Symptoms of Apathy Independently Predict Incident Frailty and Disability in Community-Dwelling Older Adults

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ABSTRACT

Objective: Although depressive symptoms are widely recognized as a predictor of functional decline among older adults, little is known about the predictive utility of apathy in this population. We prospectively examined apathy symptoms as predictors of incident slow gait, frailty, and disability among non-demented, community-dwelling older adults.

Methods: We examined 2 independent prospective cohort studies—the LonGenity study (N = 625, 53% women, mean age = 75.2 years) and the Central Control of Mobility in Aging (CCMA) study (N = 312, 57% women, mean age = 76.4 years). Individuals were recruited from 2008 to 2014. Apathy was assessed using 3 items from the Geriatric Depression Scale. Slow gait was defined as 1 standard deviation or more below age- and sex-adjusted mean values, frailty was defined using the Cardiovascular Health Study criteria, and disability was assessed with a well-validated disability scale.

Results: The prevalence of apathy was 20% in the LonGenity cohort and 26% in the CCMA cohort. The presence of apathy at baseline, independent of depressive symptoms (besides apathy), increased the risk of developing incident slow gait (hazard ratio [HR] = 2.10; 95% CI, 1.36–3.24; $P = .001$), frailty (HR = 2.86; 95% CI, 1.96–4.16; $P < .001$), and disability (HR = 3.43; 95% CI, 1.73–6.79; $P < .001$) in the pooled sample. These associations remained significant when accounting for demographics, medical illnesses, and cognitive function.

Conclusions: Apathy is associated with increased risk of developing slow gait, frailty, and disability, independent of other established risk factors, in non-demented older adults. Apathy should be screened for as a potentially preventable cause of functional decline in clinical psychiatric settings.

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Apathy is one of the most common neuropsychiatric symptoms in older adults[1–4] and is increasingly prevalent with advancing age.[1,3,4] Defined as concurrent reduction in cognitive, emotional, and motoric goal-directed behavior,[5] apathy is hypothesized to result from damage to the frontal-subcortical pathways.[5–7] Although nosologically similar to depression, apathy is now widely considered a distinct neuropsychiatric condition that can occur in the presence or absence of depression.[8,9]

Apathy has been identified as a prominent behavioral symptom in Alzheimer's and Parkinson's diseases and is associated with greater morbidity and mortality in these conditions.[10,11] Additionally, it is associated with multiple adverse health outcomes among older adults with varying degrees of neurologic impairment in both cross-sectional and longitudinal studies.[12–14] For instance, apathy predicts gait dysfunction, disability, and cognitive decline in individuals with dementia.[11–15] Furthermore, apathy predicts conversion to dementia among those with mild cognitive impairment (MCI)[16–18] and increases risk of mortality in nursing home residents.[19] However, despite the widely researched function of apathy as a marker of decline among these vulnerable disease populations, little is known about the predictive validity of apathy in healthy older adults.

Identifying risk factors for functional decline in the community-dwelling elderly population is particularly important, as these individuals are still easily able to participate in targeted psychiatric interventions. Behavioral markers, such as apathy and depression, can be screened quickly and inexpensively at routine clinical visits. While depression has been extensively studied as a predictor of functional decline in healthy older adults,[20–25] few have looked at apathy,[3] and, to our knowledge, no one has assessed longitudinal associations of apathy with frailty and motor status in this population.

To address these knowledge gaps, we examined the longitudinal relationship between apathy and subsequent functional decline in 2 prospective cohorts of community-dwelling, cognitively-intact, and non-disabled older adults. Researchers recommend utilizing complementary measurements of functioning to provide a more holistic understanding of health status[26]; therefore, we examined new onset of slow gait, frailty, and disability as our primary outcomes. Slow gait, frailty, and disability predict multiple adverse health outcomes in older adults, including falls, dementia, morbidity, and death, making them robust indicators of functioning.[27–31] Expanding upon previous research,[11–17] we hypothesized that baseline apathy, independent of depressive symptoms, would predict incident slow gait, frailty, and disability in community-dwelling older adults. If confirmed, our findings will lend support to the clinical utility of apathy in psychiatric settings.

