

## RESEARCH PAPER

# Long-term conditions, multimorbidity, lifestyle factors and change in grip strength over 9 years of follow-up: Findings from 44,315 UK biobank participants

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## Abstract

**Background:** Weak grip strength is associated with a range of adverse health outcomes and an accelerated decline in grip strength confers an even greater risk. The factors associated with change in grip strength in mid-life remain to be fully determined.

**Methods:** We used data from 44,315 UK Biobank participants who had grip strength measured at baseline (2006–10) and a subsequent visit approximately nine years later. At baseline, participants' long-term conditions (LTCs) were categorised against a hierarchy, with multimorbidity characterised by the number of LTC categories. Lifestyle factors were assessed. Change in grip strength was grouped into four patterns: decline, stable low, stable high or reference (no change or increase) and used as the outcome in multinomial logistic regression.

**Results:** Most LTC categories were associated with adverse patterns of change in grip strength (stable low and/or decline): for example, musculoskeletal/trauma conditions were associated with an increased risk of the stable low pattern (Relative Risk Ratio [RRR] = 1.63; 95% confidence interval [CI]: 1.49–1.79). Multimorbidity and lifestyle factors had independent associations with grip strength change. Those with 3+ categories of LTCs were more likely to experience decline in grip strength (RRR = 1.18; 95% CI: 1.08–1.28) compared to those with none. Low physical activity was associated with adverse patterns of grip strength, while raised body mass index (BMI) had divergent associations.

**Conclusions:** Individuals living with multimorbidity and those with lifestyle risk factors such as low physical activity are at increased risk of low muscle strength and the loss of strength over time.

**Keywords:** multimorbidity, long-term conditions, sarcopenia, grip strength, mid-life, later-life, lifestyle, older people

## Key Points

- There is limited research into the factors associated with change in grip strength in mid-life
- Individuals living with multimorbidity and those with lifestyle risk factors are at increased risk of low muscle strength and loss of strength over time
- Our findings suggest potential target groups in mid-life for assessment of grip strength, leading to established interventions such as resistance exercise training and the identification of participants for future research studies.

## Introduction

Grip strength is a key feature in the diagnosis of sarcopenia [1], the accelerated loss of muscle strength and mass. Weak grip strength is associated with a range of adverse health outcomes such as disability [2] and mortality [3], with an accelerated loss of grip strength conferring an even greater health risk [4, 5]. The revised European consensus guidelines on sarcopenia highlighted the need for more research into the factors that may influence sarcopenia across the life course, both to understand causes of this condition and also to identify opportunities for prevention [1]. Mid-life is a particularly relevant period since this appears to be when individuals transition from a period of broadly stable grip strength to age-related decline [6]. It is also a time when assessments of future health including cardiovascular risk are already conducted as part of clinical care [7].

Two important areas to consider are long-term conditions (LTCs), which can be used to identify individuals at increased risk of sarcopenia using routine health records, and lifestyle factors, which are potentially modifiable and targets for intervention. The presence of multimorbidity, commonly defined as the presence of multiple LTCs, has been associated with an accelerated loss of grip strength [8]. Multimorbidity becomes increasingly common with age [9] and there is an urgent need to understand which categories of LTCs pose the greatest risk of strength loss and should therefore be a focus for further assessment. We have previously shown that the presence of musculoskeletal, endocrine and neurological/psychiatric conditions had the strongest associations with weak grip strength in a cross-sectional analysis [10]. To our knowledge there have not been similar studies examining such relationships with change in grip strength.

Lifestyle factors including physical inactivity, smoking and overweight and obesity influence the development of many long-term conditions [11–13] and are associated with multimorbidity [14]. Some evidence suggests that these lifestyle factors are also associated with decline in grip strength over time [15, 16]. These factors have also been combined into a risk factor score and related to a number of patterns of grip strength change in mid-life [17]. Such patterns capture the heterogeneity in change in grip strength, including the fact that many individuals do not experience significant decline in mid-life and may remain at a stable level, including those who are persistently weaker than typical for their age. Finally, there is evidence for the role of diet in the development of sarcopenia [18, 19], yet we are not aware of studies evaluating change in grip strength that have considered the role of dietary factors.

Using data from UK Biobank the present study aims to investigate the associations of long-term conditions, multimorbidity and lifestyle factors with patterns of change in grip strength over approximately 9 years of follow up.

