

Review Article

A Narrative Review of the Utilisation of the SHARE Frailty Instruments (SHARE-FI and SHARE-FI75+) in the Literature

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Abstract

This narrative literature review aimed to examine the utilisation of the Survey of Health, Ageing and Retirement in Europe (SHARE) frailty instruments: SHARE-FI and SHARE-FI75+. We used the Google Scholar “cited by” function (accessed on February 20th, 2023) to identify all citations of the original SHARE-FI and SHARE-FI75+ studies. Included articles were categorised into four themes: epidemiological studies (prevalence and associated factors); associations with geriatric syndromes, diseases and health outcomes; randomised clinical trials (RCTs); and expert consensus and practice guidelines. Of 529 articles screened (446 citing SHARE-FI and 83 citing SHARE-FI75+), 64 (12.1%) were included. Sixteen (25.0%) were epidemiological; 35 (54.7%) described associations; 10 (15.6%) were RCTs; and 3 (4.7%) were expert consensus or practice guidelines. Frailty was associated with older age; female sex; higher morbidity; lower education; social isolation; worse nutrition and mobility; rheumatological, cardiovascular, and endocrine diseases; and greater healthcare utilisation and mortality. SHARE-FI was used in RCTs as entry criterion, controlling variable, and intervention outcome. SHARE-FI and SHARE-FI75+ have been recommended to aid the management of atrial fibrillation anticoagulation and hypertension, respectively. SHARE-FI and SHARE-FI75+, two open access phenotypical frailty measurement tools, have been utilised for a range of purposes, and mostly in epidemiological/associational studies.

Keywords: Frailty, Geriatric assessment, Review, SHARE-FI, SHARE-FI75+

Introduction

Frailty refers to a multidimensional geriatric syndrome characterised by an increase in an older person's vulnerability to adverse outcomes^{1,2}. As such, it is recognised as an important syndrome for geriatric medicine with substantial healthcare costs and decreased quality of life for patients. The considerable impact of frailty calls for proactive efforts to identify, assess and manage it to improve patients' outcomes and reduce societal burdens^{2,3}. The identification of frailty has therefore become a topic of interest with numerous frailty operationalisations and measurement tools having been developed⁴. Since its original publication in 2001, Fried et al.'s physical frailty phenotype (defined by exhaustion, unexplained weight loss, weakness, slowness and low physical activity) has been one of the most popular and validated tools in the literature^{5,6}. However, it is not

well adapted for use in primary care settings due to the need for post hoc calculations on a reference sample. Santos-Eggimann et al. were the first to adapt Fried's frailty phenotype to a large population-based sample using the first wave of the Survey of Health, Ageing and Retirement in Europe (SHARE)⁷. Since SHARE did not collect information