Clinical Points

- Although apathy is one of the most common neuropsychiatric symptoms in older adults, little is known of its effect on frailty and motoric decline.
- Presence of apathy was associated with increased risk of developing slow gait, frailty, and disability in older adults.
- Apathy screenings may prevent functional decline and should become a routine part of psychiatric visits with older adults.

METHODS

Participants

Participants were recruited from 2 independent ongoing cohort studies at the Albert Einstein College of Medicine—the LonGenity study[32] and the Central Control of Mobility in Aging (CCMA) study.[33]

LonGenity. The goal of the LonGenity study is to identify genotypes associated with longevity and successful aging in Ashkenazi Jewish seniors.[32] Participants seen between March 2008 and September 2014 were included in this analysis. As previously described,[32] Ashkenazi Jewish adults aged 65 years and older were systematically recruited using public records such as voter registration lists. A smaller sample was identified through contacts at synagogues, community organizations, and advertisements in Jewish newspapers. Potential participants were contacted by mail and then telephone to rule out the presence of baseline dementia. Participants received comprehensive neuropsychological, psychological, and quantitative gait assessments at baseline and annual follow-up visits. Exclusion criteria were inability to speak English, dementia, significant loss of vision or hearing, and having a sibling already enrolled in the study. Of the 847 individuals recruited at baseline, 213 had not received follow-up assessments at the time of data analysis and 9 were missing data. These participants were excluded from the study. Excluded individuals did not significantly differ with respect to age, sex, education, or illness index from eligible participants. Following exclusions, 625 individuals with median follow-up of 3 years (range, 1–6 years) were included in the current study (mean [SD] age = 75.21 [6.4] years; 53.3% were female).

Central Control of Mobility in Aging. The primary goal of the CCMA study is to determine cognitive predictors of mobility decline and disability in aging.[33] Participants seen between June 2011 and September 2014 were included in this analysis. The study procedure has been previously described.[33] Briefly, individuals aged 65 years and older residing in lower Westchester County, New York, were identified from population lists. Potential participants were contacted by mail and then telephone to rule out the presence of baseline dementia. Exclusion criteria were inability to speak English, inability to ambulate independently, dementia, significant loss of vision or hearing, and major psychiatric disorders. Eligible participants received comprehensive neuropsychological, psychological, and quantitative gait assessments at baseline and annual follow-up visits. Of the 496 individuals recruited at baseline, 182 had not received follow-up assessments at the time of data analysis and 2 were missing data. These participants were excluded from the study. Excluded individuals did not significantly differ with respect to age, sex, education, or illness index from eligible participants. Following exclusions, 312 individuals with median follow-up of 2 years (range, 1–3 years) were included in the current study (mean [SD] age = 76.4 [6.87] years; 56.7% were female).

For both cohorts, the institutional review board of the Albert Einstein College of Medicine approved the experimental procedures and all participants provided written informed consent. Participants received complete clinical and neuropsychological evaluations annually in both studies, and diagnoses of dementia and mild cognitive impairment were assigned according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition,[34] using all available clinical, neuropsychological, and laboratory information at consensus case conferences attended by at least 1 study neurologist and 1 neuropsychologist, as previously described.[35]

Outcome Measures

We selected 3 common motor and functional outcomes (slow gait, frailty, and disability) associated with poor physical and cognitive aging.[27–31,36] Each of these outcomes was assessed at baseline and annual follow-up visits in both cohorts. All of these assessments were conducted with raters blinded to participants' apathy status at baseline and follow-up visits.

Slow gait. Gait speed (cm/s) was measured while participants walked at their normal pace on an 8.5-meter–long computerized walkway (180 × 35.5 × 0.25 inches) with embedded pressure sensors (GAITRite, CIR systems, Havertown, Pennsylvania). Excellent reliability and validity for GAITRite assessments have been reported.[30,37] Slow gait was defined as 1 standard deviation or more below previously outlined age- and sex-appropriate mean values.[38] A similar procedure was previously used to define slow gait in these 2 cohorts as well as other cohorts.[39]

Frailty. Frailty diagnosis was operationalized using the Cardiovascular Health Study criteria,[36] defined as meeting 3 or more of the following: unintentional weight loss of more than 10 pounds in the past year, self-reported decrease in energy in the past year, muscle weakness (weak grip strength), slow gait speed (cutoff scores described in the previous paragraph), and self-reported decrease in physical activity in the past year.[36] Similar to previous reports,[40–42] subjective grip strength ("Do you feel as though your grip is weak?") was used since objective measures were not available for all participants at follow-up. Among individuals in our sample with both objective and subjective measurements (n = 451), these 2 ratings showed substantial interrater agreement ($\kappa = 0.681$).