## Methods

We used data from UK Biobank participants who had grip strength measured at baseline and also at a subsequent study

visit (referred to as imaging visit hereon) approximately nine years later. At baseline, participants' LTCs were self-reported and categorised against a hierarchy with multimorbidity characterised by the number of LTC categories present (0, 1, 2 and 3+). Lifestyle factors (body mass index (BMI), smoking, diet and physical activity) were also assessed. Further details about UK Biobank, and the assessment of long-term conditions, lifestyle factors and grip strength are available in Supplementary Methods.

## Characterisation of the outcome: Change in grip strength

Characterising change in a clinical outcome when data are available at only two time points is challenging as the outcome may be subject to the effects of regression to the mean and measurement error. We employed the patterns of change as previously reported by Cooper et al [17]. We calculated age (grouped by decade) and sex-specific Z-scores separately at the baseline and imaging visits: that is, the number of standard deviations an observation is above the mean for the relevant age group and sex, at the visit in question. We classified each Z-score value into three groups: low (less than  $-1$ ), intermediate (between  $-1$  and  $1$ ), and high (greater than  $1$ ). Participants who were unable to complete grip strength assessment for health reasons such as arthritis, stroke or limb injury were considered to have a Z-score in the low group for the purpose of analyses.

We then grouped change in grip strength between the baseline and imaging visits into four patterns based on the Z-score groups: (i) reference (low/intermediate at baseline and intermediate/high at the imaging visit), (ii) decline (high at baseline and low/intermediate at imaging visit, or intermediate at baseline and low at follow-up), (iii) stable high (high at both visits), and (iv) stable low (low at both visits) [17].

## Statistical analyses

We restricted the sample to participants of UK Biobank with complete data on lifestyle factors, LTCs, and patterns of grip strength change. Descriptive statistics were stratified by sex, with differences between males and females analysed using chi-squared tests in the case of categorical variables, t-tests in variables deemed to be normally distributed and Wilcoxon rank-sum tests in those not.

We used multinomial logistic regression to assess associations between the exposures (categories of LTCs, multimorbidity and lifestyle factors) and the outcome (pattern of grip strength change). We did this using two models: (i) a model containing binary variables for the presence/absence of each category of LTCs, and (ii) a model containing a variable for the number of categories of LTCs combined with variables for lifestyle factors. As the outcome was based on age and sex-specific Z-scores for grip strength, we did not include adjustments for age and sex in the regression models.

We repeated the above analyses for males and females separately to look for sex differences in the associations tested, as shown in [Supplementary Figures 1 and 2](#).

We performed sensitivity analyses by repeating models on sub-samples, removing (i) those unable to perform the grip strength test due to health reasons ( $n = 101$ , [Supplementary Figures 3 and 4](#)), and (ii) those with a change in grip strength greater than two standard deviations removed ( $n = 1,591$ , [Supplementary Figures 5 and 6](#)). The findings were unchanged in both sets of sensitivity analyses. All statistical analyses were performed using R version 3.6.0 [20].

## Results

A total of 44,315 (51.1% female) participants at ages 40–70 had information available on LTCs, lifestyle factors, and grip strength change (i.e. grip strength measured at baseline and imaging visit). The most common categories of LTCs were cardiovascular (present in 27.9% of the sample), musculoskeletal (17.0%), and respiratory/ENT (ear, nose and throat) (16.3%). The sample was approximately divided into thirds by number of categories of LTCs: zero (30.2%), one (33.9%), and two or more (36.0%), with the latter group considered to have multimorbidity. [Table 1](#) shows the characteristics of the sample by sex (with additional information provided in [Supplementary Table 1](#)). Male participants tended to be older, to have less than three categories of LTCs, to have higher BMI, to be current/previous smokers, to undertake higher levels of LTPA and to consume more processed meat, and less fruit and vegetables.

The median time between visits was 9.2 (7.6, 10.3) years. Within participant grip strength declined by a mean of 2.0 (5.7) kg in females and 3.5 (7.4) kg in males over this period. In terms of patterns of grip strength change (please see Methods for definitions), 6.2% had stable low strength, 6.9% had stable high strength, 15.5% experienced a decline in strength and the remainder (71.4%) were in the reference pattern. The mean values in each pattern of grip strength change at the two visits by number of LTC categories are shown in [Supplementary Table 2](#).

