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Publication Date	2023-11-27
Publisher	Oxford University Press
Repository DOI	<a href="https://doi.org/10.1093/ageing/afad214">https://doi.org/10.1093/ageing/afad214</a>

## RESEARCH PAPER

# Comparing frailty prevalence between countries: validation of the Global Burden of Disease study Frailty Index (GBD-FI) in the survey of health, ageing and retirement in Europe

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## Abstract

**Background:** Accurate comparable prevalence proportions are required to better understand the epidemiology of frailty. Estimates in many countries are missing or incomparable. The Global Burden of Disease Frailty Index (GBD-FI) applies the deficit accumulation model to generate frailty scores from items available in the Global Burden of Disease study.

**Objective:** To externally validate the GBD-FI.

**Methods:** Data were obtained from the Survey of Health Ageing and Retirement in Europe (SHARE). A 20-item modified GBD-FI was compared with established frailty measures: a 70-item frailty index (FI-70), the Clinical Frailty Scale (CFS), Frailty Phenotype (FP) and SHARE-FI. Area under receiver operating characteristic curves (AUC) were fitted to examine diagnostic accuracy for frailty and predictive validity for 2-year mortality.

**Results:** In total, 31,624 participants aged  $\geq 50$  years from 15 countries were included. Frailty prevalence was 22% using the GBD-FI (ranging from 8% in Switzerland to 41% in Poland). The GBD-FI had good to excellent diagnostic accuracy for frailty, irrespective of approach; the AUC ranged from 0.86 (95% confidence interval: 0.85–0.87) measuring frailty using the CFS to 0.94 (0.93–0.94) with the FI-70. The GBD-FI had similar accuracy for 2-year mortality (AUC 0.71, 0.69–0.74) compared with the CFS (0.73;  $P = 0.186$ ), FP (0.73;  $P = 0.392$ ) and SHARE-FI (0.70;  $P = 0.255$ ) but lower than the FI-70 (0.76;  $P < 0.001$ ).

**Conclusion:** The GBD-FI demonstrated concurrent and predictive validity, suggesting it is a valid measure of frailty. It has the potential to be an efficient, replicable and consistent approach to comparing frailty between countries and regions across time using GBD data.

**Keywords:** frailty index, Global Burden of Disease study, predictive validity, mortality, prevalence, older people

## Key Points

- The GBD-FI showed strong concurrent validity compared with other frailty tools (AUC: 0.86–0.94).

- The GBD-FI had similar predictive validity for mortality compared with other frailty tools (CFS, FP, SHARE-FI: AUC: 0.70–0.73).
- Frailty prevalence among people  $\geq 50$  years in 15 European countries was 22% according to the GBD-FI; ranging between 8% (Switzerland) and 41% (Poland).
- The GBD-FI is a valid measure of frailty to compare prevalence proportions between countries and territories.

## Introduction

The number of adults aged  $\geq 65$  years is projected to rise from 703 million to over 1.5 billion globally by 2050 [1]. In this setting, frailty, an important age-associated health state [2], will become an increasingly important clinical and public health priority [3]. Accurate and comparable measures of frailty are necessary to examine epidemiological trends and appropriately target care and resources. Multiple approaches to measure frailty at both individual and population-level are accepted. This includes the physical model of frailty as represented by the Frailty Phenotype (FP), focusing on physical signs and symptoms [4], and the accumulation of deficits model, asserting that cellular and systemic damage, through the acquisition of health deficits over time, results in a diminished ability to respond to stressors, predisposing individuals to adverse events [5].

In the latter model, deficits can be observed across multiple domains including diseases, symptoms, function, cognition and laboratory readings [6]. An individual's overall health state (i.e. their risk of adverse outcomes) can then be quantified using a Frailty Index (FI), scored as the proportion of a list of non-specific ageing-related deficits an individual has accumulated. Studies examining FIs have consistently illustrated that the number of deficits present rather than their nature best predicts risk [5] and that despite comprising different deficits, the predictive ability of FIs generally stabilises when at least 25 items are considered [7]. A recent systematic review and meta-analysis has shown that frailty measured by the FI is a significant predictor of mortality [8].

Given the absence of frailty prevalence estimates for many countries and concerns about comparability between regions [9], a novel FI was recently proposed for use with the Global Burden of Disease (GBD) study to support country and regional comparisons [10]. This GBD Frailty Index (GBD-FI) uses 36 items available within the GBD dataset. The GBD study is a large international effort to globally map morbidity and mortality using data from 204 countries and an increasing number of territories [11]. Such subnational estimates are already available for 21 countries including the United Kingdom and United States of America. While GBD studies provide robust comparable population estimates for a comprehensive range of diseases and risk factors, no estimates of frailty prevalence are available. The GBD-FI deficits include a broad selection of age-associated diseases, signs and symptoms including dementia, depression, sensory impairments, physical inactivity and metabolic disorders, although specific measures of function relating to activities of daily living (ADL) are not available in the GBD.

