- 23. Australian Institute of Health and Welfare. *Aged Care*. 2017 [cited 2017 January 12]. http://www.aihw.gov.au/aged-care/.
- **24.** National Coroners Information System. *About NCIS*. [cited 2017 March 3]. www.ncis.org.au/data-collection/.
- 25. StataCorp. Stata Statistical Software. College Station, TX: StataCorp LP, 2015.
- **26.** The Joint Commission. *Comprehensive Accreditation Manual for Hospitals Update 2*. 2015 [cited 2017 March 25]. www. mitsstools.org/uploads/3/7/7/6/3776466/psc_for_web.pdf.
- 27. de Vries E, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care 2008; 17(3):216–23.
- 28. Australian Institute of Health and Welfare. Residential Aged Care and Aged Care Packages in the Community 2011–12. 2013 [cited 2017 March 2]. http://www.aihw.gov.au/aged-care/residential-and-community-2011-12/.
- **29.** Ferrah N, Lovell J, Ibrahim J. Systematic review of the prevalence of medication errors resulting in hospitalization and death of nursing home residents. JAGS 2017; 65: 433–42.

- **30.** Bugeja L, Ibrahim JE, Ferrah N, Murphy B, Willoughby M, Ranson D. The utility of medico-legal databases for public health research: a systematic review of peer-reviewed publications using the National Coronial Information System. Health Res Policy Syst 2016; 14: 28. 10.1186/s12961-016-0096-1.
- **31.** World Health Organization. *Communication During Patient Hand-Overs*. Patient Safety Solutions 2007 [cited 2017 January 21]; pp. 1–4. www.who.int/patientsafety/solutions/patientsafety/PS-Solution3.pdf.
- **32.** McCusker J, Cole M, Abrahamowicz M, Han L, Podoba JE, Ramman-Haddad L. Environmental risk factors for delirium in hospitalized older people. JAGS 2001; 49(10): 1327–34.
- **33.** Ibrahim J, Bugeja L, Ranson D. Using existing information from medico-legal death investigations to improve care of older people in residential aged care services. J Law Med 2013; 21(2):255–561.

Received 3 August 2017; editorial decision 11 October 2017

Age and Ageing 2018; **47:** 233–241 © The Author 2017. Published by Oxford University Press on behalf of the British Geriatrics Society. doi: 10.1093/ageing/afx157 All rights reserved. For permissions, please email: journals.permissions@oup.com Published electronically 21 September 2017

Frailty and healthcare costs—longitudinal results of a prospective cohort study

André Hajek^{1†}, Jens-Oliver Bock^{1†}, Kai-Uwe Saum², Herbert Matschinger^{1,3}, Hermann Brenner^{2,4}, Bernd Holleczek^{2,5}, Walter E. Haefeli⁶, Dirk Heider^{1†}, Hans-Helmut König^{1†}

Address correspondence to: A. Hajek, Department of Health Economics and Health Services Research, University Medical Center Hamburg-Eppendorf, Hamburg Center for Health Economics, Hamburg, Germany. Tel: +49-40-7410-52877; Fax +49-40-7410-40261. Email: a.hajek@uke.de

Abstract

Objective: to investigate how frailty and frailty symptoms affect healthcare costs in older age longitudinally. **Methods:** data were gathered from a prospective cohort study in Saarland, Germany (two waves with 3-year interval, n = 1,636 aged 57–84 years at baseline). Frailty was assessed by the five Fried frailty criteria. Frailty was defined as having at least three criteria, the presence of 1–2 criteria as 'pre-frail'. Healthcare costs were quantified based on self-reported healthcare use in the sectors of inpatient treatment, outpatient treatment, professional nursing care and informal care as well as the provision of pharmaceuticals, medical supplies and dental prostheses.

¹Department of Health Economics and Health Services Research, Hamburg Center for Health Economics, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

²Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), Heidelberg, Germany

³Institute for Social Medicine, Occupational Health and Public Health, University of Leipzig, Leipzig, Germany

⁴Network Aging Research, University of Heidelberg, Heidelberg, Germany

⁵Saarland Cancer Registry, Saarbrücken, Germany

⁶Department of Clinical Pharmacology and Pharmacoepidemiology, University of Heidelberg, Heidelberg, Germany

[†]These authors contributed equally to this work.

Results: while the onset of pre-frailty did not increase (log) total healthcare costs after adjusting for potential confounders including comorbidity, progression from non-frailty to frailty was associated with an increase in total healthcare costs (for example, costs increased by ~54 and 101% if 3 and 4 or 5 symptoms were present, respectively). This association of frailty onset with increased healthcare costs was in particular observed in the inpatient sector and for informal nursing care. Among the frailty symptoms, the onset of exhaustion was associated with an increase in total healthcare costs, whereas changes in slowness, weakness, weight loss and low-physical activity were not significantly associated with an increase in total healthcare costs.

