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Impact of Persistent Pain on Function, Cognition, and Well-being of Older Adults

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Abstract

Background: We sought to determine the population-level associations between persistent pain and subsequent changes in physical function, cognitive function, and well-being, outcomes important to older adults.

Methods: We used data from National Health Aging Trends Study (NHATS) of community-dwelling Medicare beneficiaries age 65+ from 2011–2019. We defined “persistent pain” as being bothered by pain in the last month in both the 2011 and 2012 interviews and “intermittent” pain including those reporting bothersome pain in one interview only. We used competing risks regression to estimate the association between persistent pain and the development of clinically meaningful declines in physical function, cognitive function, and well-being, adjusting for age, sex, race, education, and marital status at baseline.

Results: Of the 5,589 eligible NHATS participants, 38.7% reported persistent pain and 27.8% reported intermittent pain. Over one-third described pain in five or more sites. Over the subsequent 7 years, participants with persistent pain were more likely to experience declines in physical function (64% persistent pain, 59% intermittent pain, 57% no bothersome pain; aHR 1.14, 95% CI 1.05–1.23) and well-being (48% persistent pain, 45% intermittent pain, 44% no bothersome pain; aHR 1.11, 95% CI 1.01–1.21), but were not more likely to experience cognitive decline (25% persistent pain, 24% intermittent pain, 23% no bothersome pain; aHR 1.02, 95% CI 0.90–1.16).

Conclusions: Persistent pain is common in older adults and occurs in multiple body sites. Persistent pain contributes to meaningful declines in physical function and well-being over 7 years and warrants proactive interventions to mitigate pain.

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Author Contributions: K. Patel and J Boscardin had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: C.S. Ritchie

Critical revision of the manuscript for important intellectual content: All authors.

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Keywords

persistent pain; chronic pain; physical function; well-being; aging

Background:

Chronic pain, defined as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” and lasting over 3–6 months, is common in older adults.¹ Surveys in the United States (US) and elsewhere report rates of between 34%–39% among those ≥65 years of age.^{2–4} This percentage is expected to increase given the growth of the older adult population and associated increase in multimorbidity in these individuals.^{5,6}

Despite its high prevalence, we are only beginning to appreciate the complexity of chronic pain in older adults. As older adults accumulate more chronic conditions and life experiences, they also are more likely to develop chronic pain related to more than one comorbid condition, often in multiple locations in the body.^{7,8} Unlike younger populations, older adults also are more likely to have more than one type of chronic pain. The BioPsychoSocial (BPS) model is a widely accepted and holistic model for the study of chronic pain; it highlights the dynamic relationships among a variety of biological, psychological, and social factors that can modulate a person’s experience of chronic pain.⁹ Relevant BPS factors are becoming elucidated as important in the development of chronic pain in older adults in specific pain populations such as those with musculoskeletal pain; however, we still know very little about pain in nationally representative samples of older adults.

We also do not have a clear picture about the longitudinal impact of chronic pain in older adults on person-centered outcomes such as physical function, cognition, and overall patient well-being. These outcomes are particularly important in older adults because studies suggest that outcomes related to physical and cognitive function and well-being may be even more important than survival in most older adults.¹⁰ Studies to date of the relationship between chronic pain and person-centered outcomes in older adults are limited to regional samples of older adults in community settings, primary care, or tertiary pain clinics or to populations at the end of life.¹¹ These studies show that the relationship between chronic pain and physical and cognitive decline may be bidirectional among older adults. Pain can be exacerbated by exercise or routine life activities. For many older adults, elicitation of pain contributes to fear of any activities potentially contributing to pain and avoidance of those activities altogether.¹² The coupling of pain and activity avoidance in specific pain syndromes has been shown to accelerate functional decline.¹³ Likewise, neural systems involved in memory and cognition are closely linked to those involved in pain processing and thus these systems may affect one another reciprocally,¹⁴ disrupting cognitive processing and contributing to a downward spiral of continuing pain, adverse neurostructural changes, and deteriorating cognitive function. Consequently, older adults with chronic pain and cognitive decline can become caught in a “disability spiral” whereby cognitive function, physical function and wellbeing worsen over time.¹⁵ These

particular relationships need to be studied longitudinally and in a representative older adult population, to guide treatment priorities and research.