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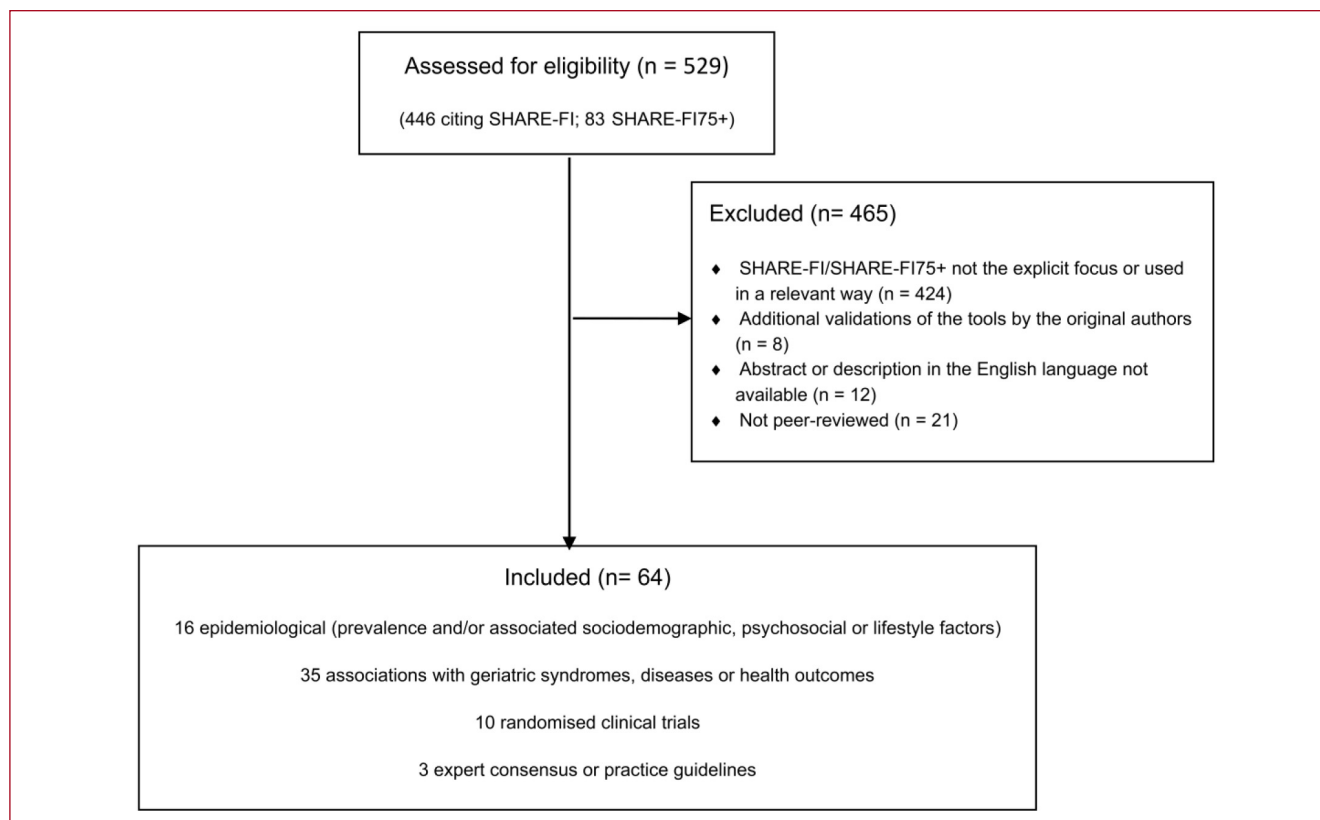


Figure 1. Flowchart of included studies.

fully fitting the original definitions of the five Fried's criteria, Santos-Eggimann et al. selected the closest SHARE variables for each criterion to investigate the prevalence of the frailty phenotype in Europeans living in the community⁷. Building on this work, Romero-Ortuno et al. investigated whether those adapted SHARE measures could be used to model frailty as a latent variable with internal and predictive validity, which in 2010 led to the publication of the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) for primary care⁸.

The aim of SHARE-FI was to provide a non-commercial, open access physical frailty identification tool for healthcare practitioners that could be simply and rapidly used in the primary care setting⁸. SHARE-FI was primarily intended for community-dwelling Europeans aged ≥ 50 years and is based on a modified frailty phenotype approach (fatigue, low appetite, weakness by handgrip strength, difficulties walking or climbing stairs, and low physical activity)⁸. Once values from an individual assessment are entered into the web-based open access calculator (one for each sex), the tool provides immediate frailty classification (robust, pre-frail and frail) and a continuous frailty score, not requiring post hoc calculations⁸. Since the publication of the original study,

SHARE-FI has been translated into Italian, French, Spanish, German, Polish and Thai⁹.

Subsequently in 2014, Romero-Ortuno et al. developed SHARE-FI75+, a modified version of the SHARE-FI tool intended for community-dwelling people aged 75 years or older, in which the handgrip strength test was replaced with an item related to gait observation¹⁰. The SHARE-FI75+ web-calculator is also freely accessible and generates age- and sex-adjusted results¹⁰.

In this narrative review, we aimed to examine the utilisation of SHARE-FI and SHARE-FI75+ in the literature. Specifically, we were interested in how these tools have been employed to study frailty and the range of subject domains it has been applied to.