Conclusions: our data stress the economic relevance of frailty in late life. Postponing or reducing frailty might be fruitful in order to reduce healthcare costs.

Keywords: healthcare costs, frailty, longitudinal study, older people

Introduction

'Frail elderly' is a Medline Medical Subject Heading since 1991. It is defined as 'older adults or aged individuals who are lacking in general strength and are unusually susceptible to disease or to other infirmity'. In addition, frailty can be described as a 'state of weakness, slowness, weight loss, exhaustion and low-physical activity' [1].

It has been shown that frailty is common in old age [2]. Furthermore, the number of frail individuals will probably increase due to demographic shifts. Stressing the importance of frailty for the healthcare system, frailty is associated with numerous health-related factors such as the admission to a nursing home [3] or cognitive impairment [4].

Some cross-sectional studies have found that frailty is associated with increased healthcare use [5, 6]. In addition, frailty has been found to be positively associated with healthcare costs in old age in Germany [7]. This finding was also supported by Butler *et al.* [8]. However, it is almost unknown how frailty affects healthcare costs longitudinally. Peters *et al.* showed that frailty at baseline may predict subsequent healthcare costs (1-year later) [9]. Furthermore, McIsaac *et al.* found that frail patients after a total joint arthroplasty showed higher total costs when compared with non-frail patients [10].

However, longitudinal studies exploiting the intraindividual changes over time are missing. These studies using panel data methods can provide insights into the causality of the relationship of frailty and healthcare costs. Therefore, based on data from a large population-based prospective cohort study, the aim of this study was to investigate whether frailty affects healthcare costs (from a societal perspective) in older age longitudinally. To this end, panel-econometric techniques were used. Hence, first insights into the causal relationship can be given which is important for designing interventions. Moreover, using panel regression models can markedly reduce the problem of unobserved heterogeneity (e.g. time-constant factors such as genetic disposition). See the 'Statistical analysis' section as well as Brüderl and Ludwig [11] for further details.

Methods

Sample

This study used data from the Epidemiological study on chances of preventing, recognising early and optimally treating chronic diseases in an elderly population', the ESTHER study. For this large, prospective cohort study, 9,949 participants aged 50-75 years were recruited via their general practitioner (GPs) in Saarland, Germany, between July 2000 and December 2002. The participants took part in comprehensive assessments conducted by study physicians and provided additional information on sociodemographic and lifestyle variables and the history of their diseases. GPs were asked to validate these data. The ESTHER study has been approved by the ethics committees of the Medical Faculty of the University of Heidelberg and the Medical Association of Saarland. A signed statement of informed consent has been obtained from all participants included in the ESTHER study.

Follow-up (FU) waves took place every 2–3 years after baseline. At the FU wave 8 years after baseline (FU Wave 1), 7,012 persons still participated in the study. They were offered an additional specific geriatric assessment by study physicians (beyond a routine, standardised self-administered questionnaire) that covered, among others, the assessment of frailty symptoms. This assessment was conducted by study physicians at participants' homes. 3,124 persons agreed to this additional assessment in FU wave 1. For 2,598 of them, their GPs provided detailed data on morbidity. FU wave 2 took place 3 years after FU Wave 1 and again offered additional volunteer geriatric assessments. FU Wave 2 comprised 5,612 participants, with 2,761 taking part in the geriatric assessments and 2,217 providing data on both, frailty and morbidity assessed by the GPs. Our longitudinal analysis is based on a subsample with complete data on frailty symptoms and morbidity in both, FU Wave 1 and FU Wave 2 (n = 1,636). Also, see Figure 1 for further details.

Frailty

We considered five frailty criteria (symptoms) according to Fried *et al.* [12]: weakness, slowness, exhaustion,

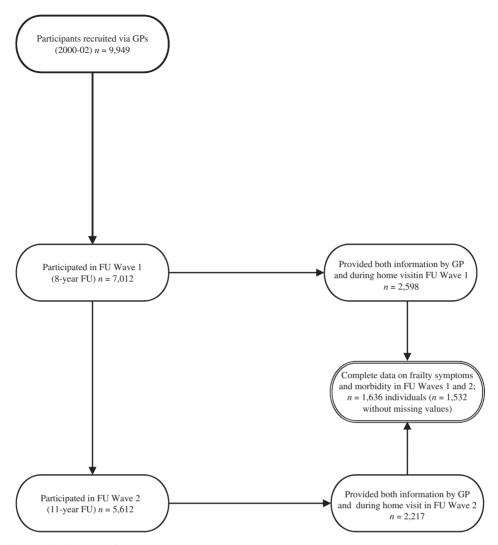


Figure 1. Flow Chart (ESTHER study).

