Published in final edited form as:

Psychosom Med. 2015 September ; 77(7): 823–832. doi:10.1097/PSY.0000000000000214.

Associations of fatigue from mid to late life with physical performance and strength in early old age: Results from a British prospective cohort study

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Abstract

OBJECTIVE—To examine associations of fatigue in mid and later life with physical performance and strength in early old age.

METHODS—Data on approximately 1800 men and women from the UK Medical Research Council National Survey of Health and Development with data on fatigue at ages 43 and 60–64 years were used. Fatigue was defined as perceived tiredness and was assessed prospectively at ages 43 and 60–64. At both ages, participants were categorized as having no, occasional or frequent fatigue. Physical performance and strength were measured at age 60–64 using four objective measures: grip strength, standing balance, chair rising, and timed get-up-and-go (TUG) tests.

RESULTS—There were associations between reports of frequent fatigue at both ages and poorer grip strength, chair rise and TUG performance at 60–64 years. Furthermore, individuals reporting frequent fatigue at both ages had weaker grip strength (β -4.09 kg, 95% CI -6.71, -1.48), and slower chair rise (β -4.65 rep./min, 95% CI -6.65, -2.64) and TUG (β -4.22 cm/s, 95% CI -12.16, -2.28) speeds when compared to those who reported no fatigue at both time points. These associations were robust and were maintained after adjustment for a range of covariates including physical activity and health status.

CONCLUSIONS—Reports of frequent fatigue were associated with poorer physical performance in early old age, especially if sustained from mid to later life. These findings indicate that it is not just fatigue but fatigue sustained across adulthood that has implications for later life functioning.

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Conflicts of Interest

The authors declare no conflict of interest.

Keywords

Aging; Life course; Fatigue; Physical performance; Strength

INTRODUCTION

Limitations in physical function and related performance tasks, strength and mobility increase with advancing age and are associated with subsequent health problems, disability, and shorter survival times.^{1–5} Consequently, with ever larger cohorts surviving to old age, to guarantee the sustainability of health and social care systems while enhancing quality of life, it is an important public health priority to find ways to promote the maintenance of functional capacity with age. Early detection of those people at greatest risk of experiencing poor physical performance in old age is central to primary prevention,⁶ especially from a life course perspective.⁷ For this purpose, knowledge of the early indicators of poor performance is important.

There has been a growing interest in fatigue as an early marker of aging-related declines in health and functional abilities. Fatigue is a common complaint among young and old adults, and one of the most common symptoms encountered in general practice.^{8,9} During the last 15 years several cross-sectional and longitudinal studies among older adults have shown that self-reported general and mobility-related fatigue are related to various adverse health outcomes such as lower levels and declines in physical performance,^{10–12} development of disability,^{13,14} increased use of social and health services,¹⁵ and mortality.^{16–18} These studies have measured fatigue at one time point, usually in old age, and then assessed risk of adverse health outcomes from that time onwards. However, some previous studies have shown rather large changes in self-reported fatigue over time^{19,20} and one study²¹ has suggested that especially frequent or sustained complaints of fatigue over time may indicate more detrimental effects on functioning compared with occasional fatigue.

Although research on fatigue in older adults has been accumulating over the last two decades with growing recognition of its importance, there remains a limited understanding of fatigue earlier in life and how it relates to outcomes in old age. For example, while associations between fatigue reported in old age and poor physical performance have been shown it is not known whether fatigue earlier in life is also associated with poorer physical performance later in life. In the present article, we aimed (1) to investigate if fatigue in mid and later life was associated with physical performance and strength in early old age; and (2) to examine whether persistency of fatigue from mid to later life was associated with physical performance and strength. It should be noted that we use the term physical performance rather than physical function because to sustain performance for most physical tasks (such as rising from a chair or walking at normal speed) requires the normal functioning of multiple underlying body systems and we wished to delineate performance at the individual level from the physiological functioning of the different underlying body systems.

METHODS

The Medical Research Council National Survey of Health and Development (NSHD) is a socially stratified sample of all births that occurred during 1 week in March 1946 across England, Scotland, and Wales.²² This cohort has been assessed prospectively at more than 20 time points across life from birth onwards.

The most recent data collection was conducted in 2006-2011 when study participants were aged 60-64 years.^{22,23} Of the 5362 original study members, at age 60-64 years the study team was still in contact with 3163 (59%); 718 had died, 594 had previously withdrawn from the study, 567 lived abroad and 320 had been untraceable for more than ten years. Study members received postal questionnaires and were invited for clinic visits. Participants unable to attend the clinic were offered a home visit by a trained nurse. Of the 3163 people in the target sample, information was obtained from the postal questionnaire and/or visits from 2661 (84%). Of these, 2462 people completed the postal questionnaire and 2229 had a clinical assessment.

Relevant ethical approval has been obtained for each data collection, with approval for the most recent collection at age 60-64 years provided by the Central Manchester Research Ethics Committee and the Scottish A Research Ethics Committee. Participants provided their written consent to participate in this study and this consent procedure was approved by the relevant ethics committees.

