

RESEARCH PAPER

Frailty—a risk factor of global and domain-specific cognitive decline among a nationally representative sample of community-dwelling older adult U.S. Medicare beneficiaries

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Abstract

Objectives: frail older adults may be more vulnerable to stressors, resulting in steeper declines in cognitive function. Whether the frailty–cognition link differs by cognitive domain remains unclear; however, it could lend insight into underlying mechanisms.

Methods: we tested whether domain-specific cognitive trajectories (clock-drawing test, (CDT), immediate and delayed recall, orientation to date, time, president and vice-president naming) measured annually (2011–2016) differ by baseline frailty (physical frailty phenotype) in the National Health and Aging Trends Study ($n = 7,439$), a nationally representative sample of older adult U.S. Medicare beneficiaries, using mixed effects models to describe repeated measures of each cognitive outcome. To determine if the association between frailty and subsequent cognitive change differed by education, we tested for interaction using the Wald test.

Results: we observed steeper declines for frail compared to non-frail participants in each domain-specific outcome, except for immediate recall. Largest differences in slope were observed for CDT (difference = -0.12 (standard deviations) SD/year, 95%CI: $-0.15, -0.08$). By 2016, mean CDT scores for frail participants were 1.8 SD below the mean (95%CI: $-1.99, -1.67$); for non-frail participants, scores were 0.8 SD below the mean (95%CI: $-0.89, -0.69$). Associations differed by education for global cognitive function ($P_{\text{interaction}} < 0.001$) and for each domain-specific outcome: CDT ($P_{\text{interaction}} < 0.001$), orientation ($P_{\text{interaction}} < 0.001$), immediate ($P_{\text{interaction}} < 0.001$) and delayed ($P_{\text{interaction}} < 0.001$) word recalls.

Conclusion: frailty is associated with lower levels and steeper declines in cognitive function, with strongest associations for executive function. These findings suggest that aetiologies are multifactorial, though primarily vascular related; further research into its association with dementia sub-types and related pathologies is critical.

Keywords: cognitive ageing, cognition, frailty, epidemiology, dementia, older people

Key Points

- Frailty is associated with lower levels and steeper declines in cognitive performance in a nationally representative cohort.
- Greatest differences were observed for executive function.
- Aetiologies are multifactorial, though likely vascular in nature.

Introduction

Cognitive impairment is common in the United States, affecting 16–20% of older adults [1]. Mild cognitive impairment (MCI) is increasingly recognised as a prodromal phase of many types of dementias [1–5], which has become a leading contributor to disability and dependence among older adults [6], as well as mounting economic and social burden [1]. However, its complex pathophysiology, slow progression and heterogeneous clinical manifestations [2, 7] complicate efforts to pinpoint underlying causes and diagnose early. Cognitive decline, the hallmark of dementia, is a critical endpoint for studies of cognitive impairment and dementia [1–5]. Therefore, it has become increasingly important to investigate potential modifiable risk factors of cognitive decline to identify prevention strategies for later life cognitive impairment and dementia.

Physical frailty, a syndrome [8–10] occurring in approximately 10–15% of community-living older adults [10, 11], is described as a deterioration in physiologic reserve manifested as a vulnerability to stressors [8–10]. While there are at least 67 identified frailty instruments [12], including the commonly investigated deficit accumulation index [13, 14], the physical frailty phenotype (PFP) [8] is the most widely used measure [12], especially in etiologic research given its distinction from co-morbidity and disability [12, 15]. Frailty is a dynamic process that is potentially preventable and modifiable as suggested by prior studies [16–18]. Together with evidence of a frailty–cognition link, it is important to investigate the role of frailty in subsequent cognitive decline to provide a potential hopeful avenue for intervention.

Studies that have demonstrated a frailty–cognition link have collectively suggested that frailty is associated with lower levels and steeper declines in cognitive function [19–23]. However, due to common research challenges including use of small samples, lack of generalizability and lack of sufficient follow-up to observe changes, results have been inconsistent. Among the few that have demonstrated a significant relationship between frailty and cognition by specific cognitive domain, stronger associations for executive function compared to memory were observed [21–24]. It is likely that in the face of acute/everyday stressors, frail older adults have lower cognitive function and steeper cognitive decline than non-frail counterparts, with strongest associations for executive function—a critical domain that deteriorates with onset of vascular dementia [25, 26]. It is also likely that education—a strong predictor of cognitive reserve, which protects against damaging effects of neuropathology—modifies this association [27].

