

Frailty, pre-frailty and employment outcomes in the Health and Employment after Fifty (HEAF) study

Professor Keith T Palmer, Professor of Occupational Medicine^{1,2}

Stefania D'Angelo, Statistician^{1,2}

Dr E Clare Harris, Research Fellow^{1,2}

Dr Cathy Linaker, Research Fellow^{1,2}

Professor Catharine R Gale, Professor of Cognitive Epidemiology^{1,6}

Professor Maria Evandrou, Professor of Gerontology⁷

Dr Holly Syddall, Statistician¹

Professor Tjeerd van Staa, Professor of Health eResearch^{8,9}

Professor Cyrus Cooper, Professor of Rheumatology^{1,2}

Professor Avan Aihie Sayer, Professor of Geriatric Medicine^{1,3,4,5}

Professor David Coggon, Emeritus Professor of Occupational and Environmental Medicine^{1,2}

Professor Karen Walker-Bone, Professor of Occupational Rheumatology^{1,2}

1. MRC Lifecourse Epidemiology Unit, University of Southampton
2. Arthritis Research UK/MRC Centre for Musculoskeletal Health and Work, University of Southampton
3. NIHR Collaboration for Leadership in Applied Health Research and Care Wessex
4. Institute of Neuroscience, Newcastle University
5. NIHR Newcastle Biomedical Research Centre, Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust
6. Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh
7. Centre for Research on Ageing, University of Southampton
8. Farr Institute, University of Manchester
9. Utrecht Institute for Pharmaceutical Sciences, Utrecht University

Correspondence to: Professor Keith Palmer, Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton SO16 6YD, UK

Tel: (023) 80777624, Fax no: (023) 80704021, e-mail: ktp@mrc.soton.ac.uk

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive licence for UK Crown and US Federal Government employees) on a worldwide basis to the BMJ Publishing Group Ltd, and its Licensees to permit this article (if accepted) to be published in Occupational and Environmental Medicine and any other BMJPGGL products and to exploit all subsidiary rights, as set out in the licence.

Key words: work, frail, job loss, sickness absence, work limitations

Word count: main text excluding references, 3,398; abstract, 250. Tables: 5 (plus 2 online supplementary tables)

What this paper adds

- In elderly care medicine, a phenotype of physical ‘frailty’ has been found to predict many adverse health outcomes and has proved a target for intervention
- The potential impact of the phenotype on employment has not been studied previously however
- Using a symptom checklist adapted from previous research, we have found that ‘frailty’ symptoms are not uncommon in people aged 50-65 years in the English general population and are very strongly associated cross-sectionally with worklessness, health-related job loss, sickness absence and not coping at work
- Our findings need to be corroborated longitudinally, and the physical function and clinical features of those with multiple symptoms characterised, as a possible prelude to developing instruments to screen for frailty in employment

Abstract

Objectives: Demographic changes are requiring people to work longer. No previous studies, however, have focussed on whether the ‘frailty’ phenotype (which predicts adverse events in the elderly) is associated with employment difficulties. To provide information, we assessed associations in the HEAF study, a population-based cohort of 50-65 year-olds.

Methods: Subjects, who were recruited from 24 English general practices, completed a baseline questionnaire on ‘pre-frailty’ and ‘frailty’ (adapted Fried criteria) and several work outcomes, including health-related job loss (HRJL), prolonged sickness absence (>20 days vs. less, past 12 months), having to cut down substantially at work and difficulty coping with work’s demands. Associations were assessed using logistic regression and population attributable fractions (PAFs) were calculated.

Results: In all, 3.9% of 8,095 respondents were classed as ‘frail’ and 31.6% as ‘pre-frail’. Three-quarters of the former were not in work, while 60% had left their last job on health grounds (odds ratio (OR) for HRJL, vs. non-frail subjects, 30.0 (95% Confidence Interval 23.0-39.2). Among those in work, ORs for prolonged sickness absence, cutting down substantially at work and struggling with work’s physical demands ranged from 10.7 to 17.2. The PAF for HRJL when any frailty marker was present was 51.8% and that for prolonged sickness absence was 32.5%. Associations were strongest with slow reported walking speed. Several associations were stronger in manual workers than in managers.

Conclusions: Fried frailty symptoms are not uncommon in mid-life and are strongly linked with economically important adverse employment outcomes. Frailty could represent an important target for prevention.

By 2060, 30% of the European population will be aged over 65 years. Increasingly, therefore, western governments have been implementing policies to encourage people to remain in work longer, to support themselves and others [1]. However, for people with chronic disease extended working life may be infeasible, particularly if their jobs require substantial physical effort. Strategies may be needed to identify workers at particular risk of health-related job loss when older, and to assist them – for example through interventions to promote their fitness in middle and later life.