Materials and Methods

We used the Google Scholar "cited by" function (accessed on February 20th, 2023) to identify all citations of the original SHARE-FI⁸ and SHARE-FI75+¹⁰ studies. These were equally distributed to five independent reviewers (HD, AHJ, MK, AN, JS) for screening. Citations were excluded if they reported additional validations of the tools by the original authors, an abstract or description in the English language was not

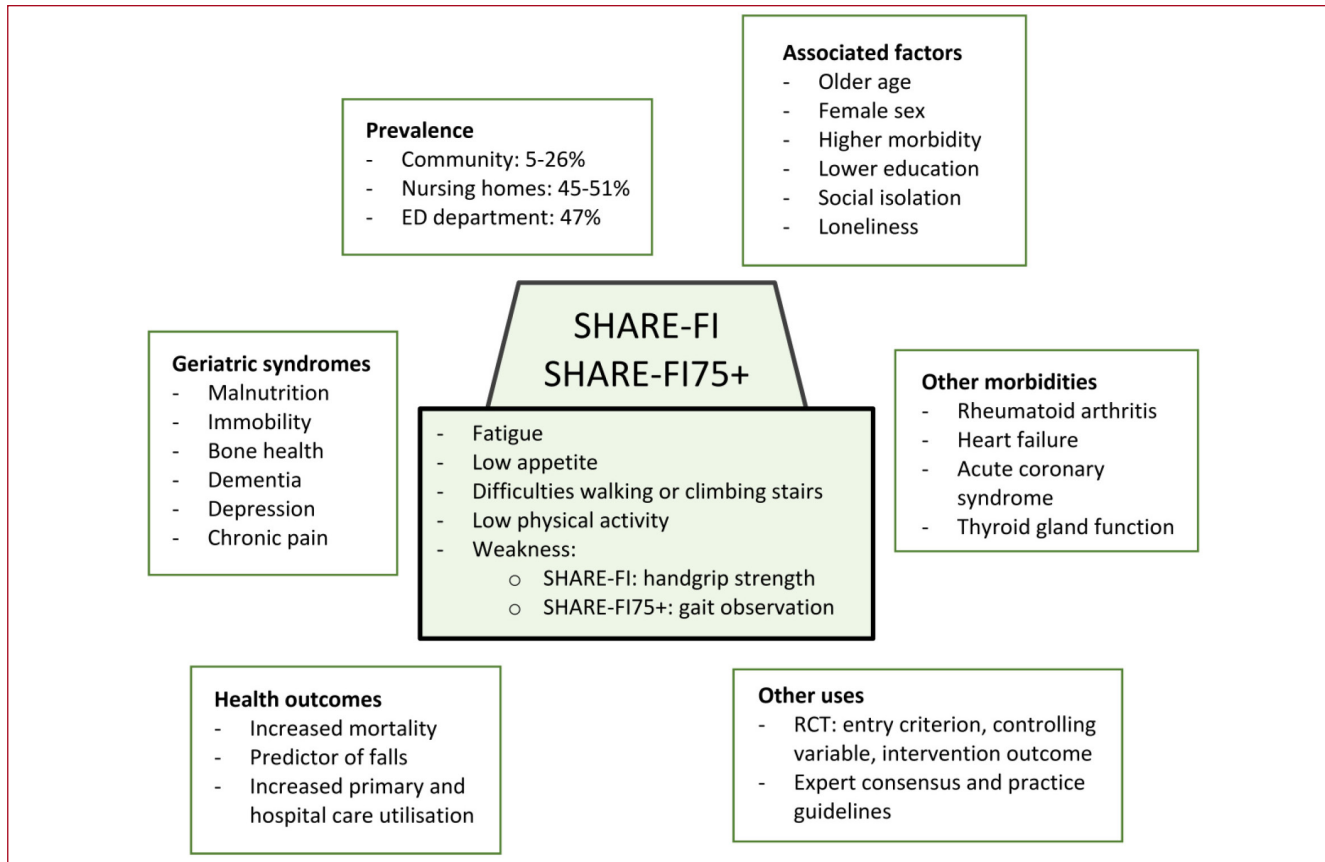


Figure 2. Summary of the narrative review.

available, they were not peer-reviewed, and if SHARE-FI/SHARE-FI75+ was not an explicit focus or used in a relevant way (e.g., not in the study methodology, or cited within the context of a review). We did not exclude articles based on the care setting described (e.g., community, hospital, nursing home). Included articles were then categorised into four themes: epidemiological studies (e.g., studies determining frailty prevalence and/or examining associated sociodemographic, psychosocial or lifestyle factors); associations with geriatric syndromes, diseases or health outcomes; randomised clinical trials; and expert consensus and practice guidelines. Disagreements among reviewers were resolved by involvement of three independent co-authors (EL, CC, RRO).

