001 |
| Less than high school | 2020 (27.1) | 906 (46.6) | 1114 (20.3) | |
| High school | 2056 (27.6) | 492 (25.3) | 1564 (28.4) | |
| Some college or vocational school | 1801 (24.2) | 307 (15.8) | 1494 (27.1) | |
| College or higher | 1570 (21.1) | 240 (12.3) | 1330 (24.2) | |
| Living arrangement, n (%) | | | | <.001 |
| Alone | 2435 (32.4) | 680 (34.3) | 1755 (31.7) | |
| With spouse/partner only | 3036 (40.5) | 538 (27.2) | 2498 (45.2) | |
| With others only | 1351 (18.0) | 568 (28.7) | 783 (14.2) | |
| With spouse/partner and with others | 684 (9.1) | 195 (9.8) | 489 (8.9) | |
| Smoking status, n (%) | | | | <.001 |
| No | 3721 (49.4) | 1064 (53.7) | 2657 (47.9) | |
| Yes | 3807 (50.6) | 919 (46.3) | 2888 (52.1) | |
| Vigorous activity, n (%) | | | | <.001 |
| No | 4970 (66.0) | 1652 (83.2) | 3318 (59.8) | |
| Yes | 2563 (34.0) | 333 (16.8) | 2230 (40.2) | |
| BMI, n (%) | | | | <.001 |
| Normal (<30 kg/m$^2$) | 5316 (72.1) | 1479 (80.0) | 3837 (70.8) | |
| Obesity (≥30 kg/m$^2$) | 1954 (28.9) | 370 (20.0) | 1584 (29.2) | |
| Visual impairment, n (%) | | | | <.001 |
| No | 6684 (89.1) | 1540 (78.2) | 5144 (93.0) | |
| Yes | 819 (10.9) | 429 (21.8) | 390 (7.0) | |
| Auditory impairment, n (%) | | | | <.001 |
| No | 5716 (75.8) | 1356 (67.7) | 4371 (78.8) | |
| Yes | 1821 (24.2) | 643 (32.3) | 1178 (21.2) | |
| Hypertension, n (%) | | | | .367 |
| No | 2467 (32.8) | 634 (32.0) | 1833 (33.1) | |
| Yes | 5061 (67.2) | 1350 (68.0) | 3711 (66.9) | |
| Diabetes, n (%) | | | | <.001 |
| No | 5631 (74.7) | 1407 (70.9) | 4224 (76.1) | |
| Yes | 1903 (25.3) | 578 (29.1) | 1325 (23.9) | |
| Stroke, n (%) | | | | <.001 |
| No | 6655 (88.4) | 1613 (81.2) | 5042 (90.9) | |
| Yes | 876 (11.5) | 373 (18.8) | 503 (9.1) | |
| Number of ADL impairments, M ± SD | 1.3 ± 0.9 | 1.8 ± 1.1 | 1.2 ± 0.6 | <.001 |
| Hospitalization, n (%) | | | | <.001 |
| No | 5770 (76.6) | 1350 (68.0) | 4420 (79.7) | |

| | | | | |
|---|---|---|---|---|
| Yes | 1759 (23.4) | 634 (32.0) | 1125 (20.3) | |
| Depressive symptoms, n (%) | | | | <.001 |
| No | 6328 (83.0) | 1444 (72.6) | 4884 (88.0) | |
| Yes | 1209 (16.0) | 544 (27.4) | 665 (12.0) | |
| Homebound, n (%) | | | | <.001 |
| No | 5652 (75.0) | 1032 (51.9) | 4620 (83.3) | |
| Yes | 1885 (25.0) | 956 (48.1) | 929 (16.7) | |

Abbreviations: M, mean; SD, standard deviations; BMI, body mass index; ADL, activity of daily living.

[a] Please note that the sample size has a range because missing values on covariates ranged from 0.1% (stroke) to 3.5% (BMI). Given the large sample size, no particular technique was used to handle missing data.

Table 2 presents the results of the associations among cognitive impairment, depressive symptoms, and homebound status in accordance with the Baron and Kenny approach to study mediation. After adjusting for demographics and health-related factors, compared to participants without depressive symptoms or homebound status, those with depressive symptoms (adjusted OR, 1.67; 95% CI, 1.42-1.97) or homebound status (adjusted OR, 1.65; 95% CI, 1.40-1.94) had higher odds of cognitive impairment. Depressive symptoms were also a significant risk factor for homebound status (adjusted OR, 2.00; 95% CI, 1.67-2.40). Additionally, both homebound status (adjusted OR, 1.58; 95% CI, 1.34-1.86) and depressive symptoms (adjusted OR, 1.60; 95% CI, 1.36-1.89) were statistically significantly associated with cognitive impairment when they were both included as independent variables in the same model.

**Table 2**. Results of logistic regression analyses of associations among depressive symptoms, homebound status and cognitive impairment

| **Independent variable(s)** | Effect size for association, OR (95% CI)[b] | | | |
|---|---|---|---|---|
| | **Dependent Variable** | | | |
| | Model 1: Cognitive Impairment | Model 2: Homebound Status | Model 3: Cognitive Impairment | Model 4: Cognitive Impairment |

| | | | | |
|---|---|---|---|---|
| Depressive symptoms | 1.67 (1.42-1.97) *** | 2.00 (1.67-2.40) *** | NA | 1.60 (1.32-1.89) *** |
| Homebound status | NA | NA | 1.65 (1.40-1.94) *** | 1.58 (1.34-1.86) *** |

Abbreviations: OR, odds ratio; NA, not applicable.

[a] * $P$ <.05, ** $P$ <.01, ***$P$<.001

[b] All models adjusted for demographics (age, sex, education, race/ethnicity, living arrangement) and health-related characteristics (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily living impairments, hospitalization).

Table 3 and Figure 1 show the indirect contribution of being homebound in the relationship between depressive symptoms and cognitive impairment. Homebound status statistically significantly mediated this relationship. It partially explained the relationship; the contribution of being homebound was 40.4% of the association between depressive symptoms and cognitive impairment in the unadjusted model (Model 1), and this proportion decreased to 12.5% after adjusting for all covariates (Model 3).

**Table 3.** Mediation of homebound status in the association between depressive symptoms and cognitive impairment

| | Model 1[b] OR (95% CI) | Model 2[c] OR (95% CI) | Model 3[d] OR (95% CI) |
|---|---|---|---|
| Natural direct effect | 1.93 (1.68-2.22) *** | 1.88 (1.61-2.18) *** | 1.61 (1.36-1.91) *** |
| Natural indirect effect | 1.56 (1.48-1.64) *** | 1.33 (1.27-1.39) *** | 1.07 (1.04-1.10) *** |
| Marginal total effect | 3.01 (2.61-3.46) *** | 2.49 (2.15-2.90) *** | 1.72 (1.46-2.03) *** |
| Proportion mediated[a] | 40.4% | 31.3% | 12.5% |

[a] Proportion meditated by homebound status were calculated as the log of the indirect effect divided by the log of the total effect.

[b] Model 1: independent variables of interest

[c] Model 2: Model 1+ demographic covariates (age, sex, education, race/ethnicity, living arrangement)

[d.] Model 3: Model 2 + health-related covariates (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily living impairments, hospitalization)

[Insert Figure 1 about here]

Results from a sensitivity analysis suggested that homebound status statistically

significantly mediated the association between depressive symptoms and cognitive impairment (adjusted OR, 1.05; 95% CI, 1.02-1.08), even after excluding data from proxy respondents (supplementary table 3, additional information see supplementary table 1 and 2).

## Discussion

We examined the mediating role of homebound status in the association of depressive symptoms and cognitive impairment using a nationally representative sample of community-dwelling older Americans. Our study found that depressive symptoms and homebound status were independently associated with cognitive impairment. Moreover, more than 10% of the effect of depressive symptoms on cognitive impairment was mediated by homebound status, suggesting that one of the ways the depression status contributes to cognitive impairment is through the decreased mobility outside the home that defines homebound status. Our findings shed light on homebound status as a target of intervention to prevent and slow cognitive impairment in later life.

Our results showed that depressive symptoms and homebound status were each independently associated with a greater risk of cognitive impairment; findings are consistent with previous studies.[13,18] Depression is a well-established predictor of cognitive impairment; however we found a similar magnitude of association between homebound status and cognitive impairment as between depression symptoms and cognitive impairment, after accounting for demographic and health-related factors. This result was inconsistent with a cross-sectional study by Meng et al., which suggested that cognitive impairment was more

strongly associated with homebound status compared with depressive symptoms.[38] Possible explanations for different results are the different measures of homebound status, differences in the covariates included, and cultural difference between the U.S. and China. Meng et al.'s study included older adults from a rural province in China, with a smaller sample size (N = 720) and adjusted for sociodemographic variables only.[38]

The mediation findings of this study may be explained through several potential mechanisms. Depressed older adults often experience loss of interest and social connection,[22] and have no energy to participate in outside activities, which for some leads to reduced mobility and becoming homebound.[15,19,39] There is robust evidence that physical activity and social participation are effective strategies to prevent cognitive impairment,[22] and that homebound older adults are less likely to benefit from these strategies. Homebound status may also mediate the effects of depression on cognitive impairment via other mechanisms such as nutrition disorders, social isolation, and hospitalization,[19,40] all of which have been associated with both depression and homebound status. The results of two previous studies (one cross-sectional[41] and one prospective[42]) found that functional disability mediated the relationship between depression status and cognitive impairment, and offer additional support to our mediation findings. Although homebound status is not equivalent to functional disability, there are overlapping characteristics between homebound older adults and those with functional disability; older adults with functional disability frequently report difficulty going outside regularly and are at increased risk of being homebound.[43]

The study has important implications for nursing practice and research. Our findings suggest the utility of efforts to improve cognitive function by reducing the effect of depressive symptoms and homebound status. For example, interventions that support depressed older adults to maintain ideal outdoor mobility through health education, psychosocial interventions, and creating a safe and convenient environment, may serve to decrease risk of cognitive impairment. Some interventions have shown their potential to reduce depressive symptoms and improve cognitive impairments in depressed older adults, such as physical exercise.[21,44,45] Yet, existing interventions are geared toward improving other outcomes of home-dwelling older adults, instead improving the status of homebound. The Centers for Medicare & Medicaid Service has suggested to improve health services for homebound older adults who receive health care at home.[46] We did not find studies of mobility interventions to reduce cognitive impairment among homebound older adults and suggest this as an area of future inquiry. Moreover, our findings suggest the utility of efforts to improve cognitive function by reducing the effect of depressive symptoms and homebound status. By recognizing the associations of depressive symptoms and homebound with cognitive impairment, nurses can screen people who are at high risk of cognitive impairment or have cognitive impairment more easily by examining their depressive symptoms and homebound status profiles in their routine practice. Last but not the least, for older adults with depressive symptoms or who are homebound, nurses can focus on whether these older adults have additional risk factors for cognitive impairment, such as physical inactivity,

obesity, and social isolation, all of which are common in depressed or homebound older adults. Proactively managing these modifiable risk factors is beneficial to delay the onset of cognitive impairment and diagnose it early.

To the best of our knowledge, this study is the first to explore the mediation role of homebound status in the relationship between depressive symptoms and cognitive impairments in older adults. The strength of the study included a large sample size, the use of nationally representative data and adjustment for potential confounders including demographics and health-related factors. However, several limitations of the study should be noted. The cross-sectional design does not examine causality. The PHQ-2 was not a diagnostic tool for depression, but for screening purposes. Although the PHQ-2 is a well-validated tool with acceptable specificity and sensitivity, measurement errors and misclassifications may still occur. All indicators were self-reported retrospectively which may cause recall bias and report errors. Particularly, when we assessed homebound status, a month recall time may be too long for participants or their proxies to recall accurately.

