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A Comparison of Frailty Indexes for the Prediction of Falls, Disability, Fractures and Mortality in Older Men

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Abstract

Objective—To compare validity of a parsimonious frailty index (components: weight loss, inability to rise from a chair, and poor energy [SOF index]) with that of the more complex CHS index (components: unintentional weight loss, low grip strength, poor energy, slowness, and low physical activity) for prediction of adverse outcomes in older men.

Design—Prospective cohort study

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Statistical Analysis: Ms. Susan Ewing performed the statistical analyses and is independent of any commercial funder. She had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

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Setting—Six U.S. centers

Participants—3132 men ≥ 67 years

Measurements—Men classified as robust, intermediate stage or frail using SOF index and criteria similar to those used in CHS index. Falls reported tri-annually for 1 year. Disability (≥ 1 new impairment in performing IADL) ascertained at 1 year. Fractures and deaths ascertained during 3 years of follow-up. Area under the curve (AUC) statistics from receiver operating characteristic curve analysis compared for models containing SOF index versus CHS index.

Results—Greater evidence of frailty as defined by either index was associated with increased risks of adverse outcomes. Frail men had a higher age-adjusted risk of recurrent falls (odds ratio [OR] 3.0–3.6), disability (OR 5.3–7.5), nonspine fracture (hazards ratio [HR] 2.2–2.3), and death (HR 2.5–3.5) ($P < 0.001$ for all models). AUC comparisons revealed no differences between models with SOF index versus models with CHS index in discriminating falls (AUC=0.63, $P=0.97$), disability (AUC=0.68, $P=0.86$), nonspine fracture (AUC=0.63, $P=0.90$), or death (AUC=0.71 for model with SOF index and 0.72 for model with CHS index, $P=0.19$).

Conclusion—The simple SOF index predicts risk of falls, disability, fracture and mortality in men as well as the more complex CHS index.

Keywords

frailty; older men; hip fracture; mortality

INTRODUCTION

Frailty, a term in clinical geriatric medicine that typically describes the presence of multisystem impairment and expanding vulnerability, has not yet emerged as a discrete clinical syndrome with a consensus definition.¹ In an attempt to standardize and operationalize the definition of frailty, Fried and colleagues systematically surveyed geriatricians and concluded that a critical mass of impairments added up to the phenotype of frailty.² Using data from the Cardiovascular Health Study (CHS), they proposed a phenotype (CHS index) in which 3 or more of the following 5 components were present: unintentional weight loss, self-reported poor energy, weakness (reduced grip strength), slow gait speed and low physical activity. Frailty as defined by the CHS index was associated with an increased risk of falls, hospitalization, disability and mortality in older people.³ Subsequently, the predictive validity of the CHS index has been confirmed in other cohorts.^{4–8} It has been proposed that the CHS index be used to screen older persons for frailty.³

However, assessment of frailty using the CHS index is unrealistic in the clinical setting for several reasons. Identification of three of its components (grip strength, walking speed, physical activity) requires knowledge of the underlying distribution of the measure in a given population and also depends on gender and/or body size. Criteria including physical activity, timed walks, and grip strength are often not feasible to evaluate in the clinic. Unintentional weight loss is a component of the CHS frailty phenotype, but reporting of intention to lose weight is not straightforward as knowing the direction of weight change may bias patient responses to a question about intention. In addition, both intentional and unintentional weight loss have been associated with an increased risk of disease in older people.^{9,10}

Based on the physiologic domains most frequently cited in the frailty literature,^{11,12} results from previous studies evaluating the predictive validity of individual components,^{9,10,13–17} and suitability of assessment of components in a clinical practice setting, we proposed a simple frailty index using 3 components (weight loss, inability to rise from a chair five times

without using the arms, and poor energy [SOF index]).¹⁸ We previously reported that this parsimonious SOF index predicted risk of adverse outcomes as well as the more complex CHS index in older women.¹⁸ To test the hypothesis that the SOF and CHS indexes have similar predictive validity in older men, we used data collected in the Osteoporotic Fractures in Men (MrOS) Study to compare the value of the SOF index with that of the CHS index for prediction of falls, disability, fracture, and death in a cohort of 3132 community-dwelling men 67 years and older.