To better understand the association between frailty and subsequent cognitive decline, we leveraged the National Health and Aging Trends Study (NHATS), a prospective, nationally representative sample of U.S. Medicare beneficiaries aged 65+ years. Our goals were to: (i) assess global and domain-specific cognitive trajectories overall; (ii) test whether global and domain-specific cognitive levels and trajectories differ by baseline frailty and (iii) investigate whether associations are modified by educational attainment. Examining the frailty–cognition relationship among a large, heterogeneous population with repeated measures of domain-specific cognitive function would provide critical insight into underlying mechanisms and aetiologies.

Methods

Study design

We used NHATS, a prospective cohort study of a nationally representative sample of U.S. Medicare beneficiaries aged 65+ years [28]. Our analytic sample included community-dwelling older adults with measures of at least three of five frailty criteria and longitudinal cognitive measures ($n = 7,439$), as described below (Supplementary Figure S1); as in prior studies [11, 19, 26], participants who had three or more frailty assessments missing were excluded from the study. All participants were followed annually for a maximum of 5 years (2011–2016), and data were collected via 2-hour, in-person interviews.

Demographic factors including age, sex, race/ethnicity, education and annual income were considered, as well as self-reported medical conditions. Additionally, participants were classified as having possible/probable dementia based on cognitive testing and self-/proxy reports using NHATS criteria [29] and based on prior studies [26, 30] (Supplementary Table S1 available in *Age and Ageing* online). Depressive symptoms (PHQ-2), subjective well-being, lower extremity function (short physical performance battery [SPPB]) and dependence in activities of daily living (ADLs) and instrumental activities of daily living (IADLs) were also considered.

Frailty

Baseline frailty was measured using the PFP [9] criteria (exhaustion, low activity, shrinking, slowness and weakness) previously operationalised in NHATS [8, 9, 19, 26] using validated interview and performance measures of functioning [31] (Supplementary Table S1 available in *Age and Ageing* online).

Each criterion was scored as 0 or 1 representing the absence or presence of the component. Criteria were then summed to create a total score (range: 0–5), and participants were defined as frail with a score of ≥ 3 , as has been validated in clinical settings for purposes of risk stratification [20, 32, 33].

Cognitive function

Trajectories for four domain-specific cognitive measures were assessed in NHATS during in-person interviews. A word-list memory test [34] required participants to recall 10 words immediately after the list of words was presented (immediate word recall) and again after a five-minute delay (delayed word recall). The number of words recalled at a given timepoint was used as either an immediate or a delayed word recall score, ranging from 0 to 10, where higher scores represent more words recalled. A clock-drawing test (CDT) for executive function was also administered to participants. Each participant was given a two-minute time limit to draw a clock face telling the time ‘10 after 11.’ Clocks were rated according to standard criteria, where higher scores represent more complete/accurate drawings [35]. Orientation to date and time was measured by asking participants for the current day, month, year and day of the week and for the name of the current president and vice-president.

We standardised scores of all four component cognitive tests using their baseline means and standard deviations (SD) and then averaged them into a global cognitive composite score, as described in prior studies [36].

Statistical analyses

We tested differences in participant characteristics by frailty using *t*-tests from logistic regressions incorporating survey weights from the sample design to compare means for all continuous variables and frequency distributions for all categorical variables by frailty. We then described cognitive trajectories for each cognitive outcome using multiple linear regression with fixed and random effects for people and time, applying analytic weights to generate nationally representative estimates. We generated autocorrelation functions to assess the variance–co-variance structure of repeated measures of each cognitive outcome and selected a first-order autoregressive model with robust variance accordingly. Models were controlled for demographic and health characteristics including centred age, sex, race, highest level of education, income quartile and number of co-morbidities. To determine if the association between frailty and subsequent cognitive change was modified by education, we tested for interaction of the association using the Wald test.

All analyses were performed using Stata 15.0, and we used a statistical significance cut-off of $\alpha < 0.05$.

Sensitivity analyses

We conducted a series of sensitivity analyses to evaluate whether findings remained robust after restricting to those without possible/probable dementia, addressing for ceiling effects (random-effects Tobit models) and addressing potential differential rates of attrition (two complementary approaches: multiple imputations by chained equations in conjunction with generalised estimating equations (GEE) and inverse probability weighting in conjunction with GEE).