In elderly care medicine, a phenotype of physical frailty has been found to be a useful target for interventions [2,3]. ‘Frailty’ thus defined is characterized by age-related declines in functional reserves across a range of physiological systems. Frail elderly people are at heightened risk of many adverse outcomes including dependency, institutionalization, falls, fractures, hospitalization, and mortality, and they have higher rates of comorbidity and disability [2-7]. Clinical trials have suggested that the frailty status may be reversible and that some of these events may thereby be avoidable [8-10].

Whilst frailty is generally regarded as a problem of old age, the symptoms by which the phenotype is identified can also occur in younger people. However, ‘frailty’ has seldom been studied in people of working age [11] and never to our knowledge investigated in relation to work incapacity. Conceivably, symptoms of frailty could be useful markers for employment difficulties in late middle age, in which case, by analogy with advances in elderly care, there could be scope to intervene to prevent health-related job loss and premature retirement.

To provide initial information in this area, we used baseline data on people aged 50-65 years who were enrolled into the Health and Employment After Fifty (HEAF) study [12] to assess the prevalence and interrelationship of symptoms of physical frailty, and to explore their associations with various adverse employment outcomes.

In previous research ‘frailty’ has been defined in more than 20 separate ways [13], among which the criteria of Fried *et al* [2] are widely used. These comprise five items of unintentional weight loss, self-reported exhaustion, slow walking speed, low physical activity levels and weakness of grip. We assessed: (1) whether ‘frailty’, defined by these criteria, was associated with adverse employment outcomes (worklessness, health-related job loss, prolonged sick leave, having to cut down a lot and failing to cope at work); (2) how much it

contributed to the population burden of such outcomes; (3) whether findings varied by the nature of a person's occupation; and (4) whether different elements of the case definition were more importantly associated with work difficulties than others.

Methods

The HEAF cohort is nested within the Clinical Practice Research Datalink (CPRD), a British primary care research database. Details of recruitment and data collection have been published elsewhere [12]. In brief, in 2013-14, a sampling frame was drawn up of patients born between 1948 and 1962 (target ages 50-64 years) who were registered with 24 English general practices contributing data to the CPRD. Questionnaires were mailed to 39,359 people (97.5% of those identified, and excluding those who had illness or recent bereavement, or had de-registered during the interval between sampling and mailing). In all 8,134 subjects returned a valid questionnaire (some of whom were aged 65 by the time they completed the form).

Relevant to this analysis were a panel of questions about physical function, health and employment outcomes. To assess frailty we adapted the Fried criteria using questionnaire items on:

- (1) Weight loss: in the past 12 months, weight loss of more than 10lbs (4.5 kg) unintentionally, i.e. without dieting and exercise (yes vs. no);
- (2) Exhaustion: in the past seven days, everything being an effort or not being able to "get going" (either or both, for most or all of the time);
- (3) Slowness: normal walking speed described as "unable to walk" or "very slow";
- (4) Weakness of grip strength: moderate or severe difficulty in opening jars that had never previously been opened;
- (5) Inactivity: in an average week, and outside any paid jobs, doing no physical activity sufficient to make the respondent hot or sweaty.

Questions 1 and 2 were those used by Fried *et al* [2]. Questions 3 to 5 approximated the corresponding criteria, which were originally based on the bottom fifths of measured walking speed, measured grip strength, and self-reported weekly physical activity. According to the Fried case definition, an elderly person meeting three or more of the five criteria would be counted as 'frail', while a person meeting one or two of the criteria would be classed as 'pre-

frail'. As in Fried's original report, we excluded subjects with three or more missing responses to the frailty items (39 subjects), leaving 8095 people in the analysis.

Employment-related questions in the HEAF baseline questionnaire included current employment status and, if not working, whether the previous job had been surrendered for a health reason (analysed as not in work vs. in work and left for a health reason vs. not); occupation or last held occupation (used to classify subjects' jobs according to the Standard Occupational Classification 2010 (SOC 2010) [14] as higher managerial, intermediate occupation or routine/manual occupation); and for those in work: total sickness absence in the past 12 months (0, <5, 5-20, or >20 days, analysed as 'any absence vs. none' and '>20 vs. ≤20 days of absence'); needing to cut down at work in the past 12 months because of health (not at all, a little or a lot, analysed as 'any vs. none' and 'a lot vs. not'); current coping with work's physical and mental demands (with some/great difficulty vs. easily); expecting to be physically and mentally able still to carry out the same kind of work in two years' time (no/not sure vs. yes); perceived job security (rather/very insecure vs. secure/very secure); ever lying awake at night, worrying or angry about work (often vs. sometimes/rarely/never). These items (other than social class) were assessed as outcomes in relation to markers of frailty.

Also, information was collected on several potential confounders of associations, namely: low well-being, according to the 14-item Warwick-Edinburgh Mental Well-being Scale (WEMWBS) [15] (bottom fifth of scores vs. the rest); and pain for a month or longer in the past 12 months which affected back or neck, arms or shoulders, or legs and which made it difficult or impossible to get washed or dressed or do household chores ('persistent' pain at 0, 1, 2-3 sites, analysed as pain at least at one site vs. no pain).