unintentional weight loss and physical inactivity. Grip strength was used to operationalise weakness. It was measured three times by means of a Jamar hand dynamometer, and the best result was taken for analyses. The Short Physical Performance Battery (SPPB) [13] measured the occurrence of slowness. Participants had to go a distance of 3 m while their average speed in m/s was recorded. Exhaustion was operationalised using two items (I felt that everything I did was an effort' and 'I could not get going') [12] of the Center for Epidemiologic Studies Depression Scale (CES-D) [14]. Unintentional weight loss defined a frailty symptom if it exceeded 5 kg within 1 year. Physical inactivity was assessed based on the Physical Activity Questionnaire for the Elderly (PAQE) [15]. We used population-independent cut-offs for determining occurrence of frailty symptoms [16]. This approach increases comparability among studies. Further details of frailty assessment have been reported elsewhere [16]. For the following analyses, a frailty index based on the number of prevalent criteria was built up. Existence of 1-2 criteria was referred to as 'pre-frail', existence of more than two points

are referred to as 'frail', while the existence of 0 points defined the status 'non-frail'. See the 'Statistical analyses' section for further details.

Healthcare costs

Following widely accepted recommendations [17], a societal perspective for calculating healthcare costs was adopted in the present study. Calculation of healthcare costs was based on patients' self-reported healthcare use. The corresponding questionnaire covered all main healthcare sectors of inpatient treatment in hospitals and rehabilitation facilities, outpatient physician and non-physician care, pharmaceuticals, professional nursing care, informal care as well as medical supplies and dental prostheses. The resource quantities, for example, days in hospital, visits to a GP or specialist, or packs of medication, were collected retrospectively for a period of 3 months. This appeared to be long enough to detect rare events like hospital stays in a sufficient number. Yet, it was probably short enough in order to enable participants to recall accurately their health-related resource

consumption [18]. The documented resource quantities were monetarily valued with corresponding unit costs. These were gathered from various sources. See the Supplementary material for further details.

Morbidity

Morbidity was assessed by the corresponding GP in 13 somatic and 1 psychiatric dimensions according to the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) [19, 20]. This comprehensive and generic instrument assigns 0 ('no problem') to 4 points ('severe problems') to the 13 somatic and one psychiatric dimensions. The CIRS-G is a validated and reliable instrument to measure general morbidity in old age [19, 20].

Other variables

As control variables, we considered age, gender, education and marital status. The latter distinguished between single, married, divorced and widowed. The educational level was assessed as length of primary and secondary school attendance that could vary between up to 9 years, 10–11 years, and more than 11 years, which corresponds to the usual three-tiered system of secondary school in Germany. In addition, the employment status was included distinguishing between 'full-time employed', 'marginally/irregularly employed', 'regular part-time employed', 'housewife/house husband', 'retired' and 'unemployed'.

Statistical analyses

In a first step, descriptive statistics for individuals at both waves were reported. In a second step, the impact of frailty on healthcare costs was examined by using panel regression models, adjusting for potential confounders. Regression models specific for each sector (inpatient treatment, outpatient treatment, pharmaceuticals, professional nursing care, informal care as well as medical supplies and dental prostheses) were calculated.

A primary motivation for using longitudinal data is to solve the problem of omitted variable bias [21]. In many panel regression models, unobserved effects are considered as random variables which were derived from the population along with the regressors and the regressand [21]. As pointed out by Wooldridge [21], the main issue is whether the unobserved factors are uncorrelated with the independent variables. If this assumption is violated, popular panel regression models such as random effects regressions are inconsistent [22]. Contrarily, when time-constant unobserved factors are correlated with the explanatory variables, fixed effects (FEs) regressions yield consistent estimates [22]. Thus, to examine the impact of time-varying independent variables on healthcare costs, FE regression analyses were performed. This was indicated by Sargan-Hansen tests, which are Hausman tests with cluster-robust standard errors.

The FE estimator is also known as 'within estimator' because this estimator exclusively uses changes within

individuals over time. The conventional FE estimation applies pooled OLS to transformed data [23, 24]. This transformation is called 'within transformation' (or 'demeaning'). For example, intra-individual changes in marital status from 'single' to 'married' were examined in the current study. Consequently, the results are often interpreted in a causal sense (average treatment effect on the treated, ATET) [11, 25]. However, in contrast to a randomised controlled trial, the current study did not have a controlled treatment. This limits causal inference from our study even though, for linguistic reasons, seemingly causal terminology was occasionally used in our report.

Because, the distribution of individual healthcare costs is highly right-skewed, the natural logarithms of these quantities were used. In addition, it is worth mentioning that time-constant factors such as sex or education are omitted in FE models because there is no within variation in these variables. The level of significance was set at a = 0.05. Our regression analysis is based on 1,532 individuals (3,064 observations) because 104 individuals were excluded due to listwise deletion. Listwise deletion means that observations with missing data were deleted and only the reduced sample of complete observations (complete case analysis) is investigated. This was done as the proportion of missing data is fairly low in the current study, indicating that a potential bias may be small [26].