Outcome ascertainment

Physical performance and strength were assessed at age 60-64 using four objective measures: grip strength, standing balance, chair rising, and timed get-up-and-go (TUG) tests. Trained nurses conducted these tests using standardized protocols as described elsewhere²⁴ and summarized here.

Grip strength was measured isometrically using an electronic handgrip dynamometer.²⁵ Three values were recorded for each hand and the highest was used in analyses (kg). *Standing balance time* was measured as the longest time, up to a maximum of 30 seconds, for which participants could maintain a one-legged stance in a standard position with their eyes closed. The distribution of these times was positively skewed and they were normalized using a natural logarithm transformation ($\ln(\text{seconds}+1)$). *Chair rise time* was measured as the time taken to rise from a sitting to a standing position with straight back and legs and then sit down again as fast as possible ten complete times. Chair rise speed was used in the analyses and calculated as repetitions/minute ($(10/\text{time}) \times 60$). In the *Timed Up and Go (TUG) test*²⁶ the participant was instructed to rise from an armless chair, walk 3 meters, turn around, return to the chair, and sit down. The test was performed once at a self-selected speed, and the time from rising out of the chair until seated again was measured. Unlike in other tests, walking aids were permitted ($n=24$). TUG speed (meters/second) was calculated and used in the analyses. Where a test was not completed for reasons of poor health ($n=49$ for grip strength, $n=136$ for chair rising, $n=89$ for standing balance and $n=34$ for TUG) values were imputed, as in previous analyses²⁷ by taking the gender specific mean of the bottom quintile for each variable. Previous analyses of the NSHD suggest that these

different tests represent slightly different underlying constructs.^{24,25,33} We thus decided *a priori* to study each of these four measures separately, rather than creating a composite score, to ensure that aetiological insights were better served and important effects specific to individual measures were not disguised. Table S1, Supplemental Digital Content 1, presents the non-parametric correlations between the individual outcome measures.

Ascertainment of fatigue

Fatigue was defined as perceived tiredness and was assessed at ages 43 and 60-64 years. At age 43, participants were asked, during a nurse home visit: "Over the last year have there been days when you felt tired out very easily?" with six response options: a) never, b) occasionally, c) sometimes, d) quite often, e) very often and f) always. At age 60-64, participants were asked: "How much of the time during the past four weeks did you feel tired?" with response options a) none of the time, b) little of the time, c) some of the time, d) a good bit of the time, e) most of the time and f) all of the time. At both ages, participants were categorized as having *no* (never at age 43, and none of the time at age 60-64), *occasional* (occasionally or sometimes at age 43, and little or some of the time at age 60-64) or *frequent* (quite often, very often or always at age 43, and a good bit, most, or all of the time at age 60-64) fatigue.

To examine whether persistency of fatigue from mid to later life was associated with physical performance and strength, participants were categorized into four groups based on reported frequency of fatigue at ages 43 and 60-64 years: (1) no fatigue at either time point, (2) only occasional fatigue at one or both time points, (3) frequent fatigue at one time point, and (4) frequent fatigue at both time points.

Covariates

Factors that could potentially confound or mediate the main associations were identified *a priori*. *Weight (kg) and height (cm)* were measured by nurses during the clinic or home visits at age 60-64 years. Highest *educational level* attained by age 26 years was categorized into five groups: (1) university degree or higher; (2) UK General Certificate of Education-Advanced level (A levels), national school qualifications usually attained at age 18 years, or their equivalents; (3) UK General Certificate of Education-Ordinary level (O levels), national school qualifications usually attained at age 16 years, or their equivalents; (4) certificate of secondary education, clerical course, or equivalent; and (5) none. At ages 53 and 60-64 the participants were asked if during the past 10 years they had been told by a doctor that they had the following health conditions: cancer, diabetes, thyroid disease or cardiovascular disease (heart attack, stroke, angina, coronary artery bypass graft, angioplasty or stent). *Physical health problems* at age 60-64 was coded accordingly as a binary variable and identified those who reported being told by a doctor during the past 20 years that she/he had had one or more of the specified health conditions. *Smoking* status at age 60-64 years was self-reported and categorized as current, ex, or never smoker. *Own occupational class* at age 53 years was categorized using the Registrar General's Social Classification into three groups: I or II (high); III (medium); IV or V (low). Leisure time *physical activity* levels were ascertained at ages 43, 53 and 60-64 years. Participation in any sports, vigorous leisure activities or exercises in study participants' spare time and the number of occasions on

which these activities were undertaken was reported. Participants were categorized as inactive (reported no participation); moderately active (participated in relevant activities one to four times in the previous 4 weeks [at ages 53 and 60-64 years] and per month [at age 43]); or most active (participated in relevant activities five or more times in the previous 4 weeks or per month). A cumulative physical activity score was then created based on reported levels of physical activity at each age. At each of age those classified as inactive were assigned a value of 0, those as moderately active a value of 1, and those as most active a value of 2. The scores from each age were then summed to create a ranging from 0 (inactive at all three ages) to 6 (most active at all three ages). For descriptive purposes the physical activity score was categorized into four groups: 0 (None), 1-2 (low), 3-4 (middle), and 5-6 (high).