Data were described using basic summary statistics and cross-tabulations were used to assess their overlap and association with one another. Associations between components of the Fried frailty criteria and employment variables were assessed by logistic regression and summarised by odds ratios (ORs) with 95% confidence intervals (95% CIs). Analyses were repeated separately for strata of social class defined from current or last held occupation. For measures of work loss, we also estimated the population attributable fractions (PAFs) associated with the presence of different numbers of Fried symptoms. A PAF represents the proportion of cases in a population that would be eliminated if all people had the same risk as

those in the reference category. Finally, in a sensitivity analysis, we assessed the further impact of adjustment for low well-being and persistent musculoskeletal pain, these being other markers of ill-health that might confound associations of frailty with the work outcomes. All analyses were conducted for men and women combined with adjustment for age (as a continuous measure) and gender and using Stata statistical software, release 14.

Results

The characteristics of the study participants are summarised in Table 1: 46% were male, the average age was 58.7 years (standard deviation 4.4 years, range 50 to 65), and 27.3% of men and 36.4% of women reported that they were no longer working. Among those not in work, 37.6% of men and 32.6% of women reported that they had left their last employment wholly or partly because of a health problem. Musculoskeletal disorders and mental illness were the most commonly cited health reasons for stopping work. In addition, many of the 2,682 men and 2,804 women who were still in work reported reduced participation in, or difficulties with, their employment. For example, 6.2% of the men and 7.2% of the women had taken 20 or more days sick leave in the past 12 months, and 28.9% of the men and 30.2% of the women reported some or great difficulty in coping with work's physical demands. About one in five reported their job to be insecure or very insecure.

Table 1: Characteristics of the participants

	Men		Women	
	N	% ^a	N	% ^a
<i>Whole sample</i>	3,689		4,406	
Age (mean (SD))		58.7 (4.4)		58.6 (4.4)
<i>Social class</i>				
Higher managerial	1,543	42.5	1,699	39.1
Intermediate occupations	795	21.9	1,437	33.0
Routine and manual occupations	1,291	35.6	1,215	27.9
<i>Employment status</i>				
In work	2,682	72.7	2,804	63.6
Not in work	1,007	27.3	1,602	36.4
- Retired (not for health reason)	517	14.0	927	21.0
- Unemployed (not for health reason)	111	3.0	152	3.4
- Left for health reason (unemployed or retired)	379	10.3	523	11.9
<i>Current workers</i>				
Any sick leave, past 12 months	1,003	37.8	1,346	48.4
≥ 20 days sick leave, past 12 months	163	6.2	200	7.2
Cutting down at work to any extent, past 12 months	669	25.1	770	27.6
Cutting down at work a lot, past 12 months	142	5.3	170	6.1
Not coping with work's physical demands	763	28.9	837	30.2
Not coping with work's mental demands	779	29.5	937	33.8
Expecting not to be able to cope at work in 2 years' time	551	21.0	791	28.5
Often lying awake worrying about work	291	11.0	412	14.8
Job insecure/very insecure	532	20.2	509	18.4

a - for current workers, percentages relate to those in work

Table 2 shows the prevalence of symptoms used to define frailty, overall and by gender. By our adapted case definition, 313 (3.9%) of the 8,095 eligible respondents were classified as 'frail' (3-5 symptoms present) and, within this subgroup, low physical activity, weakness of grip, and slow walking speed were reported by 77%, 87% and 82% of subjects respectively. Some 2,560 (31.6%) subjects were counted as 'pre-frail' (1 or 2 symptoms present) by our adapted Fried criteria. Women were more likely than men to report symptoms, both individually and in combination, with 4.9% of women but 2.7% of men reporting ≥ 3 symptoms.

Table 2. Prevalence of Fried symptoms

Symptoms	All	Men	Women	'Pre-frail' ^a	'Frail' ^a
	N (%)	N (%)	N (%)	N (%)	N (%)
Low physical activity	1,355 (18.8)	589 (17.5)	766 (20.0)	1,161 (51.5)	194 (77.0)
Weakness of grip	1,001 (12.5)	192 (5.3)	809 (18.6)	730 (28.8)	271 (87.1)
Unintentional weight loss	753 (9.4)	327 (8.9)	426 (9.7)	605 (23.7)	148 (47.7)
Slow walking speed	536 (6.6)	233 (6.3)	303 (6.9)	278 (10.9)	258 (82.4)
Exhaustion	526 (6.5)	194 (5.3)	332 (7.6)	333 (13.1)	193 (61.7)
Number of frailty symptoms:					
None	5,222 (64.5)	2597 (70.4)	2625 (59.6)		
1-2 symptoms ('pre-frail')	2,560 (31.6)	993 (26.9)	1567 (35.5)		
≥3 symptoms ('frail')	313 (3.9)	99 (2.7)	214 (4.9)		

a 'Pre-frail', 1-2 symptoms; 'frail', 3-5 symptoms

Certain symptoms associated with one another particularly strongly, notably slow walking speed with weak grip (OR 11.9) and exhaustion (OR 10.5), but also slow walking speed with low physical activity (OR 6.1) and weak grip with exhaustion (OR 6.1). By contrast, associations of unintentional weight loss and low physical activity with other frailty indicators tended to be weaker (online supplementary Table 1).