No nationally representative studies of older adults assess chronic pain and its longitudinal impact. NHATS does not assess chronic pain in the previous 3 months but does allow for investigation of pain spanning 12 months, which is a likely indicator of chronic pain and which we call “persistent pain.” Using eight years of data from the National Health and Aging Trends Study (NHATS), a population-based study of United States older adults, we sought to characterize persistent pain as an indicator of chronic pain among older adults and assess its impact on associations between persistent pain and physical function, cognition, and well-being.

Methods:

Design

We used longitudinal data from the NHATS, a nationally representative survey of community-dwelling Medicare beneficiaries age 65+ from 2011–2019. NHATS is sponsored by the National Institute on Aging (grant number NIA U01AG32947) and conducts annual in-home interviews.¹⁶ Response rates ranged from 71% in 2011 to 91% in subsequent interviews.¹⁷

Participants: Our sample included all participants enrolled in 2011 and 2012 who responded to the question about bothersome pain in both the 2011 and 2012 interviews. In the 2011 cohort, 7609 community-dwelling older adults completed interviews. Of these 7609, 6559 participants completed interviews in both 2011 and 2012. After excluding proxy respondents (n=964) and 6 participants with missing data, 5589 participants assessed the bothersome pain questions in both rounds.

Exposure

Persistent Pain—NHATS does not query about the presence of chronic pain directly. Rather, at each interview, participants are asked the following pain-related question: “In the last month, have you been bothered by pain?”. Based on responses to this question, we grouped participants into 3 groups: those who answered no to the presence of bothersome pain in both rounds (no bothersome pain); those who answered no in one interview round (intermittent pain), and those who answered yes in both rounds (persistent pain). NHATS also asks “in the last month, [whether] pain ever limited [participants] activities, “how often [participants] take medication for pain (Response choices: every day, most days, some days, rarely or never), and location of pain.

Comparison

NHATS participants with no bothersome pain in the last month in both rounds served as the comparison group; the second comparison group was comprised of those with what we call intermittent pain (those with bothersome pain in the previous month in one interview round only).

Outcome Measures

Function, Cognition, and Well-being

Physical function: The Gill score includes four self-care activities (eating, getting cleaned up, using the toilet, and dressing) and three mobility activities (going outside, getting around inside, and getting out of bed) and creates hierarchical categories for each activity: fully able (no device use, reduction in activities, difficulty, or assistance); accommodations (device use but no reduction in activities, difficulty, or assistance); reduced activities (reductions in activities but no difficulty or assistance); difficulty (difficulty performing activities by oneself, when using devices, if needed, but no assistance); and assistance (help from another person or, rarely, not doing the particular activity).^{18,19} Using the NHATS, Gill et al showed the version that defined vulnerability on the basis of accommodations, reduced activities, or difficulty, had a more consistent mortality gradient compared to alternative formulations. The Gill function score demonstrates strong predictive validity for mortality and related changes in physical performance, with a 2-point change in the Gill function score being considered clinically meaningful.¹⁸ A 2-point decrease represents a transition from being vulnerable to requiring assistance (disabled) in a single activity, or from being fully able to vulnerable with respect to any two activities. We reversed the direction of the total score such that a lower score indicated worse function (range 7–28, higher scores indicate better function).

Cognitive function: NHATS classifies participants' cognitive function into one of three groups—no dementia, probable dementia, or possible dementia. This classification was established using an algorithm that designates probable dementia based on a NHATS participant or a proxy respondent reporting that: 1) a doctor told the participant that s/he had dementia or Alzheimer's disease; 2) via proxy respondents reporting answers to the AD8 that met criteria for probable dementia (a score of >2) or 3) through participants who had NHATS cognitive test information where impairment (defined as scores at or below 1.5 standard deviation (SD) from the mean for self-respondents) on 2 of 3 cognitive domains on the self-reported cognitive tests (memory, orientation, executive functioning) were used. Participants were considered to have possible dementia if a self-respondent's NHATS cognitive test information demonstrated scores below 1.5 SD of the mean in only 1 domain.²⁰ We defined cognitive decline as participants with no dementia developing probable dementia or possible dementia or those participants with possible dementia developing probable dementia during the follow-up period. We excluded participants who had probable dementia at baseline (from Table 1, n=470) for the cognition outcome.