Results

Of 529 articles screened (446 citing SHARE-FI and 83 citing SHARE-FI75+), 64 (12.1%) were included in the narrative review. Sixteen (25.0%) were epidemiological and 35 (54.7%) principally described associations, with some overlap between those two types of studies; 10

(15.6%) were RCTs; and 3 (4.7%) were expert consensus or practice guidelines. The flowchart of included studies is shown in Figure 1. The highlights of the included articles are represented in Figure 2 and narrated below.

Epidemiology

Prevalence

A large systematic review and meta-analysis reviewing 62 papers (representing 68 unique datasets) and completed in 22 European countries found that SHARE-FI was the second most frequently used tool (after the original Fried's frailty phenotype) in the community setting (17.6% of studies), with studies carried out in Austria, France, Germany, Greece, Italy, Spain, The Netherlands, Belgium, Ireland, Norway, and Poland¹¹. The pooled average frailty prevalence in the community setting by SHARE-FI was 18% (95% CI 13-25%), similar to the overall pooled estimate of the meta-analysis which was 18% (95% CI 15-21%) and 17% (95% CI 13-21%) when the analysis was limited to high-quality studies¹¹, but higher than the pooled average frailty prevalence by Fried's phenotype which was 10%

(95% CI 8–11%). Manfredi et al. found that countries in the north of Europe had lower frailty prevalences¹².

Some studies used SHARE-FI to measure the prevalence of frailty outside its originally intended community-based setting, resulting in higher frailty proportions compared to community-based samples. For example, in a study of 662 volunteers from 28 nursing homes in Belgium, the authors reported frailty prevalence according to different frailty scales and found that 45.1% were frail, 36.6% pre-frail and 18.2% robust using SHARE-FI, which was higher than the prevalence found by Fried's phenotype (25.5% frail, 60.8% pre-frail and 13.7% robust)¹³. In a series of 289 New Zealand aged-care residents, 51% were frail, 33% pre-frail and 16 non-frail¹⁴. In a study conducted with 180 Polish people aged over 60 years, the overall prevalence of frailty was 26%, but the subgroup living in nursing homes (n=90) had a prevalence of 48%, compared to 5% in those living in the community¹⁵. In another study completed with 198 patients aged ≥ 70 years presenting to an Irish Emergency Department (ED), almost half were frail (47%), 21% were pre-frail and 32% robust¹⁶. In a sample of 62 patients aged ≥ 75 years assessed within the first day of admission to an acute English hospital, Hartley et al. showed a median SHARE-FI score of 3.4 (IQR 1.6–4.3)¹⁷, where an individual SHARE-FI score of ≥ 2.14 and ≥ 3.01 identify frailty in women and men, respectively⁸.

Associated factors

In a study of 2289 people living in five European countries, frailty was found associated with older age (OR 1.06, 95% CI 1.04–1.08), female sex (OR 2.20, 95% CI 1.75–2.76), lower education (OR 1.58, 95% CI 1.05–2.37), living alone (OR 2.11, 95% CI 1.68–2.66), worse nutritional status (OR 3.06, 95% CI 2.22–4.22), and multi-morbidity (OR 2.54, 95% CI 1.69–3.81) and more prescribed medications (OR 1.33, 95% CI 1.24–1.42)¹⁸. As regards association with sex, a large SHARE-based cross-sectional study showed that European women were generally frailer, especially in Southern Europe (OR 1.84, 95% CI 1.72–1.96)¹⁹. Consistently with previous literature, a large SHARE-FI-based study showed that women can expect to live longer with frailty or activity limitation, despite the fact that men's life expectancy is generally shorter²⁰. One study used the SHARE dataset to analyse temporal trends in the proportion of life expectancy spent as robust (robust-LE) or as frail (frail-LE) between 2004 and 2015²¹. While the robust-LE increased overall, there were important regional and sex disparities. Frail-LE increased for central European men, while robust-LE increased most for northern European women and southern European men²¹.