Statistical analysis

Multiple linear regression models were used to test the associations between fatigue and each of the four outcome measures. The main associations were calculated among those with data on fatigue at ages 43 and 60-64 years, weight, height, and outcome measure of interest (n=1827 for grip strength, n=1899 for balance, n=1897 for chair rise speed and n=1782 for TUG speed). In these and all subsequent models where there was evidence of an interaction between fatigue and gender, analyses were stratified by gender, but where not, analyses were gender-adjusted. To explore the effect of covariates on the main associations, the analyses were replicated using a subsample of participants with data on main variables and all of the covariates, and adjusting the gender, weight and height adjusted models one by one for each of the covariates (socioeconomic position [occupational class and educational level], physical health problems, smoking and cumulative physical activity score).

Sensitivity analyses

To help differentiate between longitudinal and cross-sectional associations, sensitivity analyses were run in which persistency of fatigue from mid to later life was categorized into five groups by splitting the frequent fatigue at one time point category used in the main analyses into two categories: (1) no fatigue at either time point, (2) only occasional fatigue at one or both time points, (3) frequent fatigue at age 43, (4) frequent fatigue at age 60-64 and (5) frequent fatigue at both time points.

Although anxiety and depression were not included in the main models as this may be an over-adjustment, sensitivity analyses were performed in which models were adjusted for symptoms of anxiety and depression at ages 43 and 60-64. Additional adjustments for other potentially important markers of health status (i.e. musculoskeletal and severe respiratory symptoms) were also performed as a further test of the robustness of the findings.

RESULTS

Baseline descriptive data are presented in Table 1. Men had better physical performance and strength at age 60-64 years and were less likely to report fatigue at ages 43 and 60-64 years than women. Eight percent of men and 3.5% of women reported no fatigue at either age, and 4.0% of men and 6.6% of women reported frequent fatigue at both ages. Reports of fatigue

at the two ages were strongly associated ($p < 0.001$); those men and women who reported fatigue at age 43 were more likely to report fatigue at age 60-64 than those who reported no fatigue at 43 (Table 2). Men were more likely to have higher occupational class and educational level, and they were less likely to be never smokers, have one or more health conditions and report low levels of physical activity than women (Table 1).

Table 3 shows the associations between fatigue at ages 43 and 60-64 years, and physical performance and strength at age 60-64. There was no association between fatigue at age 43 and grip strength at age 60-64 in men, but women who reported frequent fatigue had weaker grip strength (β -1.57 kg, 95 % CI -2.43, -0.56) than those who reported no fatigue ($p = 0.04$ from test of gender interaction) when adjusting for weight and height. Frequent fatigue at age 43 was also associated with poorer balance (β -0.13 ln(s), 95 % CI -0.21, -0.06) and slower chair rise (β -2.28 rep./min, 95 % CI -3.32, -1.23) and TUG speeds (β -3.32 cm/s, 95 % CI -5.85, -0.80) when adjusting for gender, weight and height. There was no evidence that these associations differed by gender ($p > 0.7$ from all tests of gender interaction).

Participants reporting frequent fatigue at age 60-64 had weaker grip strength (β -2.59 kg, 95 % CI -4.39, -0.76) and slower chair rise (β -3.10 rep./min, 95 % CI -4.50, -1.71) and TUG (β -4.95 cm/s, 95 % CI -8.32, -1.53) speeds when compared with those with no fatigue and after adjusting for gender, weight and height (Table 3) and there was no evidence that these associations differed by gender ($p > 0.20$ from all tests of gender interaction).

The main associations between sustained fatigue frequency at ages 43 and 60-64 years, and physical performance and strength at age 60-64 years are presented in Table 4. Reporting only occasional fatigue at ages 43 and/or 60-64 was not associated with physical performance and strength at age 60-64 years. However, participants reporting frequent fatigue at one of the time points had slower chair rise speed (β -3.04 rep./min, 95 % CI -4.61, -1.46), and those reporting frequent fatigue at both ages had weaker grip strength (β -4.09 kg, 95 % CI -6.71, -1.48), and slower chair rise (β -4.65 rep./min, 95 % CI -6.65, -2.64) and TUG (β -4.22 cm/s, 95 % CI -12.16, -2.28) speeds when compared to those who reported no fatigue at either age after adjustment for gender, weight and height (Table 4). There was no evidence that these associations differed by gender ($p > 0.60$ from all tests of gender interaction). The observed associations between sustained frequent fatigue from age 43 to 60-64 years and physical performance and strength were maintained after further adjustments (Table 5), although slight attenuation of the effects was observed when adjusting for physical health problems and the cumulative physical activity score. Balance was not carried forward into these analyses as there was no evidence of association with basic adjustments (Table 4).