## Conclusion

Based on a nationally representative sample of older adults in the U.S., we found that depressive symptoms and homebound status were associated with cognitive impairment, and homebound status partially mediated the relationship between depressive symptoms and cognitive impairment. Therefore, for future public health policy on preventing cognitive impairment in depressed older adults, homebound status should be taken into account.

**Author contributions**

*Wenting Peng:* Concept and design, analysis, drafting of the initial manuscript and revision.

*Christina E. Miyawaki*: Critical feedback and revision of the manuscript.

*Safiyyah M. Okoye:* Critical feedback and revision of the manuscript.

*Wenru Wang:* Critical feedback and revision of the manuscript.

*Yuqian Luo:* Revision of the manuscript.

*Cen Mo:* Revision of the manuscript.

*Minhui Liu:* Supervision, validation, interpretation of data and critical revision of the manuscript.

**Funding**

The publication of this manuscript was supported by the Youth Grant from National Natural Science Foundation of China (Grant No.72004237) and Natural Science Foundation of Changsha City (Grant No.kp2007080).

**Competing interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Ethics approval**

NHATS was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board (JHSPH IRB # 00002083). NHATS participants completed written informed consent prior to being interviewed. The current analyses were deemed exempt from review by the Xiangya School of Nursing Ethic Committee of Central South University. The study was conducted according to the guidelines of the Declaration of Helsinki.

**Data availability statement**

The NHATS data analyzed in the current study are available for research purposes at www.nhats.org.

## References

1. Bahureksa L, Najafi B, Saleh A, et al. The Impact of Mild Cognitive Impairment on Gait and Balance: a Systematic Review and Meta-Analysis of Studies using Instrumented Assessment. *Gerontology*. 2017;63(1):67-83. doi:10.1159/000445831

2. Yates JA, Clare L, Woods RT, Cognitive Function and Ageing Study: Wales. What is the Relationship between Health, Mood, and Mild Cognitive Impairment? *J Alzheimers Dis*. 2017;55(3):1183-1193. doi:10.3233/JAD-160611

3. Hale JM, Schneider DC, Mehta NK, Myrskylä M. Cognitive impairment in the U.S.: Lifetime risk, age at onset, and years impaired. *SSM - Popul Health*. 2020;11:100577. doi:10.1016/j.ssmph.2020.100577

4. Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. *N Engl J Med*. 2013;368(14):1326-1334. doi:10.1056/NEJMsa1204629

5. Jin-Won N, Young Dae K, Jumin P, In-Hwan O, Jinseok K. Relationship between Physical Disability and Depression by Gender: A Panel Regression Model. *PloS One*. 2016;11(11). doi:10.1371/journal.pone.0166238

6. Ge L, Yap CW, Ong R, Heng BH. Social isolation, loneliness and their relationships with depressive symptoms: A population-based study. *PloS One*. 2017;12(8):e0182145. doi:10.1371/journal.pone.0182145

7. Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease:

a clinical review. *Eur Heart J*. 2014;35(21):1365-1372. doi:10.1093/eurheartj/eht462

8. Baumgart M, Snyder HM, Carrillo MC, Fazio S, Kim H, Johns H. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimers Dement*. 2015;11(6):718-726. doi:10.1016/j.jalz.2015.05.016

9. Lisko I, Kulmala J, Annetorp M, Ngandu T, Mangialasche F, Kivipelto M. How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med*. 2021;289(6):807-830. doi:10.1111/joim.13227

10. Wiels W, Baeken C, Engelborghs S. Depressive Symptoms in the Elderly—An Early Symptom of Dementia? A Systematic Review. *Front Pharmacol*. 2020;11:34. doi:10.3389/fphar.2020.00034

11. Cooper C, Sommerlad A, Lyketsos CG, Livingston G. Modifiable predictors of dementia in mild cognitive impairment: a systematic review and meta-analysis. *Am J Psychiatry*. 2015;172(4):323-334. doi:10.1176/appi.ajp.2014.14070878

12. Mourao RJ, Mansur G, Malloy-Diniz LF, Castro Costa E, Diniz BS. Depressive symptoms increase the risk of progression to dementia in subjects with mild cognitive impairment: systematic review and meta-analysis. *Int J Geriatr Psychiatry*. 2016;31(8):905-911. doi:10.1002/gps.4406

13. Tan EYL, Köhler S, Hamel REG, Muñoz-Sánchez JL, Verhey FRJ, Ramakers IHGB. Depressive Symptoms in Mild Cognitive Impairment and the Risk of Dementia: A Systematic Review and Comparative Meta-Analysis of Clinical and Community-Based

Studies. *J Alzheimers Dis*. 2019;67(4):1319-1329. doi:10.3233/JAD-180513

14. Xiang X, An R, Oh H. The Bidirectional Relationship Between Depressive Symptoms and Homebound Status Among Older Adults. *J Gerontol B Psychol Sci Soc Sci*. 2020;75(2):357-366. doi:10.1093/geronb/gbx180

15. Ornstein KA, Leff B, Covinsky KE, et al. Epidemiology of the Homebound Population in the United States. *JAMA Intern Med*. 2015;175(7):1180-1186. doi:10.1001/jamainternmed.2015.1849

16. Xiang X, Brooks J. Correlates of Depressive Symptoms among Homebound and Semi-Homebound Older Adults. *J Gerontol Soc Work*. 2017;60(3):201-214. doi:10.1080/01634372.2017.1286625

17. Richardson TM, Friedman B, Podgorski C, et al. Depression and its correlates among older adults accessing aging services. *Am J Geriatr Psychiatry*. 2012;20(4):346-354. doi:10.1097/JGP.0b013e3182107e50

18. Negrón-Blanco L, de Pedro-Cuesta J, Almazán J, et al. Prevalence of and factors associated with homebound status among adults in urban and rural Spanish populations. *BMC Public Health*. 2016;16:574. doi:10.1186/s12889-016-3270-z

19. Cohen-Mansfield J, Shmotkin D, Hazan H. Homebound older persons: prevalence, characteristics, and longitudinal predictors. *Arch Gerontol Geriatr*. 2012;54(1):55-60. doi:10.1016/j.archger.2011.02.016

20. Qiu WQ, Dean M, Liu T, et al. Physical and mental health of homebound older adults: an

overlooked population. *J Am Geriatr Soc*. 2010;58(12):2423-2428. doi:10.1111/j.1532-5415.2010.03161.x

21. Neviani F, Belvederi Murri M, Mussi C, et al. Physical exercise for late life depression: effects on cognition and disability. *Int Psychogeriatr*. 2017;29(7):1105-1112. doi:10.1017/S1041610217000576

22. US Preventive Services Task Force, Owens DK, Davidson KW, et al. Screening for Cognitive Impairment in Older Adults: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2020;323(8):757-763. doi:10.1001/jama.2020.0435

23. Freedman VA, Kasper JD. Cohort Profile: The National Health and Aging Trends Study (NHATS). *Int J Epidemiol*. 2019;48(4):1044-1045g. doi:10.1093/ije/dyz109

24. Kasper JD, Freedman VA, Spillman BC. Classification of persons by dementia status in the National Health and Aging Trends Study. Published online 2013. Accessed March 7, 2021. https://www.nhats.org/sites/default/files/inline-files/DementiaTechnicalPaperJuly_2_4_2013_10_ 23_15.pdf

25. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003;41(11):1284-1292. doi:10.1097/01.MLR.0000093487.78664.3C

26. Podcasy JL, Epperson CN. Considering sex and gender in Alzheimer disease and other dementias. *Dialogues Clin Neurosci*. 2016;18(4). doi:10.31887/DCNS.2016.18.4/cepperson

27. Wilson RS, Capuano AW, Sampaio C, et al. The link between social and emotional

isolation and dementia in older black and white Brazilians. *Int Psychogeriatr*. Published online June 15, 2021:1-7. doi:10.1017/S1041610221000673

28. Song YN, Wang P, Xu W, et al. Risk Factors of Rapid Cognitive Decline in Alzheimer's Disease and Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2018;66(2):497-515. doi:10.3233/JAD-180476

29. Roystonn K, Abdin E, Shahwan S, et al. Living arrangements and cognitive abilities of community-dwelling older adults in Singapore. *Psychogeriatr Off J Jpn Psychogeriatr Soc*. 2020;20(5):625-635. doi:10.1111/psyg.12532

30. Karssemeijer EGA, Aaronson JA, Bossers WJ, Smits T, Olde Rikkert MGM, Kessels RPC. Positive effects of combined cognitive and physical exercise training on cognitive function in older adults with mild cognitive impairment or dementia: A meta-analysis. *Ageing Res Rev*. 2017;40:75-83. doi:10.1016/j.arr.2017.09.003

31. Chen SP, Bhattacharya J, Pershing S. Association of Vision Loss With Cognition in Older Adults. *JAMA Ophthalmol*. 2017;135(9):963-970. doi:10.1001/jamaophthalmol.2017.2838

32. Dawes P, Emsley R, Cruickshanks KJ, et al. Hearing Loss and Cognition: The Role of Hearing Aids, Social Isolation and Depression. *PLoS ONE*. 2015;10(3). doi:10.1371/journal.pone.0119616

33. Wu X, Fan L, Ke S, He Y, Zhang K, Yang S. Longitudinal Associations of Stroke With Cognitive Impairment Among Older Adults in the United States: A Population-Based Study.

*Front Public Health*. 2021;9:637042. doi:10.3389/fpubh.2021.637042

34. Lindbergh CA, Dishman RK, Miller LS. Functional Disability in Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. *Neuropsychol Rev*. 2016;26(2):129-159. doi:10.1007/s11065-016-9321-5

35. Li E, C L, K N, et al. Hospitalization, surgery, and incident dementia. *Alzheimers Dement J Alzheimers Assoc*. 2019;15(4). doi:10.1016/j.jalz.2018.12.005

36. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol*. 1986;51(6):1173-1182. doi:10.1037//0022-3514.51.6.1173

37. *StataSE*. TX: StataCorp LLC; 2017.

