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Frailty in NHANES: Comparing the frailty index and phenotype

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ABSTRACT

The two most commonly employed frailty measures are the frailty phenotype and the frailty index. We compared them to examine whether they demonstrated common characteristics of frailty scales, and to examine their association with adverse health measures including disability, self-reported health, and healthcare utilization. The study examined adults aged 50+ (n = 4096) from a sequential, cross-sectional sample (2003–2004; 2005–2006), National Health and Nutrition Examination Survey. The frailty phenotype was modified from a previously adapted version and a 46-item frailty index was created following a standard protocol. Both measures demonstrated a right-skewed distribution, higher levels of frailty in women, exponential increase with age and associations with high healthcare utilization and poor self-reported health. More people classified as frail by the modified phenotype had ADL disability (97.8%) compared with the frailty index (56.6%) and similarly for IADL disability (95% vs. 85.6%). The prevalence of frailty was 3.6% using the modified frailty phenotype and 34% using the frailty index. Frailty index scores in those who were classified as robust by the modified phenotype were still significantly associated with poor self-reported health and high healthcare utilization. The frailty index and the modified frailty phenotype each confirmed previously established characteristics of frailty scales. The agreement between frailty and disability was high with each measure, suggesting that frailty is not simply a pre-disability stage. Overall, the frailty index classified more people as frail, and suggested that it may have the ability to discriminate better at the lower to middle end of the frailty continuum.

1. Introduction

Chronological age – the number of years since birth – differs from biological age – the active rate at which the body is aging (Searle, Mitnitski, Gahbauer, Gill, & Rockwood, 2008). Biological age may be better at describing quality of life, life expectancy and current level of health (Mitnitski, Graham, Mogilner, & Rockwood, 2002). The measurement of frailty could represent an assessment of biological age and thereby is a useful estimate of an individual's health status (Rockwood, 2005a; De Lepeleire, Iliffe, Mann, & Degryse, 2009). Frailty signifies an increased vulnerability to adverse health outcomes, reflecting an age-associated decline in multiple physiological systems (Fried et al., 2001; Rockwood & Theou, 2012; Rockwood, 2005b; Xue, 2011). The two most commonly used approaches to frailty differ, viewing frailty either as a syndrome (frailty phenotype approach) (Fried et al., 2001) or as a state (frailty index approach) (Mitnitski et al., 2002; Rockwood, 2005b). Although the frailty phenotype and frailty index have been compared (Kulminski et al., 2008; Malmstrom, Miller, & Morley, 2014; Ravindrarajah et al., 2013; Rockwood, Andrew, & Mitnitski, 2007; Theou, Brothers, Mitnitski, & Rockwood, 2013; Woo, Leung, & Morley, 2012), their similarities and differences are still not fully agreed upon. Many studies have demonstrated that frailty scores and characteristics from the two measures are comparable (Malmstrom et al., 2014; Woo et al., 2012; Mitnitski, Fallah, Rockwood, & Rockwood, 2011), while others have provided evidence that the frailty index can define the risk of adverse outcomes more precisely than does the phenotype

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(Hubbard, O'Mahony, & Woodhouse, 2009; Malmstrom et al., 2014; Rockwood et al., 2007; Theou et al., 2013).

The majority of studies that compared the frailty phenotype and the frailty index have focused solely on people over the age of 65 (Theou et al., 2013; Kulminski et al., 2008; Rockwood et al., 2007; Woo et al., 2012; Mitnitski et al., 2011; Jung et al., 2014), despite emerging evidence suggesting that frailty begins much earlier than that (Rockwood, Song, & Mitnitski, 2011). Studies that have examined a younger age group have focused on a smaller sample that is not representative of the general population such as the European Male Aging Study (Ravindrarajah et al., 2013) or a the African American Health cohort (Malmstrom et al., 2014). Cesari, Gambassi, van Kan, and Vellas (2014) recently suggested that the two constructs should be considered complementary to one another rather than interchangeable and thus should not be compared. Even so, contrasting the two measures can help us understand the frailty construct, especially using data from a general population.

