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The association of comorbid depression and anxiety symptoms with disability onset in older adults

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Abstract

Objective: Despite the high prevalence of late-life depression and anxiety at threshold and subthreshold levels, their joint role in the disablement process remains unclear. This study aims to examine the association of comorbid occurring depression and anxiety across the full spectrum of symptom severity with disability onset in older adults.

Methods: The study included 3663 participants from the 2011 National Health and Aging Trends Study who reported no limitations in self-care and mobility activities at baseline. Disability onset was defined as a report of receiving help from another person in any of the activities for three consecutive months. Depression and anxiety symptoms were measured using the 4-item Patient Health Questionnaire, grouped into low, mild and moderate/severe symptom groups. Cox proportional hazards models were used to estimate relative risks for disability onset over a five-year period by depression/anxiety symptom groups.

Results: A total of 1047 participants developed disability (24.6%; 6.0 per 1000 person-months). At baseline, one-fifth of the sample reported mild ($n=579$, 16%; 31.6% with disability onset) or moderate/severe symptoms ($n=156$, 4%; 38.1% with disability onset). After adjustment for socio-demographics, there was a dose-response relationship between depression/anxiety symptom groups and disability onset (mild vs low: Hazard Ratio [HR]=1.43, 95% Confidence Interval [CI]=1.20–1.70; moderate/severe vs low: HR=1.94, 95% CI=1.45–2.59). The increased risk remained significant after adjustment for health status variables for the mild symptom group (HR=1.26, 95% CI=1.07–1.49), but not for the moderate/severe symptom group (HR=1.30, 95% CI=0.94–1.79), possibly reflecting lower statistical power.

Conclusions: Findings suggest that the full spectrum of depression and anxiety symptoms are associated with increased risk for disability in late life. Their role in the disablement process warrants further investigation.

Keywords

depression; anxiety; disability; aging; epidemiology

INTRODUCTION

Symptoms of depression and anxiety are common among older adults and often co-occur (1, 2). The prevalence of clinically significant depressive symptoms in late life range from 8–16% in community settings to 35% in long-term care settings (3), with subthreshold depression being two to three times more prevalent than major depression (4). Depression is highly comorbid with anxiety at threshold and subthreshold levels (5–8), and comorbid anxiety disorders are strongly associated with depression severity and persistence (9).

Depression is generally accepted as an important risk factor for late-life disability. However, the role for anxiety disorders and symptoms as an independent risk factor for disability among older adults is less clearly established (10). Evidence from longitudinal studies suggests that anxiety increases risks for limitations in subjective physical functioning, social participation, and activities of daily living (11–13). The prevalence of disability itself increases sharply at older ages; and late-life disability is associated with reduced quality of life, loss of independence, and greater personal care needs (14, 15).

Evidence from primary care settings suggests that the effects of comorbid depression and anxiety on functional limitations exceed their independent contributions (16). However, the degree to which this finding pertains to the full spectrum of severity of these symptoms, including subthreshold levels, is presently unknown. Depression or anxiety symptoms at subthreshold levels are also disabling and predictive of disability onset (17, 18), but existing studies of the joint influence of these symptoms on disability are mainly cross-sectional with mixed findings (7, 19–22). Therefore, the objective of this study is to examine the association of comorbid depression and anxiety symptoms with disability onset in older adults across the full spectrum of severity of these symptoms.

METHODS

Study participants

Data were obtained from the National Health and Aging Trends Study (NHATS), which is a nationally representative longitudinal study designed to study trends and trajectories of late-life disability. Annual interviews were conducted among Medicare beneficiaries aged 65 and over in the United States. The first cohort of 8,245 participants was enrolled in 2011, with oversampling of older adults. More details of the study have been described elsewhere (23).