Table 3 presents the associations between number of frailty symptoms and work outcomes, and provides estimates of the relevant PAFs. Relationships with employment status, including whether the previous job was surrendered for a health reason, were explored in all subjects, whereas those with sickness absence, needing to cut down a lot at work, and various perceptions about work (e.g. self-reported coping, future expectations, worry over work, job dissatisfaction) were restricted to the 5,486 respondents in paid work.

Table 3. Associations between number of frailty symptoms and employment outcomes and perceptions

Outcomes	N (%) with work outcome among participants with no frailty symptoms	Risk factor					
		'Pre-frail' (1-2 vs. 0 symptoms)			'Frail' (3-5 vs. 0 symptoms)		
		N (%) positive	OR (95% CI)	PAF	N (%) positive	OR (95% CI)	PAF
<i>Entire Sample (n =8,095)</i>							
Not in work vs. in work	1468 (28.1)	906 (35.4)	1.4 (1.2,1.6)	9.7%	235 (75.1)	10.5 (7.9,14.1)	8.2%
Left for a health reason vs. not	280 (5.4)	433 (16.9)	3.7 (3.1,4.3)	34.9%	189 (60.4)	30.0 (23.0,39.2)	20.3%
<i>Those in work (n=5,486)</i>							
Sick leave, days past 12 months (max n=5,457):							
Any vs. none	1468 (39.4)	827 (50.8)	1.5 (1.4,1.7)	12.2%	54 (70.1)	3.4 (2.1,5.5)	1.6%
>20 days vs. ≤20 days	168 (4.5)	169 (10.4)	2.5 (2.0,3.1)	27.6%	26 (33.8)	10.7 (6.5,17.7)	6.5%
Cut down on work, past 12 months:							
Any vs. none	787 (21.1)	596 (36.5)	2.2 (1.9,2.4)	22.2%	56 (72.7)	10.0 (6.0,16.6)	3.5%
A lot vs. not a lot (none/a little)	128 (3.4)	155 (9.5)	3.0 (2.3,3.8)	33.0%	29 (37.7)	17.2 (10.5,28.4)	8.8%
Coping with work's physical demands (vs. easily):							
With some/great difficulty	848 (22.9)	691 (42.0)	2.4 (2.2,2.8)	25.5%	61 (81.3)	14.8 (8.2,26.6)	3.6%
Coping with work's mental demands (vs. easily):							
With some/great difficulty	1029 (27.9)	640 (38.9)	1.7 (1.5,1.9)	14.8%	47 (62.7)	4.5 (2.8,7.3)	2.1%
Expecting to be able to cope in 2 years' time (vs. yes):							
No/not sure	717 (19.4)	566 (34.6)	2.1 (1.9,2.4)	22.3%	59 (78.7)	14.5 (8.2,25.4)	4.1%
Lying awake at night worrying about work (vs. sometimes/rarely/never):							
Often	375 (10.1)	300 (18.2)	2.0 (1.7,2.3)	20.8%	28 (36.8)	1.2 (1.0,1.4)	3.2%
Job security (vs. secure/very secure):							
Insecure/very insecure	671 (18.2)	341 (20.8)	5.1 (3.2,8.3)	5.6%	29 (38.7)	3.0 (1.9,4.8)	1.9%

PAF – population attributable fraction; all estimates are adjusted for age and gender

Three-quarters of those classed as 'frail' were no longer working, and 60% reported leaving their last job for a health reason; corresponding proportions among the 'non-frail' (those with no Fried symptoms) were 28% and 5% respectively ($p \leq 0.001$ for differences). The odds of not being in paid work were elevated 10.5-fold in 'frail' vs. 'non-frail' subjects, and the OR for health-related job loss was even higher (OR 30.0, 95%CI 23.0-39.2). Adverse work outcomes were also more frequent in those classed as 'pre-frail', although associations were weaker (ORs vs. 'non-frail', 1.4 and 3.7 respectively).

