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Original Article

## Discrimination ability of comorbidity, frailty, and subjective health to predict mortality in community-dwelling older people: Population based prospective cohort study

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### ABSTRACT

**Objective:** To investigate the added value of comorbidity, frailty, and subjective health to mortality predictions in community-dwelling older people and whether it changes with increasing age.

**Participants:** 36,751 community-dwelling subjects aged 50–100 from the longitudinal Survey of Health, Ageing, and Retirement in Europe.

**Methods:** Mortality risk associated with Comorbidity Index, Frailty Index, Frailty Phenotype, and subjective health was analysed using Cox regression. The extent to which health indicators modified individual mortality risk predictions was examined and the added ability to discriminate mortality risks was assessed.

**Main outcome measures:** Three-year mortality risks, hazard ratios, change in individual mortality risks, three-year area under the receiver operating characteristic curve (AUC).

**Results:** Three-year mortality risks increased 41-folds within an age span of 50 years. Hazard ratios per change in health indicator became less significant with increasing age ( $p$ -value  $< 0.001$ ). AUC for three-year mortality prediction based on age and sex was 76.9% (95% CI 75.5% to 78.3%). Information on health indicators modified individual three-year mortality risk predictions up to 30%, both upwards and downwards, each adding  $< 2\%$  discriminative power. The added discrimination ability of all health indicators gradually declined from an extra 4% at age 50–59 to  $< 1\%$  in the oldest old. Trends were similar for one-year mortality and not different between sexes, levels of education, and household income.

**Conclusion:** Calendar age encompasses most of the discrimination ability to predict mortality. The added value of comorbidity, frailty, and subjective health to mortality predictions decreases with increasing age.

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### 1. Introduction

Prognosis is the cornerstone of medicine, yet predicting outcome is one of the biggest challenges professionals face in day-to-day clinical practice [1]. Not only does it reflect the trajectory of how a disease will develop along with its associated outcomes, it also guides decision making on the character and the timing of interventions. Without an accurate prediction of what is going to happen in future, it is sheer impossible to weigh up benefits and risks of implementing a potentially harmful strategy over watchful waiting, and subsequently for patients to make a properly informed decision. Estimating prognosis in old age is an even more strenuous task as many patients have atypical

presentations of several diseases at the same time and use manifold pharmaceutical treatments [2]. The underlying pathogenesis of these comorbidities is a random accumulation of permanent damage [3], a notion that sparked an intensive search for a 'biomarker of ageing' that accurately reflects the functional status of our body. Currently we lack markers that reflect biological age better than calendar age [4], and hence we rely on clinical disease markers for decision making [5,6].

Even in the absence of a clinical diagnosis of disease, the ageing process results in a poor resolution towards homeostasis after a stressful event, which has been coined as 'frailty' [7]. In order to prevent the risk of adverse outcomes of (pharmaceutical) interventions, numerous studies have developed and validated indicators of frailty [8–10], as well as subjective health [11,12] to help identify older people at risk. The generalized message from these studies is that these frailty indicators serve as warning signs in identifying older people at risk and provide a decision point to start or withhold specific interventions in order to improve outcomes of older people. However, there is only

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limited evidence as yet that the routine use of these instruments for decision making improves the outcomes of our interventions [13].

To have a better understanding on to what extent current health indicators capture information for decision making, we set out to determine how much mortality prediction based on age and sex can be improved by information on comorbidity, frailty, and subjective health using data from SHARE; a European effort of 27 European countries and Israel on determinants of health, ageing, and retirement. First, we assessed how health indicators and age interact in their ability to discern mortality risks in subjects from the general population. Second, we explored to what extent the health indicators modify individual mortality risk predictions based on age and sex. Third, we prospectively assessed the added value of health indicators to the discrimination ability of mortality predictions and analysed whether the added value changes with increasing age.