A study in SHARE showed that loneliness and social isolation were associated with the risk of developing frailty or pre-frailty status, with relative risk ratio of 1.14 and 1.68, respectively, with the presence of loneliness; and 1.17 and 1.84, respectively, with social isolation²². Another study analysed the six waves of the SHARE study and extracted

data from 79874 participants in partnerships and 3620 participants who lost their partners, finding that while men and women experienced an initial drop in frailty after the loss, women were more likely to recover the lost frailty points overtime while the effects on frailty persisted in men²³. Also using SHARE, Ilinca and Calciolari showed that frailty was associated with greater utilisation of primary healthcare and hospital services²⁴.

Outside community settings, age was also found to be positively correlated with frailty^{15,25}. However, an observational study with patients presenting to an Irish Emergency Department (ED) study found no correlation with age¹⁶. Lower education and socioeconomic status, and living alone were found to be associated with frailty in one study including a mix of community-dwelling and nursing home participants¹⁵; while another study in hospitalised older patients found no significant associations²⁵. In a study with 22 institutionalised older adults in Italy (mean age 84), frailty as assessed by SHARE-FI was associated with more variance and cross-correlation in self-rated physical, mental, and social health over 100 consecutive days²⁶.

Relationship with geriatric syndromes, diseases and health outcomes

Geriatric syndromes

Malnutrition. A study using SHARE-FI75+ showed that adverse nutritional markers were independently associated with frailty in 1430 older participants from two Danish cohorts. In this study, after adjusting for age, sex, chronic conditions and physical function, having one more nutrition risk factor significantly increased the risk of pre-frailty/frailty (OR 1.39, 95% CI 1.07–1.80)²⁷. In an observational study carried out with 112 patients aged 65 years or older in Italy (62 patients hospitalised for a hip fracture and 50 outpatients without fracture), 65% of frail patients were at risk of malnutrition and 10% were malnourished as per Mini-Nutritional Assessment (MNA)²⁸. Another cross-sectional study with 133 acutely hospitalised older patients in Austria also examined the association between malnutrition (MNA) and frailty (SHARE-FI), finding malnutrition or risk of malnutrition in 47% of robust, 69% of pre-frail, and 93% of frail participants²⁹. Good association between SHARE-FI and MNA was also documented by Muszalik et al. in older hospitalised patients in Poland³⁰.

Immobility. A SHARE-based study showed a negative correlation between fulfilment of the minimal aerobic physical activity recommendations and frailty ($R=-0.745$; $p=0.008$)³¹. Another SHARE study looked at the impact of physical activity on frailty over 11 years, finding that higher physical activity was significantly and negatively correlated with frailty, with higher protein intake seeming to have an additive effect³².

An observational study by Danilovich et al. in the USA with 139 older Medicaid waiver recipients (mean age 74), showed that SHARE-FI (both categorical and continuous

scores) significantly predicted timed up and go (TUG) time, all domains of the short physical performance battery (SPPB), gait speed, and inability to perform the chair rise test³³. The Irish study by McCullagh et al. observed a median walking speed of 0.46 m/s in 32 older acute hospital inpatients (mean age 78), 50% of whom were frail by SHARE-FI³⁴.

Bone health. In a sample of 309 older residents from 16 residential aged-care facilities in New Zealand, those on vitamin D supplements had adequate serum vitamin D levels, regardless of their SHARE-FI frailty level³⁵. Furthermore, SHARE-FI has been employed as a tool to aid the investigation of Osteoprotegerin (OPG) as a potential biomarker of frailty. A small observational study from Italy showed that the SHARE-FI continuous score was directly associated with serum OPG concentration in non-fracture older participants³⁶.

