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Keywords:	terminal decline, motor function, walking speed, grip strength, ADL and IADL limitations

Terminal decline in objective and self-reported measures of motor function over 10-years before death: results from the Whitehall II cohort study

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ABSTRACT

OBJECTIVES Accelerated decline in cognitive function, referred to as terminal decline, is observed in the years preceding death. Motor function is robustly associated with mortality but the manner in which it declines before death remains unclear. Using repeat measures of motor function we examined objective and self-reported measures of motor function in relation to mortality.

DESIGN Prospective cohort study.

SETTING UK based Whitehall II cohort study, participants aged 35-55 years recruited in 1985-1988; motor function component was added to the study at the 2007-2009 wave.

PARTICIPANTS 6,194 participants with motor function measures in 2007-2009 (mean age 65.6, standard deviation 5.9), 2012-2013, and 2015-2016. Walking speed, grip strength, and timed 5 chair-rises comprised objective measures; physical component summary (PCS) score of the Short Form-36 and limitations in activities and instrumental activities of daily living (ADL/IADL) the self-reported measures.

MAIN OUTCOME MEASURES All-cause mortality between 2007 and 2019.

RESULTS Standardized motor function measures from 2007-2009 (mean follow-up 10.6 years, N cases/N total=610/5,645) were associated with mortality in Cox regression adjusted for sociodemographic characteristics, health behaviours, body mass index and chronic diseases: walking speed (hazard ratio 0.82, 95% Confidence Interval 0.75 to 0.90), grip strength (0.87, 0.80 to 0.94), timed 5 chair-rises (1.14, 1.07 to 1.23), PCS (0.86, 0.79 to 0.92), and ADL/IADL limitations (1.30, 1.07 to 1.58). These associations were progressively stronger when motor function measures were drawn from 2012-2013 (mean follow-up 6.8 years) and 2015-2016 (mean follow-up 3.7 years). Analysis of trajectories showed differences between survivors (N=6,194) and decedents (N=484) in standardized motor function scores up to 10 years before death for timed 5 chair-rises (-0.35, -0.59 to -0.12), 9 years for walking speed (0.21, 0.05 to 0.36), 6 years for grip strength (0.10, 0.01 to 0.20), 7 years for PCS (0.15, 0.05 to 0.25), and 4 years for ADL/IADL (-2%, -4% to 0%). These differences increased in the period leading to death for timed 5 chair-rises (p<0.001), PCS (p<0.001), and ADL/IADL limitations (p=0.04) and remained unchanged for walking speed (p=0.20) and grip strength (p=0.50).

CONCLUSION Motor function in early old age has a robust association with mortality, with evidence of terminal decline in motor function emerging early in measures of overall motor function (timed 5 chair-rises and PCS) and late in ADL/IADL limitations.

Summary box

What is already known on this topic

- Motor function declines with age, with considerable heterogeneity in the rate of decline.
- In older adults, performance-based measures of motor function and functional limitations are associated with mortality.
- An accelerated decline in motor functioning, specifically ADL/IADL limitations has been observed in the last few months or years of life but whether this decline spans a longer time frame and is present for objective and self-reported measures of motor function is unknown.

What this study adds

- Motor function assessed at mean age 65, 69, and 72 showed walking speed, grip strength, timed 5 chair-rises, physical functioning score (SF-36), and ADL/IADL limitations to be associated with mortality; all associations were stronger with later life measures of motor function.
- Trajectories of motor function over 10 years using a backward time scale showed divergence, or terminal decline, in timed 5 chair-rises, physical functioning score (SF-36), and ADL/IADL limitations starting 10, 7, and 4 years before death respectively. Differences in walking speed were present 9 years before death but did not increase in the period leading to death.
- Analyses were adjusted for sociodemographic factors, health behaviours, body mass index, and chronic diseases (diabetes, coronary heart disease, stroke, cancer, dementia, Parkinson's disease, COPD, depression, arthritis).

INTRODUCTION

Ageing is characterized by decline in cognitive[1 2] and motor[3 4] function over the adult lifecourse along with an increase in heterogeneity in individual trajectories, partly due to pathological processes of age-related chronic diseases.[5 6] In the years immediately preceding death an accelerated decline in functioning has been observed,[7 8] referred to as "terminal decline".[9] As described in a recent review, terminal decline is observed in multiple domains although much of the research is confined to cognitive decline.[10]

While better understanding of changes in functional status in one or two years before death is useful for planning care, it has minimal utility for identifying individuals who could benefit from clinical or behavioural interventions. Consideration of longer spans to study decline preceding death is also supported by findings showing decline in motor[4] and cognitive function[2] to be manifest starting in midlife. Furthermore, several studies have shown midlife cognitive and motor function to be associated with mortality.[11-14] The long-term change in trajectories of functioning prior to death is less well characterized in relation to motor function. For cognitive function, long-term trajectories are known, and change-point studies show differences in different measures to emerge up to 15 years before death.[15]

Change in motor function in the years before death is a dynamic process and may reflect changes over a longer period than at end of life examined in several studies.[9 16 17] To date, few studies have considered a longer follow-up. An exception is a study showing decline in walking speed starting at 10 years before death.[18] Some studies have used composite measures of motor function[16 19 20] where the role played by strength, upper and lower body function cannot be separated. A further limitation, apart from notable exceptions,[9] is a lack of studies assessing both objective and self-reported measures of function. To address these limitations, the aim of this longitudinal cohort study was to examine multiple measures of motor function for their associations with mortality using time-to-event analyses to capture the importance of between-person differences in motor function and retrospective trajectory analyses to compare within-person change in motor function over 10 years in survivors and deceased participants. Use of this twin analytic strategy allows both between- and within-person differences in motor function to be examined in relation to mortality in the same study, the latter being reflected in the shape of the change in motor function leading to death.