38. Meng LD, Liu YC, Feng X, Zhai YX, Liu kun. The mediating role of depression on the relationship between housebound status and cognitive function among the elderly in rural communities: A cross-sectional study. *Arch Gerontol Geriatr*. 2018;78:58-63. doi:10.1016/j.archger.2018.05.019

39. Mickler AK, Leff B, Eaton England A, et al. Understanding the Daily Experiences and Perceptions of Homebound Older Adults and Their Caregivers: A Qualitative Study. *J Appl Gerontol*. Published online February 1, 2021:733464821990171. doi:10.1177/0733464821990171

40. Ganguli M, Fox A, Gilby J, Belle S. Characteristics of rural homebound older adults: a community-based study. *J Am Geriatr Soc*. 1996;44(4):363-370. doi:10.1111/j.1532-

5415.1996.tb06403.x

41. Chen CM, Liu LF. The effect of disability and depression on cognitive function and screening factors. *Arch Gerontol Geriatr*. 2017;73:154-159. doi:10.1016/j.archger.2017.07.019

42. Chen C, Mullan J, Su Y, Griffiths D, Kreis IA, Chiu H. The longitudinal relationship between depressive symptoms and disability for older adults: a population-based study. *J Gerontol A Biol Sci Med Sci*. 2012;67(10):1059-1067. doi:10.1093/gerona/gls074

43. De-Rosende Celeiro I, Santos-Del-Riego S, Muñiz García J. Homebound status among middle-aged and older adults with disabilities in ADLs and its associations with clinical, functional, and environmental factors. *Disabil Health J*. 2017;10(1):145-151. doi:10.1016/j.dhjo.2016.06.006

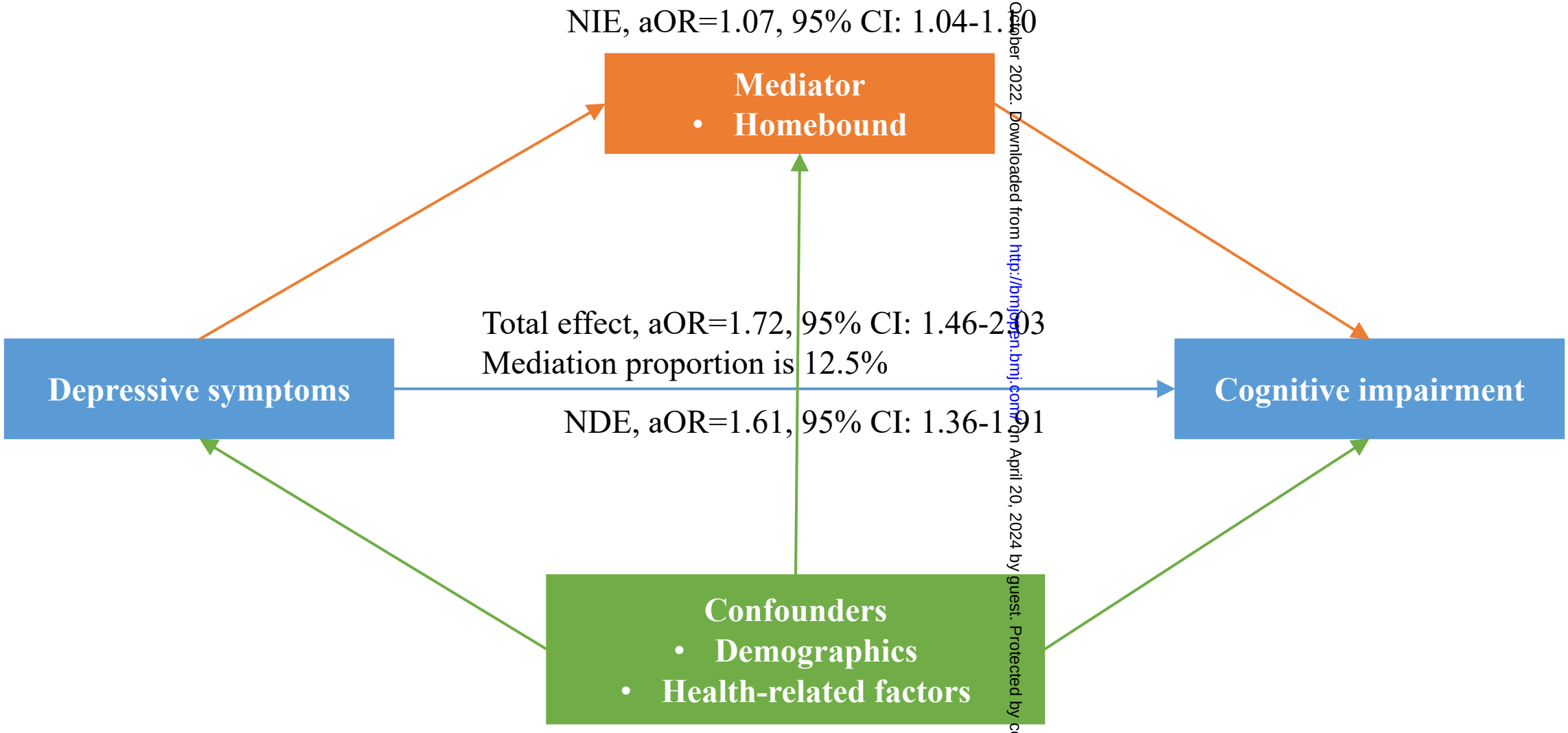
44. Miller KJ, Gonçalves-Bradley DC, Areerob P, Hennessy D, Mesagno C, Grace F. Comparative effectiveness of three exercise types to treat clinical depression in older adults: A systematic review and network meta-analysis of randomised controlled trials. *Ageing Res Rev*. 2020;58:100999. doi:10.1016/j.arr.2019.100999

45. Makizako H, Tsutsumimoto K, Doi T, et al. Exercise and Horticultural Programs for Older Adults with Depressive Symptoms and Memory Problems: A Randomized Controlled Trial. *J Clin Med*. 2019;9(1):99. doi:10.3390/jcm9010099

46. CMS. Improve Home Health Services for Older Adults and People with Disabilities. Published June 28, 2021. Accessed September 17, 2021.

https://www.cms.gov/newsroom/press-releases/cms-improve-home-health-services-older-adults-and-people-disabilities

Figure 1. Mediation model of homebound status between depressive symptoms and cognitive impairment.




Abbreviations: OR, odds ratio; NIE, natural indirect effect; NDE, natural direct effect.

The figure depicts that homebound status significantly mediated the relationship between depressive symptoms and cognitive impairment (NIE, aOR; 95% CI, 1.04, 1.10), with significant direct effect of depressive symptoms (NDE, aOR=1.61; 95% CI, 1.36, 1.91) and significant total effect (aOR,1.72; 95% CI, 1.46, 2.03) after adjusting for all covariates.

# Supplement

Supplementary table 1. Characteristics distribution stratified by self-reported cognitive status, M ± SD, N (%)

Supplementary table 2. Results of logistic regression analysis of associations among depressive symptoms, homebound and cognitive impairment excluding proxy respondents (N=6,746-6,978)

Supplementary table 3. Mediation of homebound status in the association between depressive symptoms and cognitive impairment excluding proxy respondents (N=6,746-6,978)

**Supplementary table 1. Characteristics distribution stratified by self-reported cognitive status**

| Characteristics | Total (N=6,746-6,978) | Cognitive impairment (n=1,416-1,530) | Nocognitive impairment (n=5,330-5,448) | *P* values |
|---|---|---|---|---|
| Age, M ± SD | 77.2 ± 7.7 | 81.2 ± 7.7 | 76.1 ± 7.3 | <.001 |
| Sex, n (%) | | | | .800 |
| Female | 4051 (58.1) | 858 (56.1) | 3193 (58.6) | |
| Male | 2927 (41.9) | 672 (43.9) | 2255 (41.4) | |
| Race/ethnicity, n (%) | | | | <.001 |
| White, non-Hispanic | 4847 (69.5) | 878 (57.4) | 3969 (72.9) | |
| Black, non-Hispanic | 1483 (21.2) | 421 (27.5) | 1062 (19.5) | |
| Hispanic | 253 (3.6) | 84 (5.5) | 169 (3.1) | |
| Other | 395 (5.7) | 147 (9.6) | 248 (4.5) | |
| Education, n (%) | | | | <.001 |
| Less than high school | 1760 (25.5) | 686 (45.6) | 1074 (19.9) | |
| High school | 1905 (27.6) | 370 (24.6) | 1535 (28.4) | |
| Some college or vocational school | 1734 (25.1) | 255 (17.0) | 1479 (27.4) | |
| College or higher | 1509 (21.8) | 191 (12.7) | 1318 (24.3) | |
| Living arrangement, n (%) | | | | <.001 |
| Alone | 2315 (33.3) | 575 (37.8) | 1740 (32.1) | |
| With spouse/partner only | 2913 (41.9) | 447 (29.3) | 2466 (45.5) | |
| With others only | 1104 (15.9) | 359 (23.6) | 745 (13.7) | |
| With spouse/partner and with others | 615 (8.9) | 142 (9.3) | 473 (8.7) | |
| Smoking status, n (%) | | | | <.001 |
| No | 3382 (48.5) | 789 (51.7) | 2593 (47.6) | |
| Yes | 3591 (51.5) | 738 (48.3) | 2853 (52.4) | |
| Vigorous activity, n (%) | | | | <.001 |
| No | 4470 (64,1) | 1235 (80.8) | 3235 (59.4) | |
| Yes | 2507 (35.9) | 294 (19.2) | 2213 (40.6) | |
| BMI, n (%) | | | | <.001 |
| Normal (<30 kg/m$^2$) | 4881 (72.3) | 1115 (78.7) | 3766 (70.7) | |
| Obesity (≥30 kg/m$^2$) | 1865 (27.7) | 301 (21.3) | 1564 (29.3) | |
| Visual impairment, n (%) | | | | <.001 |
| No | 6347 (91.2) | 1281(83.9) | 5066 (93.2) | |
| Yes | 615 (8.8) | 246 (16.1) | 369 (6.8) | |
| Auditory impairment, n (%) | | | | <.001 |
| No | 5381 (77.1) | 1079 (70.5) | 4302 (79.0) | |
| Yes | 1597 (22.9) | 451 (29.5) | 1146 (21.0) | |
| Hypertension, n (%) | | | | .905 |
| No | 2306 (33.1) | 503 (33.0) | 1803 (33.1) | |
| Yes | 4663 (66.9) | 1023 (67.0) | 3640 (66.9) | |

| | | | | |
|---|---|---|---|---|
| Diabetes, n (%) | | | | <.001 |
| No | 5218 (74.8) | 1074 (70.3) | 4144 (76.1) | |
| Yes | 1757 (25.2) | 453 (29.7) | 1304 (23.9) | |
| Stroke, n (%) | | | | <.001 |
| No | 6246 (89.6) | 1289 (84.4) | 4957 (91.1) | |
| Yes | 726 (10.4) | 239 (15.6) | 487 (8.9) | |
| Number of ADL impairments, M ± SD | 1.2 ± 0.7 | 1.5 ± 1.0 | 1.2 ± 0.6 | <.001 |
| Hospitalization, n (%) | | | | <.001 |
| No | 5428 (77.9) | 1071 (71.2) | 4357 (80.0) | |
| Yes | 1542 (22.1) | 455 (29.8) | 1087 (20.0) | |
| Depressive symptoms, n (%) | | | | <.001 |
| No | 5974 (85.6) | 1177 (76.9) | 4797 (88.1) | |
| Yes | 1004 (14.4) | 353 (23.1) | 651 (11.9) | |
| Homebound, n (%) | | | | <.001 |
| No | 5509 (79.0) | 937 (61.2) | 4572 (83.9) | |
| Yes | 1469 (21.0) | 593 (38.8) | 876 (16.1) | |

Abbreviations: M, mean; SD, standard deviations; BMI, body mass index; ADL, activity of daily living.

**Supplementary table 2. Results of logistic regression analysis of associations among depressive symptoms, homebound and cognitive impairment excluding proxy respondents (N=6,746-6,978)**

| Independent variable(s) | Effect size for association, OR (95% CI)[b] | | | |
|---|---|---|---|---|
| | Dependent Variable | | | |
| | Model 1: Cognitive Impairment | Model 2: Homebound Status | Model 3: Cognitive Impairment | Model 4: Cognitive Impairment |
| Depressive symptoms | 1.52 (1.27-1.81) *** | 1.92 (1.59-2.33) *** | NA | 1.47 (1.23-1.75) *** |
| Homebound status | NA | NA | 1.51 (1.27-1.80) *** | 1.46 (1.23-1.75) *** |

Abbreviations: OR, odds ratio; NA, not applicable.

a * P <.05, ** P <.01, ***P<.001

b All models adjusted for demographics (age, sex, education, race/ethnicity, living arrangement) and health-related characteristics (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily living impairments, hospitalization).