The associations between LTC categories and grip strength change are shown in [Figure 1](#). All categories of LTCs had significant independent associations with grip strength change except the renal/urology, and the gynaecology/breast categories. The strongest associations were seen for the outcome of stable low grip strength such as musculoskeletal/trauma conditions (RRR = 1.63 (95% CI: 1.49–1.79)) or eye conditions (RRR = 1.49 (95% CI: 1.24–1.80)). Several categories also had independent associations with decline in grip strength including haematology/dermatology, gastrointestinal and immunological/systemic conditions. There was evidence of a sex difference in these findings, with stronger associations typically seen in females. Some categories had stronger associations in males, including endocrine/diabetes and haematology/dermatology ([Supplementary Figures 1a and b](#)).

We saw graded associations between the degree of multimorbidity (characterised as the number of categories of

long-term conditions) and pattern of change in grip strength, independent of lifestyle factors as shown in [Figure 2](#). For example, those with three or more categories of LTCs were at increased risk of decline in grip strength (RRR = 1.18 (95% CI: 1.08–1.28)), a marked increase in stable low grip strength (RRR = 2.11 (95% CI: 1.87–2.38)) and were less likely to experience stable high grip strength.

The associations between lifestyle factors and grip strength change, independent of multimorbidity, are also shown in [Figure 2](#). All lifestyle factors had significant associations except frequent consumption of processed meat. We saw that overweight and obesity were associated with increased risk of both a decline and stable high grip strength. Current smoking was associated with slightly reduced risk of stable low grip strength. Infrequent consumption of fruit and vegetables was associated with a decreased risk of stable high grip strength, while infrequent consumption of oily fish was associated with an increased risk of stable low grip strength. Levels of LTPA had a graded association with the stable grip strength categories, for example those with low LTPA were at increased risk (RRR = 1.62 (95% CI: 1.37–1.92)) of stable low and decreased risk (RRR 0.69 (95% CI: 0.61, 0.79)) of stable high strength.

The overall pattern of these findings was consistent in males and females, although we did observe stronger associations for BMI and LTPA in males, and stronger associations for multimorbidity in females, as shown in [Supplementary Figures 2a and b](#).

## Discussion

We investigated the associations of long-term conditions, multimorbidity and lifestyle factors with patterns of change in grip strength over approximately 9 years of follow-up using data from UK Biobank. We found heterogeneity in grip strength change, with 16% of the sample experiencing decline between the two time-points, and a further 6% having low strength at both time-points. Several categories of LTCs were associated with adverse patterns of change in grip strength, with the strongest association seen between musculoskeletal LTCs and stable low grip strength. We also saw a graded relationship between the degree of multimorbidity present and adverse patterns of grip strength change: a reduced risk of stable high strength, along with an increased risk of stable low and decline in strength. A range of lifestyle factors were independently associated with adverse patterns of grip strength including obesity, infrequent consumption of fruit, vegetables and oily fish, and lower LTPA.

Our findings on change in grip strength are consistent with previous work indicating that a significant proportion of people may not experience meaningful decline in grip strength across midlife [17]. We are not aware of previous investigations that have examined individual categories of long-term conditions and change in grip strength. However, our group has previously shown that the presence of musculoskeletal conditions is strongly associated with probable

