



## Review

# Modifications to the frailty phenotype criteria: Systematic review of the current literature and investigation of 262 frailty phenotypes in the Survey of Health, Ageing, and Retirement in Europe

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## ARTICLE INFO

## Article history:

Received 15 December 2014

Received in revised form 31 March 2015

Accepted 1 April 2015

Available online 4 April 2015

## Keywords:

Frailty

Ageing

Phenotype

Survey of Health, Ageing, and Retirement in Europe

Systematic review

Secondary analysis

## ABSTRACT

We conducted a systematic review to determine variability in how the criteria of the frailty phenotype (grip strength, weight loss, exhaustion, walking speed, physical activity) were assessed. We then evaluated the impact on estimating prevalence and mortality of modifying the criteria, using the Survey of Health, Ageing, & Retirement in Europe (SHARE). Five databases were searched for original research articles published after 2000, which evaluated frailty using the phenotypic criteria. Among the 264 included studies, 24 studies provided enough information to demonstrate that all criteria were assessed as proposed in the original frailty phenotype study by Fried et al. (2001). Physical inactivity and weight loss were the criteria most often modified. We then created 262 phenotypes from SHARE based on common modifications found in the review. Among these phenotypes, frailty prevalence ranged from 12.7% to 28.2%. Agreement with the primary frailty phenotype ranged from 0.662 to 0.967 and internal consistency ranged from 0.430 to 0.649. Women had 2.1–16.3% higher frailty prevalence than men. Areas under receiver operating characteristic curves for discriminating five-year mortality ranged from 0.607 (95% CI: 0.583–0.630) to 0.668 (0.645–0.691). The frailty phenotype often has been modified, and these modifications have important impact on its classification and predictive ability.

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## 1. Introduction

Frailty challenges healthcare professionals and has pervasive impact on health and the outcomes of health care. It has been proposed that frailty should always be considered when treating the older patient (Theou and Rockwood, 2012). Various instruments have been developed to measure frailty (deVries et al., 2011); the “frailty phenotype” is the most commonly used way. The phenotype determines frailty based on five criteria: weight loss, exhaustion, physical inactivity, slow walking speed, and weak grip strength. Individuals with three or more of these problems are classified as frail, those with one or two are said to be “prefrail” and those with none are nonfrail, or robust. Since the first publication of this frailty measurement tool in 2001 (Fried et al., 2001), the five phenotypic criteria have been measured in different ways across studies, including by its originators (Bandein-Roche et al., 2006; Makary et al., 2010; Eckel et al., 2011), which potentially limits the comparability of studies using this definition. Various studies (Johansen et al., 2014; Eckel et al., 2011; Saum et al., 2012; Freiheit et al., 2011; Shamliyan et al., 2013) showed that modifying the phenotypic criteria could change estimates of the prevalence of frailty and the predictive ability of the phenotype, leading to potentially different classifications and results. Kutner and Zhang (2013) recently commented on a study using a modified frailty phenotype, stating that “assignment of frailty classification is very dependent on the particular criteria and operational measures that are applied”. In particular, they commented on the replacement of the performance-based measures (grip strength, walking speed) in the original frailty phenotype definition with self-reported items. This modification is very common due to the inconvenience and infeasibility of assessing performance-based measures in the measurement of frailty, especially in clinical settings. Therefore, the aims of this study were to (1) conduct a systematic review of the literature to determine variability in measurement methods for the frailty phenotype’s five criteria, and (2) compare whether modifying the phenotypic criteria available in the Survey of Health, Ageing, & Retirement in Europe (SHARE) would have an impact on the classification and predictive ability of the frailty phenotype.

## 2. Methods

### 2.1. Systematic review

We searched Medline, Embase, Psycinfo, Scopus and Eric up to November 2012. Two arms of the search strategy were developed and intersected using the Boolean term “AND”: Frail AND all reasonable descriptors of the frailty phenotype (see Appendix 1 of Supplementary material for Medline search strategy). The database search results were uploaded into Refworks, which was used to manage the screening process. Two members of the review team independently screened the title and abstracts of the articles that were extracted from the literature search and for those that met reviewers’ agreement the full text was retrieved. Any disagreement between the two reviewers was resolved by a third reviewer. We included original research articles published after 2000 that evaluated participants’ frailty status using the phenotypic criteria. For each article that satisfied these criteria, we extracted the following descriptive data: language in which article was written, country

where the study was conducted, number, age, and sex of participants, study setting and whether this study was part of a larger study. We then extracted the following data regarding the frailty phenotype included in each study: number of phenotypic criteria; how each criterion was measured; how the deficit for each criterion was identified; how the frailty score was calculated; how frailty categories were classified, and; how missing data were handled.

### 2.2. Secondary analysis

We conducted secondary analyses of data from the first wave of the Survey of Health, Ageing, & Retirement in Europe (SHARE). SHARE began in 2004 and represents the non-institutionalized population aged 50 and older in the participating countries (Austria, Belgium, Denmark, France, Germany, Greece, Israel, Italy, Netherlands, Spain, Sweden, and Switzerland) who speak the official language of the country, as well as their spouses/partners independent of age if they live in the same household (first wave  $n = 31115$ ). Walking speed (one of the frailty phenotype criteria) was only measured among individuals aged 76 years or older; therefore, participants younger than 76 were excluded from this secondary analysis, yielding 5139 participants aged 76–104 (mean age  $81.4 \pm 4.6$ , 58.4% women). Mortality data up to five years follow up were obtained from the second (2006/2007), third (2008/2009), and fourth (2010/2011) waves of SHARE.

Weight loss, fatigue, and physical activity were measured with self-reported responses to survey questions. Walking speed was measured twice at the respondent’s usual pace for a distance of 2.5 m. The walking test started with the individual standing behind the start line. Timing started when first foot crossed the start line and ended when the first foot completely crossed the end line (no acceleration or deceleration phase was used). Walking aids were allowed, if needed. Only walking speed scores of more than 0.54 s and less than 30 s were recorded as valid. Grip strength was measured twice in each hand with a dynamometer (Smedley, S Dynamometer, TTM, Tokyo, 100 kg), alternating between hands. The dominant hand was identified. Only grip strength scores of more than 0 kg and less than 100 kg were recorded as valid. Also if the difference between trials on one hand was more than 20 kg and/or if grip strength was only measured once in one hand then the measurements of that hand were considered invalid.

Frailty phenotypes have previously constructed using the SHARE data (Romero-Ortuno, 2011, 2012; Romero-Ortuno et al., 2010, 2011; Santos-Eggimann et al., 2009; Etman et al., 2012). Here based on common modifications of the phenotypic criteria that we found in the systematic review, we created 262 frailty phenotypes using the SHARE data. First we created one primary frailty phenotype including five criteria as close to the original frailty phenotype criteria as possible (Table 1). We then created 251 other phenotypes using various published adaptations of the walking time and grip strength criterion; 12 potential variables were created for walking time and 21 potential variables were created for grip strength (see Table 2 for 9 major modifications among these 252 phenotypes). Weight loss, fatigue and physical activity items were identical across phenotypes. Modifications were made with regards to the type of measure (performance vs. self-report), cut-points (population independent vs. population dependent), and number of trials (using score of first trial vs. average score vs. maximum

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