## Objectives

The objectives of this study were to (i) operationalise an internally valid GBD-FI, modified for the available dataset, (ii) assess concurrent validity and diagnostic accuracy of this modified GBD-FI for frailty at individual level, measured against four other established frailty instruments applying different models of frailty: a 70-item FI (FI-70), the Clinical Frailty Scale (CFS), the Fried FP and the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) [12] and (iii) examine the predictive validity of the modified GBD-FI against these measures of frailty for mortality.

## Methods

### Data source

This study is a secondary analysis of a large longitudinal cohort: the Survey of Health, Ageing and Retirement in Europe (SHARE), which includes a population-based cohort of adults aged  $\geq 50$  years. Computer-assisted interviews were delivered by trained personnel and proxy participants (relatives, friends or neighbours) [13]. This analysis excluded those aged  $< 50$  years, nursing home residents and those with missing self-reported frailty items. To incorporate previously validated frailty measures [12] and maximise the number of items applicable in the GBD-FI, the baseline sample was taken from wave 2 (2006/7) [14]. Mortality data were obtained from the next available wave [15]. A total of 15 countries participated in wave 2 (Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Ireland, Israel, Italy, Netherlands, Poland, Spain, Sweden and Switzerland).

### Frailty measures

The GBD-FI was operationalised for the SHARE and compared with four previously validated frailty measures, summarised below. A full description is provided in the **Appendix**.

### Operationalisation of the GBD-FI

The original GBD-FI was created using 36 items from the GBD 2017 study, which includes more than 350 diseases and injuries [16] and 84 risk factors [17]. The approach to item selection is described in detail elsewhere [10]. In summary, standard criteria for creating a FI proposed by Searle et al. [6] were applied and redundant items were removed. In all, 20 variables were available in SHARE wave 2, and are presented and compared with the original GBD items in

**Table 1.** Frailty status for the GBD-FI in the SHARE was defined by the accepted FI cut-off score of  $\geq 0.25$  out of 1.0 [6].

#### 70-item FI

The 70-item FI has previously been published for the SHARE waves 1 and 2 [12]. The FI-70 included biological deficits [ $n = 29$  (41%) including 16 co-morbidities and 13 signs/symptoms], cognitive deficits [ $n = 4$  (6%)], deficits in mental wellbeing [ $n = 11$  (14%)], functional ADL deficits [ $n = 25$  (36%)], and two others [self-rated health and hospitalisation in past year (3%)]. Frailty was defined using a cut-off of  $\geq 0.25$  [6].

#### Clinical frailty scale

This study used an adaption of the CFS previously applied in the SHARE, which uses an eight-stage approach considering independence in ADL, self-rated health, frequency of self-reported vigorous activity, self-reported limitation in activities because of health, the number of ADL and finally the number of instrumental ADL (IADL), scoring participants from 1 (very fit) to 8 (very severely frail), taking a cut-off of  $\geq 5$  [12].

#### Frailty phenotype

Frailty was defined as the presence of at least three of the five physical frailty items (reduced appetite/eating less, fatigue, weak grip strength, walking difficulties and low moderate physical activity) [12, 18]. Items were self-reported apart from grip strength, which was measured as the maximum of two readings for each hand using a handheld dynamometer [19]. Those missing the weak grip strength criterion were imputed as 0 [12].

#### SHARE-FI

The SHARE-FI is a weighted FP [20], which uses an ordinal version of the physical activity criterion, continuous scores for grip strength and does not require body mass index (BMI) for grip strength cut-offs [21]. The five questions are then combined using sex-specific weights and cut-offs [21]. Those missing the weak grip strength criterion were imputed as 0 [12].

#### Covariates and outcomes

Information on age, biological sex and living arrangements (dichotomised into living alone or not) were included. Self-reported educational level was based on International Standard Classification of Education 1997 codes (2–6). Employment status was dichotomised into employed (including self-employed) and not employed (any reason). Financial insecurity was taken as a response of ‘with great difficulty’ or ‘with some difficulty’ to the question ‘Thinking of your household’s total monthly income, would you say that your household is able to make ends meet?’. Quality of life (QoL) was obtained from the CASP-12 scale, ranging between

12 (lowest) and 48 (highest) [22]. BMI was constructed from self-reported height and weight. Low self-rated health was defined as responses of ‘fair’ or ‘poor’. Mortality data were obtained from follow-up at the next wave. Deaths in the SHARE were determined via contact with consenting relatives, friends or neighbours of the study participants, as mortality data from census or registry data were not available.

#### Statistical analysis

Analyses were performed using R version 4.1.1. Calibrated cross-sectional survey weights for individuals provided in the SHARE dataset were applied to produce more representative estimates [13] (**Appendix**). The statistical significance of associations between the GBD-FI and other variables were assessed using weighted t-tests and weighted chi-square tests. Correlations were tested using weighted Pearson’s or Spearman’s coefficients. Agreement between the frailty cut-off values was measured using weighted Cohen’s Kappa statistic. The rate of deficit accumulation with age was examined using weighted linear regression [6]. Weighted logistic regression was used to calculate odds ratios (ORs) for mortality comparing non-frail and frail groups. Accuracy for frailty according to each measure and for mortality at follow-up were compared using weighted area under the curve (AUC) from Receiver Operating Characteristic curves and bootstrap replicates were used to generate 95% confidence intervals (CI). The statistical significance of AUC differences were tested using a paired t-test of bootstrap replicates [23]. Covariate-adjusted (age and sex) AUC values were estimated using a ‘Semiparametric Bayesian inference’ approach. Further details and sample R codes are provided in the **Appendix**.