First, our main regression models included the frailty score as independent variable (with five categories: non-frail (0; reference); pre-frail (1), pre-frail (2), frail (3), frail (4 and 5)). The highest level of frailty (5) was collapsed into the category frail (4 and 5) due to the low number of cases. Second, regression models were conducted with the frailty criteria as independent variables instead of the frailty score in order to disentangle their individual impact. Third, regression models without morbidity were performed since morbidity is likely to be associated with frailty, and disentangling their effects on healthcare costs might often be difficult.

Results

Sample characteristics

Table 1 depicts the sample characteristics. Data were reported for n = 1,636 individuals, which had data on both morbidity and frailty symptoms available for FU waves 1 and 2.

For example, among the non-frail individuals at FU Wave 1, 286 individuals remained unchanged afterwards, whereas 251 individuals became pre-frail and 20 individuals became frail.

Regression analysis

Table 2 presents the findings of FE regressions of (log) healthcare costs with frailty score used as independent variable (log-linear regression). Thus, regression coefficients are semi-elasticities, i.e. they show the approximate percentage change in costs for a one-unit increase in an explanatory

Table I. Descriptive statistics over time

	FU Wave 1 $(n = 1,636)$	FU Wave 2 $(n = 1,636)$
Age in years: mean (SD); range	69.1 (6.0); 57–84	71.7 (6.1); 60–87
Female: N (%)	839 (51.3)	839 (51.3)
Marital status: N (%)	(31.3)	037 (31.3)
Single	52 (3.2)	50 (3.1)
Married	1,198 (73.6)	1,158 (71.6)
Divorced	115 (7.1)	113 (7.0)
Widowed	262 (16.1)	297 (18.3)
Education: N (%)*	()	
9 school years	1,047 (64.9)	1,047 (64.9)
10–11 school years	301 (18.7)	301 (18.7)
≥12 school years	265 (16.4)	265 (16.4)
Employment status: N (%)		
Full-time employed	132 (8.1)	51 (3.2)
Marginally employed	49 (3.0)	31 (1.9)
Regular part-time employed	26 (1.6)	18 (1.1)
Housewife/house husband	244 (15.0)	254 (15.7)
Retired	1,153 (71.0)	1,253 (77.6)
Unemployed	21 (1.3)	8 (0.5)
Morbidity (CIRS-G): mean (SD); range	6.5 (5.2); 0–32	7.8 (5.7); 0–49
Healthcare costs (3 months): mean (SD); 25%-percentile; i	median; 75%-percentile; range	
Total		
	€773.7 (€2,080.1);	€914.8 (€2,262.1);
	€124.3; €274.9; €536.9;	€144.0; €286.3; €597.7
	€0–€41,884.9	€0–€34,914.1
Inpatient		
	€326.9 (€1,696.4);	€390.4 (€1,862.8);
	€0; €0;	€0; €0; €0;
	€0–€30,948.6	€0-32,496.0
Outpatient		
	€197.0 (€262.2);	€197.0 (€213.8);
	€61.7; €128.0; €244.2	€62.4; €134.7; €250.6
	€0–€4,904.0	€0–€2,061.2
Pharmaceuticals		
	€133.6 (€236.5);	€160.4 (€353.6);
	€20.4; €70.7; €164.0	€32.4; €84.7; €182.8
	€0–€5,361.7	€0–€10,090.2
Professional nursing care		
	€4.2 (€72.2);	€19.4 (€510.3);
	€0; €0;	€0; €0; €0;
	€0–€2,340.0	€0–€20,304.0
Informal care		
	€29.2 (€401.4);	€58.7 (€783.1);
	€0; €0; €0;	€0; €0; €0;
	€0–€10,152.0	€0–€20,304.0
Medical supplies and dental prostheses	000 0 (0405 0)	000 0 (0400 0)
	€82.8 (€495.8);	€88.9 (€488.8);
	€0; €0; €0;	€0; €0; €0;
E 3. N 00/144	€0–€9,677.0	€0–€7,600.0
Frailty: N (%)**	500 (05 F)	500 (04.0)
Non-frail (0)	580 (35.5)	502 (31.8)
Pre-frail (1)	683 (41.9)	528 (33.5)
Pre-frail (2)	267 (16.4)	359 (22.7)
Frail (3)	75 (4.6)	141 (8.9)
Frail (4 and 5)	26 (1.6)	49 (3.1)
Frailty symptoms: N (%)	E00 (25 E)	(00, 07.0)
Slowness (yes)	580 (35.5)	609 (37.2)
Weakness (yes)	466 (28.5)	542 (33.1)
Weight loss (yes)***	54 (3.3)	88 (5.6)
Exhaustion (yes)	169 (10.3)	152 (9.3)
Low-physical activity (yes)****	286 (17.5)	532 (32.5)

The variables sex and education were not included in FE regressions as independent variables since they are time-constant. These two variables are only depicted for descriptive purposes. SD, standard deviation, CIRS-G, Cumulative Illness Rating Scale for Geriatrics.