METHODS

Study population

The Whitehall II study is an ongoing prospective cohort of 10,308 British civil servants, 6,895 men and 3,413 women, aged 35-55 in 1985-1988.[21] Since baseline, follow-up clinical examinations have taken place approximately every 4-5 years using home-based assessment for those who choose this option and clinic-based assessments (London and major cities in the UK) for others; each wave takes approximately two years to complete. Measurement of motor function was introduced to the study at the 2007-2009 clinical examination and repeated in 2012-2013 and 2015-2016 (flow chart in **eFigure 1**). In addition to clinical examinations within the study, data over the follow-up are obtained via linkage to electronic health records of the UK National Health Service (NHS). The NHS provides most of the health care in the country, including in- and out-patient care, and record linkage is undertaken using a unique NHS identifier held by all UK residents. At each wave, participants provided informed written consent and research ethics approval was obtained from the National Health Service London - Harrow Research Ethics Committee (latest reference number 85/0938).

Patient involvement

Participants of the Whitehall II study were not involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design, or implementation of the study. No participants were asked advice on interpretation or writing up of results but all results are disseminated to study participants via newsletters and our website, which has a participant portal, https://www.ucl.ac.uk/epidemiology-health-care/research/epidemiology-and-public-health/research/whitehall-ii/participants-area.

Motor function (2007-2009, 2012-2013, and 2015-2016)

Objective measures

Walking speed was measured over an 8-ft (2.44 m) marked course, with no obstructions for an additional 2 feet at either end. Participants wore either low-heeled close-fitting footwear or walked barefoot with instructions to 'walk to the other end of the course at your usual walking pace, just as if you were walking down the street to go to the shops. Walk all the way past the other end of the tape before you stop'. Three tests were conducted and the time taken to complete the test was recorded by a research nurse using a stop-watch; the mean of three trials (meters per second) was used in the analysis. Use of a walking stick, if habitual, was allowed.

Grip strength was measured using a Smedley hand grip dynamometer. Participants were seated, their elbow on the table, forearm pointing upwards, palm of the hand facing up. The dynamometer was adjusted to suit participants' dominant hand and they were instructed to squeeze the dynamometer as hard as possible for 2 seconds. Three tests were performed with one minute rest between each test, the maximum of these values was used in the analyses.[22]

Timed 5 chair-rises was recorded with participants sitting on an armless chair with feet resting on the floor and arms folded across their chest. Participants were instructed to stand up and sit down five times as quickly as possible without using their arms. In order to retain 275 participants with data on all other measures of motor function except timed 5 chair-rises, we imputed these data using sex-specific mean score of the bottom quintile of performance as in a previous study.[23]

Self-reported measures (2007-2009, 2012-2013, and 2015-2016)

Self-reported functioning was measured using the physical component summary (PCS) score of the Short Form 36 General Health Survey.[24] A low PCS score indicates limitations in self-care and daily activities, suffering from severe pain, and poor general health.

Self-reported functional limitations were assessed using difficulties in basic activities of daily living (ADLs)[25] and instrumental activities of daily living (IADLs).[26] ADLs were composed of questions on the following 6 items: dressing, walking, bathing, eating, getting in bed, and using the toilet; IADLs included difficulty in cooking, shopping for grocery, making telephone calls, taking medication, doing housework, and managing money. Impaired functional status was determined by one or more limitations on a combined ADLs and IADLs scale.

Mortality

Death from any cause was defined using mortality records drawn from the British national mortality register (National Health Services Central Registry) until October, 2019. The tracing exercise was carried out using the National Health Service identification number (NHS-ID) of each participant.

Covariates

Socio-demographic variables included age, sex, ethnicity (white or non-white), marital status (living with a partner or single), and occupational position[21] at age 50 (high, intermediate and low, reflecting income and status at work).

Health behaviours included smoking (never smoker, ex-smoker, current smoker), alcohol consumption (no alcohol in the previous week; moderate, 1-14 units/week; high, >14 units/week), time spent in moderate and vigorous physical activity (less than 150 minutes per week, at least the recommended amount of physical activity), and frequency of fruits and vegetables consumption (less than daily, at least once a day).

Body mass index, estimated using height and weight assessed at the clinical examination, was categorized as <20 Kg/m², 20-24.9 Kg/m², 25-29.9 Kg/m², and ≥30 Kg/m².

Chronic diseases were ascertained using data from multiple sources: clinical examinations in the study and linkage to electronic health records; three national databases were used: the national hospital episode statistics (HES) database with in- and out-patient data, the Mental Health Services Data Set which in addition to in- and out-patient data also has data on care in the community, and the cancer registry. Chronic conditions considered were: diabetes (fasting glucose ≥ 7.0 mmol/l, reported doctor-diagnosed diabetes, use of diabetes medication, ICD10: E10-E14), coronary heart disease (12-lead resting ECG recording, ICD10: I20-I25), stroke (MONICA-Ausburg stroke questionnaire, ICD10: I60-I64), cancer (cancer registry with malignant cancer ICD10: C00–C97 to include colorectal, lung, breast, prostate, smoking related cancers and melanoma skin cancers), dementia (ICD10: F00-F03, F05·1, G30, G31), Parkinson's disease (self-report of longstanding illness, ICD10: G20), chronic obstructive pulmonary disease (self-report of longstanding illness, ICD10: J41-J44), depression (self-report of longstanding illness, use of antidepressants, ICD10: F32-F33), and arthritis (self-report of longstanding illness, ICD10: M05, M06, M15-M19). A multimorbidity score was created as the count of these chronic conditions, ranging from 0 to 9.

