Age and Ageing 2019; **48:** 547–552
doi: 10.1093/ageing/afz040
Published electronically 27 April 2019

Fluctuations in frailty among older adults

Erwin Stolz, Hannes Mayerl, Wolfgang Freidl

Institute of Social Medicine and Epidemiology, Medical University of Graz, Universitätsstraße 6/I, 8010 Graz, Austria

Address correspondence to: Erwin Stolz. Tel: +43 316 385 71587; Email: erwin.stolz@medunigraz.at

Abstract

Background: frailty fluctuations, that is, within-person up and down deviations from individual long-term frailty index trajectories represent a hitherto both conceptually and empirically untapped facet of frailty among older adults.
Objective: to assess the size of frailty fluctuations in old age and their association with frailty levels, frailty growth as well as sex and socio-economic position.
Methods: a total of 18,704 biannual observations from 4,514 community-dwelling older adults (65+) in 10 European countries over 12 years from the Survey of Health, Ageing and Retirement in Europe (SHARE) were analysed. A frailty index was constructed based on 50 items. Long-term frailty trajectories and fluctuations were modelled simultaneously using Bayesian mixed-effects location-scale regression models.
Results: frailty index fluctuations were non-negligible among older adults, amounting to 0.04/0.05 FI or 2.0/2.5 health deficits on average. 30% of fluctuations were between 0.04 and 0.1 FI (2 and 5 health deficits) and 8% were larger than 0.1 FI (5 health deficits). Fluctuations increased with age and frailty levels, and were higher among women, those with low socio-economic position (education) and individuals who died during follow-up.
Conclusions: frailty index fluctuations refer to instabilities in an older person's health status and represent a hitherto untapped but relevant aspect of vulnerability in old age. Future analysis of frailty fluctuations should be based on a larger number of repeated observations with shorter time intervals.

Keywords

frailty, fluctuations, intra-individual variability, socio-economic position, mixed-effects location-scale regression model, older adults

Key points

- Frailty index fluctuations are a hitherto untapped facet of frailty among older adults.
- Frailty index fluctuations increased with age and frailty levels.
- Frailty index fluctuations were higher among women and individuals with low socio-economic position.
- Frailty index fluctuations amounted to 0.05 FI or 2.5 health deficits on average

Introduction

Frailty results from cumulative decline in multiple physiological systems and is defined as a state of increased vulnerability among older adults with regard to adverse outcomes [1], such as further rapid health decline, hospitalisation, institutionalisation and death (e.g. [2–5]) after the exposure to (minor) stressors. The cumulative deficit model is a principal and well-established model of frailty [1, 6] and depicts frailty as a non-specific state of risk due to a variety of health deficits [3, 7, 8] including symptoms, signs, disabilities, diseases and laboratory measurements summarised in a continuous frailty index (FI).

A large number of studies based on health survey data from various countries and settings (e.g. [8–14]) showed that the FI increases progressively with age. Irrespective of this general trend of progressive deficit accumulation, there is substantial heterogeneity, i.e. individuals enter old age at broadly varying health states and proceed in a variety of FI trajectories, including gradual as well as steep increases but also phases of stability or improvement ('deficit diminution') [8, 11, 15]. Thus, frailty as depicted by the FI can be described as a dynamic, and to some degree, reversible process, for example due to interventions (e.g. [16]).

One aspect of frailty dynamics that has received little attention so far are fluctuations in frailty, that is intra-individual variability [17] which describes within-individual vertical deviations in the FI from the long-term frailty trajectory. Although frailty has been associated with instability [18] before, this referred to unstable disability as a consequence of frailty [1] but not instability in frailty itself. Figure 1 illustrates the concept of frailty fluctuations by depicting two individuals with identical long-term frailty trajectories (solid lines) but different levels of fluctuations. It is currently unclear how large such instabilities are on average, whether and how they are related to chronological age as well as to overall frailty levels and frailty growth, and whether frailty fluctuations are similarly patterned with regard to sex or socio-economic position (SEP), that is, whether women and individuals with low SEP do not only show higher average frailty levels [9, 12–14], but whether they also show elevated levels of frailty fluctuations.