## Results

### Sample description

From a total of 37,143 participants from 15 countries, 31,624 were included after excluding those aged  $< 50$  years old ( $n = 1,065$ ), nursing home residents ( $n = 240$ ), and those missing data for frailty ( $n = 1,614$ ), mortality ( $n = 2,492$ ) and cross-sectional sampling weights ( $n = 108$ ). Baseline characteristics by GBD-FI frailty status are provided in **Table 2**. The mean age was 65.58 (range 50–102) years and 54% were female. Frailty prevalence ranged from 8% for the SHARE-FI to 22% for the GBD-FI. The mean GBD-FI score was 0.16 (SD:  $\pm 0.12$ ), similar to the mean FI-70 score of 0.16 (SD:  $\pm 0.13$ ). Frailty according to the GBD-FI was most strongly correlated with FI-70 denoted frailty ( $r = 0.67$ ) (**Appendix**).

### Characteristics of the GBD-FI compared with the other frailty instruments

The GBD-FI and FI-70 followed a right-skewed distribution, typically seen when FIs are applied to a healthy population (**Appendix**) [6]. For individual scores, the upper

**Table 1.** Operationalization of the GBD-FI for the SHARE wave 2 (2006/7)

GBD-FI items selected from the GBD 2017 ( <i>N</i> = 36)*	GBD-FI items modified for the SHARE Wave 2 ( <i>N</i> = 20)
Communicable, maternal, neonatal, and nutritional diseases	
Enteric infections	
Diarrheal diseases	N/A
Nutritional deficiencies	
Protein-energy malnutrition	N/A
Non-communicable diseases	
Neoplasms	
Neoplasms	Malignant cancers (excluding mild skin cancers)
Cardiovascular diseases	
Ischemic heart disease	
Heart failure (impairment)	A heart attack including myocardial infarction or coronary thrombosis or any other heart problem including congestive heart failure
Non-rheumatic valvular heart disease	
Cardiomyopathy and myocarditis	
Atrial fibrillation and flutter	
Stroke	Stroke/cerebrovascular disease
Peripheral artery disease	N/A
High systolic blood pressure (risk factor)	High blood pressure or hypertension
Other cardiovascular and circulatory diseases <sup>3</sup>	N/A
Chronic respiratory diseases	
Chronic respiratory diseases	Chronic lung disease OR asthma OR persistent cough
Digestive diseases	
Peptic ulcer disease	Stomach or duodenal ulcer, peptic ulcer
Gallbladder and biliary diseases	N/A
Neurological disorders	
Alzheimer's disease and other dementias	Alzheimer's disease, dementia, organic brain syndrome, senility or any other serious memory impairment
	Parkinson disease
Parkinson's disease	
Mental disorders	
Major depressive disorder	Depression screening (EURO-D score $\geq 4$ )
Diabetes and kidney diseases	
Diabetes mellitus	Diabetes or high blood sugar
Chronic kidney disease	N/A
Skin and subcutaneous diseases	
Skin and subcutaneous diseases	N/A
Sense organ diseases	
Blindness and vision impairment (impairment)	Eyesight rated fair/poor (close OR distant)
Hearing loss (impairment)	Hearing rated fair/poor
Other sense organ diseases <sup>b</sup>	Dizziness, faints or blackouts
Musculoskeletal disorders	
Rheumatoid arthritis	Arthritis (including osteoarthritis or rheumatism)
Osteoarthritis	
Low back pain	N/A
Gout	N/A
Low bone mineral density (risk factor)	Osteoporosis
Other non-communicable diseases	
Urinary system diseases <sup>c</sup>	Incontinence (self-reported 'bothered by')
Genital prolapse	N/A
Endocrine, metabolic, blood and immune disorders <sup>d</sup>	N/A
High LDL cholesterol (risk factor)	High blood cholesterol
Edentulism and severe tooth loss	Dentures use
Injuries	
Unintentional injuries	
Falls (injurious)	Falling down (self-reported 'bothered by')
Risk factors (some included above, these deficits are ordinal)	
Low physical activity (risk factor)	Low physical activity (risk factor) <sup>e</sup>

**N/A = not available** \*NOTE Items are categorised by GBD group [10], and details on residual GBD cause groups [16] are provided below: <sup>a</sup>Composed of cardiovascular diseases other than rheumatic heart disease, ischemic heart disease; stroke; hypertensive heart disease; non-rheumatic valvular heart disease; cardiomyopathy and myocarditis; atrial fibrillation and flutter; aortic aneurysm; peripheral artery disease and endocarditis. <sup>b</sup>Includes a plethora of eye and ear disorders such as disorders of the eyelids and vertiginous syndromes. <sup>c</sup>Includes urinary tract infections, urolithiasis, benign prostatic hyperplasia and other urinary diseases. <sup>d</sup>Includes mainly thyroid disorders, metabolic and immune disorders, and blood disorders. Does not include anaemia, diabetes, obesity or hypercholesterolemia. <sup>e</sup>Calculated from the sum of two self-reported questions: moderate activity (More than once a week = 0, Once a week = 1/6, One to three times a month = 2/6, Hardly ever, or never = 3/6) and vigorous activity (More than once a week = 0, Once a week = 1/6, One to three times a month = 2/6, Hardly ever, or never = 3/6).