The present study uses the 2011 NHATS interview as baseline. Of the 8,245 participants, 7,609 non-nursing home participants completed the baseline interview. Of these, an additional 3,225 were excluded due to either receiving personal assistance with self-care or mobility activities at baseline ($n=1,717$), reporting an activity reduction or difficulty in performing ADLs ($n=1,506$) or having missing values on the disability classification ($n=2$), leaving a sample of 4,384 participants. An additional 721 participants were excluded due to having neither in-person nor proxy interviews at the first follow-up interview ($n=719$) or lacking data on disability measures during the follow-up visits ($n=2$), leaving a final analytical sample of 3,663 participants who were followed-up over a 5-year study period.

Measures

Disability onset—The outcome measure was time from age 65 to first onset of disability, which was a continuous time-to-event variable. Disability was defined as receiving help from others in performing self-care (eating, dressing, bathing and toileting) or mobility (getting out of bed, getting around inside and going outside) activities for at least three months. The outcome was created from information provided at each interview about help received during the past 12 months or since the last interview. If participants started receiving help during the past year, they were asked to indicate the month the help was first received, and if they were no longer receiving the help at the time of the interview, they were asked to report the month help ended. Participants who did not have any disability onset lasting at least 3 months were censored at the fifth follow-up interview. Participants who were lost to follow up were censored at the time of last known contact, and those who died before disability onset at the time of the proxy interview for deceased participants.

Depression and anxiety symptoms at baseline—Depression and anxiety symptoms at baseline were assessed using the Patient Health Questionnaire for Depression and Anxiety (PHQ-4) (24). The PHQ-4 has been shown to have excellent factorial and criterion validity, and to have concurrent correlations with several important health and quality of life outcomes that were stronger than either symptom scale on its own (24, 25). The PHQ-4 is composed of a depression subscale from the 2-item Patient Health Questionnaire (PHQ-2) (26), and an anxiety subscale from the 2-item Generalized Anxiety Disorder scale (GAD-2). Participants are asked “over the last month, how often have you (a) had little interest or pleasure in doing things; (b) felt down, depressed, or hopeless; (c) felt nervous, anxious, or on edge; (d) been unable to stop or control worrying” (24). Each item is scored on a four-point scale from “not at all” (0), “several days” (1), “more than half the days” (2) to “nearly every day” (3). Each subscale ranges from 0 to 6, and the total score of the four items ranges from 0 to 12.

We used the previously established criteria to categorize participants based on symptom severity (24, 26–28). The PHQ-4 severity groups are low (0–2), mild (3–5), moderate (6–8), and severe symptom groups (9–12). We combined the moderate group with the severe group due to the small number of participants in these two categories. The subscale severity groups are no symptom (0), subthreshold symptoms (1–2) and threshold symptoms (≥ 3) for the PHQ-2 and GAD-2, respectively.

Covariates—Covariates included in the analysis were sociodemographic characteristics and health factors at baseline.

Sociodemographic characteristics were age, sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), educational attainment (below high school, high school, above high school but no bachelor’s degree, at least bachelor’s degree) and annual total income. Participants’ incomes were classified by weighted quartiles of total income at baseline.

Health factors at baseline included number of medical conditions (none or one, two, three, at least four), cognitive impairment (no dementia, possible dementia, probable dementia) and

physical capacity (low, medium, high). Medical conditions included self-reported history of heart disease, hypertension, arthritis, osteoporosis, diabetes, lung disease, stroke and cancer. Cognitive function was assessed using a battery of cognitive tests for non-proxy participants (memory, orientation and executive function), and the AD8 Dementia Screening Interview for proxy informants. The three-category dementia classification was generated using a previously described approach (29).