Results from sensitivity analyses confirmed that those people who reported frequent fatigue at both time points had slower chair rise and TUG speeds and weaker grip strength than those people who only reported frequent fatigue cross-sectionally (Table 6 and Table S2, Supplemental Digital Content 2). In addition, sensitivity analyses confirmed that the main findings were robust; the results were largely unchanged after additional adjustments for symptoms of anxiety and depression and other markers of health status (see Table S3, Supplemental Digital Content 3).

DISCUSSION

In a representative sample of the British population, frequent complaints of fatigue in both mid and later life were associated with poorer physical performance and weaker strength in early old age, especially if fatigue was sustained from mid to later life. These associations were robust and were maintained after adjustment for a range of covariates.

These results support the previously found associations between fatigue and poor physical performance among older populations^{10–12} and extend the existing literature by providing evidence of: (1) associations between midlife fatigue and poorer physical performance and strength measured 20 years later, and; (2) strong associations between sustained reports of frequent fatigue across mid to later life and poorer physical performance and strength in early old age. We observed consistent patterns of association with objectively measured grip strength, chair rise and TUG performance, all important measures of physical performance known to correlate and integrate with daily mobility tasks.^{26,28–30} Given that lower levels of muscle strength and physical performance are associated with increased risk of subsequent health problems, loss of independence, and shorter survival times^{1–5} our results suggest that fatigue may be an important early indicator of those people at greatest risk of experiencing poor outcomes in old age.

Compared to other outcome measures of this study, we observed only a modest non-significant trend between fatigue and balance. The associations between self-reported fatigue and balance performance are poorly understood in the general population with one study among older adults suggesting a significant association between tiredness in daily activities and poor balance performance when measured with a piezoelectric force platform.³¹ It is possible that the balance measure used in this study was not sensitive enough to observe significant differences in the performance between participants with and without fatigue. However, these rarely investigated associations need to be clarified in future studies.

When adjusting for covariates we found that socioeconomic position and smoking had very little impact on the main associations (Table 4). Adjustment for self-reported health problems and the cumulative physical activity score attenuated associations by up to 4 % and 11 %, respectively, suggesting that these factors may partially explain the associations found. It is possible that fatigue may affect people's activity levels^{14,32} with this affecting physical performance and strength,³³ and many physical health problems may cause both fatigue and poor physical performance and strength.^{8,9,34–36} Although the current study cannot comprehensively address the mechanisms by which fatigue affects physical performance and strength, the previously reported associations of fatigue with multiple markers of mental and physical health suggests that it may represent a general state of altered physiology.^{8,9,37} For example, fatigue in midlife could be the symptomatic presentation of subclinical disease,¹⁷ increased inflammation,^{38–40} or it may result from limitations in oxygen supply or energy production.^{8,41} Furthermore, fatigue may be a result of functional disabilities that decrease efficiency, such as rheumatoid arthritis,⁴² or a result of physical or mental effort.⁸ In addition, fatigue and psychiatric disorders frequently occur comorbidly, and may share similar phenomenological features.⁴³ More research is needed to

understand the pathophysiologic origins of fatigue as well as mediating factors between fatigue and physical performance and strength.

Methodological considerations

To enable the study of fatigue across adulthood we utilised measures of fatigue ascertained at two time points. It is acknowledged that different questions were used at these ages and that at each age only a single item was used. However, the responses to the questions could be categorised in a comparable way and so do resemble each other relatively well. Moreover, using these comparable questions enabled us to construct a variable describing the persistency of fatigue frequency from mid to later life, thus providing new information on sustained fatigue and its associations with subsequent physical performance and strength.

The NSHD was established using a sampling frame that ensured that it was nationally representative of the population born in England, Scotland, and Wales in 1946. Since then, losses to follow-up due to death, emigration, loss of contact, and permanent refusal have occurred. Despite this, in all recent waves of data collection, the sample has remained representative of the national population born at a similar time in most respects.^{22,44,45} Lower educational attainment, lower childhood cognition, lifelong smoking, not owning one's home and not being married at 53 years predicted lower likelihood of overall response at 60-64 years.²² However, the occupational social class and unemployment profiles of the participants were similar to the 2001 England Census reference population²² and so it is expected that findings will be generalizable to the generation of post war baby boomers currently reaching old age.