**Table 2.** Characteristics of participants in total and by their GBD-FI frailty status comparing non-frail and frail participants

Baseline characteristics	Total ( <i>N</i> = 24,620)	Non-frail ( <i>n</i> = 19,927)	Frail ( <i>n</i> = 4,693)	<i>P</i> -value
Age (years $\pm$ SD)	65.58 ( $\pm$ 10.3)	63.84 ( $\pm$ 9.53)	71.73 ( $\pm$ 10.5)	<0.001
Female	54%	51%	65%	<0.001
Lives alone	23%	21%	32%	<0.001
Education (post-primary)	68%	74%	48%	<0.001
Employed	26%	32%	6%	<0.001
Financial insecurity	44%	39%	60%	<0.001
QoL (CASP-12 score $\pm$ SD)	36.46 ( $\pm$ 6.38)	37.84 ( $\pm$ 5.65)	31.46 ( $\pm$ 6.37)	<0.001
BMI ( $\pm$ SD)	26.69 ( $\pm$ 4.45)	26.47 ( $\pm$ 4.26)	27.48 ( $\pm$ 5.00)	<0.001
Hospitalisation (in last year)	15%	12%	28%	<0.001
Low self-rated health (fair/poor)	40%	28%	82%	<0.001
FI-70 deficits: comorbidities ( $\geq$ 2)	55%	43%	97%	<0.001
FI-70 deficits: signs & symptoms	84%	80%	100%	<0.001
FI-70 deficits: mental wellbeing	73%	67%	95%	<0.001
FI-70 deficits: cognitive tests	52%	46%	75%	<0.001
FI-70 deficits: function	77%	71%	97%	<0.001
Activities limited by health <sup>a</sup>	44%	34%	81%	<0.001
IADL disability	17%	8%	45%	<0.001
ADL disability	11%	5%	32%	<0.001
FI-70 measured frailty <sup>b</sup>	20%	6%	71%	<0.001
CFS measured frailty <sup>b</sup>	15%	6%	45%	<0.001
FP measured frailty <sup>b</sup>	11%	4%	36%	<0.001
SHARE-FI measured frailty <sup>b</sup>	8%	2%	29%	<0.001

Abbreviations: ADL, activities of daily living; IADL, instrumental activities of daily living; SD, standard deviation. Note: Missing data (unweighted): education (post-primary): 534, employed: 17, financial difficulty: 9905, CASP-12: 1496, BMI: 864. <sup>a</sup>Activity limitation was measured using the Global Activity Limitation Indicator (GALI): 'For the past six months at least, to what extent have you been limited because of a health problem in activities people usually do? . . . Severely limited/Limited, but not severely; Not limited'. <sup>b</sup>Frailty proportions measured using the following cut-offs:  $\geq 0.25$  out of 1.00 for the GBD-FI and FI-70 scores,  $\geq 5$  positive criteria out of 8 for the CFS and  $\geq 3$  positive criteria out of 5 for the FP. The SHARE-FI is weighted and determined from sex-specific equations detailed in the **Appendix**.

limit for both the GBD-FI (99th percentile = 0.50) and FI-70 (99th percentile = 0.59) were as expected, markedly less than 1.0, given the high mortality associated with extreme deficit accumulation [6]. GBD-FI scores were moderately correlated with age ( $r = 0.41$ ) and the rate of deficit accumulation ( $\beta$ ) was 0.030 per year, again characteristic of a typical FI [6]. Values were similar for the FI-70 ( $r = 0.45$ ;  $\beta = 0.036$ ). The GBD-FI had higher mean scores and frailty prevalence proportions among females, similar to the other frailty instruments (**Appendix**). GBD-FI scores correlated strongly with the FI-70 scores ( $r = 0.85$ ) and at a cut-off of  $\geq 0.25$  for frailty, there was substantial agreement; Cohen Kappa ( $\kappa$ ) score 0.67. The GBD-FI also had moderate correlation and agreement with the CFS ( $r = 0.61$ ;  $\kappa = 0.44$ ), FP ( $r = 0.60$ ;  $\kappa = 0.4$ ) and SHARE-FI ( $r = 0.57$ ;  $\kappa = 0.34$ ).

### Country-level comparisons

Country-specific frailty prevalence proportions according to all five measures are presented in **Table 3**. The prevalence estimated using the GBD-FI was 22% with the lowest value observed in Switzerland and highest in Poland. As expected, a higher prevalence was found for instruments applying the deficit accumulation rather than physical models of frailty [9]. Country-level frailty prevalence according to the GBD-FI correlated very strongly with the FI-70 ( $r = 0.98$ ), CFS ( $r = 0.96$ ), FP ( $r = 0.95$ ) and SHARE-FI ( $r = 0.95$ ).