Results

Study population

Of 7,439 community-dwelling older adults (mean age = 75.23 years) in NHATS followed for a mean of 3.21 years (SE = 0.03), 56.44% were women, 81.53% self-reported as White, and 20.30% had possible/probable dementia at baseline (Table 1).

Frailty at baseline

At baseline, 1,313 (14.1%) were frail. Frail participants tended to be older (mean = 78.94 versus 74.62 years) and were more likely than non-frail participants to be female (63.72% versus 55.25%), Black (11.93% versus 7.59%) and Hispanic (10.81% versus 6.00%). Frail older adults were also more likely to have a highest education attainment of ≤ 8 th grade (20.13% versus 8.50%) and be within the lowest income quartile (41.74% versus 22.68%). Additionally, frail older adults were more likely to have ≥ 4 co-morbidities (26.66% versus 7.18%), severe depressive symptoms (38.93% versus 10.36%), dependence (IADL: 50.17% versus 7.16%; ADL: 53.53% versus 7.11%) and lower mean SPPB scores (2.37 versus 7.41) (Table 1).

Cognitive levels and trajectories among all community-dwelling older adults

After adjustment, reference participants (a 75-year-old, White male with 0 co-morbidities, educational attainment of ≤ 8 th grade and lowest income quartile) scored significantly below the mean for all cognitive tests at baseline (Figure 1). On average, reference participant scores ranged from 0.40 SD below the mean level for the delayed word recall (–0.40 SD, 95% confidence interval (CI): –0.48, –0.32) to 0.60 SD below the mean level for immediate word recall (–0.60 SD, 95%CI: –0.78, –0.32).

Over the 5-year follow-up, community-dwelling older adults demonstrated decline in global cognitive function (–0.010 SD/year, 95%CI: –0.014, –0.006) and in all domain-specific cognitive performance tests with the exception of orientation (Figure 1). Steepest declines occurred for CDT (–0.098 SD/year, 95%CI: –0.107, –0.089), immediate word recall (–0.030 SD/year, 95%CI: –0.036, –0.025) and delayed word recall (–0.018 SD/year, 95%CI: –0.024, –0.013), respectively (Table 2).

Table 1. Baseline participant characteristics by frailty status of community-dwelling older adults in the National Health and Aging Trends Study, 2011–2016 ($n = 7,439$)

Characteristic	Overall ($n = 7,439$)	Non-frail ($n = 6,126$)	Frail ($n = 1,313$)
Age (years)**	75.23 (0.10)	74.62 (0.10)	78.94 (0.24)
Female (%)**	4,320 (56.44)	3,479 (55.25)	841 (63.72)
Race (%)**			
White	5,129 (81.53)	4,346 (82.72)	783 (74.27)
Black	1,641 (8.20)	1,263 (7.59)	378 (11.93)
Hispanic	440 (6.68)	322 (6.00)	118 (10.81)
Other	229 (3.59)	195 (3.69)	34 (2.99)
Income (%)**			
1st quartile	2,302 (25.37)	1,683 (22.68)	619 (41.74)
4th quartile	1,339 (22.92)	1,245 (25.27)	94 (8.60)
Education (%)**			
8th Grade or less	953 (10.14)	643 (8.50)	310 (20.13)
9th–12th Grade (no diploma)	1,042 (11.36)	790 (10.33)	252 (17.64)
High school diploma or equivalent	2,041 (27.58)	1,694 (27.41)	347 (28.59)
Some college but no degree	1,483 (21.54)	1,285 (22.18)	198 (17.60)
Associates or bachelor's degree	1,182 (17.94)	1,034 (18.89)	148 (12.18)
Graduate degree	714 (11.44)	665 (12.68)	49 (3.86)
Subjective well-being score**	17.30 (0.05)	17.69 (0.05)	14.44 (0.18)
Depressive symptoms**	1,179 (14.39)	690 (10.36)	489 (38.93)
Co-morbidity (%) ^a **			
0 Co-morbidities	1,256 (18.37)	1,188 (20.56)	68 (5.04)
1 Co-morbidities	2,184 (30.19)	1,952 (32.47)	232 (16.27)
2 Co-morbidities	2,048 (26.65)	1,681 (26.48)	367 (27.68)
3 Co-morbidities	1,163 (14.86)	843 (13.30)	320 (24.35)
4+ Co-morbidities	788 (9.93)	462 (7.18)	326 (26.66)
SPPB, mean (SD)	6.73 (0.06)	2.37 (0.09)	7.41 (0.05)
ADL (%)**			
Moderate	1,684 (21.15)	1,343 (20.12)	341 (27.44)
Severe	1,284 (13.66)	544 (7.11)	740 (53.53)
IADL (%)**			
Moderate	1,625 (21.06)	1,276 (19.55)	349 (30.28)
Severe	1,327 (13.23)	586 (7.16)	741 (50.17)
Global cognition composite score**	0.20 (0.01)	0.26 (0.01)	-0.26 (0.03)
Clock-drawing test score**	0.16 (0.02)	0.25 (0.02)	-0.39 (0.04)
Immediate word recall**	0.18 (0.21)	0.25 (0.02)	-0.33 (0.04)
Delayed word recall**	0.20 (0.02)	0.25 (0.02)	-0.22 (0.04)
Orientation to date & time**	0.15 (0.02)	0.24 (0.02)	-0.41 (0.04)
Dementia (possible or probable) (%)**	1,941 (20.30)	1,270 (16.27)	671 (44.84)

