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# The SHARE operationalized frailty phenotype: A comparison of two approaches

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# ABSTRACT

*Purpose*: The phenotype defined by Fried et al. is one of the main operationalizations of frailty. Santos-Eggimann et al. pioneered the adaptation of the phenotype criteria to the Survey of Health, Ageing and Retirement in Europe (SHARE, http://www.share-project.org/). Using the adapted criteria, Romero-Ortuno et al. created and validated the SHARE Frailty Instrument for Primary Care (SHARE-FI). In SHARE-FI, the cut-offs for the phenotypic categories (i.e. non-frail, pre-frail and frail) are automatically derived from latent variable modelling, while Fried et al. (and also Santos-Eggimann et al.) use a rule based on the number of criteria present (Ncriteria):  $\geq$  3: frail; 1 or 2: pre-frail; 0: non-frail. The aim of the present study was to compare the mortality prediction of these two different approaches (latent variable modelling in SHARE-FI vs. Ncriteria in Santos-Eggimann et al.).

*Subjects and methods:* The subjects were 15,420 women and 12,742 men from the first wave of SHARE. A correspondence analysis was used to assess the degree of agreement between phenotypic classifications. The ability of the continuous measures (Ncriteria and SHARE-FI score) to predict mortality (mean follow-up of 2.4 years) was compared using receiver operating characteristic plots and areas under the curve (AUC).

*Results:* In both women and men, there was a high degree of correspondence between phenotypic categories. The two continuous measures performed similarly as mortality predictors (women: SHARE-FI-AUC = 0.77; Ncriteria-AUC = 0.75. Men: SHARE-FI-AUC = 0.76; Ncriteria-AUC = 0.72).

*Conclusion:* The two approaches to the SHARE operationalized frailty phenotype performed equally well to predict mortality.

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#### 1. Introduction

Frailty is a state of vulnerability to poor resolution of homoeostasis after a stressor event and is a consequence of cumulative decline in many physiological systems during a lifetime [1]. Although there is no international consensus on the definition of frailty [2,3] a popular operationalization is the frailty phenotype developed by Fried et al. [4,5].

According to the phenotypic approach, frailty is defined as a clinical syndrome consisting of unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity [6,7]. Fried et al. operationalized these criteria in the Cardiovascular Health Study, according to very explicit definitions [6], and defined three frailty categories:

• frail (i.e. three or more criteria present);

- pre-frail (i.e. one or two criteria present);
- non-frail (i.e. none of the criteria present) [6].

The phenotype approach has represented an important step in the operationalization of frailty in epidemiological and clinical practice [8,9].

Fried et al. have shown that surrogates for individual frailty phenotype criteria are possible [10]. In that regard, Santos-Eggimann et al. pioneered the adaptation of the phenotypic frailty criteria to the contents of the Survey of Health, Ageing and Retirement in Europe (SHARE, http://www.share-project.org/) [11], and they subsequently validated the adapted criteria [12]. Using those adapted phenotypic criteria, Romero-Ortuno et al. created and validated the SHARE Frailty Instrument for Primary Care (SHARE-FI) [13–15].

In SHARE-FI, the frailty score and the cut-offs for the definition of the frailty categories (i.e. non-frail, pre-frail and frail) are based on latent variable modelling, and not on Fried et al.'s rule (also in use by Santos-Eggimann et al.) based on the number of criteria met:  $\geq$  3 criteria: frail; 1 or 2 criteria: pre-frail; 0 criteria: non-frail. In SHARE-FI, frailty was constructed as an unobserved (latent) variable that is indicated by five different (but related) observed variables (i.e. the adapted phenotypic criteria). By using the Latent GOLD<sup>®</sup> statistical package, the SHARE-FI latent variable was

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specified as being ordinal and having three categories, thus conforming to the non-frail, pre-frail, frail classification. In SHARE-FI, the cut-offs for the frailty categories are automatically generated by Latent GOLD<sup>®</sup>, and not arbitrarily defined [15]. The SHARE-FI calculators (one for each sex) are freely accessible on *BMC Geriatrics* (http://www.biomedcentral.com/1471-2318/10/57/additional), and translated versions can be accessed on https://sites.google.com/a/tcd.ie/share-frailty-instrument-calculators/. When data is entered into the calculator, the tool provides a continuous Frailty score (i.e. the 'predicted discrete factor score', whose formulae are in the paper) and enables automatic classification into phenotypic frailty categories: non-frail, pre-frail and frail.

To date, it was not known how the automatic SHARE-FI classification compares *vis-à-vis* the 'manual' calculation method based on the number of frailty criteria met. Thus, the aim of the present study was to compare the mortality prediction of these two different approaches to the SHARE operationalized frailty phenotype.