Missing values (if occurred): *23 missing values in the first wave and 23 missing values in the second wave; **5 missing values in the first wave and 57 missing values in the second wave; ***1 missing value in the second wave.

Table 2. Factors affecting (log) healthcare costs with frailty status as main predictor. Results of FEs regressions

Independent variables	(1) Total	(2) Inpatient	(3) Outpatient	(4) Pharmaceuticals	(5) Professional nursing care	(6) Informal care	(7) Medical supplies and dental prostheses
Potential confounders			· · · · · · · · · · · · · · · · · · ·	✓			✓
Changes from 'Non-frail' (0) to 'Pre-frail' (1)	0.06	0.06	0.08	0.08	-0.04	0.03	0.00
	(0.08)	(0.14)	(0.08)	(0.08)	(0.03)	(0.04)	(0.13)
Changes from 'Non-frail' (0) to 'Pre-frail' (2)	0.13	0.29	0.06	0.09	-0.03	0.05	-0.09
	(0.10)	(0.20)	(0.10)	(0.09)	(0.04)	(0.06)	(0.17)
Changes from 'Non-frail' (0) to 'Frail' (3)	0.43**	1.13***	0.07	0.11	0.04	0.42**	-0.01
	(0.14)	(0.33)	(0.14)	(0.13)	(0.09)	(0.16)	(0.27)
Changes from 'Non-frail' (0) to 'Frail' (4 and 5)	0.70**	1.17	0.27	0.31	0.55*	0.52	0.38
,	(0.23)	(0.65)	(0.19)	(0.22)	(0.23)	(0.35)	(0.48)
Constant	2.36*	-1.54	3.98***	-2.49*	-0.57	-1.05	0.88
	(1.11)	(2.11)	(1.11)	(1.07)	(0.43)	(0.78)	(1.88)
Observations	3,064	3,064	3,064	3,064	3,064	3,064	3,064
R^2	0.02	0.02	0.00	0.04	0.03	0.02	0.01
Number of individuals	1,532	1,532	1,532	1,532	1,532	1,532	1,532

Beta-coefficients were reported. Cluster-robust standard errors in parentheses. Observations with missing values were dropped (listwise deletion). Listwise deletion means that observations with missing data were deleted and only the reduced sample of complete observations (complete case analysis) is investigated. ***P < 0.001, **P < 0.05, *P < 0.10. All estimations include age, marital status, employment status and morbidity.

variable. For small values of $\hat{\beta}$, $e^{\hat{\beta}} \approx 1 + \hat{\beta}$. For example, for $\hat{\beta} = .05$, $e^{0.05} \approx 1.05$. Consequently, a one-unit change in X corresponds approximately to an expected increase in Y of 5%.

FE regressions were used since, for example, the Sargan–Hansen statistic with (log) total healthcare costs as outcome variable was 101.7, P < 0.001. The FE regressions revealed that changes from 'non-frail' to 'pre-frail' (1 and 2) were not associated with an increase in total healthcare costs nor in sector-specific healthcare costs. However, changes to 'frail' were associated with an increase in total healthcare costs by 54% (3) and 101% (4 and 5) (frail (3): $\beta = 0.43$, P < 0.01; frail (4 and 5): $\beta = 0.70$, P < 0.01). Furthermore, changes to 'frail' (3) were associated with an increase in inpatient costs by 200% ($\beta = 1.13$, P < 0.001) and an increase in informal care costs by 52% ($\beta = 0.42$, P < 0.01). In addition, changes to 'frail' (4 and 5) were associated with an increase in professional nursing care costs by 73% ($\beta = 0.55$, P < 0.05).

Table 3 reports the findings of FE regressions of log healthcare costs with frailty criteria used as predictors (instead of frailty score). FE regressions revealed that the onset of exhaustion was associated with an increase in total healthcare costs by 36% (β = 0.3, P < 0.01), whereas the other frailty criteria were not significantly associated with this outcome measure. Furthermore, the onset of slowness was associated with an increase in informal care costs by 21% (β = 0.2, P < 0.001). The onset of weakness was associated with an increase in professional nursing care costs by 7% (β = 0.07, P < 0.05). Furthermore, while the onset of exhaustion was associated with an increase in inpatient costs by 92% (β = 0.65, P < 0.05) and

pharmaceuticals costs by 32% (β = 0.28, P < 0.01), changes in weight loss were not associated with any of the outcome measures. In addition, the onset of low-physical activity was associated with an increase in inpatient costs by 48% (β = 0.39, P < 0.05).

In additional analysis, morbidity was removed from regression analysis because it is associated with frailty (r = 0.28, P < 0.001). In terms of significance and effect sizes, findings remained virtually the same.

Discussion

Main findings

The present study examined to which extent changes in frailty were associated with changes in healthcare costs in older age longitudinally. While changes from 'non-frail' to 'pre-frail' were not associated with increased total healthcare costs after adjusting for potential confounders, the onset of frailty was associated with an increase in total healthcare costs. For example, costs increased by ~54 and 101% if 3 and 4 or 5 symptoms were present, respectively.