Fried et al. (2001) identify frailty as the presence of three or more of the five criteria: unintentional weight loss, low energy, slow gait, reduced grip strength and reduced physical activity. The frailty index (Rockwood et al., 1999) operationalizes frailty as the fraction of deficits present in an individual (Searle et al., 2008). Multiple studies have examined frailty in the National Health and Nutrition Examination Survey (NHANES), a large-scale series of cross-sectional surveys that have been used to extensively describe the health of the U.S population. The majority of these studies have followed an adapted version of the phenotype proposed by Wilhelm-Leen et al. (Bowling & Muntner, 2012; Eichholzer, Richard, Walser-Domjan, Linseisen, & Rohrmann, 2013; Singh, Bailey, Noheria, & Kullo, 2012; Smit et al., 2012; Smit, Winters-Stone, Loprinzi, Tang, & Crespo, 2013; Wilhelm-Leen, Hall, Tamura, & Chertow, 2009; Wilhelm-Leen, Hall, Deboer, & Chertow, 2010). This definition can no longer be used, as components of the phenotype were not measured in cohorts after 2002. Of note, no study has examined frailty using NHANES cohorts past 2002, suggesting that a validated adapted phenotype is necessary. Furthermore, although a frailty index is feasible, it has not yet been employed in the NHANES dataset.

This study compared two alternative measures of frailty using the NHANES data: a modified 4-item version of the frailty phenotype and a frailty index. The objectives were two-fold. First, to examine whether the frailty index and modified frailty phenotype demonstrate common characteristics in terms of distribution, mean score, sex differences in frailty scores, limit (99th percentile), relationship of frailty with age, prevalence of frailty, and second to examine the association between each definition of frailty and adverse health measures including disability, self-reported health, and healthcare utilization.

2. Methods

2.1. Sample and study design

We conducted secondary analysis of the cross-sectional data from the 2003–2004 and 2005–2006 cohorts of the United States National Health and Nutrition Examination Survey (NHANES) (CDC, 2014). This study was part of a larger study that examined the association between frailty and physical activity (Blodgett, Theou, Kirkland, Andreou, & Rockwood, 2014). Frailty was not directly measured, however frailty level could still be identified through the data available using the frailty index and phenotype approach. We excluded individuals with missing frailty index or modified phenotype data (see below) for a final sample size of 4096. The NHANES survey protocol was approved by the Institutional Review Board of the Centers for Disease Control and Prevention and all patients provided written informed consent.

2.2. Construction of the frailty index

Any frailty indexes operationalizes frailty by counting deficits; the more health deficits an individual has, the frailer they will be – i.e., the more susceptible to adverse health outcomes (Searle et al., 2008). The frailty index, calculated as a ratio of deficits present out of the total number of possible deficits, gives a continuous score from total fitness (0) to total frailty (1). Here, we constructed a 46-item frailty index (including deficits related to disability, comorbidity, symptoms and irregular laboratory values) (Table 1) following a standard protocol (Searle et al., 2008). All variables were screened to ensure they were (1) health-related, (2) age-associated, (3) neither overly common (deficit was present in 80% or more of individuals by age 80), (4) nor overly uncommon (present in less than 1% of the study population). Deficits were screened to confirm that they encompassed a broad range of systems. All variables included in the frailty index were recoded such that 0 signified the absence of a deficit, while the presence of the deficit was given a score of 1 (Blodgett et al., 2014). Any individual who was missing 20% or more of the variables were excluded from the study ($n = 664$). The high number of excluded cases, which is atypical of frailty indexes, is due to the inclusion of lab values in the frailty index; 426 individuals (out of the 664 excluded) did not have any lab tests done. The frailty index is meant to be used as a continuous score, however in order to compare it with the phenotype, it was also categorized based on proposed cut-off scores identified using stratum specific likelihood ratios (Hoover, Rotermann, Sanmartin, & Bernier, 2013). A FI score of $FI \leq 0.10$ was considered 'non-frail', a score of

Table 1
46 deficits included in frailty index.

Comorbidities	*Signs/symptoms*
• Stroke	• Heart rate at rest
• Thyroid condition	• Systolic blood pressure
• Cancer	• Cough regularly
• Heart attack	• Leaked/lost control or urine
• Heart disease	• General vision
• Ever had high blood pressure	• Difficulty seeing steps/curbs in dim light
• Angina/angina pectoris	• General hearing
• Osteoporosis	• Confusion or inability to remember things
• Diabetes	
• Arthritis	*Lab values*
• Ever had broken hip	• Homocysteine (μmol/L)
	• Folatc, scrum (nmol/L)
• Cataract operation	• Glycohemoglobin (%)
• Weak/failing kidneys	• Red blood cell count (million cells/μL)
	• Hemoglobin (g/dL)
Function	• Red cell distribution width (%)
• Difficulty using fork and knife	• Lymphocyte percent (%)
• Difficulty dressing yourself	• Segmented neutrophils percent (%)
• Difficulty getting in/but of bed	
• Difficulty standing up from armless chair	*Other*
• Difficulty managing money	• Medications
• Difficulty preparing meals	• Self-reported health
• Difficulty standing for long periods of time	• Health compared to 1 year ago
• Difficult stooping, crouching, kneeling	• Frequency of healthcare use
• Difficulty grasping/holding small objects	• Overnight hospital stays
• Difficulty lifting or carrying	
• Difficulty pushing or pulling large objects	
• Difficult attending social event	

$0.10 < FI \leq 0.21$ was 'vulnerable', a score of $0.21 < FI \leq 0.45$ was 'frail,' and $FI > 0.45$ was 'most frail'.

