

Journals of Gerontology: Medical Sciences cite as: J Gerontol A Biol Sci Med Sci, 2019, Vol. 74, No. 8, 1257–1264 doi:10.1093/gerona/gly232

Advance Access publication October 11, 2018



Research Article

The Burden of Frailty Among U.S. Veterans and Its Association With Mortality, 2002–2012

Ariela R. Orkaby, MD, MPH,^{1,2,3} Lisa Nussbaum, MA, MBA,² Yuk-Lam Ho, MPH,² David Gagnon, MD, PhD,^{2,4} Lien Quach, PhD,^{2,5} Rachel Ward, MPH, PhD,² Rachel Quaden, MA,² Enzo Yaksic, BS,² Kelly Harrington, PhD,^{2,6} Julie M. Paik, MD, MPH, MSc,^{1,7} Dae H. Kim, MD, MPH, ScD,^{8,9} Peter W. Wilson, MD,^{2,10,11,12} J. Michael Gaziano, MD, MPH,^{2,3} Luc Djousse MD, ScD,^{2,3} Kelly Cho, PhD,*^{2,3} and Jane A. Driver, MD, MPH*,^{1,2,3}

¹New England Geriatric Research, Education, and Clinical Center (GRECC), VA Boston Healthcare System, Massachusetts. ²Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), Boston, Massachusetts. ³Division of Aging, Department of Medicine, Brigham & Women's Hospital, Boston, Massachusetts. ⁴Department of Biostatistics, Boston University School of Public Health, Massachusetts. ⁵Department of Gerontology, University of Massachusetts Boston, Massachusetts. ⁶Department of Psychiatry, Boston University School of Medicine, Massachusetts. ⁷Renal Section, Department of Medicine, VA Boston Healthcare System, Massachusetts. ⁸Division of Gerontology, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts. ⁹Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts. ¹⁰Atlanta VA Medical Center, Decatur, Georgia. ¹¹Division of Cardiology, Emory University School of Medicine, Atlanta, Georgia, and ¹²Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta.

*These authors share senior authorship.

Address correspondence to: Jane A. Driver, MD, MPH, New England Geriatric Research, Education and Clinical Center (GRECC), VA Boston Healthcare System, 150 S Huntington St, Boston, MA 02130. E-mail: Jane.Driver@va.gov

Received: June 12, 2018; Editorial Decision Date: September 14, 2018

Decision Editor: Anne Newman, MD, MPH

Abstract

Background: Frailty is a key determinant of clinical outcomes. We sought to describe frailty among U.S. Veterans and its association with mortality. Methods: Nationwide retrospective cohort study of regular Veterans Affairs (VA) users, aged at least 65 years in 2002–2012, followed through 2014, using national VA administrative and Medicare and Medicaid data. A frailty index (FI) for VA (VA-FI) was calculated using the cumulative deficit method. Thirty-one age-related deficits in health from diagnostic and procedure codes were included and were updated biennially. Survival analysis assessed associations between VA-FI and mortality.

Results: A VA-FI was calculated for 2,837,152 Veterans over 10 years. In 2002, 35.5% were non-frail (FI = 0-0.10), 32.6% were pre-frail (FI = 0.11-0.20), 18.9% were mildly frail (FI = 0.21-0.30), 8.7% were moderately frail (FI = 0.31-0.40), and 4.3% were severely frail (FI > 0.40). From 2002 to 2012, the prevalence of moderate frailty increased to 12.7% and severe frailty to 14.1%. Frailty was strongly associated with survival and was independent of age, sex, race, and smoking; the VA-FI better predicted mortality than age alone. Although prevalence of frailty rose over time, compared to non-frail Veterans, 2 years' hazard ratios (95% confidence intervals) for mortality declined from a peak in 2004 of 2.01 (1.97-2.04), 3.49 (3.44-3.55), 5.88 (5.79-5.97), and 10.39 (10.23-10.56) for pre-frail, mildly, moderately, and severely frail, respectively, to 1.51 (1.49-1.53), 2.36 (2.33-2.39), 3.68 (3.63-3.73), 6.62 (6.53-6.71) in 2012. At every frailty level, risk of mortality was lower for women versus men and higher for blacks versus whites.

Conclusions: Frailty affects at least 3 of every 10 U.S. Veterans aged 65 years and older, and is strongly associated with mortality. The VA-FI could be used to more accurately estimate life expectancy and individualize care for Veterans.

Keywords: Epidemiology, Frailty, Mortality.

The accelerated pace of population aging presents a formidable challenge to health care systems worldwide. This is especially true for the Department of Veterans Affairs (VA), as over 4.5 million U.S. Veterans are now 75 and older (1), creating an urgent need to promote healthier aging and target resources to those who need them most. VA has been a leader in using risk prediction to identify vulnerable Veterans, and has disseminated a tool nationally for determining short-term clinical risk (2). Like most models used to identify the risk of adverse clinical outcomes, this tool is strongly age driven. However, age itself is not the bearer of risk; rather, age-associated health deficits create vulnerability to adverse health events, leading to a state known as frailty (3–7). Because the minority of people older than 85 years become frail (4, 7–11), conventional prediction models lose accuracy when they rely heavily on age (5, 12).