Dementia. In an Irish study by Timmons et al. in 598 acutely hospitalised patients aged ≥ 70 years, patients living with dementia (pwD) were more likely to be frailer by SHARE-FI ($\chi^2=17.18$, $p<0.001$)³⁷.

Depression. SHARE-FI was used in a SHARE-based 5-year longitudinal study involving 17 European countries, which found that frailty significantly predicted depressive symptoms in this population aged 50+ (after adjusting for other variables, OR for pre-frailty was 1.81 (95% CI 1.65–2.00) and for frailty 2.50 (95% CI 2.14–2.92)³⁸.

Chronic pain. In a Spanish study with 154 community-dwelling participants (mean age 77), participants reporting moderate and severe pain were more likely to be frail or pre-frail, after adjustment for potential confounders (OR: 4.20, 95% CI 2.10–8.40) (39). SHARE-FI was used in Italy in a case-control study with 170 symptomatic knee osteoarthritis outpatients (mean age 70) and 186 healthy controls and showed that frailer subjects reported significantly higher mean values of pain⁴⁰.

Other diseases

Rheumatological. Two studies utilised SHARE-FI specifically in patients living with rheumatoid arthritis (RA)^{41,42}. An Austrian monocentric cross-sectional study by Haider et al. measured the prevalence of frailty in seropositive RA patients aged 18–65 years, showing that only 55% were robust and that pre-frailty/frailty was directly associated with the Clinical Disease Activity Index (CDAI) score and higher levels of inflammatory parameters in blood (CRP, TNF- α and IL-6)⁴¹. Salaffi et al. measured frailty in 210 Italian outpatients living with RA (mean age 60) and 100 healthy subjects, finding that both the categorical and continuous SHARE-FI scores were directly associated with the modified Rheumatic Disease Comorbidity Index (mRDCI) and the Simplified Disease Activity Index (SDAI)⁴².

Cardiovascular. In 811 patients (mean age 77) recruited across the 24 acute hospitals of The New South Wales (NSW) Heart Failure (FH) Snapshot study, SHARE-FI independently predicted death within 12 months post discharge, but was not

associated with 30-day readmission⁴³. In adult participants of the FRAilty MEasurement in Heart Failure (FRAME-HF) study, SHARE-FI was able to discriminate between inpatients and outpatients⁴⁴. In a small pilot Australian study with 131 adults with HF (mean age 54), SHARE-FI seemed to have, together with the Deficits Accumulation Index (DAI), the highest C-statistic value (0.73) for the prediction of rehospitalisation and/or mortality at 12 months, followed by the original Frailty Phenotype (FP) (0.72), and the St Vincent's Frailty instrument (0.71)⁴⁵; however, results for the multiple logistic regression models were not statistically significant. A Polish study proposed a novel model to predict frailty (based on SHARE-FI) in HF patients using the following five variables: age >50 years, systolic blood pressure (SBP) on admission <110 mmHg, total cholesterol <4.85 mmol/L, bilirubin ≥ 15.5 mmol/L, and ALT ≤ 34 U/L⁴⁶. An Australian study with 83 men and 37 women (mean age 53) showed that the prevalence of frailty was 33% among patients with advanced symptomatic HF referred for heart transplantation and was associated with increased mortality⁴⁷. In another Australian cohort of 137 patients (mean age 72) admitted to hospital with HF and atrial fibrillation (AF), the prescription of anticoagulant drugs at discharge was significantly associated better survival at 12 months, but there was a non-statistically significant trend that patients who were identified as frail were less likely to be discharged on anticoagulant medications⁴⁸.

Spanish studies by Alonso Salinas et al. using SHARE-FI in the context of acute coronary syndrome (ACS) showed that frailty was associated with higher risk of 30-day major bleeding⁴⁹, as well reinfarction and mortality up to 1 year⁵⁰⁻⁵².

Endocrine. Two studies from Italy and New Zealand investigated the relationship between frailty and thyroid gland function. The former found in 112 older patients (mean age 79) a significant inverse correlation between SHARE-FI score and serum free T3 (FT3) concentration in patients with and without hip fractures; this study also found that an FT3 cut-off of <2.3 pg/mL was able to distinguish between frail and non-frail patients with sensitivity and specificity of 74%⁵³. In the New Zealand study, in 309 residents from 16 aged-care homes (median age 85) there was no significant difference in iodine deficiency between frail and non-frail residents, but frailty was associated with elevated thyroglobulin⁵⁴. A small Polish study suggested an association between elevated HbA1c levels and risk of frailty measured by SHARE-FI⁵⁵.