**Supplementary table 3. Mediation of homebound status in the association between depressive symptoms and cognitive impairment excluding proxy respondents (N=6,746-6,978)**

| | Model 1[b] | Model 2[c] | Model 3[d] |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Natural direct effect | 1.71 (1.46-1.98) *** | 1.63 (1.39-1.93) *** | 1.47 (1.24-1.78) *** |
| Natural indirect effect | 1.36 (1.29-1.43) *** | 1.19 (1.14-1.24) *** | 1.05 (1.02-1.08) *** |
| Marginal total effect | 2.33 (2.00-2.71) *** | 1.95 (1.66-2.30) *** | 1.54 (1.30-1.86) *** |
| Proportion mediated[a] | 57.3% | 36.5% | 12.7% |

[a] Proportion meditated by homebound status were calculated as the log of the indirect effect divided by the log of the total effect.

[b] Model 1: independent variables of interest

[c] Model 2: Model 1+ demographic covariates (age, sex, education, race/ethnicity, living arrangement)

[d] Model 3: Model 2 + health-related covariates (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily life impairment, hospitalization)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | Page 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Page 5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | Page 6-7 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | Page 7 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Page 7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | Page 7 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Page 7-10 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Page 7-10 |
| Bias | 9 | Describe any efforts to address potential sources of bias | N/A |
| Study size | 10 | Explain how the study size was arrived at | Page 11 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Page 10-11 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Page 10-11 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | N/A |
| | | (*c*) Explain how missing data were addressed | Page 7 |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | N/A |
| | | (*e*) Describe any sensitivity analyses | Page 11 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | In Page 7 |
| | | (b) Give reasons for non-participation at each stage | In Page 7 |
| | | (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Page 12 |
| | | (b) Indicate number of participants with missing data for each variable of interest | Page 7 |

| | | | |
|---|---|---|---|
| Outcome data | 15* | Report numbers of outcome events or summary measures | Page 12 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Page 12-13 |
| | | (*b*) Report category boundaries when continuous variables were categorized | Page 12 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Page 13 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | Page 13-14 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Page 16-17 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Page 13-17 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Page 17 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Page 19 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# Mediating Role of Homebound Status between Depressive Symptoms and Cognitive Impairment among Community-Dwelling Older Adults in the U.S.: A Cross-Sectional Analysis of a Cohort Study



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2022-065536.R1 |
| Article Type: | Original research |
| Date Submitted by the Author: | 23-Sep-2022 |
| Complete List of Authors: | Peng, Wenting; Central South University<br>Miyawaki, christina; University of Houston,<br>Okoye, Safiyyah M; Johns Hopkins University<br>Wang, Wenru; National University of Singapore<br>Luo, Yuqian; Central South University<br>Mo, Cen; Central South University<br>Liu, Minhui; Central South University |
| Primary Subject Heading: | Epidemiology |
| Secondary Subject Heading: | Epidemiology, Mental health, Nursing, Public health |
| Keywords: | EPIDEMIOLOGY, GERIATRIC MEDICINE, MENTAL HEALTH, Dementia < NEUROLOGY, Depression & mood disorders < PSYCHIATRY |
| | |

*I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.*

*The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.*

*Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.*

# Mediating Role of Homebound Status between Depressive Symptoms and Cognitive Impairment among Community-Dwelling Older Adults in the U.S.: A Cross-Sectional Analysis of a Cohort Study

**Title:** Mediating Role of Homebound Status between Depressive Symptoms and Cognitive Impairment among Community-Dwelling Older Adults in the U.S.: A Cross-Sectional Analysis of a Cohort Study

**Authors:** Wenting Peng, BSN, RN[1]; Christina E Miyawaki, PhD, MSW, MA[2]; Safiyyah M Okoye, PhD, RN[3]; Wenru Wang, PhD[4]; Yuqian Luo, BSN, RN[1]; Cen Mo, BSN, RN[1]; Minhui Liu, PhD, RN[1*]

**Affiliations:**
[1] Xiangya School of Nursing, Central South University, Changsha, China
[2] Graduate College of Social Work, University of Houston, Houston, Texas, USA
[3] Johns Hopkins School of Nursing, Baltimore, MD, USA
[4] Alice Lee Centre for Nursing Studies, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

***Correspondence to:**
Minhui Liu, PhD, RN
Associate Professor
Central South University, Xiangya School of Nursing
172 Tongzipo Road of Yuelu District
Changsha, China 410013
Phone: +86 133-7894-9466
Email: mliu62@jhu.edu
Twitter: @MinhuiLiu2

## Abstract

**Objective:** Depressive symptoms are known modifiable factors of cognitive impairment in older adults. However, the pathway through which depressive symptoms lead to cognitive impairment is not well understood. This study aimed to investigate whether homebound status (defined as usually unable to leave home unassisted) mediates the association between depressive symptoms and cognitive impairment in community-dwelling older adults in the United States.

**Design:** A secondary analysis of cross-sectional data.

**Setting(s):** Communities in the United States.

**Participants:** Community-dwelling older adults (N=7,537) from the 2011 National Health and Aging Trends Study (NHATS), a nationally representative survey of Medicare Beneficiaries in the United States.

**Main outcome measures:** Participants' cognitive impairment status was classified using a composite measure. Depressive symptoms were assessed using Patient Health Questionnaire-2. Homebound status was determined by the frequency, difficulty, and needing help in getting outdoors. We used logistic regression and the Paramed command in STATA to analyze whether homebound mediated the association between depressive symptoms and cognitive impairment.

**Results:** Participants were on average, 77.7 years old, female (58.3%), and non-Hispanic white (68.1%). About 26% of the participants were classified as having cognitive

impairment, 16% reported depressive symptoms, and 25% were homebound. Depressive symptoms (adjusted OR, 1.60; 95% CI, 1.36-1.89) and homebound status (adjusted OR, 1.58; 95% CI, 1.34-1.86) were independently associated with cognitive impairment. Homebound significantly mediated 12.5% of the total effect between depressive symptoms and cognitive impairment, with significant indirect effect (OR, 1.07; 95% CI, 1.04-1.10), direct effect (OR, 1.61; 95% CI, 1.36-1.91) and total effect (OR, 1.72; 95% CI, 1.46-2.03).

**Conclusions:** This study supports a mediating role of homebound status in the relationship between depressive symptoms and cognitive impairment. Interventions to promote outdoor mobility should be studied for their ability to delay cognitive impairment for older adults with depressive symptoms.

***Keywords:*** homebound; depressive symptoms; cognitive impairments; older adults; mediation

## Strengths and limitations of this study

- The strengths of this study include the use of nationally large sample data and adjustment for potential confounders including demographics and health-related factors.
- The cross-sectional design does not examine causality.
- All indicators were self-reported retrospectively which may cause recall bias and report errors.
- The measurement of homebound did not collect reasons why individuals did not leave their homes.

## Introduction

Cognitive impairment (including mild cognitive impairment and dementia [1]) causes disabilities in older adults' physical and psychological functions and is a major public health concern [2,3]. Approximately 25% of U.S. adults aged 50 and over suffer from cognitive impairment and this rate increases with age [1], bringing a huge economic burden to families and society [4]. Older adults with cognitive impairments have a high and growing demand for long-term care, which poses a significant challenge for healthcare systems, healthcare providers, and families. Thus, it is imperative to identify the modifiable factors and develop effective strategies to prevent and slow the progression of cognitive impairment in older adults.

Depressive symptoms are common in older adults and are associated with physical disability [5], social isolation [6], and cardiovascular diseases [7], all of which have been identified as contributors to declines in cognition [8,9]. A systematic review concluded that depressive symptoms are an independent risk factor for dementia [10]. In addition, multiple systematic reviews found that depressive symptoms are associated with the progression of mild cognitive impairment to dementia [11–13]. Despite these well-established associations between depressive symptoms and cognitive impairment, the mediating mechanisms of the association remain unclear.

In this paper, we examined homebound status as a potential mediator between depressive symptoms and cognitive impairment. Being homebound, defined as limited at

home, is closely related to depression and cognitive impairment. Homebound older adults have consistently been found to experience depression in high numbers; in one population-based study, 59% of older adults who had not left their homes in the previous month had positive depressive symptoms [14–17]. Prior research has also found cognitive impairment more prevalent in the homebound population than the non-homebound population [18,19]. The confluence of mental health, physical, and social impairments that result in homebound status [20], may lead to cognitive impairment and should be better understood as a potential target of intervention. For example, previous studies have shown that older adults with depressive symptoms were more likely to have physical impairments and loss of interest or energy in social participation [5,21], resulting in homebound status [19,20], Rates of physical activity and social participation, well-known protective factors against cognitive impairment [22], are low in homebound older adults and may contribute to the higher rates of cognitive impairment in this population [20].

Fortunately, homebound status is modifiable and can be improved using assistive devices, modifying the home environment, and accessing transportation [15]. It is therefore important to investigate the potential of homebound status as a target of interventions to improve cognitive function. However, to the best of our knowledge, no study has attempted to investigate whether homebound status mediates the association between depressive symptoms and cognitive impairment, suggesting the pathway through homebound status remains unclear. Given the reversibility of homebound status and depressive symptoms and

the heavy burden of cognitive impairment, it is also important to understand the mediating role of homebound status between cognitive impairment and depressive symptoms. The study was to examine whether homebound status mediates the association between depressive symptoms and cognitive impairment in a nationally representative sample of community-dwelling older adults in the U.S. We hypothesized that homebound status is a significant mediator between depressive symptoms and cognitive impairment in community-dwelling older adults.

## Methods

### Design and Sample

We used the first round (2011) of data from the National Health and Aging Trends Study (NHATS) [23], a nationally representative longitudinal cohort study of older adults in the U.S. who are Medicare beneficiaries aged 65 and older [24]. The NHATS study began in 2011 and aimed to understand the disability trends of older adults in late life. In the current study, data obtained from older adults who were aged 65 or above and lived in the community were included in data analyses. In the initial round, a total of 7,609 participants who lived in the community completed the sample person interview. We excluded 72 participants who had incomplete data on depressive symptoms, homebound or cognitive function, for a resulting analysis sample size of 7,537. Excluded participants were older, living alone, with less education, were less likely to perform vigorous activities, had a stroke, and tended to have more activities of daily living (ADL) impairments, visual impairment, and

auditory impairment, compared to those who were not excluded. The NHATS used downloadable, nonidentifiable and publicly available data and was approved by the Johns Hopkins University Institutional Review Board (No.00002083). Prior to being interviewed, all NHATS participants completed a written informed consent form [25]. The current analyses were deemed exempt from review by the Xiangya School of Nursing Ethic Committee of Central South University.

**Measurement**

***Dependent variables***

Cognitive function was determined by a previously modified NHATS dementia definition including a diagnosis from physicians (self-reported), assessment of cognitive function in 3 domains (memory, orientation, and executive function) and AD8 Dementia Screening Interview provided by proxy respondents [26]. The AD8 contained 8 items and ranged 0 to 8. Cognitive impairments were determined by a cut-off of 2 and higher. The Cronbach's α coefficient of AD8 was 0.84 [27]. Participants were classified into three groups as follows *probable dementia*, *possible dementia*, and *no dementia*. *Probable dementia* was assessed by i) a diagnosis of dementia; ii) the AD8 scores $\geq$ 2; or iii) scores $\leq$ 1.5 Standard Deviation (SDs) below the mean in at least 2 of 3 cognitive performance tests; *Possible dementia* was determined by a score of $\leq$ 1.5 SDs below the mean in 1 cognitive performance test. All other participants were classified as having *no dementia*. We considered participants with a classification of probable dementia or possible dementia as having cognitive

impairment; we considered participants with a classification of no dementia as without cognitive impairment. The NHATS dementia definition (defined as probable or possible dementia) has shown high sensitivity (85.7%) and specificity (83.7%) compared to a structured in-home clinical measurement in the landmark Aging, Demographics, and Memory Study [26]. For terminology consistent with the cognitive impairment instrument, the term "cognitive impairment" was used throughout this article to replace dementia.