Physical capacity was assessed using six pairs of activities at two difficulty levels, including walking 6 blocks or 3 blocks, walking up 20 stairs or 10 stairs, lifting and carrying 20 pounds or 10 pounds, kneeling down or bending over (without holding on to anyone or anything), putting a heavy object on a shelf overhead or reaching up over head, and opening a sealed jar using hands only or grasping small objects (30). For each pair, a participant received 2 points for reporting being able to do the more challenging task, 1 point for the less challenging task, and 0 points for neither. The total score ranges from 0–12, with higher scores representing better physical capacity. We generated a four-category variable for physical capacity based on the distribution of the total scores in the study sample: full capacity (12), slightly reduced (11), moderately reduced (9–10) or severely reduced (0–8).

Statistical analysis

We examined baseline sample characteristics by PHQ-4 severity group and by sex, and compared the study sample with those who did not have follow-up interviews after baseline. We then examined the distribution of threshold-level depression and anxiety by PHQ-4 severity group.

We used age as the time scale, with age 65 being the time origin (31); and accommodated left truncation (entering the study after age 65) by the modeling strategy (31). We examined survival functions by PHQ-4 severity group using Kaplan-Meier estimates, tested the equality of the survival functions using the Cox regression-based test, and evaluated dose-response relationship across the PHQ-4 severity groups using the log-rank test. We then computed the overall and group-specific incidence rates.

We used Cox proportional hazards models to examine the association of the PHQ-4 composite measure with disability onset. The models estimated relative risks for disability onset using hazard ratios (HR) and 95% confidence intervals (CI), with the low symptom group serving as the reference category. To disentangle the effects of potential confounders, we fit three models with sequential adjustment for covariates. Model 1 adjusted for socio-demographic characteristics (sex, race/ethnicity, education and annual total income). Model 2 additionally adjusted for dementia classification and number of medical conditions at baseline. Model 3 adjusted for Model 2 covariates and baseline physical capacity. The proportional hazard assumption was tested based on the Schoenfeld residuals for each model (32). Variables violating the assumption were specified as strata variables, and stratified estimates were calculated. We then repeated the analysis for the PHQ-2 and GAD-2 subscales. In secondary analysis, we stratified by sex to explore potential sex differences in the associations.

We conducted two sensitivity analyses. In the first, we explored the influence of physical capacity on the overall pattern of findings by re-testing the primary associations among participants who reported being at (almost) full capacity. This was done after restricting the sample to participants with capacity scores ≥ 11 at baseline. In the second, we explored the influence of disability definition by re-testing the primary associations using a different definition of disability onset; i.e., a first report of disability that lasted for at least one month instead of three months.

The analyses were conducted using statistical software Stata, version 14.2 (Stata Corp, College Station, TX), accounting for the complex survey design of the NHATS. All significance tests were evaluated at the level of 0.05.

RESULTS

Among older adults without activity limitations represented in this study ($n=3,663$), approximately three fifths were between ages 65 and 74, half were female, over four-fifths were non-Hispanic white, over half had educational attainment above high school, and about half had full physical capacity (Table 1). At baseline, 80.9% ($n=2,928$) were in the low symptom group, 14.9% ($n=579$) were in the mild symptom group, and 4.2% ($n=156$) were in the moderate/severe symptom group (see top Table 1; percentages reported are weighted). Approximately half of the moderate/severe symptom group had both depression and anxiety, while half of the mild symptom group had neither depression nor anxiety (Figure 1). Compared to participants in the low symptom group, those in the mild or moderate/severe symptom groups were more likely to be female, had lower education and income, and had poorer health in terms of dementia classification, number of medical conditions and physical capacity. Participants who were lost to follow-up after the baseline interview did not differ from the study sample in terms of baseline depression, anxiety and PHQ-4 symptom severity. Despite the equal distribution of sex in the study sample, women had more subthreshold- and threshold-level symptoms of depression and anxiety and greater impairment in physical capacity compared to men (Table S1, Supplemental Digital Content).

There was substantial overlap in depression and anxiety symptoms. These symptoms were highly comorbid, with 71% in the mild group and 97% of the moderate/severe group reporting both depression and anxiety symptoms. At threshold levels, 28.1% of the participants with depression met screening criteria for anxiety, and 34.1% of those with anxiety met screening criteria for depression.