METHODS

Participants

From March 2000 through April 2002, 5,995 men who were at least 65 years of age were recruited for participation in the baseline examination of MrOS.¹⁹ Men were recruited from population based listings in six regions of the United States.²⁰ Men with a history of bilateral hip replacement and men who were unable to walk without the assistance of another person were excluded from the study.

From December 2003 through March 2005, MrOS participants were invited to participate in an ancillary study to identify outcomes of sleep disorders in older men (MrOS Sleep study). Of the 5995 men enrolled in the overall study, 3135 (>100% of goal of 3000) completed the MrOS Sleep (2nd) examination. Of these, a total of 3132 men provided data for frailty components and are the subject of this analysis. The Institutional Review Board (IRB) at each center approved the study protocol and written informed consent was obtained from all subjects.

Measurements

Participants completed a questionnaire and were interviewed at the 2nd examination. A selected medical history was obtained. Participants were asked to bring all current medications with them to the 2nd examination for verification of use. Physical activity was assessed using the Physical Activity Scale for the Elderly (PASE).²¹ Depressive symptoms including the question, “Do you feel full of energy?”, were evaluated using the 15-item Geriatric Depression Scale. Cognitive function was assessed with the Teng Modified Mini-Mental State Exam (3MS).²² To assess functional disability, men were asked whether they had any difficulty performing any of five instrumental activities of daily living (IADL). Tests of physical function included grip strength (using a hand-held Jamar dynamometer), walk speed (time in seconds to walk 6 meters at usual pace expressed as m/sec), and inability to rise from a chair (without using his arms) five times. Body weight and height measurements were used to calculate a standard body mass index (BMI). Bone mineral density of the hip was measured using dual energy x-ray absorptiometry (QDR 4500, Hologic, Waltham, MA).

SOF Frailty Index

Frailty defined by the SOF index¹⁸ was identified by the presence of ≥ 2 of the following 3 components at the 2nd examination:

1. *Weight loss* (irrespective of intention to lose weight) of $\geq 5\%$ between the baseline and 2nd examination (mean years between examinations 3.4 (± 0.5)),
2. *Inability to rise from a chair* five times without using the arms, and
3. *Poor energy* as identified by an answer of “no” to the question “Do you feel full of energy?” on the Geriatric Depression Scale.

Men with none of the above components were considered to be robust and those with 1 component were considered to be in an intermediate stage.

CHS Frailty Index

Frailty defined by the CHS index as proposed by Fried and colleagues³ was identified by the presence of ≥ 3 of the following 5 components at the 2nd examination:

1. *Shrinking* as identified by an unintentional weight loss of $\geq 5\%$ between the baseline and 2nd examination (mean years between examinations 3.4 (± 0.5)),
 2. *Weakness* as identified by a maximal grip strength in the lowest quintile stratified by body mass index quartile,
 3. *Poor energy* as identified by an answer of “no” to the question “Do you feel full of energy?” from the Geriatric Depression Scale (GDS),
 4. *Slowness* as identified by an average walk speed in the lowest quintile stratified by median standing height, and
 5. *Low physical activity* level as identified by a PASE score in the lowest quintile.
- Measurements used to define the components of shrinking, poor energy and low physical activity were similar, but not identical, to those used in the original phenotype proposed by Fried and colleagues.³ Men with none of the above components were considered to be robust and those with 1 or 2 components were considered to be in an intermediate stage.