That FI fluctuations have not received much attention so far is likely attributable to the fact that both adequate data and statistical methods were lacking. The increasing number of repeated observations available in health surveys and mixed-effect location-scale models [20] allow for the first time to assess and model frailty fluctuations in population-representative data among older adults. Technically, fluctuations are captured by observation-level residuals, which are often considered to only represent measurement error or random statistical noise [19, 21]. Conceptually, fluctuations in frailty could be thought of as a sign of a loss of homoeostasis and thus a facet of system vulnerability besides the overall frailty level or its long-term change. Consequently, we expect frailty fluctuations to be closely associated with mean frailty levels and growth but also with mortality. The aim of this paper is to answer these open questions based on cross-national European panel survey data.

Methods

Data

We used longitudinal data of up to five repeated observations during 12 years of follow-up from community-dwelling older adults aged 65 years and over from 10 European countries (Austria, Belgium, Denmark, France, Germany, Italy, Netherlands, Spain, Sweden, Switzerland) provided in the Survey of Health, Ageing and Retirement in Europe (SHARE). Personal computer-assisted interviews were conducted bi-annually with one exception (2004/05, 2006/07, 2011/12, 2013, 2015). We included only individuals who provided valid information for all 50 frailty index items in each wave and who, after the baseline interview (2004/2005) participated at least twice more (43.8%) as three observations are a minimum in order to have a meaningful vertical deviation from a trajectory. In total, this amounted to 4,514 respondents and 18,704 observations.

The central outcome variable was frailty as operationalised by the health deficit accumulation approach (frailty index: range = 0–1) [3, 7, 8, 22] based on 50 health deficits (Appendix 1, available in *Age and Ageing* online).

As time variables, we used chronological age (in years) at the time of the interview and 5-year birth cohort (1 < 1920, 2 = 1920–1924, 3 = 1925–1929, 4 = 1930–1934, 5 = 1935–-1939). Predictor variables included sex (male/female) and SEP, which was approximated by the level of education based on the International Classification of Education (low = primary and lower secondary education, medium = upper secondary education, high = post-secondary and tertiary education). Finally, we included the number of interviews (3–5) and whether a respondent had died (no/yes/unknown) in order to adjust for sample attrition.

Statistical model

In order to assess the role of fluctuations in frailty, we used mixed-effects location-scale regression models [20], which allow to model the mean ('location') and the variation ('scale') simultaneously. 'Scale' refers to the logarithmised residual standard deviation of FI values, that is, the observation-level residuals vertically deviating from individual-level growth curves based on fixed and random effects. In comparison to two-step procedures (e.g. [19]), mixed-effects location-scale regression models retain the uncertainty of estimated observation-level residuals [23],

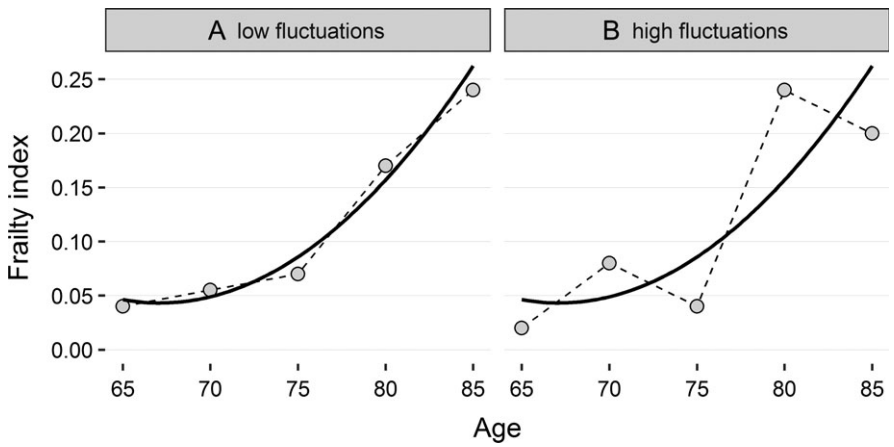

Figure 1. Illustration of fluctuations in frailty among two hypothetic individuals.

allow to assess the relevance of frailty fluctuations directly via model fit comparisons [23], and to model the association between fluctuations and mean FI levels as well as FI growth via correlations between individual-level random effects. Further details on the statistical model and estimation procedure can be found in the appendix (Appendix 2, available in *Age and Ageing* online).