Statistical analysis

All continuous measures of motor function were standardized using sex-specific mean and standard deviation from baseline (2007-2009). The association between motor function and mortality was examined in two ways, first using time to event analysis and then comparison of retrospective trajectories of motor function over 10 years.

Time to event analysis: Cox proportional hazards regression was used to examine the association of motor function in 2007-2009, 2012-2013, and 2015-2016 (separate models) with mortality. Age was used as the time-scale, participants were left-truncated at age at assessment and right-censored at age of death or end of mortality follow-up (October 2019), whichever came first. Proportional hazards assumption was verified by plotting Schoenfeld residuals. Analyses were first adjusted for socio-demographic factors (sex, ethnicity, marital status, and occupational position at age 50) (Model 1); additionally for health behaviours (physical activity, alcohol, tobacco and fruits/vegetable consumptions) (Model 2), and then for BMI and the multimorbidity score (Model 3). The associations were expressed as hazard ratio (HR) per standard deviation higher motor function for continuous measures and for having at least one limitation versus none for ADL/IADL.

<u>Retrospective analysis of motor function trajectories over 10 years</u>: Trajectories of motor function were examined using a backward time-scale such that time 0 was 31st December 2017 for survivors and date of death for participants who died between baseline (2007-2009) and 31st December 2017. Deaths after this date were not considered in these analyses in order to restrict analyses on mortality occurring not long after the last measure of motor function. Retrospective trajectories were defined using linear mixed models for all motor function measures except ADL/IADL limitations for which logistic regression with generalized estimated equation (GEE) and an unstructured correlation matrix was used. Time and time^2 and their interactions with age at time 0, sex, ethnicity, marital status and occupation position were included in Model 1, subsequent adjustment for covariates was the same as that in the fully adjusted Cox regression (Model 3). Age was centred at the overall mean at time 0 and in the linear mixed models random effects for the intercept and time were used to allow for differences in motor function at the intercept (time = 0) and change in motor function over time. The difference in motor function for the continuous measures and prevalence of ADL/IADL limitations in survivors and decedents were estimated for each year, over the 10 years preceding end of follow-up or death.

All analyses were conducted using R software (R Core Team, 2019, version 4.0.3). Cox regression, linear mixed models, GEE, and comparisons between survivors and decedents were performed using the *survival* (version 3.2-7), *nlme* (version 3.1-149), *geepack* (version 1.3-2) and *emmeans* (version 1.5.2-1) packages, respectively. Estimates were reported with 95% confidence intervals (95%CI) and two-tailed p-values considered significant at 0.05 level.

Additional analyses

First, in addition to considering the motor function measures separately in Cox regression in the main analyses, we undertook analyses including all motor function measures in the same model. Second, to examine the impact of missing data the Cox regression analysis was repeated using inverse probability weighting to reflect the study population at recruitment (1985).[27] This involved calculation of the probability of being included in the present study among those alive using data from baseline on sociodemographic factors and health behaviours as well as data on chronic conditions over the follow-up; then the inverse of these probabilities was used as weights in the Cox regression. Third, the role of chronic diseases was examined in time-to-event analyses stratified by the status of multimorbidity at the assessment of motor function. Fourth, the possible influence of cognitive function was examined by adding a measure of global cognition (the Mini Mental State Examination) as a covariate to the analyses. Fifth, as IADLs and ADLs were combined in the main analyses, we examined them separately to determine whether trends in long-term terminal decline were similar in these two measures of functional limitations. Finally, in an alternate approach to assessment of change in motor function we examined the association between change in motor function over the first two measures of motor function and subsequent mortality using Cox regression and the same covariates as in the main analyses drawn from the 2012-2013 assessments.

RESULTS

Assessment of motor function was introduced to the study protocol at the 2007-2009 wave of data collection when the age range of participants was 55 to 79 years, and repeated in 2012-2013 and 2015-2016 leading to smaller numbers in analyses due to drop-out and mortality (**eFigure 1**). The analyses of motor function trajectories were based on 6,194 of participants with data on at least 1 out of 3 waves of motor function and the covariates. Compared to those excluded from these analyses, participants included in the analyses were younger (44.0 vs. 45.6 years at recruitment in 1985-1988; p<0.001), more likely to be men (72.0% vs. 64.0%; p<0.001), Caucasian (92.5% vs. 88.8%, p<0.001), and have higher occupational position (43.2% vs. 33.3%; p<0.001).

Among the 6,194 participants included in the analyses, 654 participants died between baseline (2007-2009) and October 2019, the mean (SD) age at death was 76.8 (6.2) years. **Table 1** shows that participants who died were more likely to be older at baseline (mean age 69.7 vs 65.1, p<0.001), to have multimorbidity (27.2%

vs %12.1, p<0.001), and poorer motor function (p<0.001 for all measures) compared to participants alive at the end of the follow-up. The motor function measures had a modest correlation with each other, ranging from 0.21 to 0.35 correlation matrix (**eTable 1**).

Time to event analysis

There were no sex differences in the association between measures of motor function and mortality, p-values for interaction term between sex and motor function measures ranged from 0.12 to 0.92. Men and women were therefore combined in the analyses with sex-specific standardization of continuous motor function measures.