Among the frailty symptoms, the onset of exhaustion was associated with an increase in total healthcare costs. The frailty symptoms had varying associations with costs depending on healthcare sectors, stressing the heterogeneity of their relationship with costs.

Previous research

Previous studies have examined associations of frailty and healthcare costs. For example, Sirven and Rapp [27] found significant excess cost for both pre-frail and frail

Table 3. Factors affecting (log) healthcare costs with symptoms of frailty as main predictors. Results of FEs regressions

Independent variables	(1) Total	(2) Inpatient	(3) Outpatient	(4) Pharmaceuticals	(5) Professional nursing care	(6) Informal care	(7) Medical supplies and dental prostheses
Potential confounders			· · · · · · · · · · · · · · · · · · ·			· · · · · · · · · · · · · · · · · · ·	
Changes to the presence of 'Slowness'	0.07	0.14	0.01	0.06	-0.01	0.19***	-0.01
	(0.08)	(0.14)	(0.07)	(0.07)	(0.03)	(0.05)	(0.13)
Changes to the presence of 'Weakness'	0.10	0.15	0.04	-0.05	0.07*	-0.05	0.17
	(0.08)	(0.14)	(0.08)	(0.08)	(0.03)	(0.05)	(0.13)
Changes to the presence of 'Weight loss'	0.29+	0.23	-0.04	0.12	0.15	0.12	-0.14
	(0.15)	(0.37)	(0.12)	(0.13)	(0.12)	(0.15)	(0.27)
Changes to the presence of 'Exhaustion'	0.31**	0.65*	0.14	0.28**	0.03	0.15	0.05
	(0.11)	(0.28)	(0.10)	(0.09)	(0.06)	(0.15)	(0.21)
Changes to the presence of 'Low-physical activity'	0.05	0.39*	0.03	0.01	0.04	0.07	-0.15
•	(0.08)	(0.16)	(0.07)	(0.07)	(0.04)	(0.07)	(0.14)
Constant	1.99+	-1.84	4.40***	-2.68*	-0.57	-1.37	0.41
	(1.14)	(2.12)	(1.11)	(1.09)	(0.47)	(0.83)	(1.94)
Observations	3,064	3,064	3,064	3,064	3,064	3,064	3,064
R^2	0.02	0.02	0.00	0.04	0.01	0.02	0.01
Number of individuals	1,532	1,532	1,532	1,532	1,532	1,532	1,532

Beta-coefficients were reported. Cluster-robust standard errors in parentheses. Observations with missing values were dropped (listwise deletion). Listwise deletion means that observations with missing data were deleted and only the reduced sample of complete observations (complete case analysis) is investigated. ***P < 0.001, **P < 0.05, *P < 0.05, *P < 0.10. All estimations include age, marital status, employment status and morbidity.

community-dwelling individuals as compared to non-frail individuals in a population-based French sample in 2012. Thereby, they limited their analysis to outpatient physician and non-physician services (like physiotherapy), finding strong associations of frailty with healthcare costs after controlling for comorbidity, limitations in activities of daily-living, and time do death. For the important inpatient sector, García-Nogueras et al. [28] revealed strong associations of frailty with inpatient costs in regression analysis controlling for the Charlson Comorbidity Index as a proxy of comorbidity. This is in line with findings of a recent literature review based on 13 studies in 8 countries which showed that frailty is an important predictor of hospitalisation [29]. Stressing and extending these findings, evidence from the present ESTHER study equally found similar associations in the inpatient and outpatient sectors, but also considered nursing care and pharmaceuticals. Thereby, pharmaceuticals have been shown to be strongly associated with costs after controlling for comorbidity in multivariate regression models [7].

The cited studies share with our findings that frailty appears to play an important role for healthcare costs. Yet, these studies were limited to cross-sectional designs. Thus far, evidence from longitudinal data is sparse. Comans *et al.* [30] showed an increase in the costs of 6 months among individuals with intermediate and high levels of frailty in comparison with individuals with low frailty following a hospital admission.

Peters *et al.* [9] used the Groningen Frailty Indicator (GFI) and a case complexity measure to predict future costs (1-year later) in all main healthcare sectors (inpatient, outpatient, pharmaceuticals and nursing care). They concluded that both frailty measures at baseline are highly predictive

for subsequent healthcare cost. McIsaac *et al.* [10] investigated the onset of frailty after total joint arthroplasty and its relationship to costs, adopting a broad payer's perspective on costs including hospital, outpatient and pharmaceutical costs. Their result of frail participants having increased total costs is comparable to our study. Yet, we used a different approach to assess frailty symptoms and the frailty index. Additionally, we analyzed the effects of the frailty symptoms on costs, showing great heterogeneity in their impact on sectoral costs. In addition, our study estimated the withineffect of frailty on costs that can be interpreted as ATET and provides therefore more insights into the causal relationship of frailty and costs.