Ascertainment of Falls, Disability, Fractures and Mortality

After the 2nd examination, participants were contacted about falls and fractures every 4 months. Over 99% of these follow-up contacts were completed. All falls reported on the first 3 postcards (covering approximately 1 year) returned after the 2nd examination were included in the falls analyses (average follow-up 9.9 (± 1.3) months). Functional status was assessed at the 2nd examination and an average of 1.2 years later at the 3rd examination; incident disability was defined as ≥ 1 new IADL impairment. Fractures were confirmed by review of radiographic reports. Average follow-up for fracture was 3.1 (± 0.7) years. Deaths were confirmed with death certificates. Follow-up for vital status was 99% complete. Average follow-up for death was 3.2 (± 0.5) years.

Statistical Analysis

We used logistic regression to analyze the association between frailty status as defined by SOF and CHS indexes and the odds of recurrent falls (≥ 2 falls vs. ≤ 1 fall) in the subsequent year and odds of disability after an average of 1.2 years of follow-up. Cox proportional hazards models were used to analyze the associations between frailty status as defined by SOF and CHS indices and subsequent outcomes including any incident nonspine fracture and death. The relative risk (approximated as hazard ratios or odds ratios) of each outcome with 95% confidence intervals was estimated for men categorized as intermediate and those categorized as frail using men categorized as robust as the referent group. We also utilized logistic regression to examine receiver operating characteristic (ROC) curves for each model and calculated area under the curve (AUC). All primary analyses were adjusted for age alone. Secondary analyses were adjusted for additional factors previously identified in the cohort to predict the outcomes.

A bootstrap procedure²³ was used to compare area under the curve (AUC) statistics from logistic regression ROC curve analysis and to compare $-2 \log$ likelihood ($-2LL$) model fit statistics for logistic regression or proportional hazards models. The full study population

was sampled (with replacement) 1000 times. Each bootstrap sample was fit to the two models being compared and the difference between the $-2LL$ statistics and between AUC statistics was calculated. The distribution of these differences was used to make statistical inference about the likelihood that the statistics from the two models were significantly different ($P < 0.05$). Findings regarding the comparison of observed AUC statistics between models were cross-validated using the 10-fold cross validation procedure (results not shown).

RESULTS

Characteristics of the Study Population

Characteristics of the cohort of 3132 men (average age 76.4 years) are shown in Table 1. Using the CHS index, 14% were classified as frail (≥ 3 components), 54% as intermediate (1–2 components) and 32% as robust (no components). Using the SOF index, 13% of men were classified as frail (≥ 2 components), 43% as intermediate (1 component) and 44% as robust (no components). Classification of frailty status using the indices was concordant in 2221 (71%) men. The Kappa statistic was 0.59. The Spearman correlation between indices was 0.70 ($P < 0.001$).

During an average follow-up of 9.9 months, 441 (14%) men experienced ≥ 2 (recurrent) falls. An average of 1.2 years after the frailty assessment, 359 (12%) men reported ≥ 1 new IADL impairment among the 2891 men with IADL data at both examinations. During an average follow-up of 3.1 (fracture) to 3.2 (death) years, 169 (5.4%) men experienced ≥ 1 nonspine fracture and 204 (7%) died.

SOF Index vs. CHS Index for Prediction of Falls, Disability, Fractures and Mortality

Greater evidence of frailty as identified using the SOF or CHS index was similarly associated with a higher odds of ≥ 2 (recurrent) falls in the subsequent year (Table 2). Compared with robust men, men in the intermediate group had a 1.6 -fold age-adjusted increase in risk ($P < 0.001$ for both models) and frail men had a 3.0 to 3.6-fold increase in risk ($P < 0.001$ for both models). ROC curves were essentially superimposed for the model containing the SOF index vs. the model containing the CHS index across a range of sensitivities and specificities, (Figure 1A). Using either index, AUC statistics were essentially identical ($P = 0.97$ for comparison of AUC statistics).

The odds of incident disability (≥ 1 new IADL impairment) were higher with increasing evidence of frailty using either the SOF or CHS index (Table 2). Compared with robust men, men in the intermediate group had an age-adjusted 2.5 to 2.6-fold increase in risk ($P < 0.001$ for both models) and frail men had a 5.3 to 7.5-fold increase in risk ($P < 0.001$ for both models). While the point estimate of the association between frailty and odds of new disability was higher in magnitude for the model with the CHS index, there was no difference between AUC statistics ($P = 0.86$) (Figure 1B).