When interpreting the results, some other limitations and strengths of the study should also be considered. In addition to the major strength of prospective ascertainment of fatigue at different time points across adulthood, another strength is the availability of standardized measures of physical performance and strength. This allowed us to examine associations between fatigue and different objective measures of physical performance and strength separately and thus elucidate potential underlying pathways. However, we acknowledge that this approach requires multiple testing and as such it is possible that some associations achieved statistical significance due to type I error. We included participants unable to perform the tests due to health problems in the analyses using imputation. These people were more likely to have health problems, have poorer performance on the other tests and report more fatigue (data not shown), and therefore, including these individuals was important to ensure that bias was not introduced. The imputation did not change the distributions (Table 2) and we assessed the impact of excluding this group in sensitivity analyses and found similar results i.e. the directions of association remained the same and effect estimates were only slightly weaker. However, we cannot rule out the possibility that results may have differed if other methods of imputation had been employed. A limitation of the study is that participants' physical performance levels were not objectively assessed at age 43 years or earlier in life. We therefore are limited in our ability to identify whether associations of fatigue in midlife with physical performance and strength were already present at age 43 years or have emerged as the cohort age and the prevalence of functional limitations has increased⁴⁶ and so we cannot establish direction of association conclusively.

Furthermore, as we used fatigue at both time points as an approximation of sustained fatigue, it is possible that interim changes in fatigue may have influenced the results.

CONCLUSION

Frequent complaints of fatigue from midlife onwards were associated with poorer physical performance and strength in early old age, especially if sustained from mid to later life. These findings indicate that it is not just fatigue but especially fatigue sustained across adulthood that has implications for later life functioning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

The authors acknowledge the crucial role of Professor Kirsten Avlund (deceased 31 August 2013) in developing the conceptual framework and scientific objectives of this paper, contributing to the interpretation of analyses and providing critical revisions to earlier versions of the manuscript. The authors are grateful to NSHD study members who took part in the latest data collection for their continuing support. We thank members of the NSHD scientific and data collection team at the following centres: MRC Unit for LHA; Wellcome Trust (WT) Clinical Research Facility (CRF) Manchester; WTCRF at the Western General Hospital in Edinburgh; WTCRF at University Hospital Birmingham; WTCRF at University College London Hospital; CRF at the University Hospital of Wales; CRF and Twin Research Unit at St Thomas' Hospital London. This work was supported by the Nordea-Foundation, The Danish National Research Foundation (M.M., K.A) and the UK Medical Research Council (Programme code MC_UU_12019/4) (D.K., R.C.).

Source of Funding

This work was supported by the Nordea-Foundation, The Danish National Research Foundation and the UK Medical Research Council (Programme code MC_UU_12019/4). The Danish Aging Research Center is supported by a grant from the VELUX Foundation and The NSHD is funded by the UK Medical Research Council. The funding agencies played no role in the design, conduct, data management, analysis, or manuscript preparation.

List of abbreviations

NSHD	The Medical Research Council National Survey of Health and Development
TUG	timed get-up-and-go

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Table 1

Characteristics of the MRC National Survey of Health and Development.

	Men (n=898 ^a)	Women (n=1001 ^a)
PHYSICAL PERFORMANCE		
AT AGE 60-64 YEARS (Mean (SD))		
Grip strength (kg)	45.7 (11.8)	26.7 (7.5)
Standing balance (seconds) ^b	3.9 (0.8)	3.4 (0.8)
Chair rise speed (repetitions/minute)	25.9 (7.0)	25.1 (7.9)
TUG speed (cm/second)	71.8 (18.1)	68.9 (16.5)
FATIGUE (N (%))		
43 years		
No fatigue	546 (60.8)	363 (36.2)
Occasional fatigue	284 (31.6)	448 (44.8)
Frequent fatigue	68 (7.6)	190 (19.0)
60-64 years		
No fatigue	88 (9.8)	64 (6.4)
Occasional fatigue	654 (72.8)	734 (73.3)
Frequent fatigue	156 (17.4)	203 (20.3)
Combined Fatigue Frequency at Ages 43 and 60-64 Years		
No fatigue	72 (8.0)	35 (3.5)
Only occasional fatigue	638 (71.1)	639 (63.8)
Frequent fatigue at 1 time point	152 (16.9)	261 (26.1)
Frequent fatigue at 2 time points	36 (4.0)	66 (6.6)
BODY SIZE AT AGE 60-64 YEARS (Mean (SD))		
Weight (kg)	85.1 (13.4)	73.2 (14.6)
Height (cm)	174.8 (6.6)	161.8 (5.9)
OTHER CHARACTERISTICS (N (%))		
	Men (n=699^c)	Women (n=827^c)
Occupational class at 53 years		
I or II (High)	407 (58.2)	336 (40.6)
III (Medium)	225 (32.2)	354 (42.8)
IV or V (Low)	67 (9.6)	137 (16.6)
Educational level at 26 years		
Degree or higher	132 (18.9)	61 (7.4)
A levels or equivalent	227 (32.5)	230 (27.8)
O levels or equivalent	110 (15.7)	224 (27.1)
CSE, clerical course or equivalent	34 (4.9)	82 (9.9)
None	196 (28.0)	230 (27.8)
Smoking status at 60-64 years		
Never	219 (31.3)	300 (36.3)
Ex	413 (59.1)	432 (52.2)
Current	67 (9.6)	95 (11.5)
Self-reported health conditions up to 60-64 years		