Disability. Disabilities in basic activities of daily living (ADLs) were assessed using standard questions with a scale developed by Gill and colleagues[43] for use in community-based cohorts. The scale has been used to assess functional status

in our aging studies as previously described.[38] Excellent test-retest reliability and interrater reliability have been reported for this scale in community samples.[43] The scale was administered by trained research assistants and characterizes self-reported performance on basic but not instrumental ADLs. Disability was coded dichotomously and defined as needing assistance with or inability to perform any 1 of the following 7 basic ADLs: bathing, dressing, walking inside the home, getting up from a chair, toileting, feeding, and grooming.

Apathy and Depressive Symptom Measures

Symptoms of apathy and depressive affect were evaluated at baseline and yearly follow-up visits using the well-validated Geriatric Depression Scale (GDS).[44,45] The 15-item GDS was used in the LonGenity study, and the corresponding 15 items were extracted from the 30-item GDS used in the CCMA study for symmetry of analysis. A similar procedure to harmonize depression assessments was previously applied in other cohorts.[46] Factor analyses have consistently identified an apathy dimension of the GDS, consisting of the following 3 items: (1) Have you dropped many of your activities and interests ("yes" or "no")? (2) Do you prefer to stay home, rather than go out and do new things ("yes" or "no")? (3) Do you feel full of energy ("yes" or "no")?[4,47,48] Consistent with previous apathy research,[2–4,18,49] we distinguished apathy (GDS-3; range, 0–3) and depressive symptoms (GDS-12, remaining items; range, 0–12) into 2 non-overlapping subscales and utilized a cutoff score of 2 or more endorsed apathy items to indicate the presence of apathy. Previous studies have demonstrated good correlation between this measurement method and clinical diagnosis of apathy,[2,4,18,50] with sensitivity and specificity of 69% and 85%, respectively.[2]

Other Covariates

As previously reported,[39,40] a summary illness index was computed based on the presence or absence of physician-diagnosed vascular diseases (diabetes, heart failure, hypertension, angina, myocardial infarction, and stroke) as well as other medical illnesses, including Parkinson's disease, chronic obstructive lung disease, and arthritis. An extensive cognitive battery was administered in both cohorts. For this investigation, we report executive functioning and processing speed, measured by verbal fluency (FAS) and digit symbol coding, respectively,[51,52] as these cognitive processes are most commonly linked with apathy.[6,7,10]

Data Analysis

Baseline characteristics were summarized with descriptive statistics. To determine the longitudinal association of baseline apathy with slow gait, frailty, and disability, we used Cox proportional hazards models with each of the 3 outcome measures as dependent variables. Individuals who met criteria for 1 of the outcome measures at baseline were excluded from subsequent analyses for that outcome but not from other analyses if they were eligible. The Cox models were examined separately in LonGenity (cohort 1) and CCMA (cohort 2), as well as in the pooled sample adjusted for cohort status.

Table 1. Baseline Characteristics of Study Population and Prevalence and Incidence Rates of Study Outcomes[a]

Variable	Cohort 1[b] (n = 625)	Cohort 2[c] (n = 312)	*P* Value
Baseline demographics			
Age, y	75.21 (6.40)	76.4 (6.87)	.01
Female, % (n)	53.3 (333)	56.7 (177)	.26
Education, y	17.5 (2.66)	14.65 (3.08)	< .01
Summary illness index (range, 0–9)	1.29 (1.04)	1.18 (0.95)	.15
No. of depressive symptoms (range, 0–12)	1 (1.33)	1 (1.12)	.99
≥ 2 Apathy symptoms, % (n)	20.2 (126)	26.0 (81)	.04
Study outcomes			
Follow-up, y	3.18 (1.43)	1.74 (0.66)	< .01
Slow gait, % (n)			
Prevalence	10.9 (68)	15.1 (47)	.06
Incidence	14.5 (81)	8.3 (22)	.03
Frailty, % (n)			
Prevalence	12.2 (76)	17.9 (56)	.01
Incidence	17.9 (98)	14.8 (38)	.31
Disability, % (n)			
Prevalence	3.8 (24)	4.5 (14)	.62
Incidence	5.3 (32)	2.3 (7)	.04