Note: Raw numbers and weighted percentages (%) for categorical characteristics, as well as weighted means and standard deviations for continuous characteristics are presented. ^aCo-morbidities were self-reported and included history of cancer, hip fracture, heart disease, high blood pressure, arthritis, osteoporosis, diabetes, lung disease or stroke. Per characteristic, comparisons were statistically significant at $**P < 0.05$

Baseline cognitive levels by frailty

After adjustment, frail community-dwelling older adults had lower global cognitive scores (-0.64 SD, 95%CI: -0.72 , -0.57) compared to non-frail community-dwelling older adults (-0.42 SD, 95%CI: -0.48 , -0.35) at baseline, and this difference was statistically significant (Cohen's $d = -0.23$ SD, 95%CI: -0.27 , -0.19). Additionally, across all domain-specific cognitive tests, frail older adults had significantly lower scores than non-frail older adults at baseline, with the greatest differences in observed for CDT (Cohen's $d = -0.47$ SD, 95%CI: -0.54 , -0.39) and orientation (Cohen's $d = -0.39$ SD, 95%CI: -0.45 , -0.33) (Table 3). At baseline, frail older adults had CDT scores that were more than two times lower (-0.82 SD,

95%CI: -0.92 , -0.71) than non-frail older adults (-0.35 SD, 95%CI: -0.44 , -0.26) (Figure 2).

Cognitive trajectories by frailty

Over the 5-year follow-up, frail older adults had steeper declines in global cognitive function (-0.03 SD/year, 95%CI: -0.04 , -0.01) than non-frail older adults (-0.01 SD/year, 95%CI: -0.012 , -0.005), and the slopes were significantly different (Cohen's $d = -0.02$ SD/year, 95%CI: -0.03 , -0.01). Frail older adults had significantly steeper declines in cognitive function than non-frail older adults across all domain-specific cognitive tests except for the immediate word recall (Cohen's $d = -0.01$

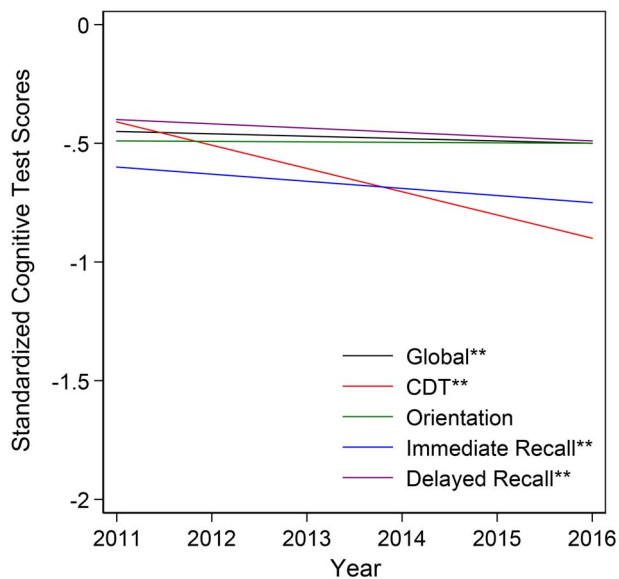


Figure 1. Adjusted cognitive trajectories by specific cognitive domain among community-dwelling older adult participants in the National Health and Aging Trends Study, 2011–2016 ($n = 7,439$). The global cognition composite score was created by standardising each of the four cognitive tests to a mean of 0 and a standard deviation of 1 based on the baseline visit, and taking the average of those standardised scores. Adjusted estimates were controlled for follow-up time, age (centred at 75 years), sex, race, education, income quartile and comorbidity index (out of 7), including arthritis, diabetes, heart disease, high blood pressure, lung disease, osteoporosis and stroke. A reference participant represents a 75-year-old, White male with 0 co-morbidities, educational attainment of 8th grade or less and in the lowest income quartile. Cognitive domains with two stars (**) represent statistical significance slopes at a cut-off of $P = 0.05$.