A total of 1047 participants developed disability during the 5-year follow-up period, with a weighted percentage of 24.6% in the full sample, 22.6% in the low symptom group, 31.6% in the mild symptom group, and 38.1% in the moderate/severe symptom group. The overall incidence rate was 6.0 per 1000 person-months (95% CI=5.6–6.5). The incidence rate clearly increased as a function of the severity of comorbid depression and anxiety symptoms, from 5.4 per 1000 person-months (95% CI=5.0–5.9) in the low symptom group, to 8.4 per 1000 person-months (95% CI=7.1–9.8) in the mild symptom group, to 10.8 per 1000 person-months (95% CI=8.1–14.4) in the moderate/severe symptom group. Cumulative survival without disability by the PHQ-4 severity groups are presented in Figure

2, and the test for trend indicated statistically significant dose-response relationship across groups ($P<0.001$).

The proportional hazard assumption was met for all variables except number of medical conditions, therefore estimates from stratified models were reported. Mild and moderate/severe symptom groups on the composite scale and subthreshold and threshold symptom groups were associated with increased risk for disability after adjustment for sociodemographic characteristics, dementia classification and medical conditions (Table 2). After additional adjustment for physical capacity, the associations were attenuated to non-significant level for the moderate/severe symptom group and threshold symptom group of the anxiety subscale.

In the secondary analysis stratifying by sex, women showed a similar pattern of associations as the total sample, with the exception that the association for the mild symptom group was no longer statistically significant in the final model after adjustment for physical capacity (Table S2, Supplemental Digital Content). The overall pattern of associations was considerably weaker in men, for whom only the association for the mild symptom group remained statistically significant in the final model (Table S2).

In the first sensitivity analysis, the overall pattern of results for the composite PHQ-4 scale was very similar as in the primary analysis. The smaller sample size in this analysis reduced statistical precision and 95% confidence intervals became wider, resulting in a borderline-significant association for the moderate/severe group (Table S3 Supplemental Digital Content). In the second sensitivity analysis, the alternative definition of disability onset produced consistent but generally weaker associations relative to the primary analysis (Table S4, Supplemental Digital Content).

DISCUSSION

This study examined the association of depression and anxiety symptoms with disability onset among adults aged 65 and older, using data from a nationally representative sample of Medicare beneficiaries in the US. We found that depression and anxiety symptoms were highly comorbid across the full spectrum of severity; and even mild symptoms on the composite scale and subthreshold symptoms on the subscales were associated with increased risk for disability onset, after adjustment for socio-demographic characteristics and several key health-related conditions. Notably, approximately half of the participants with mild symptom severity as measured by the PHQ-4 composite scale did not meet the threshold for depression and anxiety on the subscales, and would have been missed with screening measures that provide separate classifications of depression and anxiety.

Our results suggest that close to one in five older adults report symptoms of depression or anxiety across the full spectrum of severity. Moreover, the comorbid presentation of these symptoms is very common, in over 70% when they are reported at mild or sub-threshold levels, and in nearly all older adults at moderate to high levels of symptom severity. The key finding of this study is that the joint occurrence of these symptoms at milder and more severe levels is not only common in older adults, but also appears to be an independent risk

factor for the development of disability in this age group. There was a dose-response relationship between depression-anxiety symptoms and disability onset after adjustment for sociodemographic characteristics, with more severe symptoms associated with greater risk for disability. Sequential adjustments for health status variables attenuated the association and also reduced the dose-response gradient, suggesting stronger confounding due to poor health status among those with moderate/severe symptom levels. Taken together, combinations of depression and anxiety symptoms such as feeling depressed or agitated may contribute to impairments in role performance and interfere with self-care and mobility activities, even at milder levels of severity when they might not meet threshold criteria for clinical disorder (5, 33). Moreover, these symptoms may interact with each other when they occur jointly and become more severe and disabling overtime (34).