[a]Values are reported as mean (SD) unless otherwise noted.
[b]LonGenity cohort.
[c]Central Control of Mobility in Aging cohort.

We used 4 models in the analysis. Because one of our main aims was to show the predictive value of apathy independent of comorbid depressive symptoms, we included the 12-item GDS (minus apathy score) as a continuous covariate in all models. In model 2, we additionally adjusted for age, sex, and education because apathy symptoms are influenced by these demographic characteristics.[1,3,4] Apathy has also been associated with poor health status and cognitive decline[3,53–55]; therefore, models 3 and 4 adjusted for summary illness index and cognitive functioning (FAS and digit symbol coding), respectively. Associations are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). Regression diagnostics for all models were examined and adequately met. All analyses in this study were carried out using SPSS version 20 (IBM Corp).

RESULTS

Baseline Characteristics

Table 1 displays baseline demographic and clinical data for subjects in both cohorts as well as prevalence and incidence rates for study outcomes. Twenty percent of individuals in cohort 1 endorsed baseline apathy versus 26% in cohort 2. In the pooled sample, 379 participants (40%) endorsed no symptoms of apathy, 351 (38%) endorsed 1, 164 (18%) endorsed 2, and 43 (5%) endorsed all 3 apathy symptoms. As expected, individuals with apathy were significantly older and had poorer health status, lower education, and a higher number of depressive symptoms (Table 2).

Longitudinal Association of Baseline Apathy Symptoms With Outcome Measures

Table 3 presents the association of baseline apathy with incident slow gait, frailty, and disability for each cohort

Table 2. Baseline Characteristics of Study Population According to Apathy Status[a]

Characteristic	Apathy (n = 207)	No Apathy (n = 730)	*P* Value
Age, y	77.38 (7.00)	75.08 (6.39)	< .01
Female, % (n)	55.07 (114)	53.70 (392)	.73
Education, y	15.86 (2.96)	16.75 (3.14)	< .01
Summary illness index (range, 0–9)	1.72 (1.09)	1.12 (0.95)	< .01
No. of depressive symptoms (range, 0–12)	3.22 (3.33)	1.24 (1.87)	< .01

[a]Values are reported as mean (SD) unless otherwise noted.

independently and with the pooled sample. Cumulative hazard functions for the pooled sample, stratified by the presence of baseline apathy, are displayed in Figure 1.

Baseline apathy increased the risk of slow gait and frailty in cohort 1 (gait HR = 1.86; frailty HR = 3.39), cohort 2 (gait HR = 2.92; frailty HR = 1.97), and the pooled sample (gait HR = 2.10; frailty HR = 2.86). These associations did not change substantively after additional adjustments for demographics, health status, and cognitive functioning. Presence of baseline apathy increased disability risk in cohort 1 (HR = 4.36) and in the pooled sample (HR = 3.43); however, this relationship was not found in cohort 2. Additional adjustments for demographics, health status, and cognitive functioning did not affect the results.

Sensitivity Analyses

We ran a series of sensitivity analyses on the pooled sample. Because apathy and depression are often comorbid conditions,[5] we wanted to show that apathy accounted for the relationships even in those without subclinical or minor depression. We reran model 1 for all 3 outcomes including only participants who endorsed 1 or fewer depressive symptoms (GDS-12 score ≤ 1) at baseline (n = 654, 105 [16%] of whom had apathy). This method is consistent with, if not more stringent than, previous reports[4,49,50] and did not affect the associations between apathy and incident slow gait (HR = 2.09; 95% CI, 1.25–3.48; *P* = .005), frailty (HR = 3.21; 95% CI, 2.03–5.10; *P* < .001), and disability (HR = 5.16; 95% CI, 2.36–11.31; *P* < .001).