### 2. Methods

### 2.1. Subjects

Fifteen thousand four hundred and twenty women and 12,742 men from the first wave of the Survey of Health, Aging and Retirement in Europe (SHARE, http://www.share-project.org/), including representative samples of twelve countries: Austria, Germany, Sweden, Netherlands, Spain, Italy, France, Denmark, Greece, Switzerland, Belgium and Israel.

### 2.2. The SHARE operationalized phenotypic frailty criteria

In both SHARE-FI [15] and Santos-Eggimann et al. [11], phenotypic frailty was defined using variables in SHARE that approximated those used in the original Cardiovascular Health Study [6]. There are, however, some differences in the way SHARE-FI and Santos-Eggimann et al. use the adapted phenotypic variables:

- *muscle weakness* was measured using a dynamometer, using the highest of 4-measurement readings (2 from each hand) of handgrip strength:
  - Santos-Eggimann et al. adjusted the grip strength reading for sex and body mass index cut-offs as specified by Fried et al. [6],
    SHARE-FI used this variable unadjusted;
- *exhaustion* criterion was met if the participant answered "yes" to the self-reported question: "In the last month have you had too little energy to do things you wanted to do?";
- unintentional weight loss was operationalized using two questions in SHARE: firstly, "What has your appetite been like?" and/or secondly, "So have you been eating more or less?". Participants scored positive for the criterion if they answered either "Diminution in desire for food" in response to the first question, or "Less" in response to the second question;
- slowness was operationalized using two questions: "Because of health problems, do you have difficulty walking 100 m, or climbing one flight of stairs without resting?". Criterion was met if participants answered positive to either of the two questions;
- low physical activity was operationalized using the question "How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car or going for a walk?":
- in Santos-Eggimann et al., participants scored positive for the criterion if responded "One to three times a month, hardly ever, or never",

• in SHARE-FI, this variable was not dichotomised. It was used as a four-category ordinal variable.

As per Santos-Eggimann et al., subjects were considered frail if they met three or more of these criteria; pre-frail if they fulfilled one or two criteria; and not frail if they met none. In SHARE-FI, the classification into frailty categories was automatic as outlined above.

#### 2.3. Mortality prediction

Wave 2 established whether wave 1 participants had died, were still alive, or had been lost to follow-up. For those who had died, the exact time to death since the initial interview was not collected. Wave 1 data were collected between 2004 and 2006 and wave 2 between 2006 and 2007. The mean individual follow-up period between wave 1 and wave 2 was 2.4 years.

#### 2.4. Statistical analyses

Statistics were computed with SPSS 16.0, separately for each sex. The level of significance was established at 0.01 throughout.

The correlation between the two continuous frailty measures, the SHARE-FI score and the number of frailty criteria (Ncriteria), was assessed with the Spearman's rank correlation coefficient. Correspondence analysis (with symmetrical normalization) was used to assess the degree of agreement between the two phenotypic classifications. Correspondence analysis examines the relationship between two categorical variables graphically in a multidimensional space, and produces plots based on the scores. Categories that are similar to each other appear close to each other in the plots. In this way, it is easy to see which categories of a variable are similar to each other or which categories of the two variables are related.

To compare the performance of the phenotypic classifications (i.e. SHARE-FI and Santos-Eggimann et al. categories) to predict mortality, Chi<sup>2</sup> cross-tabulations were used with the *Phi* statistic as measure of association. To compare the ability of the two continuous measures (i.e. SHARE-FI score and Ncriteria) to predict mortality, we used receiver operating characteristic (ROC) plots and areas under the curve (AUC).

## 2.5. Ethics

This is a secondary analysis of data obtained under the SHARE Data Access Rules (http://share-dev.mpisoc.mpg.de/data-accessdocumentation/research-data-center-data-access.html). SHARE received ethical approval by the university of Mannheim's Internal Review Board. All participants consented to the study.

#### 3. Results

Fifteen thousand five hundred and seventy-eight women and 12,783 men from the first wave of SHARE had information on SHARE-FI [15]; and 15,420 women and 12,742 men had information for the Santos-Eggimann et al. operationalization (with the latter approach, some cases were lost due to missing information on body mass index, which is needed for the stratification of grip strength). Overall, 15,420 women and 12,742 men had information for both SHARE-FI and Santos-Eggimann et al. operationalizations.

Two hundred and sixty-seven women and 361 men had died at follow-up.

# 3.1. Correlation between SHARE-FI score and number of frailty criteria (Ncriteria)

In women, the bivariate correlation between SHARE-FI score and Ncriteria was strong and highly significant (two-tailed Download English Version:

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