There are several other explanations for an association between co-morbid symptoms of depression and anxiety and disability onset. For example, these symptoms are common in patients with age-related chronic conditions such as coronary heart disease, stroke, diabetes, and dementia (35, 36). These chronic conditions tend to be primary drivers of disability in late life, and thus may account for the observed association between these symptoms and disability onset in this study. Statistical adjustment for these conditions reduced but did not eliminate the association, suggesting that these symptoms may have a residual independent effect on disability. These symptoms may also serve as a marker of the clinical severity of the underlying medical conditions that lead to subsequent functional limitations and disability (37). We are unable to exclude this possibility due to lack of detailed clinical data on disease severity in this study.

A second possibility is that these symptoms increase risk for the development of age-related chronic conditions. For example, depression is considered a risk factor for cardiovascular conditions and diabetes (38, 39), and are common prior to and in milder stages of cognitive impairment and dementia (5, 40). In other words, symptoms of depression and anxiety may have contributed to the development of disabling medical conditions during follow-up, and statistical control for these conditions may therefore have amounted to over-adjustment for potential mediators. Although we cannot entirely exclude this possibility, we are not able to distinguish between these symptoms contributing to the underlying chronic disease process itself, or merely being a manifestation of the prodromal phase of these conditions (36).

A third possibility is that these symptoms emerge as a consequence of impairments in physical capacity. Such impairments may be the result of multiple co-morbid chronic medical conditions that affect adults as they age and may cause symptoms of depression or anxiety in their own right (41). They typically precede the onset of overt disability, and are considered an earlier stage in the disablement process (30). Like medical conditions, however, impairments in physical capacity may act as a potential confounder in the association of depression and anxiety symptoms with disability onset, and also as a mediator in this relationship. To gain further insight in these mechanisms, we adjusted for physical capacity in a separate step in the statistical analysis and conducted a sensitivity analysis after restricting the sample to those who reported being at (almost) full capacity. Overall, our results suggest that both mechanisms could be relevant to understanding the role of symptoms of depression and anxiety in disability onset. Adjustment for physical capacity

resulted in somewhat attenuated associations between these symptoms and disability onset, especially for the group of moderate/severe symptoms levels. At the same time, our findings indicate that depression and anxiety symptoms were predictive of disability onset even in the absence of impairments in physical capacity at baseline, although this relationship did not reach statistical significance for the moderate/severe symptom group. Taken together, the findings suggest that a composite measure like the PHQ-4 may have utility in identifying patients at risk for disability in the early stage of the disablement process.

Results of the sex-stratified analyses did not produce clear evidence for potential sex differences in the association of depression and anxiety symptoms with disability onset. Although the overall pattern of associations was reasonably similar to those in the main analysis, the risk estimate with moderate/severe symptom levels was noticeably higher among women. The other deviation from the overall pattern was the risk estimate for the moderate/severe group among men, which was lower than in the main analysis and in the analysis for women. This finding, however, may have been due in part to the small size of this group. In other words, our data suggest that these symptoms, especially at moderate to high levels, may be more disabling for women than for men, but this potential sex difference needs further clarification in future studies.

The study has several limitations. First, the PHQ-4 is not a diagnostic instrument for psychiatric disorders but an ultra-brief screening tool that is easy to administer. Despite its satisfactory psychometric properties and practical utility in primary care settings, measurement errors and misclassifications may still exist, especially for older adults whose symptom manifestations may differ from that in the general adult population (42). Future studies should seek to replicate the findings using diagnostic examinations for depression and anxiety. Second, the measure of disability onset was based on self-reported receipt of help, which may be subject to recall bias, especially for older adults with cognitive impairment. However, such biases are unlikely to have a substantial impact on the findings, because only a modest proportion of participants were classified as having possible or probable dementia at baseline. Third, because death is a potential competing risk for disability onset, estimates of disability onset may be biased; however, competing risks are unlikely to have a substantial influence on the analysis because disability was reported before death in most cases (43). Forth, our measure of medical conditions reflected overall disease burden rather than specific health consequences of certain diseases, such as pain and inflammation, which may have resulted in residual confounding. Fifth, the small sample size of the moderate/severe symptom groups may have limited the power to reach statistical significance in the stratified and subgroup analyses. Sixth, we did not explore whether disability onset captured during the study period was incident or recurrent.