Research-ethical assessments of the Survey of Health, Ageing and Retirement in Europe (SHARE) project have been carried out by the ethics committee of the University of Mannheim and then taken over by the Ethics Council of the Max Planck Society.

Results

56.1% of the sampled older adults were women. Average age at the time of enrolment was 72.8 (SD = 5.4, min = 65, max = 94) years. 61.7% had a low, 21.2% a medium and 17.1% a high level of education. 22.7% of the respondents provided three observations, 29.5% four and 47.8% five observations. 13.0% of the sampled older adults died during follow-up and the vital status was unknown for 11.6%. Respondents with only one or two observations who were excluded, were older and in poorer health than those with three or more observations who were retained for analysis (Appendix 4, available in *Age and Ageing* online).

Mean/median frailty levels at baseline were 0.11/0.09 (SD = 0.08) and 0.16/0.14 (SD = 0.11) for men and women, respectively; 95th/99th percentile frailty values were 0.35/0.49 for both men and women. Mean/median frailty levels had increased to 0.17/0.14 (SD = 0.13) for men and 0.23/0.20 (SD = 0.15) for women 12 years later, that is, among those who remained in the sample. With each subsequent wave, the right skewed gamma distribution of frailty became more normal (Appendix 5, available in *Age and Ageing* online). Heterogeneity between respondents with regard to both frailty level and growth was considerable as can be seen from plots of raw data (Appendix 6, available in *Age and Ageing* online) and individual-level random effects (Table 1). The latter showed FI levels to range between 0.06 and 0.22 (−/+ 1 SD) and that (linear) frailty growth ranged between 0.02 and 0.13 (−/+ 1 SD) per 10 years. The dynamic nature of frailty trajectories and fluctuation also shows in Appendix 7, available in *Age and Ageing* online. It depicts fitted individual frailty index growth curves and actual observations for 30 randomly selected respondents, thereby illustrating the measurement of frailty fluctuations. Based on absolute values of observation-level residuals, the median intra-individual standard deviation (iSD) [17] was 0.04 for men and 0.05 for women. In other words, average within-person frailty fluctuations amounted to 2.0–2.5 health deficits. Furthermore, observation-level residuals were positively skewed (= 2.2), i.e. the majority of vertical deviations were below 0.04 (61.9%), 29.9% were between 0.04 and 0.1, and 8.2% were larger than 0.1 FI-points.

Table 1. Bayesian mixed-effects location-scale regression model of frailty among older adults (65+).

	Frailty level FI-μ (95CI)	Frailty fluctuations FI-σ (95CI)
Population-level (fixed) effects		
Intercept (γ_{00})	0.14 [0.12, 0.16]	0.06 [0.05, 0.07]
Age10 (γ_{01})	0.07 [0.06, 0.07]	1.52 [1.43, 1.61]
Age10^2 (γ_{02})	0.02 [0.02, 0.02]	–
Female (ref: Male) (γ_{04})	0.04 [0.04, 0.05]	1.21[1.16, 1.26]
Female * Age10 (γ_{05})	0.01 [0.01, 0.02]	0.92 [0.87, 0.97]
Medium education (ref: low) (γ_{06})	−0.01 [−0.02, −0.01]	0.90 [0.85, 0.95]
High education (ref: low) (γ_{08})	−0.02 [−0.03, −0.02]	0.85[0.80, 0.90]
Medium education * Age10 (γ_{07})	0.00 [−0.00, 0.01]	1.03 [0.96, 1.09]
High education * Age10 (γ_{09})	−0.01 [−0.01, −0.00]	1.06 [0.99, 1.14]
Vital status unknown (ref: alive) (γ_{11})	0.01 [−0.00, 0.02]	1.05 [0.97, 1.13]
Vital status dead (ref: alive) (γ_{12})	0.03 [0.02, 0.04]	1.21 [1.11, 1.30]
Individual-level (random) effects		
SD (Intercept) (u_{0i})	0.08 [0.08, 0.08]	0.52 [0.50, 0.53]
SD (Age) (u_{1i})	0.05 [0.04, 0.05]	–
Corr μ (Intercept FI-μ, Age μ)	0.69 [0.64, 0.73]	–
Corr (Intercept FI-μ, Intercept FI-σ)	0.92 [0.90, 0.94]	0.92 [0.890, 0.94]
Corr (Intercept FI-σ, Age μ)	0.69 [0.63, 0.74]	0.69 [0.63, 0.74]
Country-level (random) effects		
SD (Intercept) (u_{0k})	0.03 [0.02, 0.05]	0.21 [0.12, 0.36]
Model fit		
WAIC/R^2	−50,275/0.20	