	Men (n=898 ^a)	Women (n=1001 ^a)
None	610 (87.3)	643 (77.8)
One or more	89 (12.7)	184 (22.2)
Cumulative leisure time physical activity levels from 43 to 60-64 years		
None	158 (22.6)	201 (24.3)
Low	210 (30.1)	286 (34.6)
Middle	212 (30.3)	219 (26.5)
High	119 (17.0)	121 (14.6)

^aThe sample includes those with data on fatigue at age 43 and 60-64 years, weight, height, and at least one of the physical performance measures. Except for grip strength: men=867, women=960; balance: men=898, women=1001; chair rise speed: men=895, women=1002; TUG speed: men=838, women=944. These estimates include those with imputed values who were unable to complete the test for health reasons. The corresponding estimates among those completing the tests (i.e with exclusion of those with imputed values) were for grip strength: men=45.9kg (11.8), women=26.9kg (7.5), balance: men=4.0s (0.8), women=3.5s (0.8), chair rise speed: men=26.3rep/min (6.9), women=25.6rep/min (7.9), TUG speed: men=80.0cm/s (18.1), women=69.0cm/s (16.5).

^b Geometric Mean and Coefficient of Variation

^cThe sample includes those with data on covariates, fatigue at age 43 and 60-64 years, and at least one of the physical performance measures.

CSE, Certificate of Secondary Education

Table 2Prevalence (%) of fatigue at age 60-64 according to fatigue at age 43 ^a

Fatigue at age 43	Fatigue at age 60-64		
	No fatigue	Occasional fatigue	Frequent fatigue
<i>Men</i>			
No fatigue	13	75	12
Occasional fatigue	5	77	18
Frequent fatigue	4	43	53
<i>Women</i>			
No fatigue	10	79	11
Occasional fatigue	6	72	22
Frequent fatigue	2	63	35

^aThe number of men and women with fatigue at both ages is presented in table 1.

Table 3Associations of Fatigue at Ages 43 And 60-64 with Strength and Physical Performance at Age 60-64 Years^a

	Difference in mean levels (95% Confidence Interval)^b		
	No fatigue	Occasional fatigue	Frequent fatigue
Grip strength, kg			
<i>Fatigue at age 43</i>			
Women, n (%)	349 (36)	431 (45)	180 (19)
Model 1	ref.	-0.91 (-2.26, 0.44)	-1.37 (-2.43, -0.31)
Model 2	ref.	-1.22 (-2.52, 0.08)	-1.57 (-2.59, -0.56)
Men, n (%)	529 (61)	277 (32)	61 (7)
Model 1	ref.	1.20 (-0.53, 2.92)	-0.10 (-3.25, 3.05)
Model 2	ref.	0.95 (-0.70, 2.61)	0.05 (-2.96, 3.06)
<i>Fatigue at age 60-64, n (%)</i>			
Model 1	ref.	-0.51 (-2.17, 1.14)	-2.58 (-4.46, -0.70)
Model 2	ref.	-0.50 (-2.09, 1.09)	-2.59 (-4.39, -0.76)
Balance, ln(balance)			
<i>Fatigue at age 43, n (%)</i>			
Model 1	ref.	-0.07 (-0.12, -0.02)	-0.15 (-0.23, -0.07)
Model 2	ref.	-0.07 (-0.12, -0.01)	-0.13 (-0.21, -0.06)
<i>Fatigue at age 60-64, n (%)</i>			
Model 1	ref.	0.04 (-0.05, 0.13)	-0.09 (-0.20, 0.01)
Model 2	ref.	0.06 (-0.03, 0.15)	-0.05 (-0.16, 0.05)
Chair rise speed, rep/min			
<i>Fatigue at age 43, n (%)</i>			
Model 1	ref.	-0.35 (-1.09, 0.40)	-2.47 (-3.53, -1.40)
Model 2	ref.	-0.29 (-1.02, 0.43)	-2.28 (-3.32, -1.23)
<i>Fatigue at age 60-64, n (%)</i>			
Model 1	ref.	-0.88 (-2.13, 0.37)	-3.65 (-5.07, -2.23)
Model 2	ref.	-0.62 (-1.85, 0.61)	-3.10 (-4.50, -1.71)
TUG speed, cm/s			
<i>Fatigue at age 43, n (%)</i>			
Model 1	ref.	-0.27 (-2.02, 1.49)	-3.69 (-6.24, -1.13)
Model 2	ref.	-0.23 (-1.96, 1.51)	-3.32 (-5.85, -0.80)
<i>Fatigue at age 60-64, n (%)</i>			
Model 1	ref.	-1.90 (-4.90, 1.10)	-6.07 (-9.49, -2.66)
Model 2	ref.	-1.33 (-4.30, 1.64)	-4.93 (-8.32, -1.53)