Among the 5,486 people in paid work, 78 (1.4%) met our criteria for 'frailty' while 1,654 (30.2%) were classed as 'pre-frail'. Relative to those with no Fried symptoms, the former group had much higher odds of prolonged sickness absence in the past year (OR 10.7, 95%CI 6.5-17.7), needing to cut down a lot on work in the past 12 months (OR 17.2, 95%CI 10.5-28.4), difficulty coping with work's physical demands (OR 14.8, 95%CI 8.2-26.6), and being unsure whether they would be able to cope with work in two years' time (OR 14.5, 95%CI 8.2-25.4). Even for 'pre-frailty', many ORs were of the order of 2 to 3 ($p < 0.001$).

A total of 873 'pre-frail' subjects were classed as such solely because they did not report physical exercise or sports in an average week sufficient to make them hot or sweaty. In case this criterion lacked specificity, we repeated the analyses for Table 3 for an alternative case definition of pre-frailty requiring the presence of two symptoms. In this sensitivity analysis, ORs for adverse work outcomes were strengthened, although below those for frailty (e.g. the OR for health-related job loss was 9.6 (95%CI 7.6-12.0, vs. 3.7) and that for sick leave >20 days in the past 12 months was 6.2 (95%CI 4.5-8.6 vs. 2.5)).

Assuming causal relationships, PAFs for health-related job loss were 20.3% for the presence of ≥ 3 Fried symptoms and 34.9% for 1-2 symptoms (Table 3), while among those in paid work, 6.2% and 26.3% of prolonged sickness absence would be attributable to these factors on the same basis. PAFs for other employment outcomes are recorded in Table 3.

Further adjustment for low well-being and persistent musculoskeletal pain, in addition to age and gender, reduced these risk estimates somewhat. However, those for 'frailty' all remained significantly and in most cases substantially elevated, and the OR for health-related job loss was still greater than 14 (online Supplementary Table 2).

To explore whether the associations presented in Table 3 differed by socio-economic status, the analyses were repeated within strata of social class determined from the current or last held job (higher managerial, intermediate, or manual/routine). Associations with not being in work, taking any sick leave, and not coping with work's demands were about 2-3 times greater amongst those from the lowest versus the highest social class, but no differential was apparent for health-related job loss, prolonged sick leave, cutting down at work, or perceived job insecurity (Table 4). However, 'frailty' was strongly associated with these adverse outcomes, even in higher managerial workers (e.g. OR for health-related job loss, 29.4 (95%CI 17.5-49.3)).

Table 4. Associations between number of frailty symptoms and employment outcomes and perceptions, by social class

Outcomes	Frail vs. not (≥ 3 vs. 0 symptoms)						P-value for interaction
	Higher managerial		Intermediate occupations		Routine and manual occupations		
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	
Entire Sample (n =8,095)							
Not in work vs. in work	7.8	(4.3,14.2)	5.2	(3.0,9.0)	15.9	(10.2,24.8)	<0.001
Left for a health reason vs. not	29.4	(17.5,49.3)	26.1	(15.2,44.8)	27.4	(18.3,41.1)	0.14
Those in work (maximum n=5,486)							
Sick leave, days past 12 months :							
Any vs. none	2.3	(0.9,5.8)	2.9	(1.2,6.7)	5.1	(2.2,12.0)	0.52
>20 days vs. ≤ 20 days	13.3	(5.1,34.8)	5.1	(2.0,13.3)	15.6	(7.1,34.1)	0.44
Cut down on work, past 12 months:							
Any vs. none	12.2	(4.4,33.9)	6.0	(2.7,13.4)	14.4	(5.8,35.7)	0.48
A lot vs. not a lot (none/a little)	21.7	(8.4,56.2)	13.2	(5.5,31.6)	23.1	(10.1,52.7)	0.92
Coping with work's physical demands (vs. easily):							
With some/great difficulty	17.8	(5.8,54.6)	7.8	(3.3,18.4)	31.9	(7.5,134.6)	0.07
Coping with work's mental demands (vs. easily):							
With some/great difficulty	3.5	(1.4,8.9)	2.7	(1.2,6.1)	10.1	(4.4,23.0)	0.01
Expecting to be able to cope in 2 years' time (vs. yes):							
No/not sure	10.9	(3.8,31.2)	9.9	(4.2,23.6)	30.1	(9.0,100.2)	0.38
Lying awake at night worrying about work (vs. sometimes/rarely/never):							
Often	6.7	(2.7,16.7)	4.1	(1.7,10.2)	8.9	(4.1,19.7)	0.24
Job security (vs. secure/very secure):							
Insecure/very insecure	3.3	(1.3,8.4)	2.9	(1.3,6.6)	3.3	(1.6,7.2)	0.90

Odds ratios (OR) are adjusted for age and gender

Finally, Table 5 considers the same employment outcomes but with symptoms of ‘frailty’ treated as individual risk factors. Almost all outcomes were more strongly associated with slow walking speed than with the other symptoms, resulting, for example, in ORs of 9.6 to 14.8 for health-related job loss, cutting down a lot at work, and difficulty coping with work’s physical demands, vs. 1.9 to 7.4 for the remaining symptoms. Strong, albeit weaker, associations were found for poor grip strength and exhaustion, and the latter had the strongest relationship to not coping mentally at work. By contrast, unintentional weight loss and our index of low physical activity were only weakly associated with the employment outcomes.