2.3. Construction of the modified frailty phenotype

From 2003 to 2004 on, gait speed-one of the five original criteria was no longer captured in NHANES participants over the age of 50. Barreto, Greig, and Ferrandez (2012) validated a four-item frailty phenotype, demonstrating that it can still identify people at risk of adverse health outcomes. As such, we created a modified four-item phenotype using four of the Wilhelm-Leen et al. (2009) criteria:

- exhaustion, defined by "some difficulty", "much difficulty", or "unable to do" when asked how much difficulty they have "walking from one room to the other on the same level".
- low physical activity, defined as "less active" when asked "Compared with most (men/women) your age, would you say that you are more active, less active, or about the same?"
- weakness, defined by "some difficulty, "much difficulty", or "unable to do" when asked how much difficulty they have "lifting or carrying something as heavy as 10 pounds [like a sack of potatoes or rice]".
- low body weight, defined by BMI ≤ 18.5 kg/m^2.

Frail individuals were those with 3 or 4 of the items, pre-frail individuals were those with 1 or 2 of the items and robust individuals were those with no items present. If an individual had missing data for any of the 4 items, they were excluded from the study ($n = 234$). Although the modified phenotype was employed as a categorical variable, the proportion of items present out of the number of items in the phenotype was also calculated in order to compare its distribution with the frailty index.

2.4. Measurement of disability, healthcare utilization, and self-reported health

All dependent variables were dichotomous as per the following criteria. ADL disability was present if there was any difficulty with at least one of the 4 ADLs measured in NHANES: using a fork or knife, dressing, getting out of bed, and walking between rooms on the same floor. Instrumental activities of daily living (IADL) disability was present if there was any difficulty with at least one of the 3 IADLs measured in NHANES: managing money; doing household chores; and preparing meals (Kalyani, Saudek, Brancati, & Selvin, 2010). Self-reported health was scored as high if the subject answered 'Excellent', 'Very good' or 'Good' to "Would you say your general health was" and low if the subject answered 'Poor' or 'Fair'. Healthcare utilization was scored as high if the subject answered 4+ and low if the subject answered 0–3 to "how many times in the last 12 months [they had] seen a doctor or other healthcare professional about their health at a doctor's office, clinic, hospital emergency room, at home or some other place".

2.5. Statistical analysis

All statistical analyses were conducted using IBM SPSS 20 and SAS 9.23. NHANES provided statistical weights to ensure that the sample was representative of the U.S population. The two-year weights for 2003–2004 and 2005–2006 are not directly comparable, as different population bases were used each year. New sample weights were rescaled such that the sum of the weights matched the survey population at the midpoint of 2003–2006. An alpha level of 0.05 was used to determine statistical significance. The distribution of frailty in each measure as well as the cumulative distribution of the frailty index with regards to the modified phenotype category were examined and compared with one-way ANOVAs. One-way ANOVAs compared mean scores by frailty measure and by sex and the 99th percentile was calculated for both frailty measures. Linear, quadratic, cubic and exponential regression models were tested to select the best fit of the association between age and frailty score. The proportion of people classified at each frailty category was calculated for both definitions; the agreement in the classification between the two definitions was examined using Kappa coefficients. Since there are four frailty index categories and three modified phenotype categories, we combined the categories into both two (non-frail, frail) and three levels (non-frail, vulnerable, frail). To create two levels of frailty, the non-frail and pre-frail categories of the modified phenotype were grouped; for the FI, we grouped the non-frail with the vulnerable and the frail with the most frail. To compare the agreement of the original three level modified phenotype with the FI, we grouped those in the frail and most frail categories of the FI together.