Our results suggest that costs increase within an individual if frailty sets on. Conversely, this means that it is likely that individual healthcare costs would decrease if a person improved from being frail to being non-frail. This is important, since correspondingly tailored interventions to prevent, delay or treat frailty might potentially lead to cost-savings. Yet, respective interventions, like screening tools, home-based support, home telecare, hospital discharge planning, physical activity or health promotion programs have to be further evaluated with regard to their effectiveness [31].

In addition, cost-effectiveness analyses (CEAs) of such interventions that proved to be effective should be conducted. However, currently, CEAs of interventions to prevent, delay or treat frailty are sparse. One example is the Ambulatory Geriatric Assessment–Frailty Intervention Trial (Age–FIT) that analyzed an intervention based on Comprehensive Geriatric Assessment for community-dwelling persons aged 75 and older and compared it to treatment as usual [32, 33] in a Swedish region using a

randomised controlled trial. Thirty-six months after the baseline assessment, mortality rates were significantly lower in the intervention group. Although total costs did not differ significantly between both groups, inpatient costs significantly decreased in the intervention group, assumingly due to decreased frailty. Besides, Yamada *et al.* [34] also found cost savings due to an effective community-based exercise program intervention, albeit not directly related to significant cost reductions in the inpatient sector but rather in total healthcare costs. These findings support our findings as they show that well-tailored interventions might lead to decreasing frailty with specific cost-savings.

Strengths and limitations

This is one of the first studies aimed at examining the relationship between frailty and healthcare costs longitudinally. Data were gathered from a large population-based prospective cohort study. However, very few participants lived in institutional settings such as nursing homes. Thus, findings may not be generalisable to institutionalised individuals. As panel data methods solve the problem of omitted variable bias, our estimations are not biased by time-constant unobserved heterogeneity. A further strength is the detailed data obtained on socio-economic factors, morbidity and frailty as well as healthcare costs. Besides the phenotype of frailty, we provide estimates of the impact of its constituting factors on healthcare costs.

Our FE estimates might be biased downwards due to panel attrition. However, it is worth noting that linear FE estimates are not biased by attrition associated with personspecific characteristics (both observed and unobserved) [21]. Our analysis was restricted to individuals who completed the voluntary additional geriatric assessments. Thus, sample selection bias is possible (e.g. individuals with a high morbidity burden or the most frail individuals might be more reluctant to participate), which in turn might lead to conservative cost estimates. Moreover, we analyzed selfreported healthcare use so that we cannot rule out recall bias of the collected data (particularly in the frailest individuals because frailty is associated with cognitive decline [4]). Yet, since the recall period was quite short, this bias should be, generally, rather small. We cannot dismiss the possibility that individuals might be omitted in FE regressions when they are still in hospital at the time of the interview. However, we assume that this is rarely the case.

Conclusion

It is most likely that the number of frail individuals in old age will increase considerably in the next decades for reasons of demographic ageing. These forecasts and our data stress the economic relevance of frailty in older adults. Because, healthcare costs rise with increasing frailty, postponing or reducing frailty might be fruitful in order to reduce healthcare costs.

Key points

- Association between frailty and healthcare costs was examined longitudinally.
- Changes to frailty were associated with an increase in total healthcare costs.
- The onset of exhaustion was associated with an increase in total healthcare costs.
- Our data stress the economic relevance of frailty in late life.
- Postponing or reducing frailty might be fruitful to reduce healthcare costs.

Supplementary Data

Supplementary data are available at Age and Ageing online.

Funding

This study was funded by the German Federal Ministry of Education and Research (grant numbers 01ET0717, 01ET0718, 01ET0719, 01ET1004A, 01ET1004B and 01ET1004C). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Conflict of interest

None.

References

- 1. Goldstein J, McVey J, Ackroyd-Stolarz S. The role of emergency medical services in geriatrics: bridging the gap between primary and acute care. CJEM 2016; 18: 54–61.
- **2.** Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc 2012; 60: 1487–92.
- Hajek A, Brettschneider C, Lange C et al. Longitudinal predictors of institutionalization in old age. PLoS One 2015; 10: e0144203.
- **4.** Hajek A, Brettschneider C, Posselt T *et al.* Predictors of frailty in old age–results of a longitudinal study. J Nutr Health Aging 2016; 20: 952–7.
- Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med 2004; 59: M255–M63.
- Gobbens RJ, van Assen MA, Luijkx KG, Schols JM. Testing an integral conceptual model of frailty. J Adv Nurs 2012; 68: 2047–60.
- Bock J-O, König H-H, Brenner H et al. Associations of frailty with health care costs–results of the ESTHER cohort study. BMC Health Serv Res 2016; 16: 1.
- **8.** Butler A, Gallagher D, Gillespie P *et al.* Frailty: a costly phenomenon in caring for elders with cognitive impairment. Int J Geriatr Psychiatry 2016; 31: 161–8.