In large clinical data sets, frailty can be defined by a frailty index (FI), a simple count of health-related deficits. The FI is based on a robust theory of aging and has been validated across diverse populations (13–16). An automated FI based on electronic medical record data was recently deployed across the entire British health care system to help primary care providers individualize clinical risk (14). Frailty has previously been defined in Veterans using claims data or prospective clinical assessments in small cohort studies (17–19) and a large VA surgical cohort (20), but its prevalence across VA is unknown. To demonstrate the potential utility of an FI for VA, we calculated an FI in a national Veteran cohort (VA-FI) based on recently validated methods in Medicare (15) and used it to describe trends in frailty and associated mortality over a period of 10 years.

Methods

Study Population

All Veterans at least 65 years who used VA services between 2002 and 2012, defined as having at least one VA clinic visit and one set of routine vitals (eg, blood pressure) and labs (eg, lipids), were included. Cohort entry required Veterans have at least one visit to a VA provider during the year of entry. Follow-up began at the last visit date in the year of cohort entry (index date). Data were queried biennially, thus a participant could contribute a single year or multiple years. The same inclusion criteria applied at each interval of 2 years. Once a Veteran entered the cohort, they were followed until death.

Frailty Definition

We defined frailty according to the cumulative deficit method, using variables in the national VA administrative data set linked to Medicare and Medicaid files (13, 16), as has been validated in Medicare and other data sets (14, 21-24). All variables included in the FI met the following four criteria (13): (a) related to health status, (b) increased in prevalence with age, (c) did not reach a prevalence of 100% before age 65, and (d) covered a range of systems such as cognition, function, and morbidity. We repeated the VA-FI calculation biennially using the same variables at each assessment (13). A minimum of 30 deficits has been recommended (13), although variations with 11-90 deficits have been published (16). The total number of deficits for an individual are counted and divided by the total number of possible variables to give a score between 0 and 1 (13). For example, a Veteran with 10 of 30 possible deficits would have a VA-FI score of 10/30 = 0.33. Given the size of our database, and based on previously published literature, we categorized the VA-FI into five groups: non-frail (0-0.1), (9, 25) pre-frail (0.11-0.20) (9, 25), and divided overall frailty into mild (0.21-0.30), moderate (0.31-0.40), and severe (>0.4) categories, respectively. In analyses

that examined frail versus non-frail, frailty was defined as a score at least 0.21 (9, 25, 26).

Deficits in the VA-FI encompassed variables related to morbidity (eg, arthritis, diabetes), functional status (codes for debility and durable medical equipment), cognition and mood (eg, dementia and depression), sensory impairment (eg, hearing or visual impairment), and other geriatric syndromes (eg, incontinence) (15). In all, 31 variables were identified from diagnostic and procedure codes (Supplementary Table A1). Variables for a given year that the VA-FI was calculated were drawn from the year in question and two preceding years, using both inpatient and outpatient codes. If a Veteran did not have any claims including the relevant codes, the variable was considered absent; thus, deficits could drop off the index in subsequent years. To ensure complete capture of claims data, Medicare and Medicaid data were included in addition to VA data.

Covariates and Outcome

We extracted data on age, sex, race, ethnicity, geographic location, and smoking status at the time of each VA-FI calculation. Smoking was identified from electronic medical records using data extraction methods and was available for all Veterans (27). Geographic region was defined according to the 21 Veterans Integrated Service Networks. Because VA data may not be all inclusive, vital status was confirmed using the National Death Index and was available for 100% of the data set. Mortality follow-up continued through 2014.

Statistical Analysis

Trends in frailty by Veterans Integrated Service Networks were described over a period of 10 years, at an intervals of 2 years from 2002 to 2012, adjusted for age, race, ethnicity, and smoking status. The 2007 cohort was used as the reference cohort for standardization purposes. We used Kaplan-Meier curves to demonstrate the relationship between frailty status and mortality. We used the STRATA statement in SAS to adjust the curves for age, race, ethnicity, and smoking status. The smooth appearance of the curves is due to the very large sample size. Follow-up began from the date of VA-FI calculation. Median survival time was calculated from 2002 through the end of follow-up for men and women to allow for a clinical interpretation of survival by an age interval of 10 years (65–75, 75-85, ≥85). Kaplan-Meier estimates were used for all categories except women aged 65-75 years for which we used a gamma model as median survival had not been achieved by the end of the study. Heat maps were used to visualize the biennial prevalence of frailty geographically across the 21 Veterans Integrated Service Networks. To reflect the most current state of frailty in available VA data, and assess the nonlinear relationship between frailty level and risk of death over 2 years, we used the most recent data available (2012-2014) and fit a restricted cubic spline plot, specifying six knots. We used a VA-FI of 0.22, the mean VA-FI score for the population in 2012, as the reference value.

All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). A two-tailed *p* value less than 0.05 was considered statistically significant.

The institutional review board at the VA Boston Medical Center approved this study.

Results

Over 10 years, 2,837,152 Veterans had at least one VA-FI calculated. In 2002, the cohort included 1,606,774 Veterans, whose mean

age was 74.6 years (SD 5.8); 98.2% were male and 91.1% were white. By 2012, the cohort had grown to 1,920,659 Veterans, mean age was 76.7 years (SD 8.1), 98.0% were male, and 88.8% were white. Over 99% had Medicare and/or Medicaid insurance in addition to VA coverage, highlighting the need to include Medicare/Medicaid information. Sample comorbidities are shown in Table 1. We found that the prevalence of heart disease, cancer, hypertension, advanced kidney disease, and stroke plateaued in 2006–2008. However, the prevalence of dementia, diabetes, incontinence, peripheral neuropathy, and mood disorders continued to rise over time (Supplementary Table A2). Due to the size of the cohort, all comparisons were statistically significant.