To explore the possibility of a reverse-causation between apathy and study outcomes, we reran model 1 excluding all participants who met criteria for each outcome within 2 years of their baseline assessment. The relationships between apathy and incident slow gait (HR = 1.90; 95% CI, 0.98–3.69; *P* = .057), frailty (HR = 3.74; 95% CI, 2.22–6.31; *P* < .001), and disability (HR = 3.76; 95% CI, 1.52–9.26; *P* = .004) remained strong.

There were 2 incident dementia cases in cohort 1 and 5 in cohort 2. Excluding these cases did not affect the relationship between apathy and the study outcomes (slow gait: HR = 2.11; 95% CI, 1.37–3.25; *P* = .001; frailty: HR = 2.84; 95% CI, 1.93–4.13; *P* < .001; disability: HR = 3.24; 95% CI, 1.57–6.73; *P* < .001).

Lastly, to explore any "dose-dependent" effect of apathy, we reran model 1 with apathy as a categorical 4-level predictor (no symptoms, 1 symptom, 2 symptoms, and 3 symptoms). Figure 2 shows that cumulative risk of incident slow gait, frailty, and disability increases with increasing apathy score (full results in Supplementary eTable 1).

DISCUSSION

In this prospective cohort-based study, the presence of apathy in non-demented, non-disabled, community-dwelling older adults increased risk of functional and motoric decline. Individuals with baseline apathy had a more than 2-fold risk of developing slow gait and frailty and a more than 3-fold risk of becoming disabled, indicating the overall risk of functional decline associated with apathy in older adults. Furthermore, individuals' risk for these outcomes increased with apathy severity. These associations were independent of depressive symptoms and remained robust after adjustment of potential confounders, such as demographics, health status, and cognitive functioning. Excluding incident cases of dementia in our sensitivity analysis did not materially affect the relationship between apathy and the study outcomes, suggesting that despite the well-established links of apathy and cognitive impairment,[7,8,13,56,57] the association of apathy with

Table 3. Longitudinal Association Between Baseline Apathy Symptoms and Incident Slow Gait, Frailty, and Disability[a]

Apathy Symptom	n	No. of Events	Model 1[b]	Model 2[c]	Model 3[d]	Model 4[e]
Slow gait						
Cohort 1	557	81	1.86 (1.11–3.12), .018	1.83 (1.08–3.10), .025	1.59 (0.94–2.70), .086	1.87 (1.10–3.18), .021
Cohort 2	265	22	2.92 (1.27–6.84), .012	2.73 (1.16–6.40), .021	3.02 (1.27–7.16), .012	2.97 (1.27–6.91), .012
Pooled sample	822	103	2.10 (1.36–3.24), .001	1.98 (1.27–3.07), .002	1.85 (1.19–2.89), .007	2.11 (1.36–3.92), .001
Frailty						
Cohort 1	549	98	3.39 (2.15–5.36), < .001	3.13 (1.98–4.93), < .001	2.87 (1.79–5.59), < .001	3.33 (2.09–5.31), < .001
Cohort 2	256	38	1.97 (1.19–3.82), .044	2.14 (1.08–4.24), .029	2.29 (1.16–4.52), .017	2.02 (1.04–3.93), .038
Pooled sample	805	136	2.86 (1.96–4.16), < .001	2.79 (1.92–4.06), < .001	2.55 (1.73–3.75), < .001	2.82 (1.93–4.12). < .001
Disability						
Cohort 1	601	32	4.36 (2.10–9.06), < .001	3.80 (1.80–8.02), < .001	3.78 (1.78–8.04), .001	3.93 (1.82–8.42), < .001
Cohort 2	298	7	0.64 (0.06–6.70), .681	0.70 (0.06–8.30), .777	0.64 (0.06–7.25), .722	1.00 (0.09–11.46), .997
Pooled sample	899	39	3.43 (1.73–6.79), < .001	2.94 (1.48–5.85), .002	3.07 (1.52–6.22), .002	3.39 (1.66–6.93), .001

[a]All analyses with pooled sample adjusted for cohort status. Cohort 1 is the LonGenity cohort, and cohort 2 is the Central Control of Mobility in Aging cohort. Results are presented as hazard ratio (95% CI), *P*.
[b]Adjusted for number of depressive symptoms minus apathy (0–12).
[c]Adjusted for baseline demographics (age, sex, and education level) and number of depressive symptoms minus apathy (0–12).
[d]Adjusted for health status: summary illness index (0–9) and number of depressive symptoms minus apathy (0–12).
[e]Adjusted for cognitive functioning (FAS and digit symbol coding) and number of depressive symptoms minus apathy (0–12).