SD/year, 95%CI: $-0.03, 0.01$) (Figure 2). However, greatest difference in slopes comparing frail to non-frail older adults occurred for CDT (Cohen's $d = -0.12$ SD/year, 95%CI: $-0.15, -0.08$), followed by orientation (Cohen's $d = -0.02$ SD/year, 95%CI: $-0.04, -0.001$) and delayed word recall (Cohen's $d = -0.02$ SD/year, 95%CI: $-0.04, -0.01$) (Table 3). By the end of the 5-year follow-up, CDT scores for frail older adults were about 1 SD lower than non-frail older adults (Cohen's $d = -1.04$, 95%CI: $-1.18, -0.89$), where non-frail older adults were 0.79 SD below the mean (95%CI: $-0.89, -0.69$), while frail older adults were 1.83 SD below the mean (95%CI: $-1.99, -1.67$).

Education significantly modified the association between baseline frailty and subsequent trajectories in global cognitive function ($\beta_{\text{interaction}} = -0.015$ SD/year, $P < 0.001$), as well as in all domain-specific cognitive performance, including CDT ($\beta_{\text{interaction}} = -0.018$ SD/year, $P < 0.001$), orientation ($\beta_{\text{interaction}} = -0.019$ SD/year, $P < 0.001$), immediate word recall ($\beta_{\text{interaction}} = -0.015$ SD/year,

$P < 0.001$) and delayed word recall ($\beta_{\text{interaction}} = -0.017$ SD/year, $P < 0.001$).

Sensitivity analyses

Across all sensitivity analyses, inferences remained consistent for differences in cognitive levels at baseline, with greatest observed differences by frailty for CDT and orientation. For cognitive trajectories, however, CDT was the only cognitive outcome that consistently demonstrated significant differences in slopes by frailty (Supplementary Tables S2–S5 available in *Age and Ageing* online).

Discussion

To our knowledge, this is the first nationally representative study of older adult U.S. Medicare beneficiaries examining the association between frailty and repeated measures of domain-specific cognitive function. Our findings are consistent with prior studies suggesting that frail older adults have lower global cognitive function (Cohen's $d = -0.23$ SD, 95%CI: $-0.27, -0.19$) and experience steeper declines in global cognitive function (Cohen's $d = -0.02$ SD/year, 95%CI: $-0.03, -0.01$) compared to their non-frail counterparts [21–24]. However, while some studies have found that greater frailty severity was predictive of cognitive decline [37–39], other studies have found that baseline cognitive performance was associated with incident frailty [40, 41]. The causal mechanisms underlying this association remain unclear, with evidence of a potential bidirectional relationship. Nevertheless, collectively, evidence suggests that many of the ageing processes catalysing frailty may also be responsible for brain ageing and cognitive decline [22, 23]. Our study extends those findings to a large, nationally representative, diverse sample with domain-specific measures, demonstrating that frail older adults had significantly lower scores in memory, executive function and orientation. Our findings suggest that with low physical reserve and the body's inability to bounce back from stressors, frail older adults are more vulnerable to lower cognitive functioning than non-frail older adults. With lower cognitive function, and steeper declines in cognitive function as they age, frail older adults may be at greater risk for cognitive impairment and dementia.