Prevalence and Limits of Frailty

In 2002, the median VA-FI score for the population was 0.16 (interquartile range = 0.13) and increased to 0.19 (interquartile

range = 0.23) by 2012. In 2002, 35.5% were classified as non-frail, 32.6% pre-frail, 18.9% mildly frail, 8.7% moderately frail, and 4.3% severely frail. Over the decade, the prevalence of mild frailty remained relatively stable (18.9% and 19.7%). By 2012, the prevalence of moderate frailty had increased by nearly 50% to 12.7%, and severe frailty had more than tripled to 14.1% (Table 1).

There was substantial variability in the prevalence of frailty by region. Crude prevalence was highest in the Southeast (>46%) and lowest in areas of the West (<37%). After adjusting for age, race, ethnicity, and smoking status, the prevalence of frailty increased over time across all regions of the country, shown in the heat maps in Supplementary Figure A1. Overall, greater than 99% of the cohort had a VA-FI $\leq\!0.7$. The maximal FI in the cohort increased from 0.87 in 2002 to 0.94 in 2012. Veterans with a VA-FI greater than 0.8 represented less than 0.01% of the cohort (Table 1). The 99th percentile VA-FI score was 0.52 in 2002 and rose to 0.65 in 2012.

Table 1. Characteristics of U.S. Veterans of age at least 65 years, 2002–2012

	2002	2004	2006	2008	2010	2012
	N = 1,606,774	N = 1,909,317	N = 1,973,895	N = 1,951,194	N = 1,900,044	N = 1,920,659
Age (mean, SD)	74.6 (5.8)	75.6 (6.2)	76.4 (6.6)	76.9 (7.1)	77.1 (7.5)	76.7 (8.1)
Male sex (%)	98.2	98.2	98.2	98.1	98.1	98.0
Race category						
White	91.1	91.0	90.8	90.4	89.8	88.8
Black	7.5	7.5	7.7	8.0	8.5	9.3
Other	1.4	1.5	1.5	1.6	1.7	1.9
Smoking status (ever)	77.8	78.0	78.4	78.9	79.1	79.2
Arthritis (%)	47.6	51.5	53.0	52.8	51.9	51.9
Cognitive impairment or dementia (%)	7.8	12.0	15.4	17.1	18.0	18.0
Diabetes (%)	32.1	34.9	37.6	39.3	40.0	40.8
Heart disease (%)	46.5	48.8	49.6	48.7	46.7	44.3
Hypertension (%)	77.7	82.6	85.7	86.4	85.2	84.1
Use of assistive device	2.6	5.7	3.9	4.0	4.9	6.5
Insurance status (%)						
VA only	0.7	0.7	0.6	0.7	0.7	1.0
VA + Medicare	90.0	90.3	90.9	91.8	92.8	93.1
VA + Medicaid	0.1	0.1	0.1	0.1	0.1	0.2
VA + Medicare and	9.2	8.9	8.4	7.4	6.4	5.7
Medicaid	7.2	0.0	0.1	,	0.1	3.7
District (%)						
Continental	15.2	15.6	15.8	16.0	16.2	16.5
Midwest	23.1	22.8	22.7	22.4	22.1	21.7
North Atlantic	24.1	23.5	23.2	23.0	22.6	22.3
West	13.4	13.8	14.2	14.6	15.1	15.6
Southeast	24.2	24.3	24.1	24.0	24.0	23.9
Frailty (%)	21.2	21.3	2111	21.0	21.0	23.7
Non-frail	35.5	28.8	25.3	24.2	24.8	25.2
Pre-frail	32.6	31.2	30.4	29.5	28.7	28.3
Mild frailty	18.9	20.7	21.1	20.9	20.2	19.7
Moderate frailty	8.7	11.5	12.8	13.2	13.1	12.7
Severe frailty	4.3	7.8	10.4	12.2	13.3	14.1
Frailty score (median,	0.16 (0.13)	0.16 (0.19)	0.19 (0.19)	0.19 (0.19)	0.19 (0.19)	0.19 (0.23)
IQR)	0.10 (0.13)	0.10 (0.17)	0.17 (0.17)	0.17 (0.17)	0.17 (0.17)	0.17 (0.23)
99% FI	0.52	0.55	0.58	0.61	0.65	0.65
Maximum FI value	0.87	0.33	0.38	0.90	0.63	0.63
% with extreme FI values	0.07	0.07	0.70	0.70	U./T	0.24
≥0.5	1.1	2.5	3.7	4.7	5.6	6.3
≥0.3 ≥0.7	0.0	0.1	0.1	0.2	0.3	0.5
∠∪./	0.0	U.1	0.1	U.Z	0.3	0.3

Frailty and Mortality

Table 2 displays 2 years' hazard ratios and 95% confidence intervals for mortality, adjusted for age, sex, race, smoking, and Veterans Integrated Service Network. The lethality of frailty peaked in 2004 with hazard ratios (95% confidence intervals) of 2.01(1.97-2.04), 3.49(3.44-3.55), 5.88(5.79-5.97), and 10.39(10.23-10.56) for pre-frail, mildly, moderately, and severely frail, respectively, to 1.51(1.49-1.53), 2.36(2.33-2.39), 3.68(3.63-3.73), 6.62(6.53-6.71) in 2012. Table 3 demonstrates 2 and 5 years' survival for men and women by age category from 2002 to 2008 and 10 years' survival from 2002. Frailty was associated with lower rates of mortality in women than men regardless of age group or frailty level (Figure 1; Supplementary Figure A2). Estimated median survival from the start of follow-up is shown for men and women in Table 4. Black Veterans had higher rates of mortality at every level of frailty throughout follow-up (Supplementary Figure A3). The relationship between frailty level and survival changed over time, even after adjusting for age, sex, race, ethnicity, and smoking status (Supplementary Figures A1 and A2.)