To examine the overlap between frailty and disability, we calculated the proportion of frail individuals who also reported ADL and IADL disability. Logistic regressions examined the strength of the association between each measure of frailty, self-reported health and healthcare utilization. Due to possible co-linearity between the adverse health measures and each measure of frailty, self-reported health and healthcare utilization were removed from the index for their respective regression analyses. Using self-reported health and health care utilization as the dependent variables, four regression models were created for both definitions. We first examined the contribution of the two frailty measures independently and then together in the same model. The fourth model examined a sub-group of those who were categorized as robust by the modified frailty phenotype to determine if frailty index score was still associated with the adverse health measures. Alcohol consumption, smoking, race, income, education, marital status, gender and age were examined as potential covariates; only those that significantly contributed to the model were retained.

3. Results

Of 4874 participants over the age of 50, 4096 (mean age 63.4 ± 10.3; 53.5% women, 18.0% ADL disability) were included in this analysis. Characteristics were comparable for those who were excluded due to missing frailty data (mean age 64.6 ± 10.9, 52.3% women, 19.3% ADL disability). See Table 2 for the demographic characteristics of the sample. The distribution of scores on both frailty scales, measured as a proportion of deficits present out of total deficits possible, resembles a right skewed distribution (Fig. 1). The mean frailty index score increased across categories of the frailty index ($p < 0.001$) (Fig. 2). Women had higher levels of frailty than men in both the frailty index, 0.20 and 0.17 respectively, and the modified frailty phenotype, 0.13 (0.52 out of 4 items) and 0.09 (0.36 out of 4 items) respectively ($p < 0.001$). The 99th percentile of frailty scores was 0.55 in the frailty index and 0.75 (3 out of 4 items) in the modified frailty phenotype. The relationship between age and frailty was best described using a non-linear, exponential model rather than a linear, logistic or quadratic model (Fig. 3). The mean frailty index score increased by 2.3% per year, in log scale, while the mean modified phenotype score increased by 1.1% per year, also on a log scale. The prevalence of frailty was 3.6% in the modified frailty phenotype and 34% in the frailty index. Although all participants classified as frail in the modified phenotype were also classified as frail in the index, 30.8% and 13.4% of the sample were categorized as robust in the modified phenotype, despite being categorized as vulnerable and frail in the frailty index (Table 3). The Kappa agreement between dichotomous frailty measures was 0.166, while the Kappa agreement examining three levels of frailty (robust, pre-frail, frail) was 0.116.

Table 2
Characteristics of the weighted sample by frailty classification.

	All $n=4096$	Frailty index categories				Modified frailty phenotype categories		
		Non-frail $n=1151$	Vulnerable $n=1551$	Frail $n=1242$	Most-frail $n=152$	Robust $n=2852$	Pre-frail $n=1098$	Frail $n=146$
Age (years ± SD)	63 ± 10	58 ± 7	63 ± 10	68 ± 10	70 ± 12	63 ± 10	64 ± 11	63 ± 10
Sex (% female)	53.5%	44.9%	55.2%	57.2%	70.3%	49.3%	62.9%	64.7%
Race/ethnicity (%)								
Non-Hispanic white	80.2%	79.5%	81.4%	79.5%	78.0%	80.9%	78.5%	77.7%
Non-Hispanic black	9.2%	8.3%	8.4%	10.5%	13.4%	8.5%	10.1%	15.6%
Mexican-American	3.9%	4.4%	4.0%	3.4%	3.2%	3.9%	4.1%	3.5%
Other	6.7%	7.8%	6.2%	6.6%	5.4%	6.7%	7.4%	3.2%
Education (%)								
Less than high school	20.0%	12.4%	17.5%	27.8%	39.1%	17.4%	25.4%	29.8%
High school	27.4%	24.5%	28.0%	29.7%	24.5%	26.9%	28.3%	30.1%
Some college/AA degree	28.7%	31.2%	28.3%	27.2%	26.7%	28.8%	28.8%	26.9%
College graduate or more	23.9%	32.0%	26.3%	15.3%	9.6%	27.0%	17.4%	13.2%
Marital status (%)								
Married	67.9%	75.0%	71.4%	61.2%	44.5%	71.4%	60.8%	53.3%
Widowed	14.9%	6.8%	13.4%	21.4%	29.4%	13.6%	17.6%	19.6%
Divorced/separated	13.2%	14.7%	11.0%	13.6%	19.2%	11.6%	16.0%	21.7%
Never married	4.0%	3.6%	4.3%	3.8%	6.9%	3.4%	5.5%	5.4%
Income (%)								
Less than $25 000	26.6%	14.0%	22.7%	40.5%	52.7%	21.8%	36.1%	49.4%
$25 000 to $75 000	48.5%	48.9%	49.5%	47.5%	43.9%	50.1%	45.5%	41.2%
More than $75 000	24.8%	37.0%	27.8%	12.0%	3.4%	28.1%	18.4%	9.4%
Smoked 100+ cigarettes ever (%)	45.6%	48.7%	47.2%	40.1%	51.3%	46.2%	44.9%	39.3%
Drank 12+ drinks in last year (%)	32.2%	26.1%	30.3%	37.7%	54.6%	30.0%	36.6%	43.0%