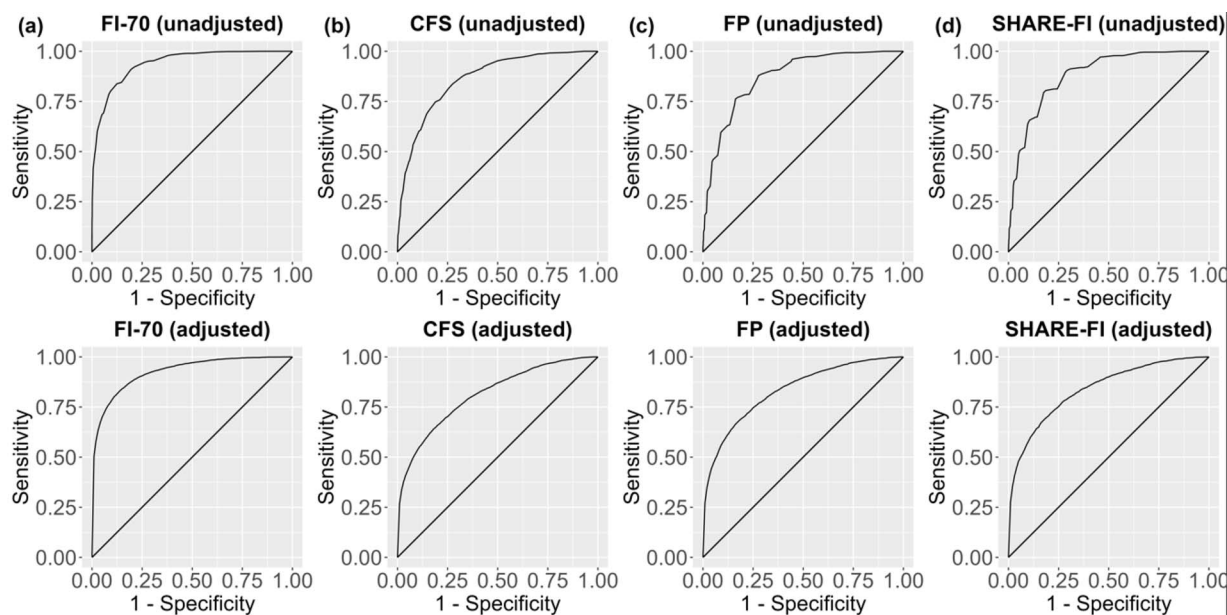
### Diagnostic and predictive accuracy of the GBD-FI

The GBD-FI had very good to excellent diagnostic accuracy for frailty, irrespective of the approach used to classify frailty. Accuracy was greatest for frailty defined by the deficit accumulation model (i.e. using the FI-70): AUC 0.94 (95% CI: 0.93–0.94), reducing only marginally after adjusting for age and sex (AUC 0.93). The overall mortality rate was 3% at a mean of 2.03 years follow-up. The ORs for each frailty scales, with and without adjustment for age and sex, are displayed in **Appendix**. For the GBD-FI, relative to the non-frail class, the unadjusted OR for mortality was 3.66 (95% CI: 3.01–4.44) for frail participants (age-sex- adjusted OR 2.01: 1.63–2.48). The same pattern was found for males and females. All instruments examined had fair accuracy for mortality. The GBD-FI (AUC 0.71, 95% CI: 0.69–0.74) was similar to the CFS (0.73: 0.70–0.76;  $P = 0.186$ ), the FP (0.73: 0.70–0.76;  $P = 0.392$ ) and the SHARE-FI (0.70: 0.67–0.73;  $P = 0.255$ ), but lower than the FI-70 (0.76: 0.74–0.79;  $P < 0.001$ ). Both age and sex had a statistically significant effect on the predictive accuracy of the frailty instruments for mortality (all  $P$ -values  $< 0.001$ ). Adjusting for age and sex, the AUC of the GBD-FI was reduced to 0.62 (0.60–0.64) and the other frailty tools were reduced to values between 0.65 and 0.68. ROC curves with AUC values comparing frailty scales are presented in **Figures 1** and **2**. Optimum GBD-FI cut-offs for the different frailty definitions are presented in the **Appendix**.

**Table 3.** Frailty prevalence according to each frailty measure, comparing SHARE countries including classification, age and sex among community-dwelling Europeans aged ≥50 years

Country	Age (mean)	Sex (% Female)	GBD-FI (% Frail)	FI-70 (% Frail)	CFS (% Frail)	FP (% Frail)	SHARE-FI (% Frail)
Austria	66.27	55%	20%	17%	17%	12%	10%
Belgium	65.71	54%	21%	18%	15%	10%	8%
Czechia	64.35	56%	20%	17%	13%	6%	5%
Denmark	64.90	53%	14%	12%	12%	7%	5%
France	65.47	55%	19%	18%	14%	10%	7%
Germany	65.61	54%	16%	16%	11%	6%	5%
Greece	65.88	53%	16%	15%	11%	10%	7%
Ireland	64.95	54%	22%	16%	14%	10%	8%
Israel	67.09	54%	33%	27%	20%	17%	12%
Italy	66.44	54%	29%	25%	17%	16%	12%
Netherlands	64.31	53%	13%	11%	10%	7%	5%
Poland	63.59	56%	41%	40%	27%	20%	15%
Spain	66.35	54%	24%	24%	14%	13%	9%
Sweden	65.46	52%	11%	10%	10%	5%	3%
Switzerland	65.51	54%	8%	7%	6%	4%	2%
<b>Total</b>	<b>65.58</b>	<b>54%</b>	<b>22%</b>	<b>20%</b>	<b>15%</b>	<b>11%</b>	<b>8%</b>