**Table 1.** Characteristics of the sample, by sex

Characteristic	Males (n = 21,658)	Females (n = 22,657)	P-value*
Age (years)	57 [50, 62]	55 [49, 60]	< 0.001
Baseline grip strength (kg)	43.4 (8.45)	26.6 (6.18)	< 0.001
Imaging visit grip strength (kg)	39.9 (8.60)	24.6 (5.92)	< 0.001
LTC(s) present in body system:			
Cardiovascular	7,207 (33.3)	5,144 (22.7)	< 0.001
Respiratory/ENT	3,637 (16.8)	3,595 (15.87)	0.009
Gastrointestinal	2,984 (13.8)	3,091 (13.6)	0.689
Renal/Urology	1,426 (6.6)	580 (2.6)	< 0.001
Endocrine/Diabetes	1,121 (5.2)	2053 (9.1)	< 0.001
Neurological/Psychiatric	2053 (9.5)	3,434 (15.2)	< 0.001
Musculoskeletal/Trauma	3,621 (16.7)	3,905 (17.2)	0.151
Haematology/Dermatology	1,082 (5.0)	1,402 (6.2)	< 0.001
Gynaecology/Breast	‡	2,315 (10.2)	
Immunological/Systemic	1979 (9.1)	2,322 (10.2)	< 0.001
Eye	696 (3.2)	698 (3.0)	0.238
History of cancer	1,065 (4.9)	1,696 (7.5)	< 0.001
Number of LTC categories			< 0.001
0	6,564 (30.3)	6,808 (30.1)	
1	7,575 (35.0)	7,431 (32.8)	
2	4,569 (21.1)	4,655 (20.6)	
3+	2,950 (13.6)	3,763 (16.6)	
BMI (kg/m <sup>2</sup> )	27.1 (3.74)	26.0 (4.53)	< 0.001
BMI category			< 0.001
<25: Normal	6,395 (29.5)	10,974 (48.4)	
25-30: Overweight	11,163 (51.5)	7,934 (35.0)	
> 30: Obese	4,100 (18.9)	3,749 (16.6)	
Smoking history			< 0.001
Never	12,288 (56.7)	14,546 (64.2)	
Previous	7,789 (36.0)	6,964 (30.8)	
Current	1,581 (7.3)	1,147 (5.0)	
Meets fruit/vegetable guidelines			< 0.001
Yes	10,282 (47.5)	13,796 (60.9)	
No	11,376 (52.5)	8,861 (39.1)	
Oily fish (> = 1 per week)			< 0.001
Yes	12,049 (55.6)	13,016 (57.5)	
No	9,609 (44.4)	9,641 (42.6)	
Processed meat (> = 2 per week)			< 0.001
No	12,697 (58.6)	18,334 (80.9)	
Yes	8,961 (41.4)	4,323 (19.1)	
Leisure-time PA category			<0.001
Low (<600)	7,520 (34.7)	10,079 (44.5)	
Moderate (600-3,000)	11,780 (54.4)	11,292 (49.8)	
High (>3,000)	2,358 (10.9)	1,286 (5.7)	

Values shown are mean (standard deviation) or median [interquartile range]. ENT, ear nose and throat. \*Differences between males and females analysed using chi-squared tests in the case of categorical variables, t-tests in continuous variables deemed to be normally distributed, and, Wilcoxon rank-sum tests in those not. ‡ Value not shown due to small numbers in this category.

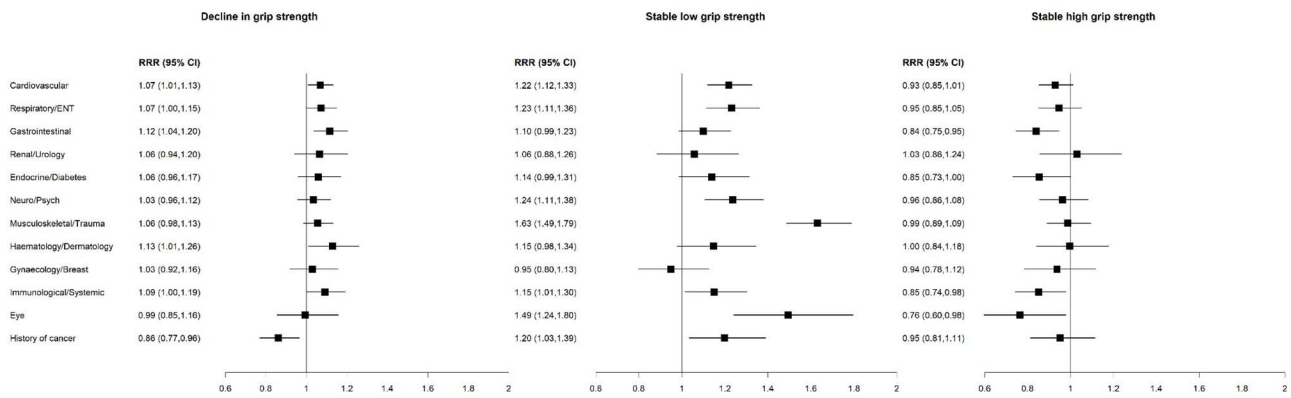
sarcopenia, as identified by weak grip strength [10]. Our findings extend this earlier work and show that some categories of LTCs such as musculoskeletal and eye conditions are associated with persistently low strength over time (stable low pattern), while others such as haematology/dermatology conditions are associated with decline in grip strength. We also found evidence of a sex difference in these associations (Supplementary Figure 1), although as above we are not aware of other studies with which to compare these findings.