Well-being: NHATS includes four items reflecting positive and negative emotions (frequency of feeling cheerful, bored, full of life, or upset in the last month on a five-point Likert scale) and three items reflecting self-realization (extent of disagreement with statements about purpose in life, self-acceptance, and environmental mastery on a 3-point Likert scale). These items have been assessed psychometrically and used in other studies to capture well-being.^{19,21} Negative items were reverse coded and ratings on the individual items were summed to create a total well-being score, ranging from 0 to 22 (Cronbach's alpha = 0.74), with a higher score indicating better well-being. Decline in well-being was defined as a decrease of > 2 points over the 7-year follow-up period. A difference of two

points represents approximately 0.63 the standard deviation of the well-being measure and is commonly considered a medium to large effect size.

Other covariates

Other covariates included: age, gender, participant-reported race and ethnicity according to investigator-defined categories, education, income, marital status, living status (live alone vs with spouse/partner or others), country of origin (born in or outside of the United States), social network (no one to talk to vs 1+ people in social network), presence and number of comorbid conditions (no comorbidity vs. 1–2 comorbidities vs. 3 comorbidities) from the following list of comorbid conditions: heart attack, heart disease, osteoporosis, diabetes, lung disease, stroke and cancer and the presence of depression or anxiety. We did not include arthritis as a comorbidity because of its high correlation with persistent pain (Table 2). Race and ethnicity were included in modeling to serve as a proxy for a complex set of social risk factors, which were hypothesized to influence pain experience and treatment.

Pain characteristics

Among the three pain groups, we characterized whether the participant reported activity limitation due to pain; the number and location of pain sites; whether the participants reported taking pain medications every day (7 days a week), most days (5–6 days a week), some days (2–4 days a week), rarely (Once a week or less), or never; and whether participants reported having a diagnosis of arthritis at the baseline round of 2012.

Data Analysis

Characteristics of the 5,589 participants were summarized using means and standard deviations for continuous data and counts and percentages for categorical data. We compared characteristics between the three pain groups using the appropriate survey-weighted tests for categorical or continuous measures.

We estimated the association of persistent pain with the development of clinically meaningful declines in physical function, cognitive function, and well-being, adjusting for age, sex, race, education, marital status, depression, anxiety, and the number of specific comorbidities at baseline and applying sampling weights to represent the 2012 US population. Primary outcomes included a 2-point decline in the Gill function score and the well-being score and the development of possible or probable dementia among participants with no dementia, or the development of probable dementia in those with possible dementia. The associations of these outcomes with the presence of persistent pain were estimated using multivariable Fine-Gray competing risks regressions with death as a competing risk. In sensitivity analyses, we estimated these associations using standard multivariable Cox models. We hypothesized that persistent pain would predict declines in physical function, cognitive function, and well-being.

We had very low amounts of missingness for the well-being score and the Gill function score. At baseline, 104 (1.9%) had missing data for well-being and 38 (0.7%) had missing data for the Gill functional score. For participants with one or more missing items, data was imputed using the scales' average score.

Results:

Of the 5,589 eligible NHATS participants, 56.3% were female, 82% were White, and median baseline age was 74 years (interquartile range, 69–80 years). Applying population weights, this sample represents 31.9 million older adults, of which 12.3 million (38.7%) experienced persistent pain, 8.9 million (27.8%) experienced intermittent pain and 10.7 million (33.5%) had no bothersome pain (Table 1). While over half of those with persistent pain (56.2%) reported activity limitations due to persistent pain; only 18.9% reported activity limitations in the intermittent pain group. Over one-third (34%) with persistent pain described pain in five or more sites (range 5–13) compared to 7.9% in those with intermittent pain. The most common painful sites among those with persistent pain were the back (62.3%), knee (49.3%), shoulder (39.2%) and leg (39.1%) (Table 2).

Participants with persistent pain were more likely to be female, Black older adults, have a less than college education, have an annual income of < \$40,800, and be unpartnered or living alone. Participants with persistent pain were more likely to report depressive symptoms, anxiety, and multimorbidity (3 or more comorbid conditions) in comparison to those reporting intermittent or no pain (Table 1).