Both objective and self-reported measures of motor function (1 SD higher score for continuous measures and 1 or more limitations in IADL/ADL) were associated with mortality (**Table 2**) in analyses adjusted for socio-demographics (Model 1) and health behaviours (Model 2) using measures of motor function in 2007-2009 (mean (SD) follow-up 10.6 (1.8) years), in 2012-2013 (mean (SD) follow-up 6.8 (1.0) years), and 2015-2016 (mean (SD) follow-up 3.7 (0.6) years). Inclusion of BMI and the multimorbidity score as covariates (Model 3) attenuated associations but all measures of motor function remained associated with mortality. The associations were stronger when follow-up was shorter, for example the HR for walking speed was 0.82 (95% CI, 0.75 to 0.90) when assessed in 2007-2009 and 0.67 (0.56 to 0.80) when assessed in 2015-2016.

When all motor function measures were entered simultaneously in the Cox regression (**eTable 2),** only walking speed was associated with mortality at all waves in the fully adjusted analyses (HR 0.88 (0.80 to 0.97), HR 0.80 (0.70 to 0.91), and HR 0.78 (0.62 to 0.97) respectively). The use of inverse probability weighting to account for missing data yielded results similar to those in the main analyses (**eTable 3**). The association of motor function with mortality was similar in those with and without multimorbidity (**eTable 4**). Further adjustment for cognitive function did not alter findings (**eTable 5**).

Among the 4,606 participants with motor function data in 2007-2009 and 2012-2013 assessments (**eTable 6**), decline of one SD in walking speed (HR 1.18, 1.05 to 1.32), grip strength (HR 1.22, 1.04 to 1.42), and PCS score (HR 1.16, 1.03 to 1.29), but not timed 5 chair-rises (HR 0.93, 0.84 to 1.03), was associated with higher risk of mortality. Compared to those with no IADL/ADL limitations at these waves, participants who developed a limitation had a higher risk of mortality (HR 1.37, 1.00 to 1.87).

Retrospective trajectories of motor function over 10 years leading to death

A total of 484 deaths among 6,194 participants were recorded between the start (2007-2009 wave of data collection) and end of follow-up (31st December 2017). The end of follow-up in these analyses was earlier than that in the Cox regression in order to restrict deaths contiguous to the last measure of motor function. Characteristics of these participants (**eTable 7**) were similar to those in participants included in the time to event analysis.

Figure 1 shows the retrospective trajectories of motor function over the ten years before death in decedents and before 31st December 2017 in those alive at this date; data are mean scores for all measures except IADL/ADL for which probabilities are presented in analyses adjusted for all covariates. The accompanying differences in each of the 10 years adjusted for socio-demographic variables are shown in **eTable 8** and adjusted for all covariates in **Table 3**. In fully adjusted analyses (Model 3, **Table 3**), mean walking speed was higher in survivors compared to decedents starting at 9 years before death (difference in standardised measure: 0.21 (0.05 to 0.36)) and persisted to time 0. Grip strength in survivors was higher from 6 (0.10 (0.01 to 0.20)) to 3 years (0.09 (0.00 to 0.18)) before death.

The shape of the overall 10-year trajectory (**Table 3**) was similar in survivors and decedents for both walking speed (p for interaction between vital status and time terms=0.20) and grip strength (p=0.50). The time for completion of 5 chair-rises was lower in survivors at year 10 (-0.35 (-0.59 to -0.12)) and the difference with decedents increased steadily with approach to time 0 (p<0.001). The PCS score was higher in survivors starting from year 7 (0.15 (0.05 to 0.25)) and increased over the period to time 0 (p <0.001). The probability of having an IADL/ADL limitation was lower in survivors started from year 4 (-0.02 (-0.04 to 0.00) with an increasing divergence to year 0 (p=0.04). Further examination of IADL and ADL limitations separately (**eTable 9**) suggested that differences between survivors and decedents were due to ADL limitations. Adjustment for cognitive function did not alter the main findings (**eTable 10**).

DISCUSSION

This study of repeated measures of objective and self-reported motor function spanning 10 years before death presents two key findings. One, time to event analysis showed all motor function measures, mean age at assessment being 65, 69, and 72 years, to be associated with mortality with stronger associations with later life measures of motor function. Two, trajectories of motor function over 10 years using a backward time scale showed divergence, or terminal decline, in timed chair rises, physical component summary score (SF-36), and ADL/IADL limitations starting 10, 7, and 4 years before death respectively. Given the definition of terminal decline as accelerated decline in functioning before death,[9] or specifically divergence in trajectories of function, our results suggest important differences in terminal decline as a function of specific measures of motor function. The difference between survivors and decedents in mean walking speed (from year 9 to year 0) and grip strength (from year 6 to year 3) did not change in the period leading to death. Difference in retrospective trajectories were largest for timed 5 chair-rises and smallest for grip strength; the increase in differences in the period leading to death was 4.7 fold in PCS, 4.5-fold in ADL/IADL limitations, and 2.3 fold in timed 5 chair-rises.

Use of the terminal decline framework allows better understanding of the relationship between motor function and mortality due to assessment of within-person changes[9 28 29] in motor function. Time-to-event analysis identifies the relevance of specific motor function measures and the HR estimates reflect between- rather than within-person differences in motor function. The originality of our approach is the use of retrospective trajectories, anchored to the date of death, so that distance to death is the same in those who died in comparisons of motor function with survivors. Increase in heterogeneity in individual trajectories is a hallmark of ageing;[5 6] our analysis shows this heterogeneity to be meaningfully associated with mortality.

Strengths and limitations

This study adds to the sparse literature on terminal decline in motor function and, to our knowledge, is the first to examine terminal and age-related long-term trajectories of multiple measures of motor function. The main strength of the study is the use of a twin approach, with modelling of trajectories along with Cox regression.