Table 5: Associations of individual symptoms of frailty with employment outcomes and perceptions

Outcomes	Risk factors									
	Weight loss		Exhaustion		Weak grip		Slow walking speed		Low activity	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)
Entire Sample (n =8,095)										
Not in work vs. in work	1.6	(1.3,1.9)	3.8	(3.1,4.6)	2.4	(2.1,2.8)	6.8	(5.4,8.4)	1.4	(1.3,1.7)
Left for a health reason vs. not	2.6	(2.1,3.2)	7.9	(6.4,9.6)	6.6	(5.5,7.8)	14.8	(12.2,18.0)	2.6	(2.2,3.1)
Those in work (n=5,486)										
Sick leave, days in past 12 months :										
Any vs. none	1.5	(1.2,1.8)	2.9	(2.2,3.8)	1.8	(1.5,2.2)	3.1	(2.2,4.4)	1.2	(1.0,1.4)
>20 days vs. ≤20 days	3.5	(2.7,4.6)	3.9	(2.8,5.5)	2.7	(2.0,3.6)	5.1	(3.5,7.5)	1.7	(1.3,2.3)
Cut down on work, past 12 months:										
Any vs. none	1.9	(1.6,2.3)	3.7	(2.9,4.8)	3.7	(3.1,4.6)	6.9	(4.8,9.7)	1.2	(1.0,1.5)
A lot vs. not a lot (none/a little)	2.6	(1.9,3.6)	5.5	(4.0,7.7)	4.4	(3.3,5.9)	9.6	(6.7,13.7)	1.4	(1.1,1.9)
Coping with work's physical demands (vs. easily):										
With some/great difficulty	1.8	(1.5,2.2)	4.2	(3.3,5.5)	5.6	(4.5,6.8)	10.6	(7.1,15.9)	1.5	(1.3,1.7)
Coping with work's mental demands (vs. easily):										
With some/great difficulty	1.4	(1.2,1.8)	3.8	(2.9,4.9)	2.4	(2.0,3.0)	1.9	(1.3,2.6)	1.3	(1.1,1.5)
Expecting to be able to cope in 2 years' time (vs. yes):										
No/not sure	1.7	(1.4,2.1)	3.6	(2.8,4.7)	4.0	(3.2,4.8)	7.4	(5.2,10.5)	1.5	(1.2,1.7)
Lying awake at night worrying about work (vs. sometimes/rarely/never):										
Often	1.6	(1.2,2.0)	5.0	(3.8,6.5)	1.9	(1.5,2.4)	2.4	(1.7,3.5)	1.4	(1.1,1.7)
Job security (vs. secure/very secure):										
Insecure/very insecure	1.3	(1.0,1.6)	1.8	(1.4,2.5)	1.6	(1.3,2.0)	2.1	(1.5,2.9)	1.0	(0.8,1.2)

Odds ratios (OR) are adjusted for age and gender

Discussion

In this analysis of over 8,000 people aged 50-65 years from English general practices, we assessed frailty using questionnaire items adapted from the Fried criteria. Almost one in three subjects was 'pre-frail' by our definition and 3.9% were 'frail'. Our case definition for frailty was associated strongly with being out of work, health-related job loss, prolonged sickness absence, having to cut down a lot on work activities, self-reports of not coping with work's demands, and negative perceptions about work, including job insecurity and worry over work with loss of sleep. PAFs were relatively high and, for the presence of any of the frailty symptoms, exceeded 50% for health-related job loss and reached almost one-third for prolonged sickness absence.

Our study had a number of strengths, including its novel focus on frailty indicators and employment outcomes, its large sample size and its geographically dispersed population-based sampling strategy. Almost everyone in Britain registers with a general practice for healthcare that is free at the point of delivery, so patient lists from general practices offer a comprehensive sampling frame. The sampling frame also allowed us to calculate PAFs, providing an estimate of the potentially avoidable burden of work incapacity and loss as judged from a population perspective.

A limitation was the relatively low response rate at baseline. The prevalence of frailty could have been underestimated if those with more Fried symptoms were less likely to return a questionnaire. A differential response of that sort would not of itself bias associations between Fried symptoms and employment outcomes, which would be unrepresentative only if the association with employment differed between responders and non-responders. If frail non-responders were more handicapped than frail responders, this might lead to an under-estimation of frailty's impact on employment. Conversely, over-estimation could arise if frail individuals with greater work handicap participated more readily in the survey; but bias of this second kind seems less likely as the items we used to assess frailty formed only a small part of a much larger question set and were dispersed through the questionnaire, helping to disguise this focus of interest from participants. Nonetheless, it will be important to confirm findings longitudinally in a cohort with good follow-up rates. (The HEAF study is well placed in this respect, as response rates at follow-up have exceeded 80%.)