At baseline, participants with persistent pain had lower Gill functional scores and well-being scores compared to those who reported intermittent or no bothersome pain. Differences were not found in cognitive status between those with and those without persistent pain at baseline (Table 1).

Over the subsequent 7 years, 64% of those with persistent pain, 59% with intermittent pain, and 57% with no bothersome pain experienced declines in physical function. One-quarter of those with persistent pain, 24% with intermittent pain and 23% with no bothersome pain experienced cognitive decline. In terms of well-being, 48% with persistent pain, 45% with intermittent pain and 44% with no bothersome pain experienced declines. After adjusting for age, sex, race, education, marital status, depression, anxiety, and number of comorbid conditions, participants with persistent pain were more likely to experience declines in physical function and well-being, but not in cognition (Table 3, Figure 1).

Discussion:

In this nationally representative sample, one in three older adults had persistent pain and one in four reported intermittent pain. At baseline, those with persistent pain had lower function and reduced well-being. Over seven years of follow up, higher rates of decline in physical function and in well-being occurred among those with persistent pain. However, we did not see an a statistically significant increased rate of cognitive impairment in those with persistent pain compared to those with intermittent or no bothersome pain.

Our prevalence rate of persistent pain is consistent with other national studies in the US and Europe of older adults that defined pain as chronic if pain continued for greater than 3 or 6 months.^{2–4} We also observed that pain was more likely to be reported by older Black participants than White participants, which is likely due to a variety of factors, including the

impact of structural racism on the assessment, diagnosis, and treatment of pain in the US.
22,23

This study is the first to include a representative sample of older Americans that demonstrates meaningful declines in physical function and well-being among those with persistent pain. In this study, we also showed that multiple sites of pain (3 or more) were the norm (63.5%). Our findings of pain in 3 or more sites were the norm, present in nearly two-thirds of our sample (63.5%) and is in line with prior studies of the prevalence of persistent pain, though methodologic differences preclude direct comparisons. In the Eggermont et al. study,⁸ for example, 40% of older adults had 2 or more sites of pain. Despite multiple sites of pain, among those with persistent pain, only about one-third took pain medications every day.

Function is closely tied to independence for older adults, and is highly prioritized by older adults, their caregivers, and loved ones.¹⁰ Our study demonstrated meaningful declines in physical function among 2/3 of older adults with persistent pain. At a population level, 7.8 of 12.3 million older adults in the US with persistent pain experienced a decrease in function over 7 years. After adjustment for potential confounders, persistent pain was associated with a 14% increase in risk for clinically significant declines in physical function compared to those with intermittent or no bothersome pain. This study extends the work of Patel et al. who evaluated the impact of bothersome pain in the previous month on function using NHATS data but did not assess persistent pain over a 12-month time period.²⁴ This rate is compatible with rates of functional disability associated with chronic pain in the Boston Maintenance of Balance, Independent Living, Intellect, and Zest in the Elderly (MOBILIZE) Study. In the MOBILIZE study, older adults with chronic pain were at substantially greater risk for developing functional disability and having clinically meaningful declines in performance status compared to their pain free peers.²⁵ In a study of Australian men ages 70 and older, pain lasting >3 months was associated with a 1.6 times greater likelihood of developing frailty at follow-up.

We saw no statistically increased rates of the development of possible or probable dementia progression in those with persistent pain. We were not able to look at more subtle changes in cognition which may explain differences in our findings from a study of older adults in the Health Retirement Study (HRS), where persistent pain (defined as reporting pain on 2 consecutive surveys) was associated with a 9.2% more rapid memory decline compared with those without persistent pain. In the HRS study, a cognitive change was based on both study participant's and proxy's responses and captured cognition as a continuous measure that may better capture smaller cognitive changes.¹¹ In the NHATS cohort, dementia was characterized as a categorical variable (i.e., of possible or probable dementia). These findings also differ from Rong et al.²⁶ who looked at moderate-severe pain and its impact on cognitive decline. NHATS does not provide insight on pain severity, only on whether pain is bothersome and whether bothersome pain is a daily experience.