Figure 1. Hazard Curves for Pooled Sample, Stratified by Apathy Status

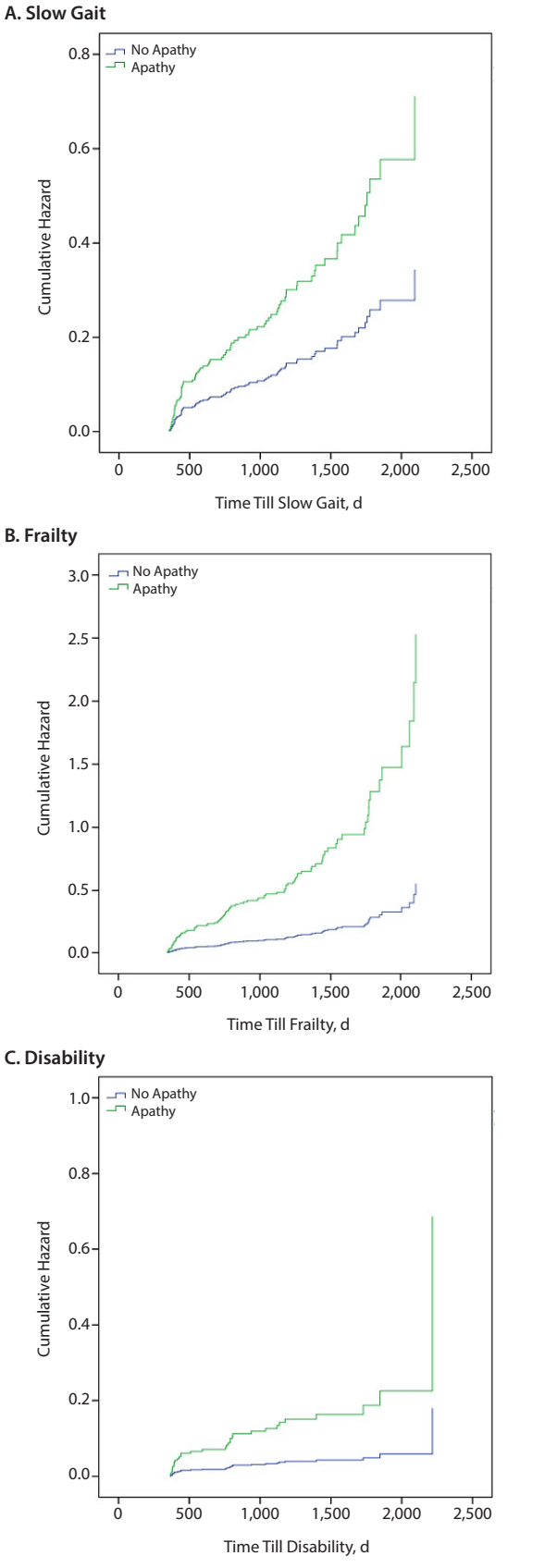
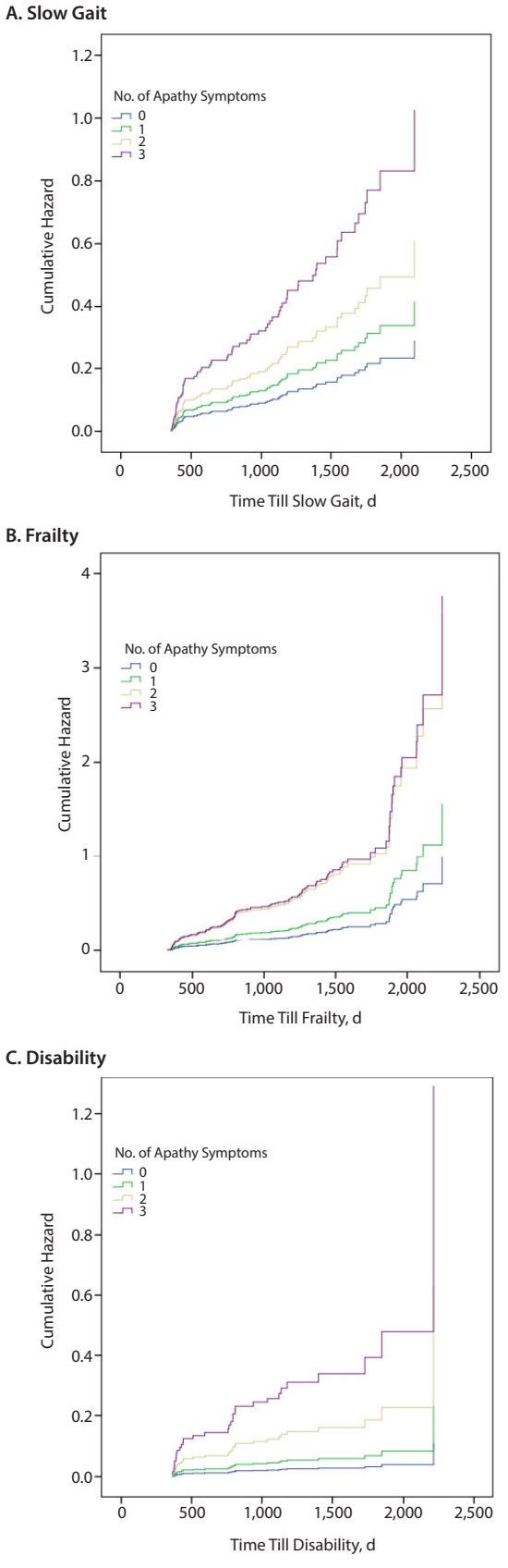