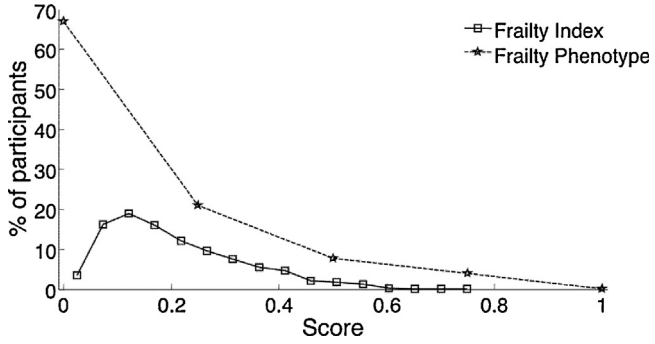

Fig. 1. Distribution of frailty index score and frailty phenotype score (out of 1).

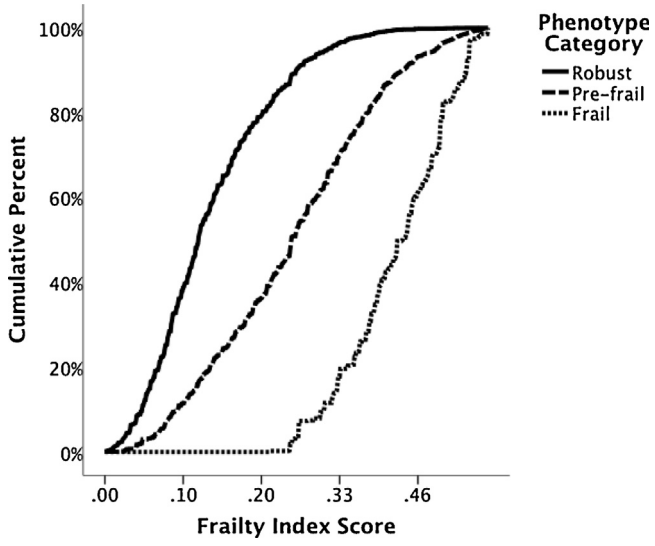

Fig. 2. Cumulative distribution of frailty index score by frailty classification according to the phenotype (robust, pre-frail or frail).

As the level of both the modified frailty phenotype and the frailty index increased, the proportion of individuals with at least one ADL or IADL increased as well. Among frail individuals, based on modified phenotype, 95% had IADL disability and 97.8% ADL disability; among frail individuals, based on FI, 85.6% had IADL disability and 56.6% ADL disability (Fig. 4). Both the frailty index

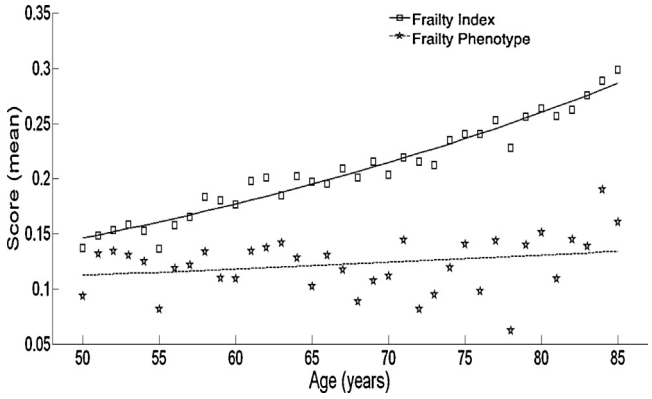

Fig. 3. Relationship of frailty with age for frailty index and frailty phenotype.

Table 3
Proportion of participants in each category of the frailty index and frailty phenotype.