Frailty as identified using either the SOF or CHS index was also similarly related to an increased risk of incident nonspine fracture (Table 2). After adjustment for age, men in the intermediate stage appeared to have a 1.3 to 1.4-fold increase in risk that did not reach the level of significance ($P = 0.15$ for model with SOF index and 0.10 for model with CHS index) and frail men had a 2.2 to 2.3-fold increase in risk ($P < 0.001$ for both models). Models containing the SOF index performed similarly to those containing the CHS index in ROC analyses (Figure 1C, $P = 0.90$ for comparison of AUC statistics).

All-cause mortality rates were higher with increasing evidence of frailty as identified using either the SOF or CHS index (Table 2). Using the model with the SOF index, men in the

intermediate group compared with robust men had an age-adjusted 1.3-fold increase in risk of death that did not reach significance ($P=0.11$), while frail men had a significant 2.5-fold increase in risk ($P<0.001$). Point estimates of the magnitude of these associations were higher for the model with the CHS index. Compared with robust men, men in the intermediate stage had a 1.8-fold increase in risk of death ($P=0.007$) and frail men had a 3.5-fold increase in risk ($P<0.001$). However, there was no difference between AUC statistics ($P=0.19$) for the models (Figure 1D).

Results were similar when $-2LL$ statistics were compared between models with the SOF index and those with the CHS index; p -values for these comparisons were 0.72 (falls), 0.42 (disability), 0.99 (non-spine fractures), and 0.43 (mortality).

For each outcome, the addition of multiple covariates (including race; living situation; health status; smoking; education; statin use; number of selected medical conditions including prior fracture, arthritis, hypo/hyperthyroidism, temporary ischemic attack or stroke, diabetes mellitus, hypertension, coronary or myocardial infarction, angina, congestive heart failure, chronic obstructive lung disease, chronic kidney disease or kidney failure, intermittent claudication, liver disease, parkinsonism, and non-skin cancer; fall history [models for fracture and mortality]; depressive symptoms; cognitive function; functional disability; body mass index; and femoral neck bone mineral density) to the age-adjusted model resulted in a small to moderate improvement in the predictive validity of the model. However, there was no difference in multivariable models with the SOF index compared to those with the CHS index in discriminating falls (AUC=0.68 for both models, $P=0.84$), disability (AUC=0.74 [SOF index] vs. 0.75 [CHS index], $P=0.36$), nonspine fracture (AUC=0.69 [SOF index] vs. 0.68 [CHS index], $P=0.79$), or death (AUC=0.75 for both models, $P=0.65$).

DISCUSSION

Measurement of frailty status using the simple SOF index based on three components (weight loss, inability to rise from a chair and poor energy) and evaluation of frailty using the more complex CHS index performed similarly in predicting falls, disability, fracture and mortality in this cohort of community-dwelling older men. In context of previously reported results in older women,¹⁸ these findings suggest that the parsimonious SOF index provides a useful operationalization of frailty to use in clinical practice to identify high-risk older people.

There is a widely held view that clinicians can easily determine whether an older patient is “frail” or not. However, there is no consensus definition or official International Classification of Diseases (ICD) diagnosis for frailty. While several instruments have been developed to operationalize the construct of frailty,¹¹ including indexes based on clinical judgment,²⁴ deficit accumulation,^{25,26} and comprehensive geriatric assessment,²⁷ the CHS index³ has been most extensively studied. The validity of the CHS index in predicting risk of adverse outcomes has been confirmed in several cohorts of older adults.^{4–8} The CHS index has also been linked to specific alterations in physiologic and biological pathways that may lead to multisystem impairment underlying the development of the clinical frailty syndrome.²⁸ It has been suggested that the CHS index might serve as the basis for screening older persons for frailty and risk of frailty³ and be integrated into the comprehensive care for older women.²⁹