Frailty and healthcare costs

- 9. Peters LL, Burgerhof JG, Boter H, Wild B, Buskens E, Slaets JP. Predictive validity of a frailty measure (GFI) and a case complexity measure (IM-E-SA) on healthcare costs in an elderly population. J Psychosom Res 2015; 79: 404–11.
- McIsaac D, Beaulé P, Bryson G, Van Walraven C. The impact of frailty on outcomes and healthcare resource usage after total joint arthroplasty. Bone Joint J 2016; 98: 799–805.
- 11. Brüderl J, Ludwig V. Fixed-effects panel regression. In: Wolf C, ed. The Sage Handbook of Regression Analysis and Causal Inference. Los Angeles: SAGE, 2015; pp. 327–57.
- Fried LP, Tangen CM, Walston J et al. Frailty in older adults evidence for a phenotype. J Gerontol A Biol Sci Med 2001; 56: M146–M57.
- 13. Guralnik JM, Simonsick EM, Ferrucci L et al. A Short Physical Performance Battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994; 49: M85–94.
- **14.** Radloff LS. The CES-D scale a self-report depression scale for research in the general population. Appl Psychol Meas 1977; 1: 385–401.
- **15.** Voorrips LE, Ravelli AC, Petra C, Dongelmans A, Deurenberg P, van Staveren WA. A physical activity questionnaire for the elderly. Med Sci Sports Exerc 1991; 23: 974–9.
- 16. Saum KU, Müller H, Stegmaier C, Hauer K, Raum E, Brenner H. Development and evaluation of a modification of the fried frailty criteria using population—independent cutpoints. J Am Geriatr Soc 2012; 60: 2110–5.
- 17. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. Methods for the Economic Evaluation of Health Care Programs. New York: Oxford University Press, 2005.
- **18.** Bhandari A, Wagner T. Self-reported utilization of health care services: improving measurement and accuracy. Med Care Res Rev 2006; 63: 217–35.
- 19. Linn BS, LINN MW, Gurel L. Cumulative illness rating scale. J Am Geriatr Soc 1968; 16: 622–6.
- **20.** Miller MD, Paradis CF, Houck PR *et al.* Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. Psychiatry Res 1992; 41: 237–48.
- **21.** Wooldridge JM. Econometric Analysis of Cross Section and Panel Data. Cambridge, Mass: MIT press, 2010.
- **22.** Cameron AC, Trivedi PK. Microeconometrics: Methods and Applications. New York: Cambridge University Press, 2005.

- 23. Brüderl J. Applied Panel Data Analysis Using Stata. Munich 2015
- 24. Gardiner JC, Luo Z, Roman LA. Fixed effects, random effects and GEE: what are the differences? Stat Med 2009; 28: 221–39.
- **25.** Gangl M. Causal inference in sociological research. Annu Rev Sociol 2010; 36: 21–47.
- **26.** Langkamp DL, Lehman A, Lemeshow S. Techniques for handling missing data in secondary analyses of large surveys. Acad Pediatr 2010; 10: 205–10.
- 27. Sirven N, Rapp T. The cost of frailty in France. Eur J Health Econ 2017; 18: 243–53.
- 28. García-Nogueras I, Aranda-Reneo I, Peña-Longobardo L, Oliva-Moreno J, Abizanda P. Use of health resources and healthcare costs associated with frailty: the FRADEA study. J Nutr Health Aging 2017; 21: 207–14.
- 29. Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. J Epidemiol Community Health 2016; 70: 722–9.
- **30.** Comans T, Peel N, Hubbard R, Mulligan A, Gray L, Scuffham P. The increase in healthcare costs associated with frailty in older people discharged to a post-acute transition care program. Age Ageing 2016; 45: 317–20.
- **31.** Wilson MG, Béland F, Julien D *et al.* Interventions for preventing, delaying the onset, or decreasing the burden of frailty: an overview of systematic reviews. Systematic reviews 2015; 4: 1.
- 32. Ekdahl AW, Alwin J, Eckerblad J et al. Long-term evaluation of the Ambulatory Geriatric Assessment: A Frailty Intervention Trial (AGe-FIT): clinical outcomes and total costs after 36 months. J Am Med Dir Assoc 2016; 17: 263–8.
- **33.** Ekdahl AW, Wirehn A-B, Alwin J *et al.* Costs and effects of an Ambulatory Geriatric Unit (the AGe-FIT Study): a randomized controlled trial. J Am Med Dir Assoc 2015; 16: 497–503.
- **34.** Yamada M, Arai H, Sonoda T, Aoyama T. Community-based exercise program is cost-effective by preventing care and disability in Japanese frail older adults. J Am Med Dir Assoc 2012; 13: 507–11.

Received 5 January 2017; editorial decision 7 August 2017