Survey of Health, Ageing and Retirement in Europe (SHARE), v6.1.1, *N*-observations = 18,704, *N*-individuals = 4.514, *N*-country = 10, unweighted data. Model adjusted for birth cohort and number of interviews. Effective sample size > 2,000 for all parameters, R-hat = 1.0. Point estimates are from the mean posterior distribution. Abbreviations: FI, frailty index; 95CI, 95% credible intervals; FI-μ, mean frailty level; FI-σ, exponentiated frailty fluctuations; SD, standard deviation; Corr, correlation coefficient; WAIC, Watanabe Akaike Information Criterion; R^2 = explained variance based on fixed effects.

Model comparison showed that model fit improved substantially when frailty fluctuations were modelled in addition to long-term frailty trajectories only (WAIC = −41,904, SE = 315 vs. WAIC = −49,781, SE = 231). Results from the final model are in Table 1 and Figure 2, which show that mean frailty levels increased progressively with age, but also that frailty fluctuations increased as people grew older (+52% per 10 years). Female older adults and those with low education were both frailer on average (ΔFI_{female} = +0.04, $\Delta FI_{lowedu.}$ = +0.02) and showed 21%, respectively, 18% more frailty fluctuations, that is, they had more unstable health compared to men and those with higher education. Additionally, those who died during follow-up were not only frailer on average (ΔFI_{dead} = +0.03), but also showed more frailty fluctuations (+21%). High correlation coefficients among individual-level random effects showed that fluctuations in frailty were strongly associated with higher mean frailty levels and frailty increases over time in individuals. Furthermore, we found that not only mean frailty levels varied across countries, which were the lowest in Switzerland (ΔFI = −0.03) and the highest in Spain (ΔFI = +0.04), but also fluctuations in frailty, which were also the lowest in Switzerland (−3%) and the highest in