Figure 2. Hazard Curves for Pooled Sample, Stratified by Number of Apathy Symptoms



functional decline may act through other non-dementia pathways in non-demented older adults.

To our knowledge, this is the first study to show that apathy symptoms predict incident frailty and motoric decline among non-demented, community-dwelling older adults. With the exception of 1 study[3] showing that apathy increases disability risk, most researchers have focused on depressive symptoms in this population. Depressive symptoms have been widely associated with frailty and disability in cross-sectional[20,22–24,58,59] and, to a lesser extent, longitudinal[60,61] studies of healthy older adults, although studies have identified a lack of correlation between apathy and depression as well as disease-specific differences in neuropathology.[9] Many previous studies that have reported the association between depressive symptoms and functional decline do not differentiate between symptoms of apathy and depression, and it is unclear how much apathy symptoms contribute to the observed findings in these studies. Additionally, many instruments that measure depressive symptoms include several apathy items, inflating depression rates and conflating the 2 psychiatric constructs.[9] It is quite possible that these previously reported associations were confounded by symptoms of apathy and that it is in fact apathy that predicts these negative health outcomes. This discovery would have significant public health implications, as clinicians routinely screen for depression, but not apathy.

Indirect evidence points to several possible explanations for the relationship between apathy and subsequent motoric and functional decline. First, apathetic individuals may be more susceptible to frailty and disability due to lifestyle factors, such as reduced physical and leisure activity, poor social support, and medication noncompliance. However, there is also evidence for shared pathophysiologic mechanisms, such as vascular pathways. Slow gait, frailty, and disability[56,62,63] have all been previously associated with vascular disease. Healthy older adults with apathy have an almost 3-fold risk of developing cardiovascular disease[50] and show greater evidence of cerebrovascular disease on magnetic resonance imaging.[49] As expected, higher numbers of vascular comorbidities were found among individuals with baseline apathy in our sample, but our summary illness index may not be sensitive to subtle vascular changes. However, the associations between apathy and slow gait, frailty, and disability remained significant when controlling for these comorbid conditions, indicating that these relationships are at least partly independent of vascular pathways.