Though we observed differences by frailty in memory and orientation, we found the strongest evidence for executive function. Specifically, frail older adults had CDT scores that were more than two times lower (-0.82 SD, 95%CI: $-0.92, -0.71$) than non-frail older adults (-0.35 SD, 95%CI: $-0.44, -0.26$) at baseline (Cohen's $d = -0.47$, 95%CI: $-0.54, -0.39$). Furthermore, by the end of the 5-year follow-up, CDT scores for frail older adults were over 1.5 SD below the mean (Cohen's $d = -1.83$, 95%CI: $-1.99, -1.67$), while scores for non-frail older adults were less than 1 SD below the mean (Cohen's $d = -0.79$ SD, 95%CI: $-0.89, -0.69$). These results are consistent with hypotheses

Table 2. Adjusted linear mixed models quantifying global and domain-specific cognitive level and slope estimates among all community-dwelling older adults in the National Health and Aging Trends Study, 2011–2016 ($n = 7,439$). The global cognition composite score was created by standardising each of the four cognitive tests to a mean of 0 and a standard deviation of 1 based on the baseline visit, and taking the average of those standardised scores. Adjusted estimates were controlled for follow-up time, age (centred at 75 years), sex, race, education, income quartile and co-morbidity index (out of 7), including arthritis, diabetes, heart disease, high blood pressure, lung disease, osteoporosis and stroke. Cognitive level represents the average level for a reference participant (75-year-old White male with 0 co-morbidities, educational attainment of 8th grade or less and in the lowest income quartile)

Cognitive outcome	Adjusted estimates Cohen's <i>d</i> (95% confidence interval)	
	Level	Slope
Global cognition composite	-0.45 (-0.51, -0.39)**	-0.010 (-0.014, -0.006)**
Clock-drawing test	-0.41 (-0.50, -0.33)**	-0.098 (-0.107, -0.089)**
Orientation	-0.49 (-0.58, -0.41)**	-0.002 (-0.007, 0.004)
Immediate recall	-0.60 (-0.78, -0.52)**	-0.030 (-0.036, -0.025)**
Delayed recall	-0.40 (-0.48, -0.32)**	-0.018 (-0.024, -0.013)**

**Statistical significance at a cut-off of $P = 0.05$

Table 3. Adjusted linear mixed models quantifying global and domain-specific cognitive level and slope estimates comparing frail ($n = 1,313$) versus non-frail ($n = 6,126$) among community-dwelling older adults in the National Health and Aging Trends Study, 2011–2016. The global cognition composite score was created by standardising each of the four cognitive tests to a mean of 0 and a standard deviation of 1 based on the baseline visit and taking the average of those standardised scores. Adjusted estimates were controlled for follow-up time, age (centred at 75 years), sex, race, education, income quartile, and comorbidity index (out of 7), including arthritis, diabetes, heart disease, high blood pressure, lung disease, osteoporosis and stroke

Cognitive outcome	Baseline cognitive levels <i>Standard deviations</i>			Slopes <i>Standard deviations per year</i>		
	Frail	Non-frail	Difference Cohen's <i>d</i> (95% CI)	Frail	Non-frail	Difference Cohen's <i>d</i> (95% CI)
Global cognition composite	-0.64**	-0.42**	-0.23 (-0.27, -0.19)**	-0.03**	-0.01**	-0.02 (-0.03, -0.01)**
Clock-drawing test	-0.82**	-0.35**	-0.47 (-0.54, -0.39)**	-0.20**	-0.09**	-0.12 (-0.15, -0.08)**
Orientation	-0.83**	-0.44**	-0.39 (-0.45, -0.33)**	-0.02**	-0.0001	-0.02 (-0.04, -0.001)**
Immediate recall	-0.79**	-0.56**	-0.23 (-0.28, -0.17)**	-0.04**	-0.03**	-0.01 (-0.03, 0.01)
Delayed recall	-0.53**	-0.38**	-0.15 (-0.21, -0.10)**	-0.04**	-0.02**	-0.02 (-0.04, -0.01)**

**Statistical significance at a cut-off of $P = 0.05$

that frailty has a stronger association with markers of executive function compared to memory [19, 21–24]. Two of the most common types of dementias, Alzheimer's disease (AD) and vascular dementia, are often distinguished by disproportionate impairments in episodic memory and executive function, respectively [25]. We therefore hypothesise that frailty's link to cognitive function likely has multifactorial aetiologies that are primarily vascular in nature. Further research into its association with dementia sub-types and related pathologies is critical.