	Frailty index category				Total
	Non-frail	Vulnerable	Frail	Most-frail	
Phenotype category					
Robust	25.2% ($n=1031$)	30.8% ($n=1261$)	13.4% ($n=550$)	0.2% ($n=10$)	69.6% ($n=2852$)
Pre-frail	2.9% ($n=120$)	7.1% ($n=290$)	14.8% ($n=605$)	2.0% ($n=83$)	26.8% ($n=1098$)
Frail	0.0% ($n=0$)	0.0% ($n=0$)	2.1% ($n=87$)	1.4% ($n=59$)	3.6% ($n=146$)
Total	28.1% ($n=1151$)	37.9% ($n=1551$)	30.3% ($n=1242$)	3.7% ($n=152$)	100% ($n=4096$)

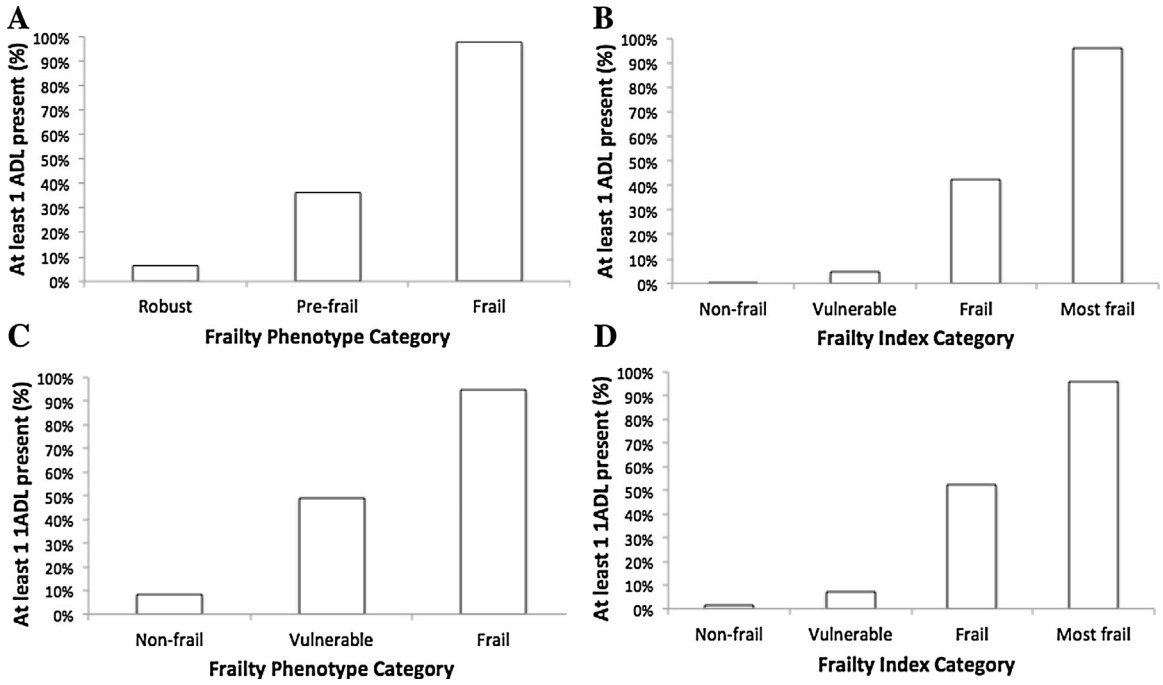

Fig. 4. Proportion of participants who experience limitation with at least one (A) ADL at each frailty phenotype category. (B) ADL at each frailty index category. (C) IADL at each frailty phenotype category. (D) IADL at each frailty index category.

and the modified phenotype were associated with self-reported health and healthcare utilization (Table 4, Models 1–3). In the combined model, the odds ratios associated with the frailty index were higher than that of the modified phenotype for both self-reported health and healthcare utilization (Table 4, Model 3). In a logistic regression examining only those categorized as robust in the modified phenotype, self-reported health and healthcare utilization were still significantly associated with frailty index (Table 4, Model 4). Due to the small number of robust individuals classified as most frail by the frailty index ($n = 10$), the frail and most frail groups were combined together in Model 4. Grouping the frail and most frail together in Model 2 and 3 yielded odds ratios of 39.08 (26.64–57.32) for self-reported health, 17.08 (11.86–24.60) for healthcare utilization in Model 2 and 22.76 (14.89–34.79) for self-reported health, 13.73 (9.36–20.14) for healthcare utilization in Model 3. Similar results were found for all models when the frailty index score was considered as a continuous variable in the regressions ($p < 0.001$).

4. Discussion

This secondary analysis of NHANES showed that the properties of both the frailty index and modified frailty phenotype were consistent with previously accepted characteristics of other frailty measures (Rockwood & Mitnitski, 2007; Theou et al., 2013) including the right skewed distribution of frailty, higher levels of frailty in women compared to men, an upper limit of deficit accumulation and an exponential increase with age. However the magnitude of these characteristics differed (e.g. prevalence was 34% for FI and 3.6% for modified phenotype). There was a high degree of overlap between frailty and disability, regardless of the definition of frailty used. Both measures were associated with self-reported health and healthcare utilization, although the frailty index had a stronger association with both measures and appeared to better discriminate at the lower to middle end of the frailty continuum.