Adverse health outcomes: mortality, falls, other

In SHARE, baseline prefrailty and frailty calculated using SHARE-FI were associated with higher risk of death over 11 years: HR 1.47 (95% CI 1.31–1.63) and 2.17 (95% CI 1.90–2.48), respectively⁵⁶. In a comparative analysis with other frailty identification tools, Theou et al. noted that the continuous SHARE-FI score had the highest AUC for 5-year mortality (0.77)⁵⁷.

The FRAILTOOLS project reported that in the 199 geriatric ward participants who had follow-up (mean age 83), SHARE-FI had the best sensitivities for the prediction of falls (89%) and mortality (86%), although it had the lowest specificities (24%, 21%)⁵⁸.

In the Belgian SENIOR study, which compared characteristics of 211 nursing home residents who had falls within 1 year of follow-up vs 354 who did not fall, among 12 frailty tools considered, the Groningen indicator was the only one with bivariate significance ($p < 0.05$), and SHARE-FI was the only with a trend towards significance ($p < 0.10$, frailty more prevalent in fallers: 29% vs 27%); however, when 1-year mortality was considered in the same cohort (93 deceased vs 491 not deceased), SHARE-FI had the best discrimination ($p = 0.01$, frailty more prevalent in the deceased: 55% vs 39%)⁵⁹.

In a study of 107 patients aged ≥ 65 years attending an ED in USA (98 patients with 30-day follow-up data), the use of SHARE-FI was associated with a composite of death, functional decline, repeat ED visit or hospital admission, or nursing home admission⁶⁰. In an Indian observational pilot study including 25 older patients (> 65 years) undergoing non-cardiac major surgery frailty as measured by SHARE-FI was associated with greater cerebral desaturation during the operation (OR 1.75, 95% CI 1.11–2.75) and longer length of stay⁶¹.

Randomised controlled trials

Frailty as entry criterion

In the randomised controlled trial (RCT) by Kapan et al., which showed that a 12-week home-based intervention program delivered by lay volunteers reduced fear of falling (FOF), participants were included if they met, among other criteria, being prefrail or frail according to SHARE-FI⁶². Kapan et al. showed that for quality of life, physical and nutritional interventions in combination were not more effective than social support in isolation⁶³. The RCT by Winzer et al., which showed positive behavioural changes of a “buddy-style” program, also used SHARE-FI for the inclusion of pre-frail or frail participants⁶⁴. The two RCTs by Haider et al. also recruited pre-frail or frail participants using SHARE-FI; the first showed that volunteer-delivered physical and nutritional interventions significantly improved grip strength and physical performance⁶⁵; the second one showed that in older adults with frailty, volunteer-delivered physical and nutritional interventions were able to slow down increases in IL-6 and CRP⁶⁶.

Frailty as controlling variable

In the RCT conducted by McCullagh et al., which demonstrated that an exercise programme in hospitalised older patients led to better physical performance, quality of life and hospital outcome, SHARE-FI was not only used to demonstrate that intervention ($n = 95$) and control ($n = 95$) groups were well matched, but also as a controlling variable in the multivariable models⁶⁷.

Frailty as intervention outcome

In the RCT by Luger et al., a 12-week home-based physical training, nutritional, and social support intervention delivered by volunteers to 80 prefrail and frail adults aged 65 years or older showed improvements in nutritional status and frailty, the latter measured by both the continuous and categorical SHARE-FI score⁶⁸.

Fransen et al.’s international multi-center trial of coordinated health and social preventative interventions showed that participants in the intervention group ($n = 986$) had less recurrent falls and a non-significant trend towards lower frailty (measured by SHARE-FI) at follow-up⁶⁹.