The use of multiple measures of motor function, both objective and self-reported measures is a further strength. The ability to consider a range of covariates in the analysis, including health behaviours, BMI and several chronic diseases, ensures that results are not driven by a certain behavioural or health profile.

The study findings need to be considered in light of some limitations. First, we were not able to examine trajectories of motor function separately by cause of death due to small number of deaths in categories of major causes of death. There is some evidence to suggest that the pattern of terminal decline differs according to cause of death.[30,31] Second, our findings are based on participants in early old age and may not be generalizable to deaths in the 9th and 10th decade of life. Third, although a wide range of chronic conditions and health behaviours were included as covariates it is likely that acute events, such as falls or hospitalizations, also affect motor function trajectories. Fourth, data are based on an occupational cohort at recruitment and participants were healthier than the general population, in terms of risk factors levels and incidence of disease. However, this does not necessarily affect risk factor-disease associations.[32] For example, the associations of walking speed with mortality risk factors in Whitehall II, such as smoking, obesity, hypertension and diabetes are comparable to those found in 21 other cohort studies[33,34] and the association between cardiovascular risk factors and CVD incidence in the Whitehall II study is similar to that in general population studies.[33] Fifth, the ethnicity distribution in the study reflects the UK population 30 years ago and the study lacks sufficient numbers to allow analyses in specific minority groups.

Comparison with previous studies

The overall results from time to event analyses in the present study are consistent with the existing literature, despite differences in the manner in which motor function was considered in the analysis. A meta-analysis that compared the lowest to highest quartile of performance found grip strength (HR: 1.67), walking speed (HR: 2.87) and chair rises (HR: 1.96) to be associated with higher risk of mortality.[35] Most studies in the meta-analysis had a short follow-up, and were based on participants older than 70 at baseline; the exception was grip strength where a wider range of data were available and these studies show stronger associations with a shorter follow-up.[35] Another pooled analysis of 9 cohort studies, mean age of participants 73.5 years and mean follow-up 12.2 years, reported walking speed to be associated with mortality.[36] In the present study, repeat assessments of motor function show stronger associations when the follow-up was shorter, particularly for ADL/IADL limitations.

The association of self-reported measures of motor function with mortality has mostly been examined using limitations in ADL in older adults, where it has a robust association with mortality,[37-39] with follow-up ranging from 1 to more than 15 years. The evidence on physical functioning scales such as the PCS score from SF-36 is more limited; a recent meta-analysis on 4 studies with a mean follow-up of 1.8 years showed associations with mortality (odds ratio for 1 unit increase: 0.95; $p < 0.001$).[40] In the present study, both these self-reported measures were associated with mortality, irrespective of the age at assessment. As with the objective motor function measures, the hazard ratio of associations with mortality were higher when self-reported function was assessed closer to death.

Studies with repeat measures of motor function have shown change in walking speed[41] and grip strength in older adults to be associated with mortality in Cox regression.[42 43] In the present study, analysis of change in motor function between 2007-2009 and 2012-2013 found change in both objective (walking speed, grip strength) and self-reported (physical component summary score and limitations in ADL/IADL) motor function to be associated with mortality (**eTable 6**). However, this approach provides only a mean hazard ratio over the follow-up, which could vary from a few months to several years, rather than change in motor function in the years leading to death. A notable study on “fast” walking speed used a 10-year backwards time scale to show more rapid decline in decedents compared to survivors but the authors did not undertake a formal comparison of differences in walking speed in the years leading to death.[18] Previous studies have examined terminal decline in ADL limitations over the last few months or years before death.[31 44 45] Our data show differences in ADL/IADL limitations to be evident 8 years and 4 years before death (**eTable 9**) in analyses unadjusted for chronic conditions and fully adjusted respectively. Terminal decline in PCS score, a measure of overall physical functioning, bodily pain, and vitality,[24] is rarely examined and our results on divergence in trajectories 4 years before death in fully adjusted analyses suggests the usefulness of this measure to monitor motor function.

Meaning of the study

There is increasing interest in objective measures of motor function, reflected in instruments such as the Short Physical Performance Battery (SPPB),[46] composed of timed tests of standing balance, walking speed, and chair rises. Performance on this battery has a robust association with mortality[19]. In the present study, we chose to examine the association of objective and subjective measures of motor function, considering each measure separately as use of composite does not allow conclusions to be drawn on the importance of each component as results could be driven by one component or all measures might make a similar contribution. Further, the SPPB does not include self-reported measures which are easier to measure. It has been suggested that measures of upper body function, assessed using a handheld dynamometer, would add to the performance battery[47] but our data do not show substantial differences or terminal decline in grip strength. Our findings also highlight the importance of self-reported measures of motor function.

Motor function is controlled by central and peripheral structures in the nervous system, which include skeletal muscles and neural connections with muscle tissues. Decline in motor function preceding death is likely to be related to disease,[48] anomalies in the physiological mechanisms of ageing,[49] quantitative and qualitative changes in muscles,[50] and more fundamental changes in mitochondria that contribute to accelerated ageing.[51] Chronic diseases are thought to be important drivers of motor decline; in the present study, adding the multimorbidity score to the analysis attenuated the associations in both time-to-event and backward trajectories analyses. The importance of chronic diseases might be due to processes of chronic inflammation and oxidative stress; these are likely to operate across the lifecourse[52] as demonstrated by diverging motor function trajectories prior to death in early old age in our study. However, in our analyses the association between motor function and mortality was also observed in participants free of multimorbidity .