In our adjusted analyses, we found that persistent pain was associated with increased reductions in well-being. To our knowledge, this is the first longitudinal study of older adults assessing the impact of persistent pain on well-being. While quality of life (QoL) is

not the same as well-being, a related review assessing the relationship between chronic pain and QoL in older adults noted that in the majority of the cross-sectional studies that were evaluated, the occurrence of chronic pain was associated with decreases in QoL.²⁷ However, we know of no study that demonstrates a longitudinal negative impact of persistent pain on well-being.

Given the high prevalence of persistent pain and its negative effects on both function and well-being, domains of the lived experience highly valued by older adults, it is incumbent on clinicians to prioritize strategies to effectively address their persistent pain. Because many older adults live with multiple chronic conditions that are painful as well, including underlying renal or liver disease or are at high risk for GI bleeding, pharmacologic management choices for older adults remain sparse. Despite an array of adverse effects associated with the use of opioids in older adults,²⁸ many clinicians still resort to their use given few accessible alternative strategies. A study of Part D prescriptions in 2018 showed that 30.4% of Medicare beneficiaries still received an opioid prescription that year.²⁹ While evidence for effective nonpharmacologic therapies are emerging, (e.g. cognitive behavioral therapy and exercise), few studies include in older adults with complex medical needs.³⁰ In our previous work,³¹ we found that many older adults lack access to effective nonpharmacologic treatments and received little guidance from their primary care providers regarding effective pain interventions. The high prevalence of pain and its untoward consequences suggest a need for a renewed policy focus on persistent pain that incorporates reimbursement for nonpharmacologic and pharmacologic approaches.

Limitations

Limitations of our findings relate to the definition of persistent pain, which we used to approximate chronic pain. The International Association for the Study of Pain or the National Pain Strategy defines chronic pain as pain that limits life or work activities on most days during the previous 6 months.³² Because NHATS interviews participants annually, we defined persistent pain as bothersome pain over the prior month reported in two consecutive rounds of interviews. Therefore, our estimates of persistent pain likely underestimate those with chronic pain of > 6 months. Further, the presence of bothersome pain in the last month” in two different years does not in itself establish that this is a persistent pain condition. It could be one acute episode each year or two different pain problems (one each year) were present the month of the survey completion. Defining “intermittent pain” as “bothersome in one interview only” also is problematic since the survey measured a one-time occurrence and not necessarily pain that occurred intermittently throughout the year. Given that NHATS does not provide data on analgesics or other pain treatment, this area also warrants further investigation. Finally, the NHATS data does not allow us to understand many important biological, psychological, or social factors relevant to pain and pain outcomes, such as the role of inflammation or psychological factors influencing pain outcomes. Nevertheless, this study highlights both the high prevalence of persistent, often multisite pain, and its negative impact on extremely important outcomes in older adults.

Conclusions

Persistent pain in older adults is prevalent in over one-third of older adults, often occurs in multiple sites, and limits activities in over half of those with persistent pain. It is associated with both lower function and well-being and with higher rates of decline in function and well-being over a seven-year period. Given that an estimated 12 million older adults experience persistent pain and close to two-thirds experience subsequent functional decline, it is critical that access to effective treatment be made available to all and that research studies focus on an evaluation of multimodal interventions to prevent decline in important outcomes in older adults.

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Key Points box

- Persistent pain is common in older adults and occurs in multiple body sites.
- Persistent pain is associated with meaningful declines in physical function and well-being over 7 years.

Why This Matters:

These findings argue for policies and reimbursement for interventions that prevent and mitigate against persistent pain.