Increased inflammatory activity is common in aging[57,64] and is hypothesized to be an important pathway for age-related physical decline.[65–68] Among the inflammatory factors, elevated levels of interleukin 6 (IL-6) have been associated with frailty, disability, and gait disturbance among community-dwelling older adults.[67–69] Elevated IL-6 is also implicated as an underlying mechanism for late-life depression[70–72]; however, its role in late-life apathy has yet to be examined. One study[73] looking at depression among poststroke individuals found that higher levels of IL-6 were associated with severity of apathetic-depressive symptoms, indicating some evidence of an apathy-inflammatory link. Future studies should further explore this connection by examining apathy and inflammatory markers in the context of age-related motoric and functional decline. Furthermore, inflammation and vascular disease commonly co-occur[74]; therefore, the relationship of apathy with functional and motoric decline may be through these pathways independently, additively, or synergistically. Future research on apathy should examine multiple biomarkers of inflammation and vascular pathology to elucidate the exact nature of these pathways and help inform potential interventions.

Yet another possible explanation for the observed relationship is the reverse-causation hypothesis. Perhaps apathy is an early behavioral manifestation of frailty and disability, such that individuals begin to display apathy symptoms during prodromal states of these conditions. However, our sensitivity analysis excluding pre-frail and pre-disabled individuals, suggests that apathy is not merely a byproduct but, rather, a predictor of these conditions.

There are several limitations of the current study that should be noted. Due to the clinical overlap between the 3 study outcomes, interpretation of apathy as a predictor of the 3 independent outcomes should be taken with caution. The disability instrument captures performance on physical or basic activities of daily living and was not developed to identify performance on instrumental activities of daily living. We assessed apathy retrospectively in 2 cohorts using 3 items from the GDS that have consistently been shown to reflect apathy[2–4,18] and have high agreement with more detailed apathy scales.[2] However, given the moderate sensitivity and specificity of the GDS, a more detailed apathy assessment might provide additional insights into specific apathy symptoms and our outcomes.[75] Furthermore, that apathy was found to have a "dose-dependent" effect on study outcomes indicates that apathy symptoms themselves, and not necessarily a clinical diagnosis of apathy, places people at risk for future decline. Vascular conditions were clinically diagnosed, and more direct measures of vascular function might have shown stronger relationships with apathy. Vascular and other biological markers should be further explored in future studies to provide mechanistic insights. Dementia was excluded through consensus case conference procedures. Future studies that examine the mediating effect of cognitive outcomes, including subtypes of mild cognitive impairment, on apathy would help delineate the relationship between apathy and functional decline.

To our knowledge, this study is the first to demonstrate apathy as an independent risk factor for frailty and motoric decline in non-disabled, non-demented, community-dwelling elderly individuals. If our findings are corroborated by other studies, apathy screening should become a routine part of psychiatric visits with older adults. Furthermore, the underlying mechanisms of these relationships should be explored via neuroimaging and biomarker techniques to inform the development of intervention strategies to prevent functional decline in high-risk apathy patients.

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Supplementary material follows this article.

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Supplementary Material

Article Title: Symptoms of Apathy Independently Predict Incident Frailty and Disability in Community-Dwelling Older Adults

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List of Supplementary Material for the article

1. eTable 1 — Results of Cox analysis examining 'dose-dependent' effect of apathy on study outcomes in pooled sample

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Supplementary eTable 1. Results of Cox analysis examining 'dose-dependent' effect of apathy on study outcomes in pooled sample

	Slow Gait	Frailty	Disability
Apathy symptoms endorsed*	N = 822	N = 805	N = 899
1 apathy symptom	1.57 (.98-2.52) .062	1.54 (1.00-2.38) .051	2.52 (1.06=5.99) .036
2 apathy symptoms	2.40 (1.40-4.11) .001	3.54 (2.23-5.62) <.001	5.22 (2.08-13.10) <.001
3 apathy symptoms	4.28 (1.86-9.84) .001	3.74 (1.76-7.94) <.001	11.00 (2,88-41.97) <.001

*compared to no apathy symptoms

All models adjusted for depressive symptoms minus apathy (0-12) and cohort status

Results presented as: HR (95% CI) p