We fit a cubic spline of the fully adjusted Cox model for 1,920,659 Veterans followed from 2012 to 2014 to examine the relationship between VA-FI level and 2 years' mortality. A score greater than 0.21 was associated with an increased risk of death; the risk increased logarithmically with the VA-FI to a limit of 0.94. Higher scores were not compatible with life, as shown in Figure 2.

To directly compare the value of age versus VA-FI, we performed a survival analysis for 2 years' mortality from 2002. VA-FI alone was found to be a better predictor of survival than age alone (Akaike information criterion [AIC] reduction of 55,633).

Discussion

We calculated an automated FI from claims data in cohort of nearly 3 million regular users of VA and found a prevalence and severity of frailty higher than that reported in other populations. The prevalence, severity, and lethality of frailty was associated not only with age, but varied substantially by sex, race, and geographic region. Frailty was strongly associated with survival and independent of age, sex, race, and smoking status, suggesting that the VA-FI could

be used to improve tools for both longer-term clinical risk prediction and shorter-term prognostication.

In 2002, life tables predicted that an average male aged 75-85 years had an additional estimated life expectancy of 7.8-10.3 years (28). When adjusted for the VA-FI, as shown in Table 4, the estimated median survival could be as low as 3.8 years and as high as 10.4 years, yielding a more accurate understanding of remaining life expectancy. For example, consider two 75-year-old male Veterans in 2008, both at moderate risk of cardiovascular disease. A VA-specific life expectancy table would attribute to both an average survival of 10.2 years (29). However, one has an FI of 0.4, predicting a 42% risk of death in 2 years, and a 70% risk of death in 5 years. If the assumptions are true, then he is unlikely to live the additional 2-5 years needed to derive benefit from primary preventive therapy such as with statins (5). The other Veteran is non-frail with an FI less than 0.1. He will likely live substantially longer than predicted, and benefit from preventive therapies with even a time of 10 years to benefit, such as screening colonoscopy (5). The first Veteran may be biologically similar to someone older than 85 years, whereas the "biological" age of the second is closer to 65 years. Like gait speed, a highly integrated measure of function that also powerfully predicts clinical outcomes (30), an FI expresses the overall state of an individual's health. An automated and readily available FI could help VA modernize its approach to the care of its population by determining where individual Veterans actually lie on the frailty spectrum (31).

The prevalence of frailty in our population ranges from 32% in 2002 to 47% in 2012. This is substantially higher than the 9%–34% prevalence found in other studies with a similar age distribution (9, 24, 25, 32). Although difficult to directly compare the results of FI across cohorts unless they are standardized to a common population, it is plausible that Veterans would have a higher burden of frailty (33). A 2016 RANS corporation report found VA users have twice the rate of diabetes and three times the rate of cancer of the general U.S. population (1). There is also mounting evidence that Veterans accumulate deficits more rapidly than their civilian counterparts; 80% of individuals with post-traumatic stress disorder have at least one other mental health condition, and substantially higher risks of obesity, hypertension, cardiovascular, and metabolic disease than expected (34, 35).

Table 2. Hazard Ratios (95% Confidence Intervals) for 2 Years' and Overall Mortality by Frailty Category Among U.S. Veterans of age at least 65 Years (2002–2014)

	Hazard Ratios† (95	% confidence intervals)				
	2002	2004	2006	2008	2010	2012	Overall (2002–2014)
Non-frail $FI \le 0.1$	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Pre-frail FI >0.1 to ≤0.2	2.06 (2.02, 2.10)	2.01 (1.97, 2.04)	1.74 (1.72, 1.77)	1.69 (1.66, 1.72)	1.57 (1.54, 1.59)	1.51 (1.49, 1.53)	1.47 (1.46, 1.48)
Mildly frail FI >0.2 to ≤0.3	3.61 (3.54, 3.67)	3.49 (3.44, 3.55)	2.95 (2.90, 2.99)	2.78 (2.74, 2.82)	2.47 (2.43, 2.50)	2.36 (2.33, 2.39)	2.07 (2.05, 2.08)
Moderately frail FI >0.3 to ≤0.4	5.94 (5.82, 6.06)	5.88 (5.79, 5.97)	4.89 (4.82, 4.96)	4.49 (4.42, 4.55)	3.87 (3.82, 3.93)	3.68 (3.63, 3.73)	2.85 (2.83, 2.87)
Severely frail FI >0.4	9.82 (9.61, 10.03)	10.39 (10.23, 10.56)	8.57 (8.45, 8.70)	7.89 (7.77, 8.00)	6.87 (6.78, 6.96)	6.62 (6.53, 6.71)	4.13 (4.10, 4.17)

Note: FI = Frailty Index.

[†]Adjusted for sex, race, age, region and smoking.