Classification of frailty status using the CHS and SOF indexes was concordant in 71% of participants. Thus, the SOF and CHS indexes similarly discriminate between groups of older men in the categorization of frailty status. In addition, our findings confirm the value of the CHS index in screening older men for risk of falls, disability, fractures and mortality, with

an AUC as high as 0.72 for death in age-adjusted models. However, similar to our previously published results in older women,¹⁸ we did not find evidence that the prediction of these events was improved using the more complicated CHS index as compared with using the straightforward SOF index that was parsimonious without significant losses in its discriminative ability. Like the CHS index, the three criteria of the SOF index reflect impairment in one or more physiological domains most frequently cited in frailty literature.^{11,12} However, unlike the CHS index, the SOF criteria are not dependent on gender, body size, underlying distribution of the components in a population, or ability to determine intention to lose weight. In addition, SOF index components are easily evaluated and inexpensively obtained in a few minutes in the clinical setting.

This study has several strengths, including its prospective design, comprehensive set of measurements, and completeness of follow-up. However, this study has a number of limitations. Participants were older men living in the community and our findings may not be applicable to other population groups. The measures used to define three components of the CHS index in this analysis were similar, but not identical to those used in the original definition proposed by Fried and colleagues.³ While prediction of all-cause mortality is of essential prognostic importance in aged populations and disability, falls and fractures are a common cause of morbidity in older adults, future research should evaluate the ability of the SOF index to predict other outcomes, including hospitalization and institutionalization. These results indicate that both the CHS and SOF indexes are limited in their ability to discriminate falls and fracture. However, it should be noted that the validity of these indexes in predicting nonspine fracture was similar to that reported for other tools based on the use of clinical risk factors alone.³⁰ Ascertainment of outcomes in this study was limited to one to three years, but our prior study in older women¹⁸ suggested that the findings regarding the predictive validity of the SOF versus CHS index persisted with longer follow-up. The objective of this analysis was to compare the ability of the SOF index to that of the CHS index in predicting adverse outcomes. Future investigations are needed to determine whether the SOF index is useful in the longitudinal characterization of change in frailty status over time. Finally, while we compared the predictive ability of the SOF index with that of the widely referenced CHS index, several indexes of frailty have been proposed and our findings are not generalizable across different frailty instruments.

The parsimonious SOF index provides an operational definition of frailty that predicts falls, disability, fracture and mortality as well as the more complicated CHS index. Thus, the SOF index provides a useful phenotype of frailty to identify high-risk older people in clinical practice.

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Conflict of Interest Disclosures:

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	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X
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Honoraria	X	X	X	X
Speaker Forum	X	X	X	X
Consultant	X	X	X	X
Stocks	X	X	X	X
Royalties	X	X	X	X
Expert Testimony	X	X	X	X
Board Member	X	X	X	X
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Employment or Affiliation		X		X		X		X
Grants/Funds		X	X			X		X
Honoraria		X		X		X		X
Speaker Forum		X		X		X		X
Consultant		X		X		X		X
Stocks		X		X		X		X
Royalties		X		X		X		X
Expert Testimony		X		X		X		X
Board Member		X		X		X		X
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Speaker Forum				X				X
Consultant				X				X
Stocks				X				X
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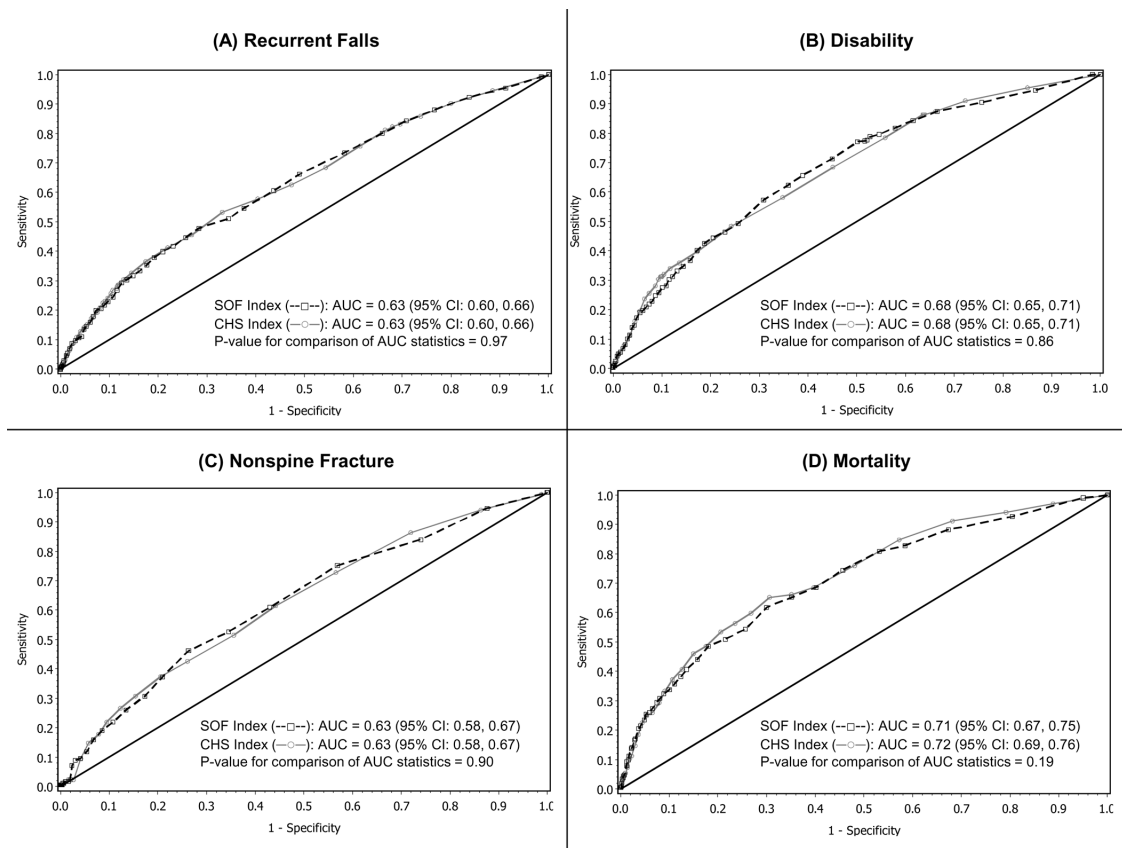


Figure 1. Age-Adjusted Receiver Operating Characteristic (ROC) Curves for Prediction of (A) Recurrent Falls, (B) Disability, (C) Nonspine Fracture, and (D) Mortality with SOF and CHS Frailty Indices*

*The black diagonal line indicates a reference AUC of 0.50 (no better than chance alone)

Table 1

Characteristics of 3132 Participants

Variable	
Age, years, mean (\pm SD)	76.4 (\pm 5.6)
Frailty status by CHS index, n (%)	
Robust	1007 (32)
Intermediate	1688 (54)
Frail	437 (14)
Frailty status by SOF index, n (%)	
Robust	1379 (44)
Intermediate	1336 (43)
Frail	417 (13)
Individual CHS index components	
Unintentional weight loss [*] , n (%)	363 (12)
Weakness, n (%)	754 (24)
Poor energy, n (%)	1401 (45)
Slowness, n (%)	624 (20)
Low physical activity level, n (%)	625 (20)
Individual SOF index components	
Weight loss [†] , n (%)	613 (20)
Inability to rise from chair [‡] , n (%)	206 (7)
Poor energy, n (%)	1401 (45)
≥ 2 falls during 1 st year, n (%)	441 (14)
≥ 1 new IADL impairment [§] , n (%)	359 (12)
≥ 1 incident nonspine fracture, n (%)	169 (5)
Deaths, n (%)	204 (7)