A second limitation is that we had no face to face contact with subjects and so were unable to perform a physical examination or conduct tests of performance. Fried's criteria are usually based on answers to two questions (reproduced in our questionnaire) in combination with measures from tests of physical performance performed according to standardised protocols. In this large cross-sectional study across England, we depended on questions about symptoms to gauge functional elements (e.g. grip strength) that we were unable to measure directly. We do not know how accurately our proxy questions reflected what would have been found had objective measurements been available. However, as yet there is no international consensus on how best to assess frailty in older people for research purposes [13], and the Fried scale has been adapted successfully in other research using proxy information when components could not be ascertained in the manner originally specified [11,16,17]. Moreover, data from another cohort study of older workers, the 10-country Survey of Health, Aging and Retirement in Europe (SHARE), which did include objective measures of physical function, estimated a broadly similar prevalence of 'frailty' and 'pre-frailty' among people of similar age to those in our study [11]. Even if the ascertainment of Fried components was accurate, the phenotype that they represent in late middle age may not be the same as in the elderly. Nevertheless, they showed consistent and strong associations with poor employment outcomes in our study sample.

Those classified as 'frail' by our study were about five times more likely to report low well-being and persistent pain, which like frailty were possible risk factors for health-related job loss, sickness absence and reduced work capacity. Adjustment for these potential confounders somewhat reduced associations between frailty and adverse work outcomes, although they remained robust and strong.

We know of no other study that has explored frailty's relations to work. However, the Work-Ability Index (WAI) is another measure that has been linked with poor employment outcomes as well as predicting poorer long-term health [18]. It assesses seven domains, all self-reported: current work capacity relative to lifetime best; work ability in relation to the physical and mental demands of the job; work impairment because of health; amount of sick leave in the past 12 months; expectations about work ability in two years' time; number of current physician-diagnosed diseases; and 'mental resources' (enjoyment, energy and hope for the future). It may be seen that none of these matches the Fried frailty criteria, although the domain of 'mental resources' partially overlaps Fried's criterion for exhaustion. An

important point of contrast between the two scales is that most of the WAI's domains are intended for application only in those in work, whereas the Fried criteria can be used without such restriction; this in turn enabled us to treat several elements of WAI (work ability in relation to the physical and mental demands of the job, sick leave, impaired work productivity, expectations of future working) as adverse work outcomes (Tables 3-5), rather than as predictors of adverse work outcomes. The Fried criteria therefore offer a flexible alternative to WAI, capable of use against a number of additional economically important end-points.

Associations between frailty and poor work outcomes appeared to be driven principally by slow walking speed, weak grip strength and exhaustion, suggesting that poor motor function could be an important underlying factor (as perhaps it may be for some people with a poor WAI score); and if so, that future interventions might focus on improving motor function. It might be supposed that heavy manual work would help to build and preserve physical strength, but paradoxically, for measured hand grip strength, there is evidence to the contrary [19,20], perhaps reflecting social inequalities in health that outweigh any advantages of physical effort at work [20]. In the current analysis, associations with not being in work, taking sick leave and not coping were strongest in manual/routine occupations. This differential could arise because of their generally poorer physical health or, more simply, a greater mismatch between physical capability and job demands – the ability of manual workers to carry out their jobs being more likely to be compromised by a given impairment of physical function.

Because our analysis was cross-sectional, interpretation of the associations is necessarily limited, particularly as all of the data were self-reported. However, the HEAF study includes a prospective component, and it has the capacity to link questionnaire responses with personal primary care medical records providing details of medical diagnoses, hospital care and prescribed treatments. In future, therefore, we plan to assess longitudinal relationships between frailty elements in middle life and medically-recorded health and health change, and between frailty and changes in employment status. We hope also to assess physical function in face to face interviews. Opportunity exists, therefore, to characterise people with multiple Fried symptoms in our study in greater clinical detail and to follow their progress over time.

A future goal may be to develop simple screening tests to identify components of physical frailty in older workers and then to devise interventions that could improve their physical function. A screening tool becomes particularly attractive if it is positive in only a small proportion of the population but accounts for a substantial proportion of that population's adverse outcomes: in this respect, the findings reported here (the low prevalence of ≥ 3 frailty symptoms but their high associated PAF) encourage us to explore this issue further in future research, especially as interventions to combat frailty in the elderly have enjoyed some success [8-10].

Funding

This work was supported by Arthritis Research UK (grant numbers ARC 19817, ARUK 20665); the Medical Research Council and the Economic and Social Research Council jointly (grant number ES/L002663/1); and a Medical Research Council programme grant (number MRC_MC_UP_A620_1018).