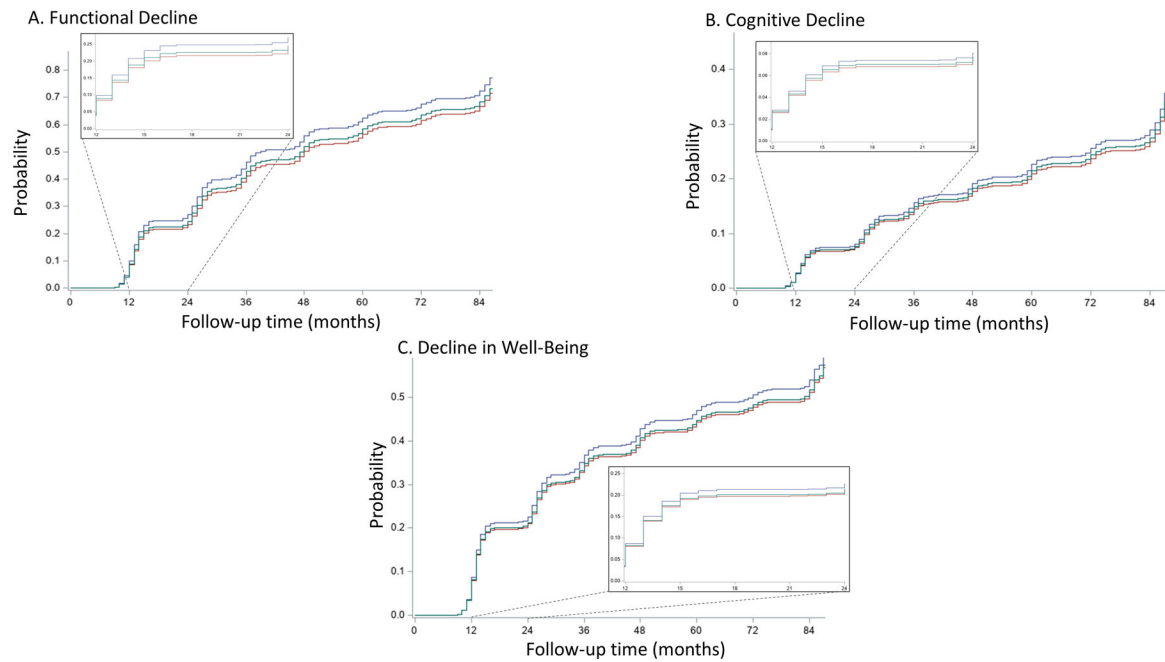


Figure 1:

Cumulative Incidence of Decline in Function, Cognition, and Well-Being by Pain Group / Legend: Functional Decline was defined as a decrease of 2 or more points on the Gill Functional Score (range 7–28). Cognitive decline was defined as a change from no cognitive impairment to possible or probably dementia, or from possible to probable dementia. Decline in well-being was defined a decrease of 2 or more points on the well-being score (range 0–22). Stepped nature of the cumulative incidence curve is due to the yearly administration of the National Health and Trends Study survey. Blue line = persistent pain group, green line = intermittent pain group and red line = no bothersome pain. The inset shows the same data on an enlarged X axis, through 12–24 months.

Table 1:

Baseline Characteristics

Characteristics, weighted column %*	Overall (n=5589, population estimate=31.9 million)	Persistent pain (n=2,215, population estimate=12.3 million)	Intermittent pain (n=1538, population estimate=8.9 million)	No bothersome pain (n=1836, population estimate=10.7 million)
Age in years, mean (SD)	75.8 (±6.99)	75.8 (±7.06)	75.8 (±7.11)	75.7 (±6.81)
Female	56.3	63.4	54.8	49.5
Race				
White	82.0	81.9	82.1	82.1
Black	8.0	9.1	7.2	7.5
Hispanic	6.2	5.8	6.8	6.0
Other	3.8	3.2	3.8	4.5
Education less than high school	20.4	22.4	20.7	17.8
Lowest quartile of income (\$0 to \$17999)	26.8	30.3	26.7	22.8
Born outside the US	10.4	9.7	10.4	11.4
Marital status				
Married/Living Together	56.3	53	58.2	58.7
Separated/Divorced/ Never married	16.2	16.7	15.6	16.1
Widowed	27.5	30.3	26.2	25.2
Live alone	30.1	32.2	28.4	29
Social network: no one to talk	4.3	3.7	4.1	5.2
Comorbidity				
No comorbidity	10.4	4.1	9.3	18.4
1–2 comorbidity	51.0	42.4	51.7	60.3
3 comorbidity	38.6	53.5	39	21.2
Depression	11.4	16.8	9.3	6.9
Anxiety	10.3	16.3	9.4	4.2
Gill functional score (mean, SD, Q1-Q3) [†]	24.82 (±3.88), 23.20–26.50	23.65 (±4.31), 21.42–25.80	24.96 (±3.83), 23.74–26.54	26.04 (±2.95), 24.95–26.94
Dementia				
Probable	6.5	7.0	6.9	5.7
Possible	9.3	9.0	9.3	9.7
No dementia	84.2	84.0	83.9	84.6
Well-being score (mean, SD, Q1-Q3) [§]	17.01 (±3.40), 14.74–18.94	16.01 (±3.68), 13.45–18.13	17.23 (±3.14), 15.14–18.91	17.99 (±2.97), 16.02–19.66