***Independent variable***

Depressive symptoms were measured using the Patient Health Questionnaire-2 (PHQ-2), a well-validated screening instrument for depression status [28]. Participants were asked: "Over the last month, how often have you: 1) had little interest or pleasure in doing things; 2) felt down, depressed, or hopeless." Responses were recorded on a 4-point Likert scale (scored 0-3) with total scores ranging from 0 to 6. A higher score suggested more depressive symptoms. Following the recommendation from previous studies, we used a cut-off of 3 and higher to determine depressive symptoms. The PHQ-2 had a good criterion validity for major depression [29]. The cut-off of 3 has a sensitivity of 0.79, a specificity of 0.86, and the area under the curve of 0.90 for any type of depressive disorder [28].

***Mediator***

Based on the measurement developed by Ornstein and colleagues, homebound status was measured using four questions based on the reported frequency of outdoor mobility [15]. First, participants were asked about the frequency of going outside, and response options

were on a 5-point Likert scale: never; rarely (≤ 1 day per week); some days (2-4 days per week); most days (5-6 days per week); and every day. Participants reporting going outside at least 2 days per week were asked whether they needed help from others to go outside. Those who reported needing help were also asked about the frequency of going outside independently. Those who reported ever going outside by themselves were asked whether they had any difficulties leaving home independently. Participants were classified as homebound if they never left home, or left home with any difficulties and assistance. All other participants were classified as non-homebound [15].

***Covariates***

Demographic and health-related characteristics that are common risk factors for depression, homebound status, and cognitive impairment were included as covariates in analyses.

Demographic characteristics included age [1], sex (male/female) [30], race/ethnicity (non-Hispanic white, non-Hispanic Black, Hispanic, and other) [31], education (less than high school, high school, college or vocational school and bachelor or higher) [32], and living arrangement (alone, with spouse/partner only, with others only, with spouse/partner and with others) [33],

Health-related characteristics included smoking status (never smoker and current/former smoker) [8]; whether they performed vigorous activities last month (yes/no) [34]; body mass index (BMI) (normal/obesity [≥30 kg/m$^2$]) [8]; visual impairment (yes/no)

[35]; auditory impairment (yes/no) [36]; diagnoses of hypertension (yes/no) [8], diabetes (yes/no) [8], and stroke (yes/no) [37]; number of activities of daily living impairments [38]; whether the subjects were hospitalized in the last 12 months (yes/no) [39].

**Statistical Analysis**

Demographic and health-related characteristics were described using frequencies, proportions, means, and standard deviations (SDs). Chi-square test and two sample t-test were used to test the differences between groups with and without cognitive impairment for categorical and continuous variables, respectively. Using Baron and Kenny's method for mediation [40], we assessed the associations among depressive symptoms, homebound status, and cognitive impairment in four logistic regression models. The first model assessed the direct relationship between the independent variable depressive symptoms and the dependent variable cognitive impairment. The second model examined whether depressive symptoms were associated with the hypothesized mediator homebound status. The third model evaluated the association between the hypothesized mediator homebound status and cognitive impairment. The fourth model estimated the association between the independent variable depressive symptoms and the dependent variable cognitive impairment upon inclusion of the hypothesized mediator homebound status to the model. All models were adjusted for demographics and health-related factors.

Because all the associations in the above models were significant, we were able to further test homebound status as a mediator following Baron and Kenny's approach and

using the Paramed command in Stata [40]. This procedure estimates the natural direct effects, natural indirect effects, and marginal total effects in the presence of exposure-mediator interaction. The product of direct and indirect effects was expressed as the total effect. We estimated direct and indirect effects using logistic regression models and performed a bootstrapping analysis with 1000 replications both with and without adjusting for covariates. The proportion of effect mediated by homebound status was calculated as the log of the indirect effect divided by the log of the total effect.

Sensitivity analyses were performed to test the robustness of the findings. We excluded any data provided by proxy respondents (n=583) and reran the analysis (see supplementary table 1, 2 & 3). Odds ratio (ORs) and 95% confidence intervals (CI) were reported. Missing values on covariates ranged from 0.1% (stroke) to 3.5% (BMI). Given the large sample size, no particular technique was used to handle missing data. *P* values less than 0.05 indicated statistical significance. All analyses were performed in Stata/SE 15.0 (Stata Corp., College Station, TX).

**Patient and public involvement**

No patients were involved in the development of the question, design, or data interpretation.

## Results

Characteristics of all participants and their comparisons by cognitive status are presented in Table 1 (N = 7,537). The mean age of the participants was 77.7 years old. Fifty-

eight percent were female and 68% were non-Hispanic white. About 26% of the participants had cognitive impairment, 16% reported depressive symptoms and 25% were homebound. Compared to participants with no cognitive impairment, those with cognitive impairment were more likely to be older and less educated, have ADL, visual and auditory impairments, have comorbidities of diabetes and stroke, and have been hospitalized ($P$<.001 for all comparisons). The prevalence of depressive symptoms and homebound status were significantly higher for those with cognitive impairment than those without (27.4% vs. 12.0% for depression status, and 48.1% vs. 16.7% for homebound).

**Table 1**. Characteristics of community-dwelling older adults, stratified by cognitive impairment status

| Characteristics | Total (N=7,270-7,537)[a] | Cognitive impairment (n=1,849-1,988) | No cognitive impairment (n=5,421-5,549) | *P* values |
|---|---|---|---|---|
| Age, M ± SD | 77.7 ± 7.9 | 81.8 ± 7.8 | 76.2 ± 7.3 | <.001 |
| Sex, n (%) | | | | .800 |
| Female | 4397 (58.3) | 1155 (58.1) | 3242 (58.4) | |
| Male | 3140 (41.7) | 833 (41.9) | 2307 (41.6) | |
| Race/ethnicity, n (%) | | | | <.001 |
| White, non-Hispanic | 5137 (68.1) | 1119 (56.3) | 4018 (72.4) | |
| Black, non-Hispanic | 1648 (21.9) | 563 (28.3) | 1085 (19.5) | |
| Hispanic | 449 (6.0) | 191 (9.6) | 258 (4.7) | |
| Other | 303 (4.0) | 115 (5.8) | 188 (3.4) | |
| Education, n (%) | | | | <.001 |
| Less than high school | 2020 (27.1) | 906 (46.6) | 1114 (20.3) | |
| High school | 2056 (27.6) | 492 (25.3) | 1564 (28.4) | |
| Some college or vocational school | 1801 (24.2) | 307 (15.8) | 1494 (27.1) | |
| College or higher | 1570 (21.1) | 240 (12.3) | 1330 (24.2) | |
| Living arrangement, n (%) | | | | <.001 |
| Alone | 2435 (32.4) | 680 (34.3) | 1755 (31.7) | |
| With spouse/partner only | 3036 (40.5) | 538 (27.2) | 2498 (45.2) | |
| With others only | 1351 (18.0) | 568 (28.7) | 783 (14.2) | |
| With spouse/partner and with others | 684 (9.1) | 195 (9.8) | 489 (8.9) | |

| | | | | |
|---|---|---|---|---|
| Smoking status, n (%) | | | | <.001 |
| No | 3721 (49.4) | 1064 (53.7) | 2657 (47.9) | |
| Yes | 3807 (50.6) | 919 (46.3) | 2888 (52.1) | |
| Vigorous activity, n (%) | | | | <.001 |
| No | 4970 (66.0) | 1652 (83.2) | 3318 (59.8) | |
| Yes | 2563 (34.0) | 333 (16.8) | 2230 (40.2) | |
| BMI, n (%) | | | | <.001 |
| Normal (<30 kg/m$^2$) | 5316 (72.1) | 1479 (80.0) | 3837 (70.8) | |
| Obesity (≥30 kg/m$^2$) | 1954 (28.9) | 370 (20.0) | 1584 (29.2) | |
| Visual impairment, n (%) | | | | <.001 |
| No | 6684 (89.1) | 1540 (78.2) | 5144 (93.0) | |
| Yes | 819 (10.9) | 429 (21.8) | 390 (7.0) | |
| Auditory impairment, n (%) | | | | <.001 |
| No | 5716 (75.8) | 1356 (67.7) | 4371 (78.8) | |
| Yes | 1821 (24.2) | 643 (32.3) | 1178 (21.2) | |
| Hypertension, n (%) | | | | .367 |
| No | 2467 (32.8) | 634 (32.0) | 1833 (33.1) | |
| Yes | 5061 (67.2) | 1350 (68.0) | 3711 (66.9) | |
| Diabetes, n (%) | | | | <.001 |
| No | 5631 (74.7) | 1407 (70.9) | 4224 (76.1) | |
| Yes | 1903 (25.3) | 578 (29.1) | 1325 (23.9) | |
| Stroke, n (%) | | | | <.001 |
| No | 6655 (88.4) | 1613 (81.2) | 5042 (90.9) | |
| Yes | 876 (11.5) | 373 (18.8) | 503 (9.1) | |
| Number of ADL impairments, M ± SD | 1.3 ± 0.9 | 1.8 ± 1.1 | 1.2 ± 0.6 | <.001 |
| Hospitalization, n (%) | | | | <.001 |
| No | 5770 (76.6) | 1350 (68.0) | 4420 (79.7) | |
| Yes | 1759 (23.4) | 634 (32.0) | 1125 (20.3) | |
| Depressive symptoms, n (%) | | | | <.001 |
| No | 6328 (83.0) | 1444 (72.6) | 4884 (88.0) | |
| Yes | 1209 (16.0) | 544 (27.4) | 665 (12.0) | |
| Homebound, n (%) | | | | <.001 |
| No | 5652 (75.0) | 1032 (51.9) | 4620 (83.3) | |
| Yes | 1885 (25.0) | 956 (48.1) | 929 (16.7) | |

Abbreviations: M, mean; SD, standard deviations; BMI, body mass index; ADL, activities of daily living.

[a] Please note that the sample size has a range because missing values on covariates ranged from 0.1% (stroke) to 3.5% (BMI). Given the large sample size, no particular technique was used to handle missing data.

Table 2 presents the results of the associations among cognitive impairment,

depressive symptoms, and homebound status in accordance with the Baron and Kenny approach to study mediation. After adjusting for demographics and health-related factors, compared to participants without depressive symptoms or homebound status, those with depressive symptoms (adjusted OR, 1.67; 95% CI, 1.42-1.97) or homebound status (adjusted OR, 1.65; 95% CI, 1.40-1.94) had higher odds of cognitive impairment. Depressive symptoms were also a significant risk factor for homebound status (adjusted OR, 2.00; 95% CI, 1.67-2.40). Additionally, both homebound status (adjusted OR, 1.58; 95% CI, 1.34-1.86) and depressive symptoms (adjusted OR, 1.60; 95% CI, 1.36-1.89) were statistically significantly associated with cognitive impairment when they were both included as independent variables in the same model.