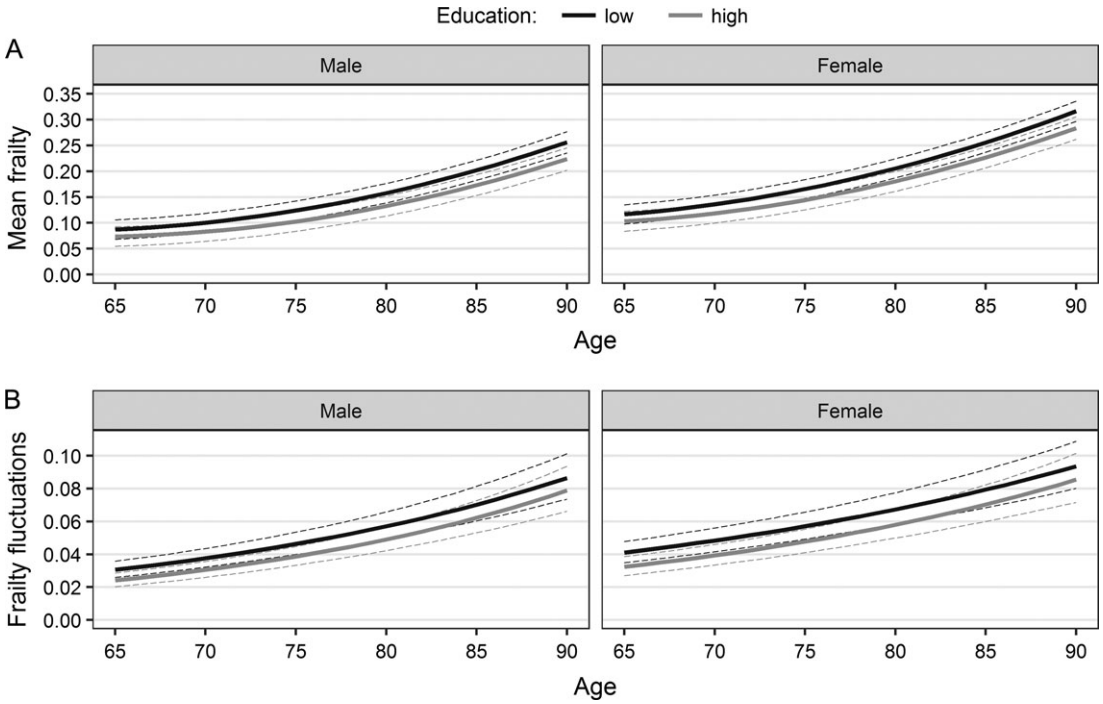

Figure 2. Estimated trajectories of mean frailty index levels (A) and fluctuations (B) by educational level for men and women (65+). *Notes*: Estimates for both mean frailty levels and frailty fluctuations are based on the final model and refer to respondents born 1925–1929 with four observations who were still alive at the end-of-follow-up. Dashed lines refer to 95% credible intervals from the fixed part of the model.

Spain (+4%). More detailed results of country-separated analyses can be found in Appendix 8, available in *Age and Ageing* online.

Discussion

To the best of our knowledge, this is the first study to investigate within-person frailty index instabilities among older adults, that is, the amount of vertical deviations from progressive long-term frailty trajectories in old age [8–14]. Fluctuations in frailty depicting repeated deteriorations and improvements in frailty could be the result of (repeated) injuries, infections and phases of increased symptoms, and subsequent recoveries, resolutions and resolves. In the current investigation, we set out to answer whether these fluctuations are negligible in size and exclusively represent measurement inaccuracy and random noise [19, 29] or rather constitute a sizeable and systematically structured facet of frailty. Our results showed, that fluctuations in frailty amounted to 2.0–2.5 health deficits on average, which is considerable. Thus average within-person FI-fluctuations deviating from long-term FI-trajectories are larger than the well-established sex- and SEP-gap (e.g. [9, 12, 13]) between individuals.

The size of frailty fluctuations likely depends on the nature of the selected items used to construct the frailty index. We followed established recommendations for the construction of the FI [10, 22] and thus one likely source of the fluctuations in our analysis is the highly dynamic character of ADL, IADL and mobility disability [18]. It has been shown [29] that disablement is a highly dynamic process characterised by a number disability episodes, that is, cycles of deterioration, recovery and recurrence even over relative short time periods. Based on data from the Health and Retirement Survey (HRS), Lin and Kelley-Moore [19] recently used an approach similar to ours finding that intra-individual variability in mobility limitations are also substantial among older adults, increase throughout late life and were higher among those who died, all of which is in line with our findings.