CONCLUSIONS

The study highlights the importance of assessing depression and anxiety symptoms across the full spectrum of severity to identify older adults at increased risk of developing disability and to prolong their independence. Depression and anxiety symptoms appear to contribute jointly to the development of disability and their interactive effects warrant further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest and Source of Funding

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Acronyms:

ADL	activities of daily living
CI	Confidence Interval
GAD	Generalized Anxiety Disorder scale
HR	Hazard Ratio
NHATS	National Health and Aging Trends Study
PHQ	Patient Health Questionnaire

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Figure 1.

Distribution of depression and anxiety by PHQ-4 severity group, the National Health and Aging Trends Study, 2011–2016

Note: PHQ-4, the Patient Health Questionnaire for Depression and Anxiety.

Figure 2.
Cumulative survival without disability by PHQ-4 severity group, the National Health and Aging Trends Study, 2011–2016
Notes: PHQ-4, the Patient Health Questionnaire for Depression and Anxiety. Disability onset was defined as first-reported receipt of help for three months or more.

Table 1.

Sample characteristics at baseline, the National Health and Aging Trends Study, 2011–2016

Variables, n (weighted %)	Comorbid depression and anxiety symptoms by PHQ-4			
	Total (n=3663)	Low (n=2928)	Mild (n=579)	Moderate/Severe (n=156)
Age (years)				
65–69	808 (31.9)	647 (32.2)	120 (29.5)	41 (34.6)
70–74	877 (27.3)	710 (27.6)	130 (25.8)	37 (26.6)
75–79	792 (19.6)	633 (19.5)	127 (20.7)	32 (18.3)
80–84	676 (12.9)	532 (12.6)	113 (14.2)	31 (14.8)
85+	510 (8.3)	406 (8.2)	89 (9.8)	15 (5.8)
Female sex	1943 (52.4)	1483 (50.1)	360 (61.7)	100 (62.9)
Race/ethnicity				
Non-Hispanic white	2675 (83.8)	2171 (84.7)	398 (80.0)	106 (80.2)
Non-Hispanic black	693 (6.8)	533 (6.4)	123 (8.5)	37 (9.1)
Hispanic	159 (5.1)	122 (4.9)	28 (5.7)	9 (7.4)
Others	136 (4.3)	102 (4.1)	30 (5.8)	4 (3.3)
Education				
Below high school	765 (16.7)	548 (15.0)	166 (22.1)	51 (29.1)
High school	1016 (27.2)	782 (25.9)	183 (31.7)	51 (34.8)
Above high school	910 (26.1)	737 (26.1)	135 (26.7)	38 (25.3)
Bachelor and above	972 (30.1)	861 (33.0)	95 (19.5)	16 (10.9)
Total income				
<1 st quartile	873 (19.6)	612 (17.1)	205 (30.8)	56 (29.0)
1 st -2 nd quartiles	909 (22.8)	702 (21.5)	153 (26.1)	54 (35.6)
2 nd -3 rd quartiles	1016 (28.7)	860 (30.3)	123 (21.9)	33 (23.8)
> 3 rd quartile	865 (28.9)	754 (31.1)	98 (21.3)	13 (11.6)
Dementia classification				
Normal	3112 (88.1)	2526 (89.3)	465 (83.5)	121 (80.9)
Possible dementia	370 (8.1)	278 (7.5)	73 (11.0)	19 (9.7)
Probable dementia	181 (3.8)	124 (3.2)	41 (5.4)	16 (9.4)
Number of medical conditions				
0–1	1269 (37.0)	1070 (39.1)	165 (29.9)	34 (22.1)
2	1023 (27.6)	849 (28.6)	132 (22.1)	42 (27.2)
3	831 (21.5)	628 (20.2)	158 (26.7)	45 (28.4)
4+	540 (13.9)	381 (12.1)	124 (21.3)	35 (22.4)
Physical capacity				
Full capacity (12)	1588 (48.1)	1364 (51.5)	195 (37.0)	29 (22.0)
Slightly reduced (11)	838 (22.8)	691 (23.3)	111 (19.6)	36 (23.7)
Moderately reduced (9–10)	625 (16.1)	460 (14.6)	132 (22.7)	33 (20.9)
Severely reduced (0–8)	612 (13.0)	413 (10.6)	141 (20.7)	58 (33.4)
Depression (PHQ-2)				