**Table 2**. Results of logistic regression analyses of associations among depressive symptoms, homebound status and cognitive impairment

| **Independent variable(s)** | Effect size for association, OR (95% CI)[b] | | | |
|---|---|---|---|---|
| | **Dependent Variable** | | | |
| | Model 1: Cognitive Impairment | Model 2: Homebound Status | Model 3: Cognitive Impairment | Model 4: Cognitive Impairment |
| Depressive symptoms | 1.67 (1.42-1.97) *** | 2.00 (1.67-2.40) *** | NA | 1.60 (1.32-1.89) *** |
| Homebound status | NA | NA | 1.65 (1.40-1.94) *** | 1.58 (1.34-1.86) *** |

Abbreviations: OR, odds ratio; NA, not applicable.

[a] * $P$ <.05, ** $P$ <.01, ***$P$<.001

[b] All models adjusted for demographics (age, sex, education, race/ethnicity, living arrangement) and health-related characteristics (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily living impairments, hospitalization).

Table 3 and Figure 1 show the indirect contribution of being homebound in the relationship between depressive symptoms and cognitive impairment. Homebound status statistically significantly mediated this relationship. It partially explained the relationship; the

contribution of being homebound was 40.4% of the association between depressive symptoms and cognitive impairment in the unadjusted model (Model 1), and this proportion decreased to 12.5% after adjusting for all covariates (Model 3).

**Table 3.** Mediation of homebound status in the association between depressive symptoms and cognitive impairment

| | Model 1[b] OR (95% CI) | Model 2[c] OR (95% CI) | Model 3[d] OR (95% CI) |
|---|---|---|---|
| Natural direct effect | 1.93 (1.68-2.22) *** | 1.88 (1.61-2.18) *** | 1.61 (1.36-1.91) *** |
| Natural indirect effect | 1.56 (1.48-1.64) *** | 1.33 (1.27-1.39) *** | 1.07 (1.04-1.10) *** |
| Marginal total effect | 3.01 (2.61-3.46) *** | 2.49 (2.15-2.90) *** | 1.72 (1.46-2.03) *** |
| Proportion mediated[a] | 40.4% | 31.3% | 12.5% |

[a] Proportion meditated by homebound status was calculated as the log of the indirect effect divided by the log of the total effect.

[b] Model 1: independent variables of interest

[c] Model 2: Model 1+ demographic covariates (age, sex, education, race/ethnicity, living arrangement)

[d.] Model 3: Model 2 + health-related covariates (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily living impairments, hospitalization)

[Insert Figure 1 about here]

Results from a sensitivity analysis suggested that homebound status statistically significantly mediated the association between depressive symptoms and cognitive impairment (adjusted OR, 1.05; 95% CI, 1.02-1.08), even after excluding data from proxy respondents (supplementary table 3, additional information see supplementary table 1 and 2).

## Discussion

We examined the mediating role of homebound status in the association of depressive symptoms and cognitive impairment using a nationally representative sample of community-dwelling older Americans. Our study found that depressive symptoms and

homebound status were independently associated with cognitive impairment. Moreover, more than 10% of the effect of depressive symptoms on cognitive impairment was mediated by homebound status, suggesting that one of the ways the depression status influences cognitive impairment is through the decreased mobility outside the home that defines homebound status. Our findings shed light on homebound status as a target of intervention to prevent and slow cognitive impairment in later life.

Our results showed that depressive symptoms and homebound status were each independently associated with a greater risk of cognitive impairment; findings are supported by previous studies [13,18]. Depression is a well-established predictor of cognitive impairment; however, we found a similar magnitude of association between homebound status and cognitive impairment as between depression symptoms and cognitive impairment, after accounting for demographic and health-related factors. This result was inconsistent with a cross-sectional study by Meng et al., which suggested that cognitive impairment was more strongly associated with homebound status compared with depressive symptoms [41]. Possible explanations for different results are differences in the homebound status measures, covariates, and the U.S. and Chinese cultures. Meng et al.'s study included older adults from a rural province in China, with a smaller sample size (N = 720) and adjusted for sociodemographic variables only [41].

The mediation findings of this study may be explained through several potential mechanisms. Depressed older adults often experience loss of interest and social connection

[22], and have no energy to participate in outside activities, which for some leads to reduced mobility and becoming homebound [15,19,42]. There is robust evidence that physical activity and social participation are effective strategies to prevent cognitive impairment [22], and that homebound older adults are less likely to benefit from these strategies. Homebound status may also mediate the effects of depression on cognitive impairment via other mechanisms such as nutrition disorders, social isolation, and hospitalization [19,43], all of which have been associated with both depression and homebound status. The results of two previous studies (one cross-sectional [44] and one prospective [45]) found that functional disability mediated the relationship between depression status and cognitive impairment, and offer additional support to our mediation findings. Although homebound status is not equivalent to functional disability, there are overlapping characteristics between homebound older adults and those with a functional disability; older adults with functional disability frequently report difficulty going outside regularly and are at increased risk of being homebound [46].

This study has important implications for public health practice and research. Our findings suggest the utility of efforts to improve cognitive function by reducing the effect of depressive symptoms and homebound status. For example, interventions that support depressed older adults to maintain ideal outdoor mobility through health education, psychosocial interventions, and creating a safe and convenient environment, may serve to decrease the risk of cognitive impairment. Some interventions have shown their potential to reduce depressive symptoms and improve cognitive impairments in depressed older adults,

such as physical exercise [21,47,48]. Yet, existing interventions are geared toward improving other outcomes of home-dwelling older adults, instead of improving the status of the homebound. Some evidence-based physical activity intervention programs, such as Community Aging in Place-Advancing Better Living for Elders (CAPABLE) and Lifestyle Interventions and Independence for Elders (LIFE), have shown the effect to increase life-space mobility, falls efficacy, and reduce cognitive frailty among community-dwelling older adults [49,50]. Future research should further identify these programs' effects on changing homebound status. The Centers for Medicare & Medicaid Services have suggested improving health services for homebound older adults who receive health care at home.[51] We did not find studies of mobility interventions to reduce cognitive impairment among homebound older adults and suggest this as an area of future inquiry. By recognizing the associations of depressive symptoms and homebound with cognitive impairment, healthcare professionals can screen people who are at high risk of cognitive impairment or have cognitive impairment more easily by examining their depressive symptoms and homebound status profiles in their routine practice. Last but not least, for older adults with depressive symptoms or who are homebound, healthcare professionals can focus on whether these older adults have additional risk factors for cognitive impairment, such as physical inactivity, obesity, and social isolation, all of which are common in depressed or homebound older adults. Proactively managing these modifiable risk factors is beneficial to delay the onset of cognitive impairment and diagnosing it early.

To the best of our knowledge, this study is the first to explore the mediation role of homebound status in the relationship between depressive symptoms and cognitive impairments in older adults. The strengths of this study include the use of nationally large sample data and adjustment for potential confounders including demographics and health-related factors. However, several limitations of the study should be noted. First, the cross-sectional design does not examine causality, suggesting future studies can further assess causal relationships among depressive symptoms, homebound status, and cognitive impairments using a prospective research design. Second, all indicators were self-reported retrospectively which may cause recall bias and report errors. Particularly, when we assessed homebound status, a month recall time may be too long for participants or their proxies to recall accurately. Third, Medicare defined a homebound individual as requiring "taxing effort" (i.e., physical, or personal assistance) to leave their home [52], which was consistent with the NHATS homebound definition. However, the measurement of homebound was limited by the items and skip patterns within the NHATS Mobility Questionnaire. For example, the mobility questions did not collect reasons why individuals did not leave their homes [15].

## Conclusion

Based on a nationally representative sample of older adults in the U.S., we found that depressive symptoms and homebound status were associated with cognitive impairment, and homebound status partially mediated the relationship between depressive symptoms and

cognitive impairment. Therefore, for future public health efforts on preventing cognitive impairment in depressed older adults, homebound status should be taken into account.

**Author contributions**

*Wenting Peng:* Concept and design, analysis, drafting of the initial manuscript and revision.

*Christina E. Miyawaki*: Critical feedback and revision of the manuscript.

*Safiyyah M. Okoye:* Critical feedback and revision of the manuscript.

*Wenru Wang:* Critical feedback and revision of the manuscript.

*Yuqian Luo:* Revision of the manuscript.

*Cen Mo:* Revision of the manuscript.

*Minhui Liu:* Supervision, validation, interpretation of data and critical revision of the manuscript.

**Funding**

The publication of this manuscript was supported by the Youth Grant from the National Natural Science Foundation of China (Grant No.72004237) and the Natural Science Foundation of Changsha City (Grant No.kp2007080).

**Competing interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Ethics approval**

NHATS was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board (JHSPH IRB # 00002083). NHATS participants completed written informed consent prior to being interviewed. The current analyses were deemed exempt from review by the Xiangya School of Nursing Ethic Committee of Central South University. The study was conducted according to the guidelines of the Declaration of Helsinki.

**Data availability statement**

Data are available in a public, open access repository. The NHATS data analyzed in the current study are available for research purposes at www.nhats.org.

## References


1 Hale JM, Schneider DC, Mehta NK, *et al.* Cognitive impairment in the U.S.: Lifetime risk, age at onset, and years impaired. *SSM - Popul Health* 2020;**11**:100577. doi:10.1016/j.ssmph.2020.100577

2 Bahureksa L, Najafi B, Saleh A, *et al.* The Impact of Mild Cognitive Impairment on Gait and Balance: a Systematic Review and Meta-Analysis of Studies using Instrumented Assessment. *Gerontology* 2017;**63**:67–83. doi:10.1159/000445831

3 Yates JA, Clare L, Woods RT, *et al.* What is the Relationship between Health, Mood, and Mild Cognitive Impairment? *J Alzheimers Dis* 2017;**55**:1183–93. doi:10.3233/JAD-160611

4 Hurd MD, Martorell P, Delavande A, *et al.* Monetary costs of dementia in the United States. *N Engl J Med* 2013;**368**:1326–34. doi:10.1056/NEJMsa1204629

5 Jin-Won N, Young Dae K, Jumin P, *et al.* Relationship between Physical Disability and Depression by Gender: A Panel Regression Model. *PloS One* 2016;**11**. doi:10.1371/journal.pone.0166238

6 Ge L, Yap CW, Ong R, *et al.* Social isolation, loneliness and their relationships with depressive symptoms: A population-based study. *PloS One* 2017;**12**:e0182145. doi:10.1371/journal.pone.0182145

7 Hare DL, Toukhsati SR, Johansson P, *et al.* Depression and cardiovascular disease: a clinical review. *Eur Heart J* 2014;**35**:1365–72. doi:10.1093/eurheartj/eht462

8 Baumgart M, Snyder HM, Carrillo MC, *et al.* Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimers Dement* 2015;**11**:718–26. doi:10.1016/j.jalz.2015.05.016

9 Lisko I, Kulmala J, Annetorp M, *et al.* How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med* 2021;**289**:807–30. doi:10.1111/joim.13227

10 Wiels W, Baeken C, Engelborghs S. Depressive Symptoms in the Elderly—An Early Symptom of Dementia? A Systematic Review. *Front Pharmacol* 2020;**11**:34. doi:10.3389/fphar.2020.00034

11 Cooper C, Sommerlad A, Lyketsos CG, *et al.* Modifiable predictors of dementia in mild cognitive impairment: a systematic review and meta-analysis. *Am J Psychiatry* 2015;**172**:323–34. doi:10.1176/appi.ajp.2014.14070878