Table 3. Two, 5, and 10 Years' Survival in Men and Women by Age and Frailty Score Categories for Years 2002 and 2008

2002	2-Year Surviv	2-Year Survival % [†] (95% CI)					5-Year Survive	5-Year Survival % [†] (95% CI)				
VA Frailty Score	Men			Women			Men			Women		
	Age	Age	Age	Age	Age	Age	Age	Age	Age	Age	Age	Age
	65–74	75–84	>85	65–74	75-84	>85	65–74	75–84	>85	65-74	75–84	>85
EI / 0 1	(00 00) 00	120 20/ 20	91 (90 91)	(00 00) 00	(00 /07 00	02 (00 05)	91 (91 92)	02 (02 02)	(7) (5) (2)	(30 707 30	(00 /07 00)	(00 07) 32
FIS U.1	95 (95,95)	96 (36,36)	91 (90,91)	97 (96,97)	96 (97,76)	90 (87 97)	91 (91,92)	75 (75 75)	64 (63,63)	93 (94,93)	00 (07,07)	(05,60)
>0.1 to <0.2	93 (93,93)	93 (93,93)	07 (00,07)	97 (36,37)	96 (93,76)	90 (87,92)	04 (04,03)	(2,(2))	47 (47 49)	94 (93 95)	03 (02,04)	59 (52 (2)
>0.2 to <0.3	91 (90,91)	88 (88,88)	81 (81,82)	95 (94,96)	92 (92,93)	86 (82,88)	(5 (/4,/5)	65 (65,66)	47 (47,48)	84 (82,83)	/6 (/3,/8)	38 (33,62)
>0.3 to ≤0.4	84 (83,84)	81 (81,82)	73 (72,74)	88 (85,90)	89 (87,90)	73 (68,78)	62 (62,62)	54 (53,54)	37 (36,38)	75 (72,78)	65 (63,67)	45 (39,51)
FI 0.4 All FI	/4 (/3,/4) 94 (94,94)	/0 (/0,/1) 90 (90,90)	62 (61,63) 81 (81,81)	82 (78,86) 96 (96,97)	81 (79,83) 93 (93,94)	70 (63,73) 84 (82,86)	47 (46,47) 84 (84,84)	39 (38,39) 70 (70,70)	25 (24,26) 49 (49,49)	60 (54,65) 89 (88,89)	51 (49,54) 78 (77,79)	33 (27,39) 57 (55,60)
2008	2-Year Surviv	2-Year Survival % [†] (95% CI)					5-Year Surviva	5-Year Survival %† (95% CI)				
VA Frailty Score	Men			Women			Men			Women		
	Age	Age	Age	Age	Age	Age	Age	Age	Age	Age	Age	Age
	65-74	75–84	>85	65-74	75-84	>85	65-74	75–84	>85	65-74	75–84	>85
FI ≤ 0.1	(26,76) 76	93 (93,93)	84 (83,84)	(66,86) 86	94 (93,95)	88 (86,90)	91 (91,91)	80 (80,80)	58 (57,58)	94 (93,95)	82 (80,84)	69 (66,72)
>0.1 to ≤ 0.2	94 (94,94)	(06,68) 68	80 (80,80)	(26,96) 26	92 (91,93)	85 (83,86)	84 (84,84)	73 (72,73)	50 (50,51)	91 (90,91)	79 (77,80)	63 (61,65)
>0.2 to ≤ 0.3	88 (88,88)	84 (84,84)	73 (73,73)	93 (92,94)	88 (86,89)	81 (79,82)	74 (74,74)	63 (62,63)	41 (41,41)	83 (82,84)	70 (68,71)	55 (53,57)
>0.3 to ≤ 0.4	(79,80)	75 (74,75)	62 (62,63)	86 (84,88)	81 (79,83)	74 (72,76)	61 (61,61)	50 (49,50)	30 (30,31)	73 (71,75)	58 (56,61)	45 (43,47)
FI > 0.4	64 (64,65)	58 (58,58)	46 (46,47)	77 (74,79)	66 (63,68)	60 (58,62)	42 (41,42)	30 (30,31)	17 (17,18)	58 (55,61)	40 (38,42)	29 (27,30)
All FI	91 (91,91)	82 (82,82)	67 (67,67)	94 (93,94)	85 (84,85)	75 (75,76)	80 (80,80)	62 (62,62)	37 (37,37)	86 (86,87)	(89,68)	49 (48,50)
2002	10-Year Survi	10-Year Survival % (95% CI)										
VA Frailty Score	Men			Women								
	Age	Age	Age	Age	Age	Age						
	65-74	75–84	≥85	65-74	75-84	>85						
FI ≤ 0.1	76 (76,76)	53 (53,53)	22 (22,23)	84 (83,85)	60 (58,61)	29 (24,35)						
$> 0.1 \text{ to} \le 0.2$	62 (62,63)	42 (41,42)	17 (17,18)	72 (70,73)	53 (52,55)	24 (21,28)						
$> 0.2 \text{ to} \le 0.3$	47 (47,48)	30 (30,30)	12 (11,12)	62 (60,64)	42 (41,44)	17 (14,21)						
$> 0.3 \text{ to } \le 0.4$	33 (33,33)	20 (20,20)	7 (7,8)	47 (43,50)	30 (28,32)	14 (10, 18)						
FI > 0.4	20 (19,20)	11 (10,11)	4 (4,4)	29 (24,34)	19 (17,22)	7 (4,11)						
All FI	63 (63,63)	38 (38,38)	13 (13,14)	72 (71,73)	47 (46,48)	19 (17,21)						