Acknowledgements

We wish to thank the CPRD and the 24 general practices that have supported data collection; also, the staff of the MRC LEU who provided invaluable support with data entry and computing, especially Helena Demetriou and Vanessa Cox.

Competing interests

CC has received consultancy and honoraria from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB. All other authors have declared no competing interests.

Authors' contributions

KTP identified the study questions and with DC designed the study and its measuring instruments. KTP supervised data collection, and with SD, DC and HS, planned the analyses. SD conducted the analyses. KTP wrote the first draft of the paper. KWB, SD, ECH, CL, AAS, CG, ME, HS, TS and CC contributed to the study's design, content, measuring instruments and plan of execution. Additionally, ECH and CL led in data collection, cleaning and preparation, and the enlistment of participating general practices. All authors read and approved the final manuscript.

References

1. Department for Work and Pensions. Fuller Working Lives: A Framework for Action. DWP, June 2014, ISBN 978-1-78425-184-0
<https://www.gov.uk/government/publications/fuller-working-lives-a-framework-for-action>
2. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56:M146–M156.
3. Clegg A, Young J, Illiffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* 2013; 381: 752–62.
4. Rockwood K, Howlett SE, MacKnight C, et al. Prevalence, attributes, and outcomes of fitness and frailty in community-dwelling older adults: report from the Canadian study of health and aging. *J Gerontol A Biol Sci Med Sci* 2004; 59: 1310–17.
5. Bandeen-Roche K, Xue QL, Ferrucci L, et al. Phenotype of frailty: characterization in the women’s health and aging studies. *J Gerontol A Biol Sci Med Sci* 2006; 61: 262–66.
6. Ensrud KE, Ewing SK, Taylor BC, et al. Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women. *Arch Intern Med* 2008; 168: 382–89.
7. Boyd CM, Ricks M, Fried LP, Guralnik JM, Xue QL, Xia J, Bandeen-Roche K. Functional decline and recovery of activities of daily living in hospitalized disabled older women; the Women’s Health and Aging Study 1. *J Am Geriatr Soc* 2009;57:1757-1766.
8. Cooper C, Dere W, Evans W, et al. Frailty and sarcopenia: definitions and outcome parameters. *Osteoporos Int* 2012;23:1839-48.
9. Faber MJ, Bosscher RJ, Chin A Paw M, van Wieringen PC. Effects of exercise programs on falls and mobility in frail and pre-frail older adults: a multicentre randomized controlled trial. *Arch Phys Med Rehabil* 2006;87:885-896.
10. Peterson MJ, Sloane R, Cohen HJ, Crowley GM, Pieper CF, Morley MC. Effect of telephone exercise counselling on frailty in older veterans: project LIFE. *Am J Mens Health*. 2007;1:326-334.

11. Santos-Eggimann B, Cuenoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009; 64A: 675-81.
12. Palmer KT, Walker-Bone K, Harris EC, Linaker C, D'Angelo S, Sayer AA, Gale C, Evandrou M, van Staa T, Cooper C, Coggon D. Health and Employment after Fifty (HEAF): a new prospective cohort study. *BMC Public Health* 2015; 15:1071.
13. Bouillon K, Kivimaki M, Hamer M, Sabia S, Fransson EI, Singh-Manoux A, Gale CR, Batty GD. Measures of frailty in population-based studies: an overview. *BMC Geriatr* 2013;13:64.
14. Office for National Statistics. Standard occupational classification 2010 (SOC2010). <http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/index.html> (accessed 10/8/16).
15. Stewart-Brown S, Janmohamed K. Warwick-Edinburgh Mental Well-being Scale. User Guide, v1 (June 2008).
<http://www.healthscotland.com/uploads/documents/7551-WEMWBS%20User%20Guide%20Version%201%20June%202008.pdf> (accessed 10/8/16)
16. Kalousova L, de Leon CM. Increase in frailty of older workers and retirees predicted by negative psychosocial working conditions on the job. *Soc Sci Med* 2015; 124:275-283.
17. Syddall HE, Westbury LD, Cooper C, Sayer AA. Self-reported walking speed: a useful marker of physical performance among community-dwelling older people? *J Am Med Dir Assoc.* 2015;16:323-8.
18. Tuomi K, Ilmarinen J, Jahkola A, Katajarinne L, Tulkki A. Work Ability Index. Finnish Institute of Occupational Health, Helsinki 1998. 2nd edition ISBN 951-802-202-X.
19. Russo A, Onder G, Cesari M, Zamboni V, Barillaro C, Capoluongo E, et al. Lifetime occupation and physical function: a prospective cohort study on persons aged 80 years and older living in a community. *Occup Environ Med* 2006;63:438-42.
20. Walker-Bone K, D'Angelo S, Palmer KT, Cooper C, Coggon DNM, Aihie-Sayer A. Heavy manual work throughout the working lifetime and muscle strength among men at retirement age. *Occup Environ Med* 2016; 73:284-286.