12 Mourao RJ, Mansur G, Malloy-Diniz LF, *et al.* Depressive symptoms increase the risk of progression to dementia in subjects with mild cognitive impairment: systematic review and meta-analysis. *Int J Geriatr Psychiatry* 2016;**31**:905–11. doi:10.1002/gps.4406

13 Tan EYL, Köhler S, Hamel REG, *et al.* Depressive Symptoms in Mild Cognitive Impairment and the Risk of Dementia: A Systematic Review and Comparative Meta-Analysis of Clinical and Community-Based Studies. *J Alzheimers Dis* 2019;**67**:1319–29. doi:10.3233/JAD-180513

14 Xiang X, An R, Oh H. The Bidirectional Relationship Between Depressive Symptoms and Homebound Status Among Older Adults. *J Gerontol B Psychol Sci Soc Sci* 2020;**75**:357–66. doi:10.1093/geronb/gbx180

15 Ornstein KA, Leff B, Covinsky KE, *et al.* Epidemiology of the Homebound Population in the United States. *JAMA Intern Med* 2015;**175**:1180–6. doi:10.1001/jamainternmed.2015.1849

16 Xiang X, Brooks J. Correlates of Depressive Symptoms among Homebound and Semi-Homebound Older Adults. *J Gerontol Soc Work* 2017;**60**:201–14. doi:10.1080/01634372.2017.1286625

17 Richardson TM, Friedman B, Podgorski C, *et al.* Depression and its correlates among older adults accessing aging services. *Am J Geriatr Psychiatry* 2012;**20**:346–54. doi:10.1097/JGP.0b013e3182107e50

18 Negrón-Blanco L, de Pedro-Cuesta J, Almazán J, *et al.* Prevalence of and factors associated with homebound status among adults in urban and rural Spanish populations. *BMC Public Health* 2016;**16**:574. doi:10.1186/s12889-016-3270-z

19 Cohen-Mansfield J, Shmotkin D, Hazan H. Homebound older persons: prevalence, characteristics, and longitudinal predictors. *Arch Gerontol Geriatr* 2012;**54**:55–60. doi:10.1016/j.archger.2011.02.016

20 Qiu WQ, Dean M, Liu T, *et al.* Physical and mental health of homebound older adults: an overlooked population. *J Am Geriatr Soc* 2010;**58**:2423–8. doi:10.1111/j.1532-5415.2010.03161.x

21 Neviani F, Belvederi Murri M, Mussi C, *et al.* Physical exercise for late life depression: effects on cognition and disability. *Int Psychogeriatr* 2017;**29**:1105–12. doi:10.1017/S1041610217000576

22 US Preventive Services Task Force, Owens DK, Davidson KW, *et al.* Screening for Cognitive Impairment in Older Adults: US Preventive Services Task Force

Recommendation Statement. *JAMA* 2020;**323**:757–63. doi:10.1001/jama.2020.0435

[Dataset] 23 National Health and Aging Trends Study. Produced and distributed by www.nhats.org with funding from the National Institute on Aging (grant number U01AG32947).

24 Freedman VA, Kasper JD. Cohort Profile: The National Health and Aging Trends Study (NHATS). *Int J Epidemiol* 2019;**48**:1044–1045g. doi:10.1093/ije/dyz109

25 NHATS Data Collection Procedures Round 1.pdf. https://www.nhats.org/sites/default/files/2021-01/NHATS%20Data%20Collection%20Procedures%20Round%201_0.pdf (accessed 10 Sep 2022).

26 Kasper JD, Freedman VA, Spillman BC. Classification of persons by dementia status in the National Health and Aging Trends Study. 2013.https://www.nhats.org/sites/default/files/inline-files/DementiaTechnicalPaperJuly_2_4_2013_10_ 23_15.pdf (accessed 7 Mar 2021).

27 Galvin JE, Roe CM, Powlishta KK, *et al.* The AD8: a brief informant interview to detect dementia. *Neurology* 2005;**65**:559–64. doi:10.1212/01.wnl.0000172958.95282.2a

28 Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003;**41**:1284–92. doi:10.1097/01.MLR.0000093487.78664.3C

29 Li C, Friedman B, Conwell Y, *et al.* Validity of the Patient Health Questionnaire 2 (PHQ-2) in Identifying Major Depression in Older People: VALIDITY OF PHQ-2 IN DETECTING DEPRESSION. *J Am Geriatr Soc* 2007;**55**:596–602. doi:10.1111/j.1532-5415.2007.01103.x

30 Podcasy JL, Epperson CN. Considering sex and gender in Alzheimer disease and other dementias. *Dialogues Clin Neurosci* 2016;**18**. doi:10.31887/DCNS.2016.18.4/cepperson

31 Wilson RS, Capuano AW, Sampaio C, *et al.* The link between social and emotional isolation and dementia in older black and white Brazilians. *Int Psychogeriatr* 2021;:1–7. doi:10.1017/S1041610221000673

32 Song Y-N, Wang P, Xu W, *et al.* Risk Factors of Rapid Cognitive Decline in Alzheimer's Disease and Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. *J Alzheimers Dis* 2018;**66**:497–515. doi:10.3233/JAD-180476

33 Roystonn K, Abdin E, Shahwan S, *et al.* Living arrangements and cognitive abilities of community-dwelling older adults in Singapore. *Psychogeriatr Off J Jpn Psychogeriatr*

*Soc* 2020;**20**:625–35. doi:10.1111/psyg.12532

34 Karssemeijer EGA, Aaronson JA, Bossers WJ, *et al.* Positive effects of combined cognitive and physical exercise training on cognitive function in older adults with mild cognitive impairment or dementia: A meta-analysis. *Ageing Res Rev* 2017;**40**:75–83. doi:10.1016/j.arr.2017.09.003

35 Chen SP, Bhattacharya J, Pershing S. Association of Vision Loss With Cognition in Older Adults. *JAMA Ophthalmol* 2017;**135**:963–70. doi:10.1001/jamaophthalmol.2017.2838

36 Dawes P, Emsley R, Cruickshanks KJ, *et al.* Hearing Loss and Cognition: The Role of Hearing Aids, Social Isolation and Depression. *PLoS ONE* 2015;**10**. doi:10.1371/journal.pone.0119616

37 Wu X, Fan L, Ke S, *et al.* Longitudinal Associations of Stroke With Cognitive Impairment Among Older Adults in the United States: A Population-Based Study. *Front Public Health* 2021;**9**:637042. doi:10.3389/fpubh.2021.637042

38 Lindbergh CA, Dishman RK, Miller LS. Functional Disability in Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. *Neuropsychol Rev* 2016;**26**:129–59. doi:10.1007/s11065-016-9321-5

39 Li E, C L, K N, *et al.* Hospitalization, surgery, and incident dementia. *Alzheimers Dement J Alzheimers Assoc* 2019;**15**. doi:10.1016/j.jalz.2018.12.005

40 Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;**51**:1173–82. doi:10.1037//0022-3514.51.6.1173

41 Meng L-D, Liu Y-C, Feng X, *et al.* The mediating role of depression on the relationship between housebound status and cognitive function among the elderly in rural communities: A cross-sectional study. *Arch Gerontol Geriatr* 2018;**78**:58–63. doi:10.1016/j.archger.2018.05.019

42 Mickler AK, Leff B, Eaton England A, *et al.* Understanding the Daily Experiences and Perceptions of Homebound Older Adults and Their Caregivers: A Qualitative Study. *J Appl Gerontol* 2021;:733464821990171. doi:10.1177/0733464821990171

43 Ganguli M, Fox A, Gilby J, *et al.* Characteristics of rural homebound older adults: a community-based study. *J Am Geriatr Soc* 1996;**44**:363–70. doi:10.1111/j.1532-5415.1996.tb06403.x

44 Chen C-M, Liu L-F. The effect of disability and depression on cognitive function and

screening factors. *Arch Gerontol Geriatr* 2017;**73**:154–9. doi:10.1016/j.archger.2017.07.019

45 Chen C, Mullan J, Su Y, *et al.* The longitudinal relationship between depressive symptoms and disability for older adults: a population-based study. *J Gerontol A Biol Sci Med Sci* 2012;**67**:1059–67. doi:10.1093/gerona/gls074

46 De-Rosende Celeiro I, Santos-Del-Riego S, Muñiz García J. Homebound status among middle-aged and older adults with disabilities in ADLs and its associations with clinical, functional, and environmental factors. *Disabil Health J* 2017;**10**:145–51. doi:10.1016/j.dhjo.2016.06.006

47 Miller KJ, Gonçalves-Bradley DC, Areerob P, *et al.* Comparative effectiveness of three exercise types to treat clinical depression in older adults: A systematic review and network meta-analysis of randomised controlled trials. *Ageing Res Rev* 2020;**58**:100999. doi:10.1016/j.arr.2019.100999

48 Makizako H, Tsutsumimoto K, Doi T, *et al.* Exercise and Horticultural Programs for Older Adults with Depressive Symptoms and Memory Problems: A Randomized Controlled Trial. *J Clin Med* 2019;**9**:99. doi:10.3390/jcm9010099

49 Liu M, Xue Q-L, Gitlin LN, *et al.* Disability Prevention Program Improves Life-Space and Falls Efficacy: A Randomized Controlled Trial. *J Am Geriatr Soc* 2021;**69**:85–90. doi:10.1111/jgs.16808

50 Liu Z, Hsu F-C, Trombetti A, *et al.* Effect of 24-month physical activity on cognitive frailty and the role of inflammation: the LIFE randomized clinical trial. *BMC Med* 2018;**16**:185. doi:10.1186/s12916-018-1174-8

51 Centers for Medicare & Medicaid Services (CMS). Improve Home Health Services for Older Adults and People with Disabilities. 2021.https://www.cms.gov/newsroom/press-releases/cms-improve-home-health-services-older-adults-and-people-disabilities (accessed 17 Sep 2021).

52 Centers for Medicare & Medicaid Services (CMS). Medicare Benefit Policy Manual. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c07.pdf