The findings of this study must be interpreted with caution. The cross-sectional nature of the NHANES study is an important limitation as no temporal order of the relationship can be drawn; it is unknown if the predictions would have been the same in a longitudinal study. The variables included in Wilhelm-Leen et al.'s phenotype were modified from the original criteria (Fried et al., 2001) in order to operationalize them for the NHANES dataset. Although this is common (Barreto et al., 2012; Rockwood et al., 2007; Singh et al., 2012; Wilhelm-Leen et al., 2009), the modifications deviated considerably from the original items. Gait speed, considered to be an important phenotype item (Green et al., 2012), was excluded from the modified phenotype, however the 'exhaustion' item defined by difficulty when "walking from one room to the other on the same level" is highly related to mobility; thus some information on mobility was likely included in the modified phenotype used in this study. The categorical nature of the phenotype and the continuous nature of the frailty index limit analyses directly comparing the two measures. As such, for certain analyses, we had to categorize the frailty index and in others, treat the phenotype as continuous.

Previous studies have demonstrated that the frailty phenotype and the frailty index have common characteristics with differing magnitudes and are both able to accurately predict adverse outcomes (Ravindrarajah et al., 2013; Rockwood et al., 2007; Theou, Brothers, Pena, Mitnitski, & Rockwood, 2014). In a European population aged 50+, researchers reported a 2% higher increase with age in the phenotype than the frailty index (Theou et al., 2014), a 0.51 kappa agreement in the dichotomized frailty measures (Theou et al., 2013) and a 10% higher frailty prevalence with the frailty index compared to the phenotype (Theou et al., 2013). A systematic review of community dwelling adults discovered that the prevalence of frailty varies significantly (from 4.0% to 59.1%), mainly due to different operationalization of frailty. In this study, the prevalence of frailty was 3.6% in the modified frailty phenotype and 34% in the frailty index. The modified frailty phenotype initially appeared to have underestimated levels of frailty in the population compared to other studies that reported

Table 4
Logistic regression examining the association of the two measures of frailty with self-reported health and healthcare utilization for the whole sample (models 1–3) and for those who were classified as robust by the phenotype (model 4).

Category	Self-reported health[a] Odds ratio (95% confidence interval)	Healthcare utilization[b] Odds ratio (95% confidence interval)
Model 1: Phenotype		
Robust (0 items/4) $n = 2852$	1	1
Pre-frail (1–2 items/4) $n = 1098$	5.34 (4.45–6.42)	2.42 (2.00–2.94)
Frail (3–4 items/4) $n = 146$	39.82 (24.02–66.03)	6.54 (4.3–9.65)
Model 2: Index		
Non-frail (FI < 0.10) $n = 1151$	1	1
Vulnerable $0.10 < FI \leq 0.21$ $n = 1551$	5.98 (4.10–8.72)	4.31 (2.98–6.22)
Frail $0.21 < FI \leq 0.45$ $n = 1242$	38.38 (26.11–56.41)	15.27 (10.61–21.99)
Most-frail FI > 0.45 $n = 152$	247.87 (133.64–459.73)	54.04 (32.28–90.45)
Model 3: Phenotype & Index		
Phenotype		
Robust $n = 2852$	1	1
Pre-frail $n = 1097$	2.52 (2.04–3.09)	1.19 (0.97–1.45) Non-significant
Frail $n = 146$	7.51(4.34–13.00)	1.42 (0.95–2.14) Non-significant
Index		
Non-frail $n = 1151$	1	1
Vulnerable $n = 1551$	5.27 (3.61–7.71)	4.23 (2.92–6.12)
Frail $n = 1242$	22.56 (15.16–33.57)	13.86 (9.43–20.37)
Most-frail $n = 152$	75.20 (38.95–145.19)	43.05 (24.19–76.6)
Model 4:[c] (n = 2852) Index		
Non-frail $n = 1031$	1	1
Vulnerable $n = 1261$	4.57 (3.00–6.97)	3.92 (2.69–5.73)
Frail ($n = 550$) & Most-frail ($n = 10$)	23.44 (14.76–37.23)	12.05 (8.00–18.51)

[a] Controlled for significant covariates (Models 1, 2: gender, age, education; Model 3: gender, age, education, income, race; Model 4: gender, age, education, race).
[b] Controlled for significant covariates (Models 1, 4: gender, age; Models 2, 3: gender, age, education).
[c] Only individuals classified as robust by the phenotype were included in this sub analysis ($n = 2852$).