CONCLUSION

The ageing of populations worldwide makes it important to understand functional status of older adults and change in functioning with age. Research on terminal decline is primarily on cognitive function,[10] and when studies examine motor function the focus in on ADL limitations in the last few years of life. Our analysis of trajectories over 10 years in early old age show the importance of objective and subjective measures of motor function. These results suggest that strategies to address accelerated decline should start prior to old age, early detection of changes in motor function might offer opportunities for prevention and targeted interventions.

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Conflict of interest disclosures

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Contributor and guarantor information: BL, SS, ASM and AF developed the hypothesis and study design. BL and AF performed the statistical analysis. BL wrote the first and successive drafts of the manuscript. All authors conceived and designed the study, analyzed and interpreted the data, and drafted or critically revised the manuscript for important intellectual content, or, in addition, acquired data. ASM and MK obtained funding for the Whitehall II study. B and AF had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis. BL is the guarantor. The corresponding author attests that all listed authors meet authorship criteria.

Data sharing: Data, protocols, and other metadata of the Whitehall II study are available to the scientific community either via the Whitehall II study data sharing portal (www.ucl.ac.uk/whitehallII/ data-sharing) or the DPUK platform (https://www.dementiasplatform.uk/).

Transparency: The lead author (BL) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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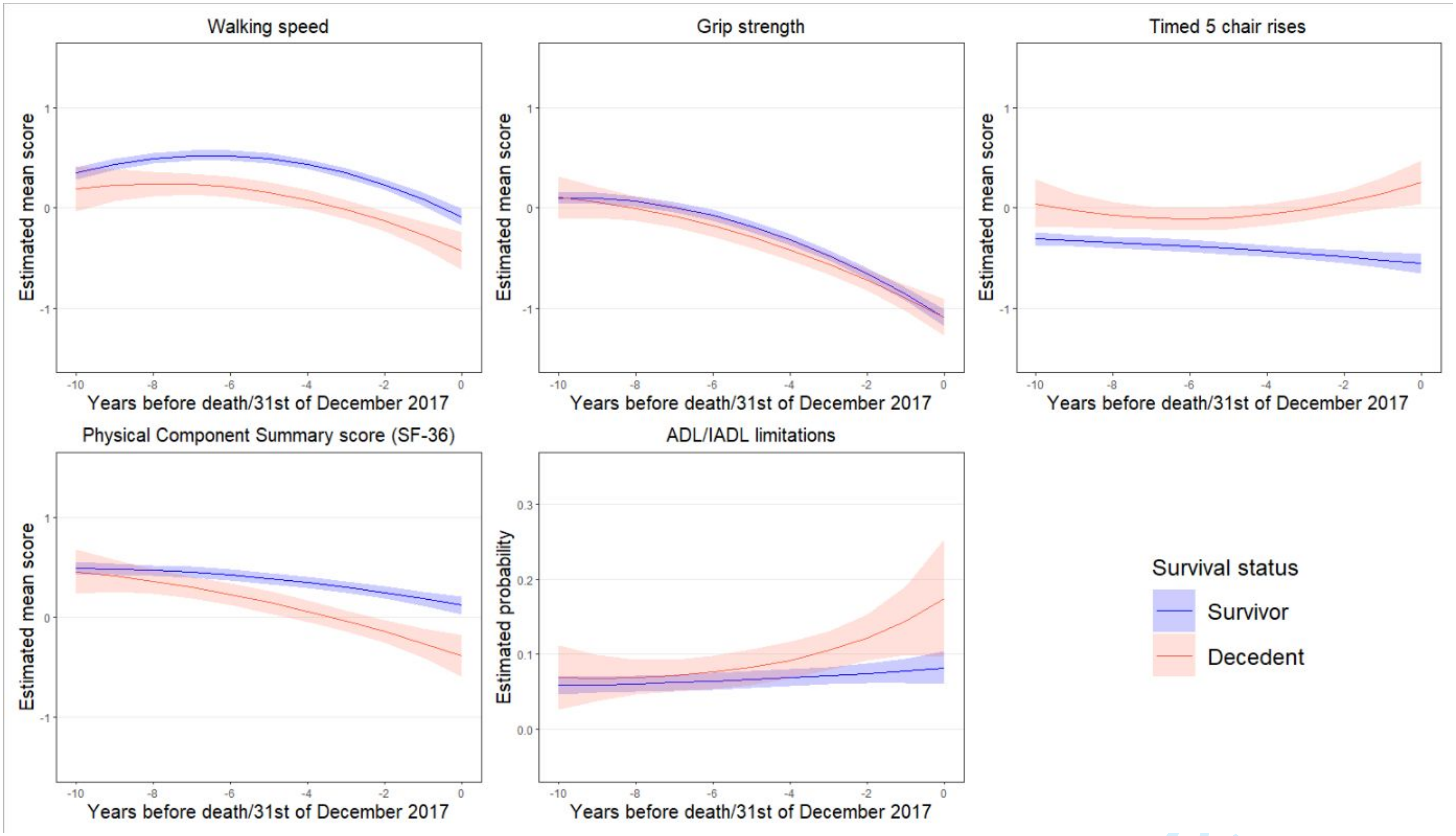
Figure 1. Trajectories of motor function over the 10 years before death (decedents, N=484) and end of follow-up (survivors, N=5,710).[a,b]



[a]Estimated mean scores from linear mixed models and estimated probability from logistic regression with generalized estimated equations. Analyses adjusted for age at year 0, sex, ethnicity, marital status, occupational position, vital status, time terms (time & time^2), interactions of these covariates with time terms, and health behaviours, BMI categories and 9-point multimorbidity score at motor function measurement.