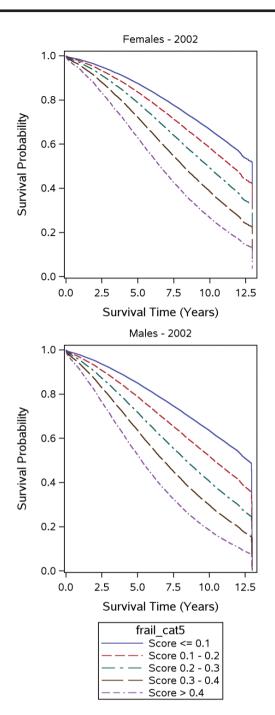


Figure 1. Kaplan-Meier curves for mortality in men and women (2002-2014).

The upper limit of the VA-FI reached 0.9 in 2012, higher than that has been reported in any other cohort (36). Data from Canada, Asia, and Europe previously suggested that an FI greater than 0.7 is not compatible with life (36, 37). The higher limit in VA users may be a reflection of the high prevalence of health deficits in Veterans. An alternative explanation is that Veterans are more resilient than other populations; they were selected on the basis of good health at their time of military service, and many are survivors of the World Wars, Korea War, and Vietnam War. Future work is needed to understand those with extreme VA-FI scores.

We observed a number of patterns seen in other cohorts, including higher frailty levels in female versus male Veterans, and a

stronger association between frailty and mortality in black versus white Veterans (22, 38). Our heat map of frailty status mirrors that of a recently published study of inequality in U.S. life expectancy at the county level from 1980 to 2014, which found up to a variability 20 years (39). Socioeconomic and race/ethnicity status, behavioral and metabolic risk factors, and health care factors explained the majority of the disparity. Of these, behavioral and metabolic risk factors were the most significant, and both are strong risk factors for frailty. Addressing these disparities may have an impact on reversing the rising prevalence of frailty seen in our cohort. Further work is needed to understand the impact of the regional variation in frailty we observed.

The overall declining lethality of frailty over time seen in our study has been described in a cohort of 1,473 older adults followed for 30 years in Sweden (40). That the decline was within only 10 years is interesting, and may reflect improvements in preventive care, such as less tobacco use, preventive treatments for cardiovascular disease, screening for cancer, and increased awareness of healthy lifestyles. It could also represent changes in coding (41); however; the prevalence of frailty as measured by definitions that do not rely on diagnostic codes has also been rising (16). This is in part due to population aging, but also to improved treatments and interventions for chronic conditions that allow people to live to ages where they accumulate age-dependent diseases. Recent data from the United Kingdom used two cohorts, all older than 65 years and predominantly female, to compare FI values over two decades (42). Mean FI values were found to have increased slightly for both men and women (0.15 to 0.16 and 0.20 to 0.2,1 respectively); however, the association between frailty and mortality remained robust. Our data are consistent with these findings, though our cohort is majority male, and in a different country, suggesting that the FI provides robust prediction of mortality across time and different populations.

An FI is most informative when age is not an accurate reflection of global health; this occurs in individuals aged 70–90 years but also in younger people with a high burden of health deficits (43). It could be used to help improve the accuracy of existing prediction models by accounting for unmeasured confounding of health deficits not considered in a parsimonious approach. A claims-based FI such as ours has been shown to have similar outcomes to a survey-based FI (15). It is also a better predictor of disability, falls, and use of long-term care resources than the commonly used Charlson index (15), which is composed only of diagnoses and does not account for deficits in functional, cognitive, or other aging-relevant domains.

Our study has several limitations. It was conducted in Veterans, limiting generalizability. Only about 2% were women; however, this translates to 30,000–40,000 women in each year of follow-up. We used only one of a number of robust methods to measure frailty (7). However, our approach has been well validated (14, 15). The VA-FI does not include laboratory or clinical data such as vital signs. We chose not to include these variables as they would introduce significant missing data that cannot be assumed to be missing at random (15). Future work to improve the VA-FI may capitalize on novel tools using natural language processing that capture data in the written electronic health record (44). Our study also has important strengths. The size and richness of the data set available allowed us to examine frailty trends over time in multiple subgroups of Veterans. Combining VA data with Medicare and Medicaid ensured very little missing

Table 4. Twelve Years' Median Survival Time According to FI Level for U.S. Veterans of age at least 65 Years

2002	Median Survival Time (years)								
	Men			Women					
	$\overline{\mathrm{Age^{\dagger}}}$	Age†	Age [†]	Age [‡]	Age†	Age†			
Frailty Score	65–74	75–84	≥85	65–74	75–84	≥85			
FI ≤ 0.1	13.0	10.4	6.4	19.2	11.6	7.4			
>0.1 to ≤0.2	12.4	8.7	5.7	15.1	10.5	6.5			
>0.2 to ≤0.3	9.5	7.0	4.8	12.0	8.8	5.6			
>0.3 to ≤ 0.4	6.8	5.4	3.8	8.5	7.0	4.5			
FI > 0.4	4.6	3.8	2.8	6.0	5.1	3.7			
All FI	12.9	8.0	4.9	15.6	9.5	5.7			

Note: FI = Frailty Index.

[‡]From gamma model because median had not been achieved by the end of the study.