This study has several limitations. First, NHATS lacks any biomarker data and heavily relies on participants self-reporting for their health history. However, self-report of chronic conditions has been shown to be reasonably accurate against medical records and claims [42]. Second, using different cognitive performance measures with varying sensitivities is especially challenging. For executive function, the CDT is known to have less education bias and language barrier and is better able to identify executive dysfunction among

people with normal MMSE [43]. Additionally, testing participants' ability for delayed verbal memory (word recall) is a strong predictor of AD pathologies [44]. Therefore, in NHATS, these tests were appropriately selected for a variety of evaluation settings where speed and ease of assessment are important in this large, diverse sample compared to more comprehensive neuropsychological batteries, which can be time-consuming and burdensome for participants. A third limitation relates to that of attrition, as is often the case with any longitudinal study; however, after accounting for potential biases due to attrition using two complementary approaches, results remained robust across all cognitive domains for differences in cognitive performance at baseline by frailty status; differences in cognitive change by frailty status were less consistent across cognitive domains, though remained robust by frailty status for global cognitive function and executive function. Finally, despite being the most widely used measure of frailty, particularly for etiologic research [12], frailty as measured by the PFP can sometimes

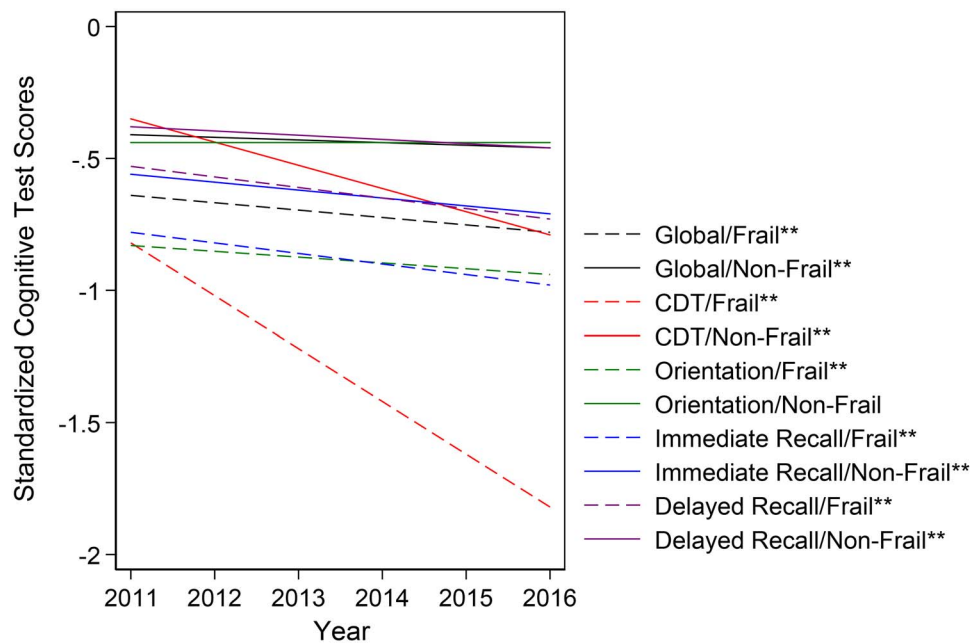


Figure 2. Adjusted cognitive trajectories by specific cognitive domain and by frailty status among community-dwelling older adult participants in the National Health and Aging Trends Study, 2011–2016 ($n = 7,439$). The global cognition composite score was created by standardising each of the four cognitive tests to a mean of 0 and a standard deviation of 1 based on the baseline visit, and taking the average of those standardised scores. Adjusted estimates were controlled for follow-up time, age (centred at 75 years), sex, race, education, income quartile and co-morbidity index (out of 7), including arthritis, diabetes, heart disease, high blood pressure, lung disease, osteoporosis and stroke. A reference participant represents a 75-year-old, White male with 0 co-morbidities, educational attainment of 8th grade or less and in the lowest income quartile. Dotted lines represent frail participants; solid lines represent non-frail participants. Trajectories with two stars (**) represent statistical significance slopes at a cut-off of $P = 0.05$.

be challenging to measure in clinical practice given time constraints, imprecision in self-reported items and inability to complete a task [45]; investigation of other rapid tools used in clinical practice, such as the FRAIL scale [46] or the Clinical Frailty Scale [47], is warranted.

Despite these limitations, this large, nationally representative study of U.S. Medicare beneficiaries aged 65 years and older has increased the generalizability of previous findings that frailty is associated with lower and steeper declines in global and domain-specific cognitive function. With widely used, repeated measures of domain-specific cognitive tests, this study has supported hypotheses that frail older adults are more vulnerable to cognitive decline, particularly in executive function. Further investigation into the direction of this relationship would lend insight into mechanisms that underlie this association, which is crucial to the development of effective, targeted interventions that may potentially prevent cognitive impairment and dementia among frail older adults.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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