CFS, Clinical Frailty Scale; FI-70, Frailty Index 70-item; FP, Frailty Phenotype; GBD-FI, Global Burden of Disease Frailty Index; SHARE-FI, Survey of Health Ageing and Retirement in Europe Frailty Instrument.



Statistics	(a) FI-70	(b) CFS	(c) FP	(d) SHARE-FI
Unadjusted AUC	0.94 (0.93–0.94)	0.86 (0.85–0.87)	0.87 (0.86–0.88)	0.88 (0.87–0.89)
<b>Covariate-adjustment for age and sex</b>				
Covariate-adjusted AUC	0.93 (0.92–0.93)	0.81 (0.80–0.82)	0.83 (0.82–0.84)	0.84 (0.83–0.85)
Coefficient for age (per year)	0.003 (p<0.001)	0.003 (p<0.001)	0.004 (p<0.001)	0.004 (p<0.001)
Coefficient for female sex	0.009 (p<0.001)	0.017 (p<0.001)	0.019 (p<0.001)	0.015 (p<0.001)

**Figure 1.** AUC for the diagnostic accuracy of the GBD-FI for frailty as defined by the (a) FI-70, (b) CFS, (c) FP and (d) SHARE-FI, including a covariate-adjustment for age and sex.

## Discussion

This study uses a large European longitudinal cohort, the SHARE, to externally validate the GBD-FI [10], a novel deficit accumulation index created from items available in the GBD study. The findings illustrate the criterion validity of the GBD-FI, supporting its future use with GBD estimates to measure and compare differences in frailty between countries and territories and over time. This is novel and important as it will allow the development of truly global, population-level frailty estimates that can be compared between all countries across the world over time. The GBD-FI demonstrated characteristics typical of a FI at the population-level including a right-skewed distribution of scores in a healthy population, higher frailty prevalence for females, a rate of deficit accumulation of  $\sim 0.03$ /year, a low upper limit (usually below 0.7) and a higher frailty prevalence than the CFS and FP approaches [6, 9].