[b]Higher scores on walking speed, grip strength, and the SF-36 PCS score reflect better motor function, the contrary is true for timed 5 chair-rises and ADL/IADL limitations.

Table 1. Population characteristics in 2007-2009 by survival status at the end of the follow-up (October 2019).

		Vital status at October 2019	
	Total	**Decedents**	**Survivors**
	(N = 5,645)	(N = 610)	(N = 5,035)
Age, M (SD)	65.6 (5.9)	69.7 (5.8)	65.1 (5.9)
Women	1,539 (27.3)	152 (24.9)	1,387 (27.5)
White	5,244 (92.9)	570 (93.4)	4,674 (92.8)
Married/Cohabiting	4,263 (75.5)	417 (68.4)	3,846 (76.4)
High socioeconomic position	2,476 (43.9)	239 (39.2)	2,237 (44.4)
Moderate alcohol consumption	2,901 (51.4)	277 (45.4)	2,624 (48.2)
Never smoker	2,722 (48.2)	249 (40.8)	2,473 (49.1)
Daily fruit & vegetable consumption	2,267 (40.2)	238 (39.0)	2,029 (40.3)
Physical activity at recommended levels	3,236 (57.3)	304 (49.8)	2,932 (58.2)
Motor function[a]			
Walking speed (cm/s), M (SD)	110.6 (26.7)	101.1 (28.2)	111.8 (26.2)
Grip strength (kg), M (SD)	38.0 (10.6)	35.3 (10.5)	38.4 (10.6)
Timed 5 chair-rises (s), M (SD)	11.3 (3.4)	12.4 (4.2)	11.1 (3.3)
SF-36 PCS score, M (SD)	48.8 (8.7)	45.3 (10.0)	49.2 (8.4)
Limitations in ADL or IADL	860 (15.2)	147 (24.1)	713 (14.2)
Chronic conditions			
Diabetes	541 (9.6)	83 (13.6)	458 (9.1)
Coronary Heart Disease	1,167 (20.7)	197 (32.3)	970 (19.3)
Stroke	216 (3.8)	60 (9.8)	156 (3.1)
Cancer	436 (7.7)	105 (17.2)	331 (6.6)
Dementia	7 (0.1)	3 (0.5)	4 (0.1)
Parkinson's disease	20 (0.4)	7 (1.1)	13 (0.3)
Chronic Obstructive Pulmonary Disease	47 (0.8)	16 (2.6)	31 (0.6)
Depression	561 (9.9)	69 (11.3)	492 (9.8)
Arthritis	496 (8.8)	68 (11.1)	428 (8.5)
BMI, M (SD)	26.7 (4.4)	27.0 (4.8)	26.7 (4.4)
Multimorbidity score[b]			
0	3,098 (54.9)	207 (33.9)	2,891 (57.4)
1	1,771 (31.4)	237 (38.9)	1,534 (30.5)
2 or more	776 (13.8)	166 (27.2)	610 (12.1)

Abbreviations: M, mean; SD, standard deviation; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.
Data are N (%) unless stated otherwise.

[a]Higher scores on walking speed, grip strength, and the physical component summary score reflect better motor function, the contrary is true for timed 5 chair-rises and ADL/IADL limitations.
[b]The score is composed of the chronic conditions listed above.

Table 2. Association between standardized measures of motor function and subsequent mortality.

	Model 1	Model 2	Model 3
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Motor function in 2007-2009[a]			
N mortality/N total = 610/5,645; Mean (SD) age, 65.6 (5.9) years; Mean (SD) follow-up, 10.6 (1.8) years			
Walking speed	0.76 (0.70 to 0.83)*	0.78 (0.72 to 0.85)*	0.82 (0.75 to 0.90)*
Grip strength	0.82 (0.76 to 0.89)*	0.84 (0.77 to 0.92)*	0.87 (0.80 to 0.94)*
Timed 5 chair-rises[b]	1.21 (1.13 to 1.30)*	1.19 (1.11 to 1.28)*	1.14 (1.07 to 1.23)*
SF-36 PCS score	0.77 (0.72 to 0.82)*	0.79 (0.74 to 0.85)*	0.86 (0.79 to 0.92)*
Limitations in ADL or IADL[b]	1.59 (1.31 to 1.91)*	1.49 (1.23 to 1.80)*	1.30 (1.07 to 1.58)*
Motor function in 2012-2013[a]			
N mortality/N total = 359/5,083; Mean (SD) age, 69.3 (5.7) years; Mean (SD) follow-up, 6.8 (1.0) years			
Walking speed	0.66 (0.59 to 0.75)*	0.69 (0.61 to 0.78)*	0.73 (0.64 to 0.82)*
Grip strength	0.83 (0.74 to 0.92)*	0.84 (0.76 to 0.94)*	0.87 (0.78 to 0.98)*
Timed 5 chair-rises[b]	1.28 (1.19 to 1.38)*	1.26 (1.16 to 1.36)*	1.20 (1.11 to 1.31)*
SF-36 PCS score	0.76 (0.70 to 0.83)*	0.79 (0.73 to 0.87)*	0.86 (0.78 to 0.94)*
Limitations in ADL or IADL[b]	1.71 (1.36 to 2.14)*	1.60 (1.27 to 2.01)*	1.38 (1.09 to 1.74)*
Motor function in 2015-2016[a]			
N mortality/N total = 150/4,440; Mean (SD) age, 72.1 (5.6) years; Mean (SD) follow-up, 3.7 (0.6) years			
Walking speed	0.59 (0.50 to 0.70)*	0.60 (0.50 to 0.71)*	0.67 (0.56 to 0.80)*
Grip strength	0.74 (0.62 to 0.88)*	0.75 (0.63 to 0.89)*	0.78 (0.65 to 0.92)*
Timed 5 chair-rises[b]	1.25 (1.15 to 1.35)*	1.24 (1.14 to 1.34)*	1.16 (1.06 to 1.27)*
SF-36 PCS score	0.71 (0.63 to 0.81)*	0.72 (0.63 to 0.82)*	0.82 (0.71 to 0.93)*
Limitations in ADL or IADL[b]	2.13 (1.52 to 3.00)*	2.08 (1.47 to 2.93)*	1.58 (1.11 to 2.27)*