* All percentages incorporate survey weights to account for the complex design of the National Health and Aging Trends Study.

[†] Gill functional measure is reverse coded, range: 7 (highest disability) –28 (no disability)

[§] Well-being range 0–22, 0 indicated low well-being

Table 2:

Characteristics of Pain among Participants Experiencing Persistent or Intermittent Pain

Weighted column %	Persistent pain (n=2,215, population estimate=12.3 million)	Intermittent pain (n=1538, population estimate=8.9 million)
Activity limitation due to pain		
No	43.8	81.1
Yes	56.2	18.9
# of total pain sites		
No pain	0.0	22.6
1–2	36.5	50.0
3–4	29.5	19.5
5+	34.0	7.9
Pain sites		
Back pain	62.3	33.4
Knee pain	49.3	26.7
Shoulder pain	39.2	19
Leg pain	39.1	17.3
Hip pain	36.4	16.3
Hand pain	34.1	14.4
Foot pain	33.5	14.8
Neck pain	30.6	13.1
Wrist pain	19.8	6.7
Arm pain	19.7	7.7
Head pain	18.4	8.5
Stomach pain	17.8	6.9
Other sites	5.2	5
Pain medications		
7 days a week	34.9	15.6
5–6 days a week	9.3	4.1
2–4 days a week	22.2	16.0
Once a week or less	20.0	27.6
Never	13.4	36.6
Don't know/Refused	0.1	0.2
Arthritis		
No	23.0	39.3
Yes	77.0	60.7

Table 3:

Risk of functional decline, cognitive decline, or decline in well-being

	Persistent pain HR (95% CI)^{**}	Intermittent pain HR (95% CI)^{**}	No bothersome pain HR (95% CI)^{**}
Functional decline [*]			
Unadjusted risk of functional decline	1.17 (1.09–1.26)	1.05 (0.97–1.14)	Ref
Age-sex-race adjusted risk of functional decline	1.18 (1.09–1.27)	1.05 (0.97–1.14)	Ref
Multivariable adjusted risk of 2+ point decrease [¶]	1.14 (1.05–1.23)	1.04 (0.95–1.13)	Ref
Cognitive decline [‡]			
Unadjusted risk of cognitive decline	1.09 (0.97–1.24)	1.03 (0.90–1.18)	Ref
Age-sex-race adjusted risk of cognitive decline	1.07 (0.94–1.21)	1.03 (0.90–1.18)	Ref
Multivariable adjusted risk of cognitive decline [¶]	1.02 (0.90–1.16)	1.02 (0.88–1.17)	Ref
Decline in well-being [§]			
Unadjusted risk of decline in well-being	1.09 (1.00–1.18)	1.02 (0.93–1.12)	Ref
Age-sex-race adjusted risk of decline in well-being	1.07 (0.99–1.17)	1.02 (0.93–1.12)	Ref
Multivariable adjusted risk of decline in well-being [¶]	1.11 (1.01–1.21)	1.02 (0.93–1.13)	Ref

^{*} Functional decline was defined as a decrease of 2 or more points on the Gill Functional Score (range 7–28).

[‡] Cognitive decline was defined as a change from no cognitive impairment to possible or probably dementia, or from possible to probable dementia.

[§] Decline in well-being was defined a decrease of 2 or more points on the well-being score (range 0–22).

[¶] Multivariable adjusted = Adjusted for age, sex, race, education, marital status, depression, anxiety, and comorbidities (heart attack, heart disease, osteoporosis, diabetes, lung disease, stroke, and cancer).

^{**} HR = Hazard ratio; CI = Confidence interval