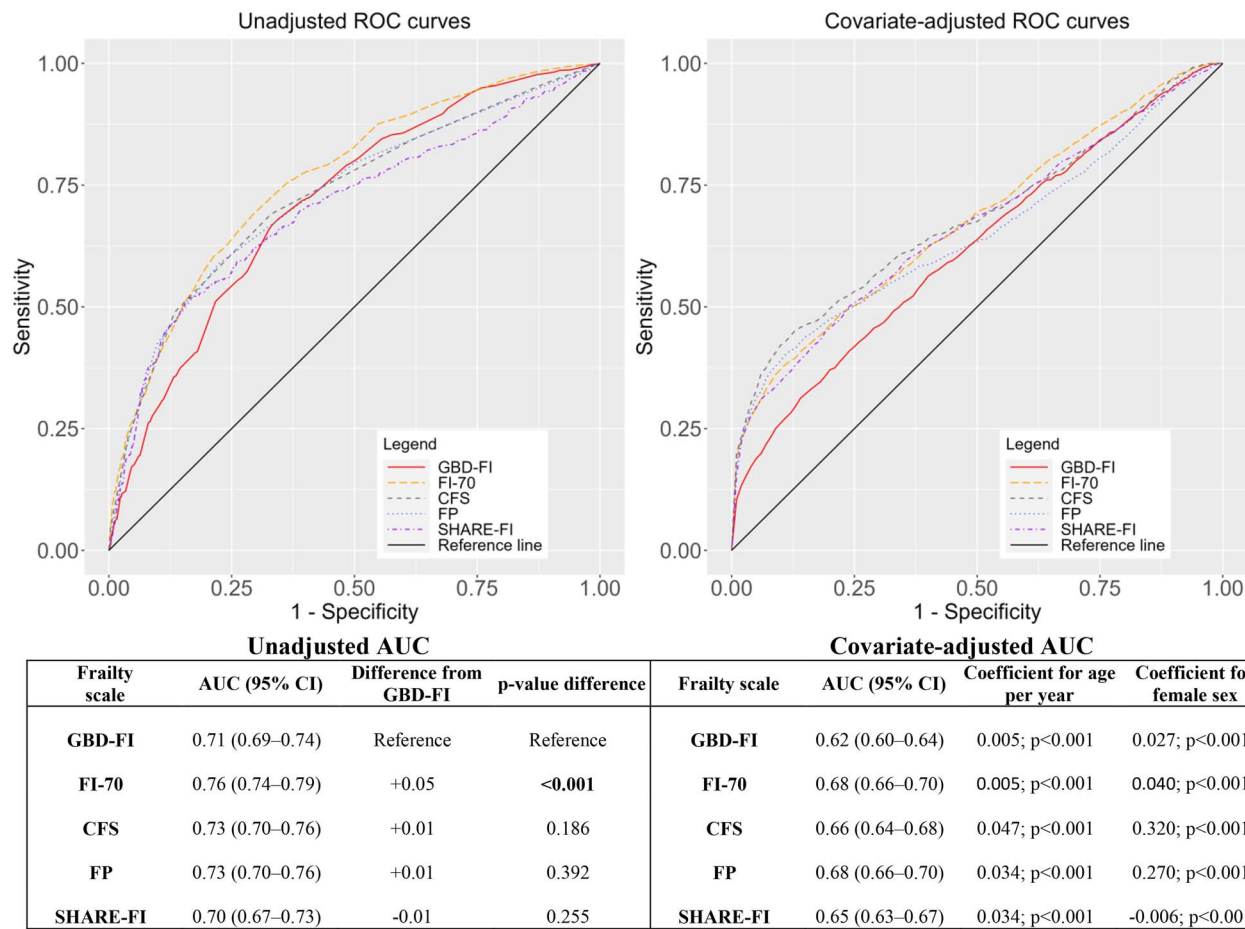
The estimated frailty prevalence using the GBD-FI was 22% for the 15 countries included, comparable with a recent meta-analysis, which also found a prevalence of 22% using any FI for all available European countries [9]. Mean GBD-FI scores correlated strongly with the FI-70 ( $r = 0.85$ ), and moderately with the other frailty measures ( $r = 0.57$ – $0.61$ ). At population-level, the GBD-FI correlated very strongly with the other frailty measures for the 15 countries included ( $r = 0.95$ – $0.98$ ), reaffirming its potential as a comparator of frailty across countries. The GBD-FI had comparable predictive validity for mortality against three other validated frailty instruments, the CFS, the FP and the SHARE-FI. Its accuracy was statistically significantly lower than a comprehensive 70-item FI. Consistent with the literature examining FIs, the GBD-FI clearly identified higher mortality with frail participants having over three times greater odds of death at follow-up (OR: 3.66) [8]. While the GBD-FI had only fair accuracy in predicting mortality, this is similar to other published frailty scales [12, 24–26] and frailty-orientated instruments measuring risk [27]. A large systematic review of prognostic indices found that few ( $n = 3$ ) had good/very good accuracy and none had excellent predictive validity for mortality [28]. When adjusted for age and sex, the predictive ability of the GBD-FI and other frailty measures for mortality decreased with increasing age and was generally lower among females. This may reflect the ‘age effect’ with growing evidence that chronological age influences the predictive accuracy of FIs [29] and the postulated male–female health-survival paradox where females may live longer but with functional impairment [30]. A colour-coded summary table of validity types explored in this paper is provided in the **Appendix**.

Despite the absence of disability-related functional items (i.e. ADLs), the GBD-FI retained the statistical characteristics of a FI and had comparable prognostic accuracy to established frailty measures incorporating ADLs. There is a significant overlap between diseases, disability and symptoms [31, 32], and previous studies have suggested that the number of deficits rather than their nature is most important for mortality prediction [7]. FIs exist on

a spectrum, ranging from those focused on function to those only including co-morbidities (see [https://www.mdpi.com/ijerph/ijerph-17-05695/article\\_deploy/html/images/ijerph-17-05695-g002-550.jpg](https://www.mdpi.com/ijerph/ijerph-17-05695/article_deploy/html/images/ijerph-17-05695-g002-550.jpg)) [10]. The GBD-FI falls within a class of deficit accumulation indices predominantly focusing on co-morbidity, similar to the Electronic FI [33], Hospital Frailty Risk Score [34], 5-Factor Modified FI [35], the Multimorbidity FI including (only co-morbidities and symptoms) [36] and FIs incorporating laboratory abnormalities [37–39]. Further research into the effect of limiting FIs to predominantly co-morbidity items is needed.

Limitations of this study include the absence and differences between the original GBD-FI items and those available in the SHARE, potentially influencing the accuracy and reproducibility of the findings. In addition, participants were community-dwellers from predominantly wealthy European countries, which may reduce generalisability. Thus, further external validation of the complete GBD-FI in other datasets including low-middle income countries and clinical setting is required to ensure values obtained in the GBD dataset for these countries are accurate. Representativeness may also be decreased by non-response bias and the exclusion of a small number of participants with missing frailty data (5%), although calibrated survey weights were applied to reduce this. These may have meant that participants with greater levels of frailty were excluded, potentially underestimating frailty prevalence and reducing the strength of agreement between frailty measures, as these would most likely have shown higher agreement for more marked frailty. The GBD-FI in this study is a modified 20-item version and previous studies suggest that  $\sim 30$  items are optimal [6]. Fewer items may lead to a less stable index, giving too much weight to individual items and this may explain why the differences between the GBD-FI and the FI-70 vary somewhat by country. The full 36-item version of the index is likely to be more stable and produce better estimates. The estimates in the GBD study may also be more complete, accurate and representative since they are based on multiple sources and are adjusted for suspected under and over reporting. This may in part explain differences between estimates between countries. However, these were mostly due to differences in the prevalence proportions of physical frailty. Hence, some of the difference may be due to true differences between populations, though as measures of physical frailty are largely self-reported, it may also be due to cultural or other such factors, which affect reporting patterns between different populations.