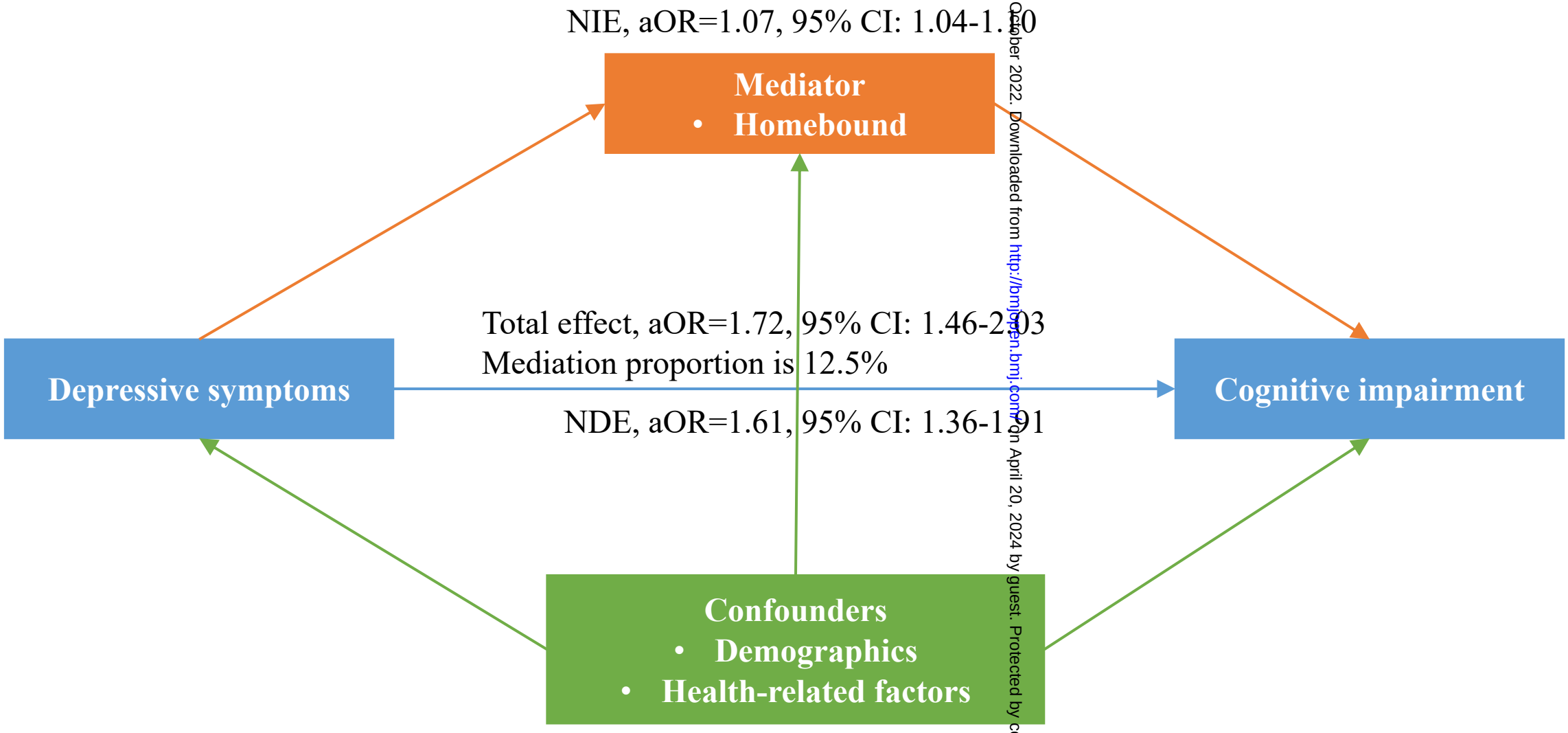
**Figure Legend**

**Figure 1.** Mediation model of homebound status between depressive symptoms and cognitive impairment.

Abbreviations: OR, odds ratio; NIE, natural indirect effect; NDE, natural direct effect.

The figure depicts that homebound status significantly mediated the relationship between depressive symptoms and cognitive impairment (NIE, aOR; 95% CI, 1.04, 1.10), with significant direct effect of depressive symptoms (NDE, aOR=1.61; 95% CI, 1.36, 1.91) and significant total effect (aOR,1.72; 95% CI, 1.46, 2.03) after adjusting for all covariates.

Figure 1. Mediation model of homebound status between depressive symptoms and cognitive impairment.




Abbreviations: OR, odds ratio; NIE, natural indirect effect; NDE, natural direct effect.

The figure depicts that homebound status significantly mediated the relationship between depressive symptoms and cognitive impairment (NIE, aOR; 95% CI, 1.04, 1.10), with significant direct effect of depressive symptoms (NDE, aOR=1.61; 95% CI, 1.36, 1.91) and significant total effect (aOR,1.72; 95% CI, 1.46, 2.03) after adjusting for all covariates.

# Supplement

Supplementary table 1. Characteristics distribution stratified by self-reported cognitive status, M ± SD, N (%)

Supplementary table 2. Results of logistic regression analysis of associations among depressive symptoms, homebound and cognitive impairment excluding proxy respondents (N=6,746-6,978)

Supplementary table 3. Mediation of homebound status in the association between depressive symptoms and cognitive impairment excluding proxy respondents (N=6,746-6,978)

**Supplementary table 1. Characteristics distribution stratified by self-reported cognitive status**

| Characteristics | Total (N=6,746-6,978) | Cognitive impairment (n=1,416-1,530) | Nocognitive impairment (n=5,330-5,448) | *P* values |
|---|---|---|---|---|
| Age, M ± SD | 77.2 ± 7.7 | 81.2 ± 7.7 | 76.1 ± 7.3 | <.001 |
| Sex, n (%) | | | | .800 |
| Female | 4051 (58.1) | 858 (56.1) | 3193 (58.6) | |
| Male | 2927 (41.9) | 672 (43.9) | 2255 (41.4) | |
| Race/ethnicity, n (%) | | | | <.001 |
| White, non-Hispanic | 4847 (69.5) | 878 (57.4) | 3969 (72.9) | |
| Black, non-Hispanic | 1483 (21.2) | 421 (27.5) | 1062 (19.5) | |
| Hispanic | 253 (3.6) | 84 (5.5) | 169 (3.1) | |
| Other | 395 (5.7) | 147 (9.6) | 248 (4.5) | |
| Education, n (%) | | | | <.001 |
| Less than high school | 1760 (25.5) | 686 (45.6) | 1074 (19.9) | |
| High school | 1905 (27.6) | 370 (24.6) | 1535 (28.4) | |
| Some college or vocational school | 1734 (25.1) | 255 (17.0) | 1479 (27.4) | |
| College or higher | 1509 (21.8) | 191 (12.7) | 1318 (24.3) | |
| Living arrangement, n (%) | | | | <.001 |
| Alone | 2315 (33.3) | 575 (37.8) | 1740 (32.1) | |
| With spouse/partner only | 2913 (41.9) | 447 (29.3) | 2466 (45.5) | |
| With others only | 1104 (15.9) | 359 (23.6) | 745 (13.7) | |
| With spouse/partner and with others | 615 (8.9) | 142 (9.3) | 473 (8.7) | |
| Smoking status, n (%) | | | | <.001 |
| No | 3382 (48.5) | 789 (51.7) | 2593 (47.6) | |
| Yes | 3591 (51.5) | 738 (48.3) | 2853 (52.4) | |
| Vigorous activity, n (%) | | | | <.001 |
| No | 4470 (64,1) | 1235 (80.8) | 3235 (59.4) | |
| Yes | 2507 (35.9) | 294 (19.2) | 2213 (40.6) | |
| BMI, n (%) | | | | <.001 |
| Normal (<30 kg/m$^2$) | 4881 (72.3) | 1115 (78.7) | 3766 (70.7) | |
| Obesity (≥30 kg/m$^2$) | 1865 (27.7) | 301 (21.3) | 1564 (29.3) | |
| Visual impairment, n (%) | | | | <.001 |
| No | 6347 (91.2) | 1281(83.9) | 5066 (93.2) | |
| Yes | 615 (8.8) | 246 (16.1) | 369 (6.8) | |
| Auditory impairment, n (%) | | | | <.001 |
| No | 5381 (77.1) | 1079 (70.5) | 4302 (79.0) | |
| Yes | 1597 (22.9) | 451 (29.5) | 1146 (21.0) | |
| Hypertension, n (%) | | | | .905 |
| No | 2306 (33.1) | 503 (33.0) | 1803 (33.1) | |
| Yes | 4663 (66.9) | 1023 (67.0) | 3640 (66.9) | |

| | | | | |
|---|---|---|---|---|
| Diabetes, n (%) | | | | <.001 |
| No | 5218 (74.8) | 1074 (70.3) | 4144 (76.1) | |
| Yes | 1757 (25.2) | 453 (29.7) | 1304 (23.9) | |
| Stroke, n (%) | | | | <.001 |
| No | 6246 (89.6) | 1289 (84.4) | 4957 (91.1) | |
| Yes | 726 (10.4) | 239 (15.6) | 487 (8.9) | |
| Number of ADL impairments, M ± SD | 1.2 ± 0.7 | 1.5 ± 1.0 | 1.2 ± 0.6 | <.001 |
| Hospitalization, n (%) | | | | <.001 |
| No | 5428 (77.9) | 1071 (71.2) | 4357 (80.0) | |
| Yes | 1542 (22.1) | 455 (29.8) | 1087 (20.0) | |
| Depressive symptoms, n (%) | | | | <.001 |
| No | 5974 (85.6) | 1177 (76.9) | 4797 (88.1) | |
| Yes | 1004 (14.4) | 353 (23.1) | 651 (11.9) | |
| Homebound, n (%) | | | | <.001 |
| No | 5509 (79.0) | 937 (61.2) | 4572 (83.9) | |
| Yes | 1469 (21.0) | 593 (38.8) | 876 (16.1) | |

Abbreviations: M, mean; SD, standard deviations; BMI, body mass index; ADL, activity of daily living.

**Supplementary table 2. Results of logistic regression analysis of associations among depressive symptoms, homebound and cognitive impairment excluding proxy respondents (N=6,746-6,978)**

| Independent variable(s) | Effect size for association, OR (95% CI)[b] | | | |
|---|---|---|---|---|
| | Dependent Variable | | | |
| | Model 1: Cognitive Impairment | Model 2: Homebound Status | Model 3: Cognitive Impairment | Model 4: Cognitive Impairment |
| Depressive symptoms | 1.52 (1.27-1.81) *** | 1.92 (1.59-2.33) *** | NA | 1.47 (1.23-1.75) *** |
| Homebound status | NA | NA | 1.51 (1.27-1.80) *** | 1.46 (1.23-1.75) *** |

Abbreviations: OR, odds ratio; NA, not applicable.

a * P <.05, ** P <.01, ***P<.001

b All models adjusted for demographics (age, sex, education, race/ethnicity, living arrangement) and health-related characteristics (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily living impairments, hospitalization).

**Supplementary table 3. Mediation of homebound status in the association between depressive symptoms and cognitive impairment excluding proxy respondents (N=6,746-6,978)**

| | Model 1[b] | Model 2[c] | Model 3[d] |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Natural direct effect | 1.71 (1.46-1.98) *** | 1.63 (1.39-1.93) *** | 1.47 (1.24-1.78) *** |
| Natural indirect effect | 1.36 (1.29-1.43) *** | 1.19 (1.14-1.24) *** | 1.05 (1.02-1.08) *** |
| Marginal total effect | 2.33 (2.00-2.71) *** | 1.95 (1.66-2.30) *** | 1.54 (1.30-1.86) *** |
| Proportion mediated[a] | 57.3% | 36.5% | 12.7% |

[a] Proportion meditated by homebound status were calculated as the log of the indirect effect divided by the log of the total effect.

[b] Model 1: independent variables of interest

[c] Model 2: Model 1+ demographic covariates (age, sex, education, race/ethnicity, living arrangement)

[d] Model 3: Model 2 + health-related covariates (smoke, body mass index, vigorous activity, visual impairment, auditory impairment, hypertension, diabetes, stroke, number of activities of daily life impairment, hospitalization)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | Page 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 2-3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Page 5-7 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | Page 7 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | Page 7 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Page 7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | Page 7 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Page 8-11 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Page 8-11 |
| Bias | 9 | Describe any efforts to address potential sources of bias | N/A |
| Study size | 10 | Explain how the study size was arrived at | Page 7 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Page 11-12 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Page 11-12 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | N/A |
| | | (*c*) Explain how missing data were addressed | Page 12 |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | N/A |
| | | (*e*) Describe any sensitivity analyses | Page 12 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | In Page 12 |
| | | (b) Give reasons for non-participation at each stage | N/A |
| | | (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Page 12-13 |
| | | (b) Indicate number of participants with missing data for each variable of interest | Page 7 |
| Outcome data | 15* | Report numbers of outcome events or summary measures | Page 12-13 |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Page 12-13 |
| | | (*b*) Report category boundaries when continuous variables were categorized | Page 12-16 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Page 16 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | Page 16-17 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Page 20 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Page 17-20 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Page 20 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Page 22 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.