Abbreviations: CHS, Cardiovascular Health Study; SOF, Study of Osteoporotic Fractures; IADL, instrumental activities of daily living

* Unintentional weight loss of 5% or more during the 3.4 years prior the exam

[†] Weight loss of 5% or more during the 3.4 years prior to the exam

[‡] Inability to rise from a chair five times without using the arms

[§] A total of 2891 men completed initial and follow-up IADL assessment

Table 2

Association between Frailty Indexes and Risk of Adverse Outcomes*

Index of Frailty	Recurrent Falls [†]	
	No. with ≥ 2 falls (%)	Odds Ratio (95% CI)
CHS		
Robust (n=1006)	86 (9)	1.0 (referent)
Intermediate (n=1680)	233 (14)	1.62 (1.24–2.11)
Frail (n=432)	122 (28)	3.56 (2.58–4.93)
SOF		
Robust (n=1378)	133 (10)	1.0 (referent)
Intermediate (n=1329)	197 (15)	1.56 (1.23–1.97)
Frail (n=411)	111 (27)	3.03 (2.27–4.05)

	Disability [‡]	
	No. with ≥ 1 new IADL impairment (%)	Odds Ratio (95% CI)
CHS		
Robust (n=968)	49 (5)	1.0 (referent)
Intermediate (n=1562)	198 (13)	2.61 (1.89–3.62)
Frail (n=361)	112 (31)	7.52 (5.14–11.02)
SOF		
Robust (n=1314)	82 (6)	1.0 (referent)
Intermediate (n=1230)	179 (15)	2.47 (1.87–3.25)
Frail (n=347)	98 (28)	5.28 (3.80–7.33)

	Nonspine Fracture [§]		
	No. with ≥ 1 fracture (%)	Age-adjusted rate per 1000 person-years	Hazard Ratio (95% CI) [†]
CHS			
Robust (n=1005)	36 (4)	12.4	1.0 (referent)
Intermediate (n=1674)	90 (5)	19.2	1.39 (0.94–2.06)
Frail (n=431)	43 (10)	31.7	2.30 (1.43–3.71)
SOF			
Robust (n=1373)	56 (4)	14.5	1.0 (referent)
Intermediate (n=1327)	73 (6)	17.9	1.30 (0.91–1.84)
Frail (n=410)	40 (10)	33.1	2.15 (1.41–3.26)

	Mortality [#]		
	No. of deaths (%)	Age-adjusted rate per 1000 person-years	Hazard Ratio (95% CI) [†]
CHS			
Robust (n=1001)	29 (3)	10.4	1.0 (referent)
Intermediate (n=1674)	104 (6)	21.0	1.77 (1.17–2.68)
Frail (n=429)	71 (17)	40.0	3.51 (2.21–5.57)
SOF			

	Mortality ^{//}		
	No. of deaths (%)	Age-adjusted rate per 1000 person-years	Hazard Ratio (95% CI) [†]
Robust (n=1368)	59 (4)	14.8	1.0 (referent)
Intermediate (n=1324)	84 (6)	19.6	1.31 (0.94–1.83)
Frail (n=412)	61 (15)	37.8	2.53 (1.75–3.66)

Note: Among the 3132 men with data for both frailty indices

Abbreviations: CHS, Cardiovascular Health Study; SOF, Study of Osteoporotic Fractures; No., number; IADL, instrumental activities of daily living

* Adjusted for age

[†] 14 who did not provide fall information at follow-up contacts during the subsequent year were excluded from this analysis

[‡] 241 who did not provide IADL information at 1.2 years of follow-up were excluded from this analysis, including 56 men who had died (n=52) or terminated study participation (n=4) in the interim period, 173 who did not provide IADL data at the follow-up exam, and 12 who were unable to attend the follow-up exam

[§] 22 men with incident clinical vertebral fracture were excluded from this analysis

^{//} 28 men whose reported deaths were in the adjudication process were excluded from this analysis