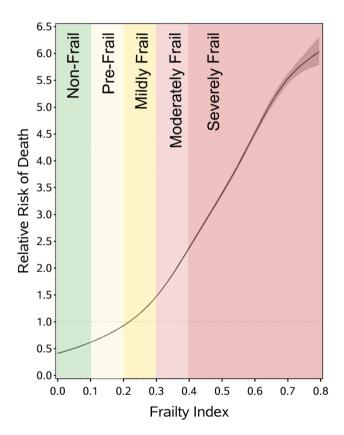


Figure 2. Association between level of frailty and 2 years' all-cause mortality in U.S. Veterans of age at least 65 years (2012–2014).

data as 100% of our population was covered by one of these three insurances.

Conclusion

Frailty affects at least 3 of every 10 U.S. Veterans age 65 and older, varying by geographic region, and is strongly associated with mortality. A simple index of health deficits easily calculated from claims data is a powerful potential tool for improving risk prediction in older and complex populations. More work is needed to determine

how this tool might complement existing models and to understand how frailty in Veterans might be prevented or mitigated.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

Funding

This work was supported by Veteran Affairs-MERIT award (5101BX003340-02). Dr. A.R.O. was supported in part by the Boston Claude D. Pepper Older Americans Independence Center, National Institutes on Aging grant P30-AG031679. Support for VA/CMS data is provided by the Department of Veterans Affairs, VA Health Services Research and Development Service, VA Information Resource Center (Project Numbers SDR 02-237 and 98-004).

Acknowledgement

We acknowledge the U.S. Veterans who made this research possible. We thank Brian Charest, MS, MPH, for his invaluable help with revisions. The sponsor had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Conflict of interest statement

None declared.

References

- Eibner C, Krull H, Brown KM, et al. Current and projected characteristics and unique health care needs of the patient population served by the department of veterans affairs. *Rand Health Q.* 2016;5:13. doi:10.1097/MLR.0b013e31827da95a
- Wang L, Porter B, Maynard C, et al. Predicting risk of hospitalization or death among patients receiving primary care in the Veterans health administration. *Med Care*. 2013;51:368–373. doi:10.1097/MLR.0b013e31827da95a
- Rockwood K, Stolee P, McDowell I. Factors associated with institutionalization of older people in Canada: testing a multifactorial definition of frailty. J Am Geriatr Soc. 1996;44:578–582.
- Fried LP, Tangen CM, Walston J, et al.; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:M146–M156.
- Lee SJ, Kim CM. Individualizing prevention for older adults. J Am Geriatr Soc. 2018;66:229–234. doi:10.1111/jgs.15216

[†]From Kaplan-Meier estimates.

- Dale W. "Staging the aging" when considering androgen deprivation therapy for older men with prostate cancer. J Clin Oncol. 2009;27:3420– 3422. doi:10.1200/ICO.2009.22.9104
- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381:752–762. doi:10.1016/S0140-6736(12)62167-9
- Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc.* 2010;58:681–687. doi: 10.1111/j.1532-5415.2010.02764.x
- Orkaby AR, Hshieh TT, Gaziano JM, Djousse L, Driver JA. Comparison of two frailty indices in the physicians' health study. *Arch Gerontol Geriatr*. 2017;71:21–27. doi:10.1016/j.archger.2017.02.009
- Sheppard VB, Faul LA, Luta G, et al. Frailty and adherence to adjuvant hormonal therapy in older women with breast cancer: CALGB protocol 369901.
 J Clin Oncol. 2014;32:2318–2327. doi:10.1200/JCO.2013.51.7367.
- Afilalo J, Alexander KP, Mack MJ, et al. Frailty assessment in the cardiovascular care of older adults. J Am Coll Cardiol. 2014;63:747–762. doi:10.1016/j.jacc.2013.09.070
- Kheirbek RE, Fokar A, Shara N, et al. Characteristics and Incidence of chronic illness in community-dwelling predominantly male U.S. veteran centenarians. J Am Geriatr Soc. 2017;65:2100–2106. doi:10.1111/jgs.14900
- Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BMC Geriatr. 2008;8:24. doi:10.1186/1471-2318-8-24
- Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. Age Ageing. 2016;45:353–360. doi:10.1093/ageing/afw039
- Kim DH, Schneeweiss S, Glynn RJ, Lipsitz LA, Rockwood K, Avorn J. Measuring frailty in Medicare data: development and validation of a claims-based frailty index. J Gerontol A Biol Sci Med Sci. 2018;73:980– 987. doi:10.1093/gerona/glx229
- Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007;62:722–727.
- Wang CP, Lorenzo C, Espinoza SE. Frailty attenuates the impact of metformin on reducing mortality in older adults with type 2 diabetes. J Endocrinol Diabetes Obes. 2014;2 pii:1031.
- Van Epps P, Tumpey T, Pearce MB, et al. Preexisting immunity, not frailty phenotype, predicts influenza post vaccination titers among older veterans. Clin Vaccine Immunol. 2017;24 pii: e00498-16. doi:10.1128/cvi.00498-16
- Hall DE, Arya S, Schmid KK, et al. Development and initial validation of the risk analysis index for measuring frailty in surgical populations. *JAMA Surg.* 2017;152:175–182. doi:10.1001/jamasurg.2016.4202
- Wahl TS, Graham LA, Hawn MT, et al. Association of the modified frailty index with 30-day surgical readmission. *JAMA Surg.* 2017;152:749–757. doi:10.1001/jamasurg.2017.1025
- Kim DH, Schneeweiss S. Measuring frailty using claims data for pharmacoepidemiologic studies of mortality in older adults: evidence and recommendations. *Pharmacoepidemiol Drug Saf.* 2014;23:891–901. doi:10.1002/pds.3674
- Hoover M, Rotermann M, Sanmartin C, Bernier J. Validation of an index to estimate the prevalence of frailty among community-dwelling seniors. *Health Rep.* 2013;24:10–17.
- Orkaby AR, Lunetta KL, Sun FJ, et al. Cross-sectional association of frailty and arterial stiffness in community-dwelling older adults: the Framingham heart study. J Gerontol A Biol Sci Med Sci. 2019:74:373–379. doi:10.1093/ gerona/gly134
- 24. Kim DH, Glynn RJ, Avorn J, et al. Validation of a claims-based frailty index against physical performance and adverse health outcomes in the health and retirement study. J Gerontol A Biol Sci Med Sci. 2019;74:1271–1276. doi:10.1093/gerona/gly197
- 25. Pajewski NM, Williamson JD, Applegate WB, et al.; SPRINT Study Research Group. Characterizing frailty status in the systolic blood