^aThe sample includes those with data on fatigue at age 43 and 60-64 years, weight, height and physical performance measure of interest (n=1827 for grip strength, n=1899 for balance, n=1897 for chair rise speed and n=1782 for TUG speed)

^bDifferences in mean levels of strength and physical performance by categories of fatigue estimated using multiple linear regression models

Model 1: Adjusted for gender(if no evidence of gender interaction)

Model 2: Model 1 + weight (kg) and height (cm)

Table 4

Associations of Combined Fatigue Frequency at Ages 43 and 60-64 Years with Strength and Physical Performance at Age 60-64 Years^a

		Difference in mean levels (95% Confidence Interval) ^b			
		No fatigue	Only occasional fatigue	Frequent fatigue at 1 time point	Frequent fatigue at 2 time points
<i>Grip strength, kg</i>	<i>n (%)</i>	106 (6)	1232 (67)	392 (22)	97 (5)
Model 1		ref.	-0.94 (-2.89, 1.01)	-1.40 (-3.52, 0.72)	-4.01 (-6.73, -1.29)
Model 2		ref.	-0.92 (-2.79, 0.96)	-1.45 (-3.49, 0.59)	-4.09 (-6.71, -1.48)
<i>Balance, ln(balance)</i>	<i>n (%)</i>	107 (6)	1277 (67)	413 (22)	102 (5)
Model 1		ref.	0.03 (-0.08, 0.14)	-0.11 (-0.23, 0.01)	-0.11 (-0.26, 0.04)
Model 2		ref.	0.05 (-0.06, 0.15)	-0.08 (-0.20, 0.03)	-0.06 (-0.21, 0.09)
<i>Chair rise speed, rep/min</i>	<i>n (%)</i>	105 (6)	1278 (67)	413 (22)	101 (5)
Model 1		ref.	-1.22 (-2.70, 0.26)	-3.40 (-4.99, -1.80)	-5.36 (-7.39, -3.32)
Model 2		ref.	-1.00 (-2.45, 0.46)	-3.04 (-4.61, -1.46)	-4.65 (-6.65, -2.64)
<i>TUG speed, cm/s</i>	<i>n (%)</i>	95 (5)	1220 (69)	377 (21)	90 (5)
Model 1		ref.	-1.12 (-4.71, 2.47)	-3.69 (-7.57, 0.20)	-8.89 (-13.86, -3.92)
Model 2		ref.	-0.54 (-4.10, 3.01)	-2.92 (-6.77, 0.93)	-7.22 (-12.16, -2.28)

^aThe sample includes those with data on fatigue at age 43 and 60-64 years, weight, height, and physical performance measure of interest (n=1827 for grip strength, n=1899 for balance, n=1897 for chair rise speed and n=1782 for TUG speed)

^bDifferences in mean levels of strength and physical performance by categories of fatigue estimated using multiple linear regression models

Model 1: Adjusted for gender(if no evidence of gender interaction)

Model 2: Model 1 + weight (kg) and height (cm)

Table 5

Associations of Combined Fatigue Frequency at Ages 43 and 60-64 Years with Strength and Physical Performance at Age 60-64 Years with Adjustment for Covariates^{a, b}

		Difference in mean levels (95% Confidence Interval) ^c			
		No fatigue	Only occasional fatigue	Frequent fatigue at 1 time point	Frequent fatigue at 2 time points
<i>Grip strength, kg</i>	<i>n (%)</i>	82 (5)	1007 (69)	305 (21)	70 (5)
Model 1	ref.		-0.25 (-2.35, 1.85)	-0.54 (-2.82, 1.75)	-4.12 (-7.11, -1.13)
Model 2	ref.		-0.36 (-2.45, 1.74)	-0.60 (-2.89, 1.68)	-4.18 (-7.16, -1.19)
Model 3	ref.		-0.19 (-2.29, 1.90)	-0.43 (-2.72, 1.86)	-3.95 (-6.95, -0.95)
Model 4	ref.		-0.24 (-2.33, 1.86)	-0.51 (-2.79, 1.79)	-4.10 (-7.09, -1.11)
Model 5	ref.		-0.33 (-2.41, 1.75)	-0.37 (-2.64, 1.91)	-3.95 (-6.92, -0.97)
<i>Chair rise speed, rep/min</i>	<i>n (%)</i>	81 (5)	1048 (69)	322 (21)	72 (5)
Model 1	ref.		-0.84 (-2.52, 0.83)	-2.81 (-4.62, -0.99)	-4.21 (-6.58, -1.84)
Model 2	ref.		-0.97 (-2.63, 0.69)	-2.82 (-4.62, -1.02)	-4.24 (-6.58, -1.89)
Model 3	ref.		-0.80 (-2.47, 0.88)	-2.73 (-4.54, -0.91)	-4.08 (-6.45, -1.71)
Model 4	ref.		-0.75 (-2.42, 0.92)	-2.61 (-4.43, -0.80)	-4.10 (-6.46, -1.73)
Model 5	ref.		-0.94 (-2.58, 0.71)	-2.55 (-4.34, -0.76)	-3.89 (-6.22, -1.56)
<i>TUG speed, cm/s</i>	<i>n (%)</i>	74 (5)	1004 (70)	293 (21)	65 (4)
Model 1	ref.		-1.66 (-5.51, 2.18)	-4.27 (-8.45, -0.10)	-8.44 (-13.40, -2.98)
Model 2	ref.		-1.80 (-5.63, 2.03)	-4.28 (-8.43, -0.11)	-8.52 (-13.96, -3.08)
Model 3	ref.		-1.60 (-5.44, 2.24)	-4.12 (-8.30, 0.06)	-8.17 (-13.64, -2.69)
Model 4	ref.		-1.48 (-5.31, 2.35)	-3.88 (-8.05, 0.28)	-8.22 (-13.66, -2.78)
Model 5	ref.		-1.86 (-5.66, 1.94)	-3.87 (-8.00, 0.27)	-7.95 (-13.34, -2.55)