Otones et al. conducted an open label RCT to evaluate the effectiveness of an eight-week physical activity and education program for pre-frail adults aged 65 years or more with chronic pain attending a primary healthcare centre in Spain (17 in intervention group, 15 in control group). Frailty was measured at baseline, after the intervention (T1) and after 3 months (T2) using SHARE-FI, and there were significant improvements in the SHARE-FI continuous score in women at both T1 and T2⁷⁰.

Travers et al. conducted an RCT in six primary care practices in Ireland showing that a home-based exercise regime with dietary protein guidance was able to improve SHARE-FI status. The absolute risk reduction was 12% and the number needed to treat was 8⁷¹.

Expert consensus and practice guidelines

In 2015, the Updated European Heart Rhythm Association (EHRA) Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation recommended that blood sampling for haemoglobin, renal and liver function be performed more frequently in older patients who are frail by physical phenotype, pointing towards the SHARE-FI online frailty calculator^{72,73}.

In 2016, the European Union Geriatric Medicine Society (EUGMS) Working Group on the Management of Hypertension in very old, frail subjects published an Expert Opinion statement, where they acknowledged the complexities of treating frail hypertensive patients aged ≥ 80 years or older; for this group, they proposed systematic screening for frailty as an aid to individualised clinical decision making, and suggested the use of the Fried’s frailty phenotype, gait speed, and SHARE-FI75+⁷⁴.

Discussion

The aim of this narrative review was to provide an overview of how the SHARE-FI and SHARE-FI75+ tools have been utilised in the literature up to February 20th, 2023. We found that of the 529 citations screened, 84.3% were related to SHARE-FI and 15.7% to SHARE-FI75+. In most of the citations screened, the tools of interest were not the primary focus (e.g., reviews, discussion of unrelated results). Of the 64 studies included in the narrative review, the vast

majority (79.7%) were epidemiological or associational, with a minority of studies utilising these tools in RCTs (15.6%) or explicitly in expert consensus statements or clinical practice guidelines (4.7%).

In the European community setting, the prevalence of frailty by SHARE-FI was low (18%(11)) and there were significant associations with older age; female sex; higher morbidity; lower education; social isolation; worse nutrition and mobility; specific rheumatological, cardiovascular, and endocrine diseases; and greater healthcare utilisation and mortality. Many of these community-based studies utilised the large SHARE dataset. On the other hand, non-community-based studies (e.g., ED, acute hospital, nursing home) reported, often in small non-probabilistic samples, higher frailty prevalences and less consistent associations.

The review highlighted significant use of these tools outside the originally intended primary care setting. As stated in the original SHARE-FI and SHARE-FI75+ studies, they are designed to be used in primary healthcare on community-dwelling adults. It is to be expected, therefore, that in ED/hospitalised/nursing home populations, some of the five criteria may be inappropriate (e.g., impaired self-report due to delirium/dementia or weakened handgrip strength due to acute illness or disability). Furthermore, in specific diseases such as HF, it was noted that patients almost universally reported difficulties walking 100 metres or 1 flight of stairs, and therefore a shorter test, such as a 5-metre walking speed test, could be more appropriate⁴⁴. As underscored by this review, frailty is a multifaceted syndrome commonly occurring with comorbidities and, therefore, developing one universal tool to measure it in patients of different backgrounds may be neither achievable nor desirable.

Some RCTs utilised SHARE-FI for the inclusion of participants, to measure frailty status at baseline or as an outcome. The most commonly studied interventions were exercise, nutrition and social support, both in isolation and combination. Multi-component interventions were effective in improving outcomes for frail older patients, but isolated social support interventions were also beneficial. In addition, SHARE-FI and SHARE-FI75+ were recommended to aid the management of atrial fibrillation anticoagulation and hypertension in older people, respectively. These are examples of challenging clinical practice areas where the balance of risks and benefits needs to be carefully considered and documented.

In conclusion, SHARE-FI and SHARE-FI75+, two open access phenotypical frailty measurement tools, have been utilised for diverse purposes. The relative paucity of RCTs and guidelines vis-à-vis epidemiological and associational studies highlights significant scope for the future utilisation of SHARE-FI and SHARE-FI75+ in studies that will be able to generate higher-level evidence.

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