Our findings on overall multimorbidity are consistent with a previous study suggesting that a greater number of long-term conditions is associated with decline in grip strength [8]. We also found that multimorbidity had

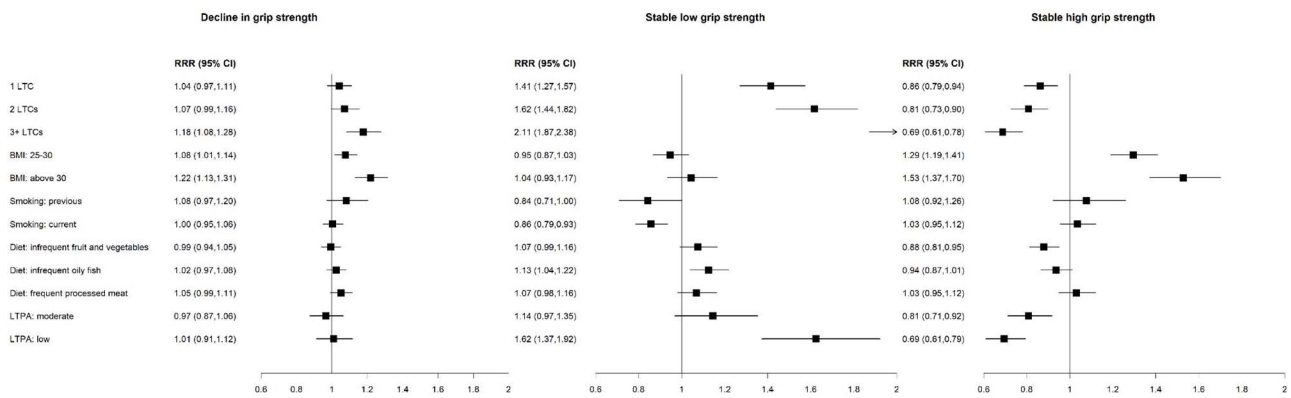
stronger associations with adverse grip strength patterns in females compared to males (Supplementary Figure 2). In keeping with this, a study of people aged 85 reported that the presence of long-term conditions was associated with lower grip strength among females but not males [16].

Previous work has demonstrated that a range of lifestyle factors including smoking [21], obesity [15] and physical inactivity [22] as well as a behavioural risk factor score [17] are associated with decline in grip strength. We observed stronger associations for LTPA in males compared with females, consistent with earlier work showing that higher levels of physical activity appeared to be protective of loss of grip strength in males but not in females [16, 23]. Although





**Figure 1.** Associations between categories of long-term conditions and patterns of grip strength change. The figure shows the independent associations of each category of LTCs at baseline with the change in grip strength category (compared to the reference category of grip strength change as defined in the Methods). ENT, ear nose and throat.



**Figure 2.** Associations between multimorbidity, lifestyle factors and patterns of grip strength change. The figure shows the independent associations of multimorbidity (expressed as the number of categories of LTCs present) and lifestyle factors at baseline with the change in grip strength category (compared to the reference category of grip strength change as defined in the Methods). The reference categories (not shown) are: zero LTCs (long-term conditions), BMI (body mass index) < 25, smoking: never, diet: frequent fruit and vegetables, diet: frequent oily fish, diet: infrequent processed meat, LTPA (leisure time physical activity) high.

previous work has highlighted the potential role of diet on the development of sarcopenia, few studies have considered the associations of dietary variables with changes in grip strength. However, greater dietary variety from a 10-item food frequency questionnaire has been previously associated with lower risk of future declines in grip strength [24].

We saw heterogeneity in the grip strength change experienced by participants. Approximately 15% of the sample experienced decline in grip strength more than that expected for their age at the two time-points, with the remainder considered stable. This is in keeping with previous cross-sectional [6] and longitudinal [25] life course studies suggesting that mid-life is a period when grip strength is broadly stable. Our results also highlight that strength may be stable around a low or high baseline, with marked differences in the profile of lifestyle factors and LTCs between these two categories.