- pressure intervention trial. J Gerontol A Biol Sci Med Sci. 2016;71:649–655. doi:10.1093/gerona/glv228
- Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc.* 2013;61:1537–1551. doi:10.1111/jgs.12420
- Wicentowski R, Sydes MR. Using implicit information to identify smoking status in smoke-blind medical discharge summaries. J Am Med Inform Assoc. 2008;15:29–31. doi:10.1197/jamia.M2440
- 28. Arias E. United States life tables, 2000. Natl Vital Stat Rep. 2002;51:1-38.
- National Center for Veterans Analysis and Statistics, Department of Veterans Affairs. Mortality Rates and Life Expectancy of Veterans. https://www.va.gov/vetdata/docs/SpecialReports/Mortality_study_ USVETS 2015 1980 2014.pdf. Accessed August 2, 2018.
- 30. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA*. 2011;305:50–58. doi:10.1001/jama.2010.1923
- Sharkey BJ. Functional vs chronologic age. Med Sci Sports Exerc. 1987;19:174–178.
- Blodgett J, Theou O, Kirkland S, Andreou P, Rockwood K. Frailty in NHANES: Comparing the frailty index and phenotype. *Arch Gerontol Geriatr.* 2015;60:464–470. doi:10.1016/j.archger.2015.01.016
- 33. Selim AJ, Berlowitz DR, Fincke G, et al. The health status of elderly veteran enrollees in the veterans health administration. *J Am Geriatr Soc.* 2004;52:1271–1276. doi:10.1111/j.1532-5415.2004.52355.x
- 34. Wolf EJ, Schnurr PP. PTSD-Related cardiovascular disease and accelerated cellular aging. *Psychiatr Ann.* 2016;46:527–532. doi:10.1002/da 22620
- Howard JT, Sosnov JA, Janak JC, et al. Associations of initial injury severity and posttraumatic stress disorder diagnoses with long-term hypertension risk after combat injury. *Hypertension*. 2018;71:824–832. doi:10.1161/HYPERTENSIONAHA.117.10496
- Bennett S, Song X, Mitnitski A, Rockwood K. A limit to frailty in very old, community-dwelling people: a secondary analysis of the Chinese longitudinal health and longevity study. Age Ageing. 2013;42:372–377. doi:10.1093/ageing/afs180
- Rockwood K, Mitnitski A. Limits to deficit accumulation in elderly people.
 Mech Ageing Dev. 2006;127:494

 –496. doi:10.1016/j.mad.2006.01.002
- Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in older adults: a nationally representative profile in the United States. J Gerontol A Biol Sci Med Sci. 2015;70:1427–1434. doi:10.1093/gerona/glv133
- Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, et al. Inequalities in life expectancy among us counties, 1980 to 2014: temporal trends and key drivers. JAMA Intern Med. 2017;177:1003–1011. doi:10.1001/ jamainternmed.2017.0918
- Bäckman K, Joas E, Falk H, Mitnitski A, Rockwood K, Skoog I. Changes in the lethality of frailty over 30 years: evidence from two cohorts of 70-year-olds in Gothenburg Sweden. *J Gerontol A Biol Sci Med Sci*. 2017;72:945–950. doi:10.1093/gerona/glw160
- Jinno S, Lu N, Jafarzadeh SR, Dubreuil M. Trends in hospitalizations for serious infections in patients with rheumatoid arthritis in the US between 1993 and 2013. Arthritis Care Res. 2018;70:652–658.doi:10.1002/ acr.23328
- Mousa A, Savva GM, Mitnitski A, et al. Is frailty a stable predictor of mortality across time? Evidence from the cognitive function and ageing studies. Age Ageing. 2018;47:721–727. doi:10.1093/ageing/afy077
- Mitnitski AB, Rutenberg AD, Farrell S, Rockwood K. Aging, frailty and complex networks. *Biogerontology*. 2017;18:433–446. doi:10.1007/ s10522-017-9684-x
- 44. Vassy JL, Ho YL, Honerlaw J, et al. Yield and bias in defining a cohort study baseline from electronic health record data. *J Biomed Inform*. 2018;78:54–59. doi:10.1016/j.jbi.2017.12.017