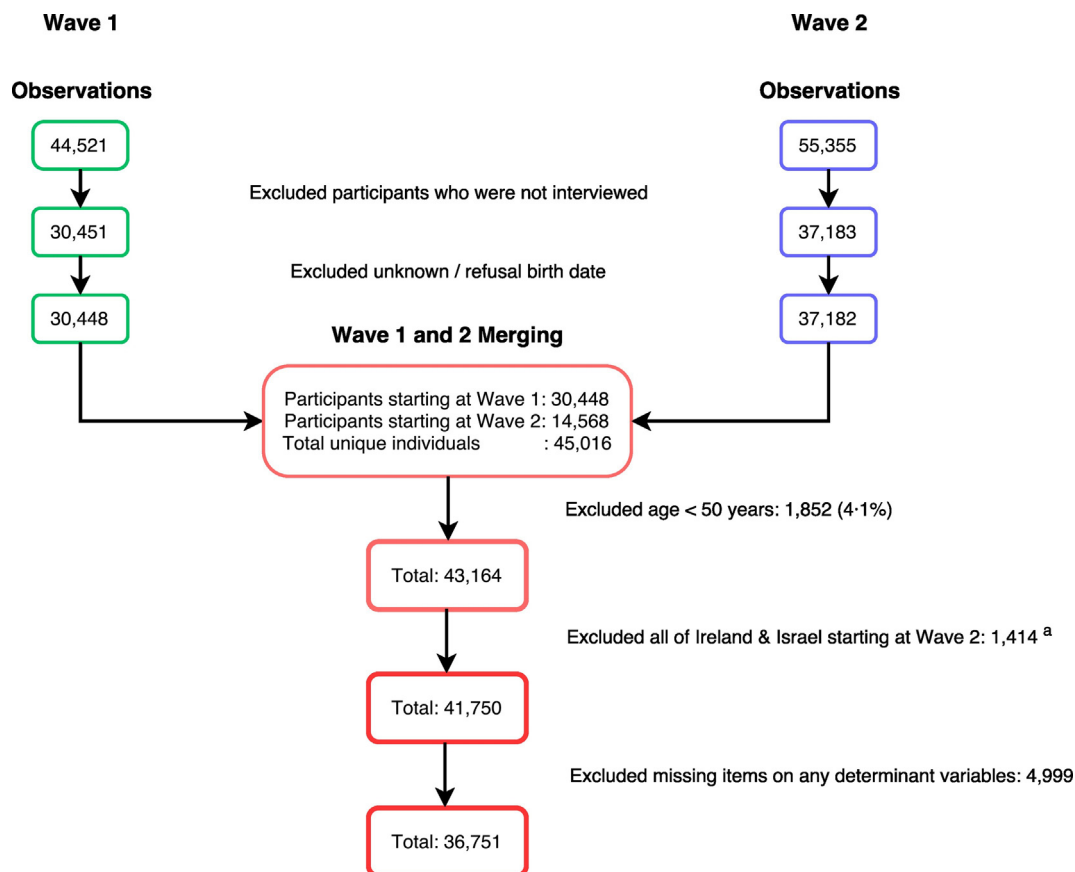
## 2. Material and methods

### 2.1. Study population

This study was based on a secondary data analysis of the Survey of Health, Ageing, and Retirement in Europe (SHARE); a multinational database including information from sequential surveys – ‘Waves’ – on health, well-being, working conditions, retirement, socio-economic status and social networks of approximately 120,000 individuals from 27 European countries and Israel [14]. The SHARE target population consisted of community-dwelling persons aged 50 years and older who have regular domicile in their respective SHARE country, as well as their spouses/partners living in the same household independent of age. SHARE data used in this study were from Wave 1 until 4 (Release 5.0.0).

We constructed a study sample consisting of participants who started at either SHARE Wave 1 or 2 and were censored for vital status in Wave 2 through Wave 4 (see Fig. 1). Out of all countries, Ireland was excluded because Ireland only started in Wave 2 and did not perform any censoring for vital status afterwards. Baseline data for demographics and health indicators were obtained from Wave 1 (2004/2005) or Wave 2 (2006/2007). New entries from the third wave were not included as that particular wave focused on retrospective interviews and did not provide data on health measurements. Dates of deaths and dates when participants were last surveyed alive were obtained from the second (2006/2007), third (2008/2009), and fourth (2011) waves of SHARE. Participants in all countries but Israel and Greece were followed up to Wave 4 for censoring of vital status. For Greece, we used Wave 3 for censoring as Wave 4 did not provide any information on vital status. For Israel, we included participants from Wave 1 in 2005 and used information from Wave 2 in 2010 for censoring vital status as Wave 2 in Israel was exceptionally late when compared to other countries. For the purpose of this study, participants with unknown birth date or aged younger than 50 were excluded. At baseline, there were 41,750 participants included in our study. We then excluded participants with any missing information on demographics and health indicators at baseline, resulting to the final study sample of 36,751 participants.

Median duration of follow up after the initial health survey was  $48.0 \pm 33.6$  months with an IQR of 75 months; it varied widely between countries due to differences in sampling regimens. As a result, censoring for vital status was available for 23,339 of the participants of whom the demographic variables and health indicators at baseline were not different from those who had no censoring information. We compared one-year Kaplan-Meier estimates with the expected mortality risk based on the mortality registers of the participating countries (see



**Fig. 1.** Flowchart generating study sample from SHARE Wave 1 and 2. The selected participants started from either SHARE Wave 1 or 2 and then followed-up until Wave 4. <sup>a</sup>Consists of participants who were excluded due to no follow-up: all participants from Ireland (N = 1,007) and participants from Israel who started at Wave 2 (N = 407).

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