Despite these limitations, this study suggests that the GBD-FI is an externally robust metric for mapping frailty as defined by the deficit accumulation model of frailty across populations. Given the need for standardised, population-level data on frailty for policy-making [40], the use of an instrument such as the GBD-FI as a comparative measure of frailty at national and regional levels is well aligned with initiatives including the strategy of the World Health Organization towards optimal ageing launched in the World Report for Ageing and Health [41]. Such comparable estimates will



**Figure 2.** AUC for the predictive validity of the GBD-FI for mortality at 2-year follow-up compared with the FI-70, the FP and the CFS, comparison between an unadjusted model comparison and a covariate-adjustment for age and sex.

support clinicians, policy-makers and healthcare planners to structure care, address existing healthcare inequalities, target limited resources and benchmark health performance across population settings.

### Conclusions, implications and future directions

This study externally validates the GBD-FI using a large sample of middle-aged and older adults from 15 European countries in the SHARE. As a first external validation of this novel instrument, this paper shows that the GBD-FI shows excellent diagnostic accuracy for frailty using different measurement approaches including measures of physical frailty and has fair predictive accuracy for mortality that is comparable with widely-applied frailty instruments. It demonstrates very strong agreement with these measures across countries. A consistent approach for frailty measurement, applying the GBD-FI to publicly-available GBD data, will increase the ability to identify more discreet areas and regions with high levels of age-related risk (i.e. frailty) globally [42]. The GBD study is an important clinical, epidemiological and research

tool to better understand population-level data for diseases and risk factors globally, between countries and increasingly within countries. As populations age, clinicians, healthcare planners and policy-makers need to better understand how frailty interacts with other conditions and risk factors and how they behave in different populations. The development of the GBD-FI opens up a new stream of research to allow this and will complement the expanding GBD study dataset. As the GBD is updated annually, data pertaining to frailty can be updated and tracked. As shown in this study, the GBD-FI can be applied to individual level data in existing longitudinal studies such as SHARE and potentially in clinical practice, allowing these to, in turn, be compared with international data such as in the GBD study. This will allow clinicians and policy-makers to better understand populations and identify gaps and differences to introduce bespoke management strategies including targeted resource utilisation, preventative measures and chronic disease management. Hence, as existing population-level studies and individual-level studies are difficult to compare, the GBD-FI could act as a ‘common language of frailty’ in clinical practice and (epidemiological and non-epidemiological) research. For example, the recent COVID-19 pandemic has

highlighted the potential benefits of understanding which areas have higher concentrations of 'at risk' older adults living with frailty. Further study examining the GBD-FI in other datasets and across the spectrum of frailty (including pre-frailty), to assess the epidemiology of these states and whether different cut-offs should be applied for these, is now required.

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

**Acknowledgements:** This paper uses data from SHARE Waves 2 and the All Waves Coverscreen (DOIs: [10.6103/SHARE.w2.800](https://doi.org/10.6103/SHARE.w2.800), [10.6103/SHARE.wXcvr.800](https://doi.org/10.6103/SHARE.wXcvr.800)).

We would like to thank Thomas Lumley (Professor of Biostatistics, University of Auckland, Australia) and Sangmin Nam (Associate Professor, CHA University, South Korea) for providing statistical advice on calculating area under the curve estimates with survey weighting.

**Declaration of Conflicts of Interest:** None.

**Declaration of Sources of Funding:** The SHARE data collection has been funded by the European Commission, DG RTD through FP5 (QLK6-CT-2001-00360), FP6 (SHARE-I3: RII-CT-2006-062193, COMPARE: CIT5-CT-2005-028857, SHARELIFE: CIT4-CT-2006-028812), FP7 (SHARE-PREP: GA N°211909, SHARE-LEAP: GA N°227822, SHARE M4: GA N°261982, DASISH: GA N°283646) and Horizon 2020 (SHARE-DEV3: GA N°676536, SHARE-COHESION: GA N°870628, SERISS: GA N°654221, SSHOC: GA N°823782, SHARE-COVID19: GA N°101015924) and by DG Employment, Social Affairs & Inclusion through VS 2015/0195, VS 2016/0135, VS 2018/0285, VS 2019/0332, and VS 2020/0313. Additional funding from the German Ministry of Education and Research, the Max Planck Society for the Advancement of Science, the US National Institute on Aging (U01\_AG09740-13S2, P01\_AG005842, P01\_AG08291, P30\_AG12815, R21\_AG025169, Y1-AG-4553-01, IAG\_BSR06-11, OGHA\_04-064, HHSN271201300071C, RAG052527A) and from various national funding sources is gratefully acknowledged (see [www.share-project.org](http://www.share-project.org)).

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**Received 26 April 2023; editorial decision 10 September 2023**