phenotype prevalence estimates of 6.9% in a US population 65+ (Fried et al., 2001), 16.6% in a Canadian population aged 65+ (Theou, Rockwood, Mitnitski, & Rockwood, 2012), and 11% in a European population aged 50+ (Gobbens, van Assen, Luijkx, & Schols, 2012). However, the prevalence was comparable to findings that used Wilheem-Leen et al.'s modified criteria in previous waves of NHANES: 6.4% (Singh et al., 2012), 2.5% (Eichholzer et al., 2013) and 2.8% (Wilhelm-Leen et al., 2009). These previous NHANES studies included individuals 65+; as such, it is likely the slightly different phenotype prevalence is due to both the younger study population as well as a change in the number of items included in the phenotype (using 4 instead of 5 items). Contrarily, the frailty index appears to have overestimated frailty when compared to other findings in Canadian populations aged 65+ including 24% (Hoover et al., 2013), 22.7% (Song, Mitnitski, & Rockwood, 2011) and finally 21.6% in a European population aged 50+ (Theou et al., 2013). This is likely due to the inclusion of lab values in the current frailty index, where the prevalence scores for the deficits were much higher compared to the remaining variables. If we constructed the frailty index without the lab values, the frailty prevalence would have been 30.0%.

While the definitions of frailty and disability remain distinct concepts, it is clear there is significant overlap between frailty and disability. In the current study ADL and IADL limitations were more common at the highest levels of frailty; 56.6% (index) and 97.8% (phenotype) of frail individuals had ADL disability, while 85.6% (index) and 95% (phenotype) of frail individuals had IADL disability. Theou et al. (2012) found comparable proportions of ADL disability in frail Canadians over the age of 65 with 66.6% disability in those classified as frail by a frailty index and 83.9% in those classified by the frailty phenotype. Wong et al. (2010) found that 29.1% and 92.7% of phenotypic frail individuals had disabilities in ADLs and IADLs in a population aged 65+; while 28% of disabled women 65+ years old in the Women's Health and Aging were frail (Guralnik, Ferrucci, Simonsick, Salive, & Wallace, 1995). Overall, recent studies, including this one, have found that agreement between frailty and disability is much more common than previously suggested (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004) and that frailty is not simply a pre-disability stage.

In addition, the frailty index was associated with adverse health measures even among people who were considered non-frail by phenotype (Theou et al., 2013). A sub-analysis in individuals categorized as robust by the modified phenotype demonstrated that frailty level was significantly associated with self-reported health and healthcare utilization suggesting that the frailty index may be a more sensitive measure of frailty due to its ability to discriminate at the lower to middle end of the frailty continuum (Kulminski et al., 2008; Rockwood & Mitnitski, 2007). The sensitive, continuous nature of the frailty index helps identify individuals who are vulnerable and allows intervention before an individual reaches an absolute frail state. While the frailty index may provide a more sensitive measure, criticism has focused on the complexity and time involved in collecting the at least 30 items needed to create a frailty index. Using data that has already been collected such as electronic medical records or secondary data could overcome this criticism. The frailty phenotype, which Cesari et al. (2014) suggests is less sensitive than the index, may be more feasible when electronic medical records are unavailable as it requires fewer items. However, reliably collected gait speed and grip strength, two performance based measures, can be problematic in the clinical setting. Furthermore, while it can immediately categorize an individual as robust, prefrail, or frail, it does not provide information on the severity of the frailty of the individual (Cesari et al., 2014). Future research should focus on the feasibility of measuring frailty in the clinical setting.

This study was the first to identify and compare two frailty measures that can be used in the NHANES population. It is also one of only a few studies to examine frailty in a population as young as 50+; frailty studies have typically focused on the older population above the age of 65. The deficit accumulation approach is based on a life course approach and suggests that frailty is not a state into which one enters but rather is a result of the accumulation of health deficits throughout life. Furthermore, most studies comparing the two measures have focused on mortality; this study compared the association between frailty and self-reported health and healthcare utilization. The identification of the index and

modified phenotype as valid measurements of frailty in NHANES is important for studies examining frailty in future NHANES cohorts. Nevertheless, one definition of frailty may not simply be agreed upon as there are strengths and weaknesses associated with each. Other definitions of frailty should continue to be explored; past studies have suggested that there are as many as eight different frailty measures that have demonstrated comparable properties (Theou et al., 2013). The ongoing research on the operational definitions of frailty can help identify and predict who is at increased risk of adverse outcomes.

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Conflict of interest

None.

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