In terms of lifestyle factors, we saw divergent associations of raised BMI with patterns of grip strength change. This was especially the case among those who were obese at

baseline and the associations seen were more marked in males. A possible explanation is effect modification by body composition: those with the combination of raised BMI but low lean mass, known as sarcopenic obesity, may have been at increased risk of grip strength decline [26]. This is an area for further research. Low physical activity at baseline increased the risk of stable low strength and decreased the risk of stable high strength. This suggests the possibility that those with low physical activity may have had both low activity and strength prior to the baseline, and there is evidence that these two factors have bidirectional associations [27]. Finally, we observed that frequent intake of fruits and vegetables, and of oily fish were associated with favourable patterns of grip strength change. There is evidence that healthier dietary patterns characterised by these foods may be protective against the development of sarcopenia [28].

We saw associations between most categories of LTCs and change in grip strength, including several categories that were associated with decline in strength. There are several possible

explanations for these findings. Some categories of LTCs such as cardiovascular conditions have been linked to loss of physical function [29] and may have direct effects on skeletal muscle. Medications used in the management of some LTCs may also play a role, with evidence of both harmful and beneficial effects for skeletal muscle [30]. For example, several of the categories of LTCs associated with decline such as haematology/dermatology and immunological/systemic conditions may require treatment with glucocorticoids, which are recognised to cause muscle loss as a side effect [31]. This is an area for further research. Finally, our results highlight how more complex degrees of multimorbidity are associated with decline in grip strength. The median time between visits was nine years and so it is possible that some categories anticipate the later development of more complex multimorbidity and associated decline in grip strength.

Our findings are directly relevant to the revised European consensus guidelines on sarcopenia [1] as well as the subsequent comprehensive review on the condition for physicians [32]. A key component of sarcopenia is the accelerated loss of muscle strength which we have characterised in terms of a decline in strength between two time-points greater than that expected for a person's age. This allowed us to identify groups at risk of strength decline, including based around the presence of different categories of LTCs as well as their overall degree of multimorbidity, both of which are routinely captured in clinical care.

We recommend that adults with two or more categories of LTCs be prioritised for assessment of sarcopenia such as during routine health checks [7]. A range of individual categories of LTCs such as gastrointestinal conditions were also associated with increased risk of decline and suggest potential priority groups for screening in secondary care settings. Identifying these specific groups would enable interventions for sarcopenia, such as resistance exercise training, to be targeted at those groups of individuals who most stand to benefit. Such screening could also help to identify individuals with sarcopenia who can be invited to join a registry for future trials in this area [33].

The associations we found between lifestyle factors and grip strength change also suggest areas for intervention. Indeed, there is interest in how to increase physical activity [34] and how to improve other lifestyle factors [35] among those living with multimorbidity. Our findings highlight a potential role for interventions that simultaneously address lifestyle factors and provide treatment for low muscle strength, for example by increasing levels of physical activity [36], performing targeted resistance exercise training [37] or increasing intake of dietary protein [18]. Our findings also reaffirm the importance of mid-life as an important window for interventions which aim to modify lifestyle behaviours to prevent the decline of muscle strength in later life [17].

Despite the healthy responder bias associated with UK Biobank [38], a key strength of our work is the large sample of participants at mid-life we were able to include. As well as considering the role of multimorbidity in grip strength decline, this has allowed us to consider individual categories

of long-term conditions. Including participants at mid-life is also useful as this may be an appropriate time to deliver targeted interventions before individuals cross a threshold of functional decline and are unable to engage. Another strength of our work is the categorical approach to grip strength change used in our analysis when only two time points are available, which still allows for heterogeneity in terms of those who have broadly stable strength as well as those who decline [17]. Evaluating specific clusters of long-term conditions with grip strength change would be an informative next step and could provide useful information that would be informative for designing and delivering targeted interventions.

### Conclusions

We have shown marked heterogeneity in grip strength change in a large sample of adults in mid-life. A range of categories of LTCs, overall multimorbidity and lifestyle risk factors were associated with stable low strength and/or decline. Our findings suggest potential target groups in mid-life for assessment of grip strength, leading to established interventions such as resistance exercise training as well as the identification of participants for future research studies.

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

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