^a The sample includes those with data on fatigue at age 43 and 60-64 years, all of the covariates and physical performance measure of interest (n=1463 for grip strength, n=1523 for chair rise speed and n=1436 for TUG speed)

^b Balance was not carried forward into these analyses as there was no evidence of association with basic adjustments (Table 3).

^c Differences in mean levels of strength and physical performance by categories of fatigue estimated using multiple linear regression models

Model 1: adjusted for gender (if no evidence of gender interaction), weight and height

Model 2: adjusted for Model 1 and socioeconomic position

Model 3: adjusted for Model 1 and health problems

Model 4: adjusted for Model 1 and smoking

Model 5: adjusted for Model 1 and midlife physical activity score

Table 6

Associations of Combined Fatigue Frequency at Ages 43 and 60-64 Years with Strength and Physical Performance at Age 60-64 Years^a

			Difference in mean levels (95% Confidence Interval) ^b			
			No fatigue	Only occasional fatigue	Frequent fatigue at age 43 only	Frequent fatigue at age 60-64 only
<i>Grip strength, kg</i>	<i>n (%)</i>	<i>106 (6)</i>	<i>1232 (67)</i>	<i>144 (8)</i>	<i>248 (14)</i>	<i>97 (5)</i>
Model 1	ref.		-0.94 (-2.89, 1.01)	0.44 (-2.05, 2.94)	-2.40 (-4.63, -0.16)	-4.01 (-6.73, -1.29)
Model 2	ref.		-0.92 (-2.79, 0.96)	0.26 (-2.13, 2.66)	-2.38 (-4.53, -0.23)	-4.09 (-6.71, -1.48)
<i>Balance, ln(balance)</i>	<i>n (%)</i>	<i>107 (6)</i>	<i>1277 (67)</i>	<i>156 (8)</i>	<i>257 (14)</i>	<i>102 (5)</i>
Model 1	ref.		0.03 (-0.08, 0.14)	-0.11 (-0.24, 0.03)	-0.11 (-0.26, 0.04)	-0.11 (-0.26, 0.04)
Model 2	ref.		0.05 (-0.06, 0.15)	-0.09 (-0.23, 0.04)	-0.09 (-0.21, 0.03)	-0.06 (-0.21, 0.09)
<i>Chair rise speed, rep/min</i>	<i>n (%)</i>	<i>105 (6)</i>	<i>1278 (67)</i>	<i>155 (8)</i>	<i>258 (14)</i>	<i>101 (5)</i>
Model 1	ref.		-1.22 (-2.70, 0.26)	-2.85 (-4.72, -0.99)	-3.70 (-5.39, -2.02)	-5.36 (-7.39, -3.32)
Model 2	ref.		-1.00 (-2.45, 0.46)	-2.65 (-4.47, -0.82)	-3.25 (-4.91, -1.60)	-4.65 (-6.65, -2.64)
<i>TUG speed, cm/s</i>	<i>n (%)</i>	<i>95 (5)</i>	<i>1220 (69)</i>	<i>143 (8)</i>	<i>234 (13)</i>	<i>90 (5)</i>
Model 1	ref.		-1.12 (-4.71, 2.47)	-2.67 (-7.18, 1.87)	-4.27 (-8.37, -0.17)	-8.89 (-13.86, -3.92)
Model 2	ref.		-0.54 (-4.10, 3.01)	-2.22 (-6.68, 2.24)	-3.32 (-7.39, 0.74)	-7.22 (-12.16, -2.28)

^aThe sample includes those with data on fatigue at age 43 and 60-64 years, weight, height, and physical performance measure of interest (n=1827 for grip strength, n=1899 for balance, n=1897 for chair rise speed and n=1782 for TUG speed)

^bDifferences in mean levels of strength and physical performance by categories of fatigue estimated using multiple linear regression models

Model 1: Adjusted for gender (if no evidence of gender interaction)

Model 2: Model 1 + weight (kg) and height (cm)