Variables, n (weighted %)	Comorbid depression and anxiety symptoms by PHQ-4			
	Total (n=3663)	Low (n=2928)	Mild (n=579)	Moderate/Severe (n=156)
No (0)	2433 (67.9)	2372 (81.9)	59 (10.6)	2 (1.3)
Subthreshold (1–2)	926 (24.4)	556 (18.1)	331 (58.2)	39 (25.6)
Threshold (≥ 3)	304 (7.7)	0 (0.0)	189 (31.2)	115 (73.1)
Anxiety (GAD-2)				
No (0)	2395 (65.2)	2283 (77.3)	109 (17.6)	3 (1.8)
Subthreshold (1–2)	1026 (28.4)	645 (22.7)	350 (61.9)	31 (19.7)
Threshold (≥ 3)	242 (6.4)	0 (0.0)	120 (20.5)	122 (78.5)

Notes: GAD, the Generalized Anxiety Disorder scale; PHQ-4, the Patient Health Questionnaire for Depression and Anxiety

Results from Cox proportional hazard models of the association of depression and anxiety symptoms with disability onset, the National Health and Aging Trends Study, 2011–2016

Table 2.

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Composite scale (PHQ-4)			
Low (0–2)	Reference	Reference	Reference
Mild (3–5)	1.43 (1.20, 1.70)**	1.33 (1.12, 1.57)**	1.26 (1.07, 1.49)**
Moderate/Severe (6–12)	1.94 (1.45, 2.59)**	1.59 (1.18, 2.14)**	1.30 (0.94, 1.79)
Depression subscale (PHQ-2)			
No (0)	Reference	Reference	Reference
Subthreshold (1–2)	1.46 (1.23, 1.73)**	1.34 (1.12, 1.60)**	1.27 (1.07, 1.51)**
Threshold (3)	1.62 (1.33, 1.97)**	1.45 (1.22, 1.73)**	1.28 (1.07, 1.53)**
Anxiety subscale (GAD-2)			
No (0)	Reference	Reference	Reference
Subthreshold (1–2)	1.43 (1.20, 1.70)**	1.35 (1.13, 1.61)**	1.34 (1.12, 1.59)**
Threshold (3)	1.64 (1.22, 2.19)**	1.37 (1.01, 1.85)*	1.18 (0.89, 1.57)

Notes: CI, confidence interval; GAD, the Generalized Anxiety Disorder scale; HR, hazard ratio; PHQ, the Patient Health Questionnaire. Disability onset was defined as first report disability that lasted for three consecutive months or more. The sample size was 3659 for all models. Model 1 adjusted for sex, race/ethnicity, education and annual total income. Model 2 adjusted for Model 1 covariates, dementia classification and number of medical conditions at baseline. Model 3 adjusted for Model 2 covariates and physical capacity. Results were stratified by number of medical conditions, to account for the violation of the proportional hazard assumption.

* $P < 0.05$;

** $P < 0.01$;

† $P < 0.1$