In our analysis, we showed that these fluctuations were not only sizeable, but also not as random as one would expect if they exclusively represented random noise or measurement error. Instead, they were closely associated with long-term frailty trajectories and also similarly structured with regard to sex, SEP and mortality. We found frailty fluctuations to increase with chronological age and FI levels (or biological age [11]), and that women, those with low SEP and those who died during follow-up did not only show higher average FI values and steeper long-term trajectories (see [9, 12–14, **25**]), but also more unstable FI levels. Similar socio-demographic associations were recently reported for mobility fluctuations [19]. The sex-difference in frailty fluctuations is in line with the sex-difference in frailty levels [30] and could be due to biological factors such as that non-lethal diseases like arthritis, which are more prevalent among women [31], could result in more dynamic symptoms and impairments. Higher fluctuations

could also be due to social factors such as that older women are more likely to live alone and/or receive inadequate care **[32]**, that is, with fewer buffers to compensate fluctuations in functioning. Finally, the sex-difference in fluctuations could also reflect sex-differences in health care utilisation and reporting behaviour [33]. Similarly, higher fluctuations among older adults with low SEP could be the result of differences in health-literacy and health behaviour [34], lower and less consistent social support [35], or lower-quality health services [19].

The fact that frailty fluctuations were closely associated with higher frailty levels, frailty growth and mortality supports the notion of frailty fluctuations as a sign of a loss of homoeostasis and a consequence of overall system vulnerability [1], for example, when small events like a change in medication or an infection results in substantial overall health deterioration and when recoveries from these spells of ill-health due to concerted intervention efforts are increasingly temporary. The close empirical association of frailty fluctuations with frailty levels, growth and mortality shows that older adults accumulate health deficits not only gradually, but that the very process of health deficit accumulation is accompanied by increasing health fluctuations. This implies that frailty measurements in late life should be based on short(er) time intervals, so that actual frailty levels can be captured accurately. Finally, cross-national differences in frailty fluctuations closely followed the geographical pattern of cross-national differences in frailty levels in this study and previous research [13]. This implies that not only are older adults in countries with lower gross domestic product and health expenditure more frail on average [36], but that their health status is also slightly more unstable compared to better-off countries in Europe such as Switzerland or the Scandinavian countries.

Although we consider our findings on frailty fluctuations a novel and promising avenue for further research—also with regard to the social determinants of frailty—this study suffers from a number of limitations which follow from the nature of the dataset analysed. First, SHARE—as most other population-representative health surveys—is characterised by a coarse temporal resolution owed to the biannual assessment intervals, which likely results in underestimated frailty fluctuations, as a lot can happen within a year or two in the lives of older adults with regard to health changes [29]. Assessments of FI dynamics based on shorter intervals could provide a more comprehensive picture of frailty dynamics among older adults in general and with regard to fluctuations in frailty in particular. Second, and relatedly, SHARE currently provides only a maximum of five subsequent panel observations, which limits the amount of observable frailty fluctuations. As the number of repeated observations in many surveys increases, estimates of fluctuations in frailty will improve given adequate retention rates. Third, the frailty index is based on self-reported health data which is subject to measurement error. Thus, some of the reported fluctuations likely reflect measurement error rather than actual frailty fluctuations. However, the size and systematic patterning of frailty fluctuations and the improved model fit indicate that these fluctuations do not exclusively reflect measurement error. Fourth, there is missing mortality data in SHARE, which likely includes deceased respondents who could not be located or contacted, which may bias the estimated effect of subsequent mortality. Fifth, and finally, we analysed the sub-sample of SHARE respondents with 3+ observations and valid information on 50 health deficits, which on average were younger and in better physical health compared to those who were excluded due to too few measurements. Also, institutionalised older adults are not systematically sampled in SHARE. Taken together, this likely results in an underestimation of average frailty levels, the steepness of long-term frailty trajectories but also the size of frailty fluctuations.

In conclusion, we found that frailty fluctuations among older adults are non-negligible, closely associated with age and long-term frailty trajectories and differ for men and women as well as between individuals with different SEP. Frailty fluctuations represent a relevant yet hitherto untapped faced of frailty, which could contribute to a better understanding of frailty development among older adults. The predictive power of frailty fluctuations with regard to negative health events and its potential clinical relevance should be investigated further using more frequent assessments regimes.

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

Declaration of Conflicts of Interest: None.

Declaration of Sources of Funding: This work was supported by no specific institution but only the Medical University of Graz. For detailed sources of funding of SHARE see Appendix 3, available in *Age and Ageing* online.

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Received 10 October 2018; editorial decision 26 March 2019