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; HR: Hazard ratio; CI: Confidence interval; SF-36: Short Form 36 General Health Survey.
[a]Standardized using mean and SD from 2007-2009, separately in men and women, for all tests except “limitations in ADL or IADL” which was dichotomized using 1 or more limitations.
[b]Higher values reflect poor motor function.
*$p<0.05$.
Model 1: adjusted for age, sex, ethnicity, marital status and occupational position.
Model 2: Model 1 + health behaviours.
Model 3: Model 2 + BMI categories and 9-point multimorbidity score.

Table 3: Differences in motor function between survivors and decedents in the 10 years preceding death, N mortality/N total = 484/6,194.[a,b]

Years preceding death	OBJECTIVE MEASURES						SELF-REPORTED MEASURES			
	Walking speed		Grip strength		Timed 5 chair-rises		SF-36 PCS score		ADL/IADL limitations	
	Difference in mean (95% CI)	*p*	Difference in mean (95% CI)	*p*	Difference in mean (95% CI)	*p*	Difference in mean (95% CI)	*p*	Difference in probabilities (95% CI)	*P*
-10	0.16 (-0.06 to 0.38)	0.16	0.00 (-0.21 to 0.20)	0.98	-0.35 (-0.59 to -0.12)	0.003	0.03 (-0.19 to 0.25)	0.78	-0.01 (-0.05 to 0.03)	0.61
-9	0.21 (0.05 to 0.36)	0.01	0.04 (-0.11 to 0.18)	0.62	-0.30 (-0.46 to -0.14)	<0.001	0.07 (-0.09 to 0.22)	0.39	-0.01 (-0.03 to 0.02)	0.54
-8	0.25 (0.14 to 0.37)	<0.001	0.07 (-0.04 to 0.18)	0.23	-0.27 (-0.39 to -0.15)	<0.001	0.11 (-0.01 to 0.22)	0.05	-0.01 (-0.03 to 0.01)	0.44
-7	0.29 (0.19 to 0.38)	<0.001	0.09 (-0.01 to 0.19)	0.07	-0.26 (-0.36 to -0.16)	<0.001	0.15 (0.05 to 0.25)	0.003	-0.01 (-0.02 to 0.01)	0.32
-6	0.32 (0.22 to 0.41)	<0.001	0.10 (0.01 to 0.20)	0.04	-0.27 (-0.37 to -0.17)	<0.001	0.19 (0.09 to 0.29)	<0.001	-0.01 (-0.03 to 0.01)	0.21
-5	0.34 (0.25 to 0.43)	<0.001	0.11 (0.01 to 0.21)	0.03	-0.31 (-0.41 to -0.20)	<0.001	0.24 (0.14 to 0.34)	<0.001	-0.01 (-0.03 to 0.00)	0.10
-4	0.35 (0.27 to 0.44)	<0.001	0.10 (0.01 to 0.20)	0.03	-0.36 (-0.46 to -0.26)	<0.001	0.29 (0.19 to 0.38)	<0.001	-0.02 (-0.04 to 0.00)	0.03
-3	0.36 (0.28 to 0.45)	<0.001	0.09 (0.00 to 0.18)	0.05	-0.44 (-0.54 to -0.34)	<0.001	0.34 (0.24 to 0.43)	<0.001	-0.03 (-0.05 to -0.01)	0.002
-2	0.36 (0.27 to 0.45)	<0.001	0.07 (-0.03 to 0.16)	0.17	-0.54 (-0.65 to -0.44)	<0.001	0.39 (0.29 to 0.49)	<0.001	-0.04 (-0.07 to -0.02)	<0.001
-1	0.36 (0.24 to 0.48)	<0.001	0.04 (-0.09 to 0.16)	0.57	-0.67 (-0.81 to -0.52)	<0.001	0.45 (0.31 to 0.58)	<0.001	-0.06 (-0.10 to -0.02)	0.001
0	0.35 (0.17 to 0.52)	<0.001	-0.01 (-0.18 to 0.17)	0.95	-0.81 (-1.02 to -0.61)	<0.001	0.51 (0.31 to 0.70)	<0.001	-0.09 (-0.16 to -0.02)	0.01
Difference in trajectories	**0.20**		**0.50**		**<0.001**		**<0.001**		**0.04**	

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; CI: Confidence Interval; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey.

[a]Higher differences in walking speed, grip strength, and the SF-36 PCS score reflect better motor function among survivors than decedents, the contrary is true for timed 5 chair-rises and ADL/IADL limitations.

[b]Estimated from linear mixed models except ADL/IADL limitations where logistic regression with generalized estimated equation models were used; analyses adjusted for age at year 0, sex, ethnicity, marital status, occupational position, vital status, time terms (time & time²), interactions of sociodemographic covariates with time terms, and health behaviours, BMI categories and 9-point multimorbidity score assessed at motor function measurement.

Terminal decline in objective and self-reported measures of motor function over 10-years before death: results from the Whitehall II cohort study

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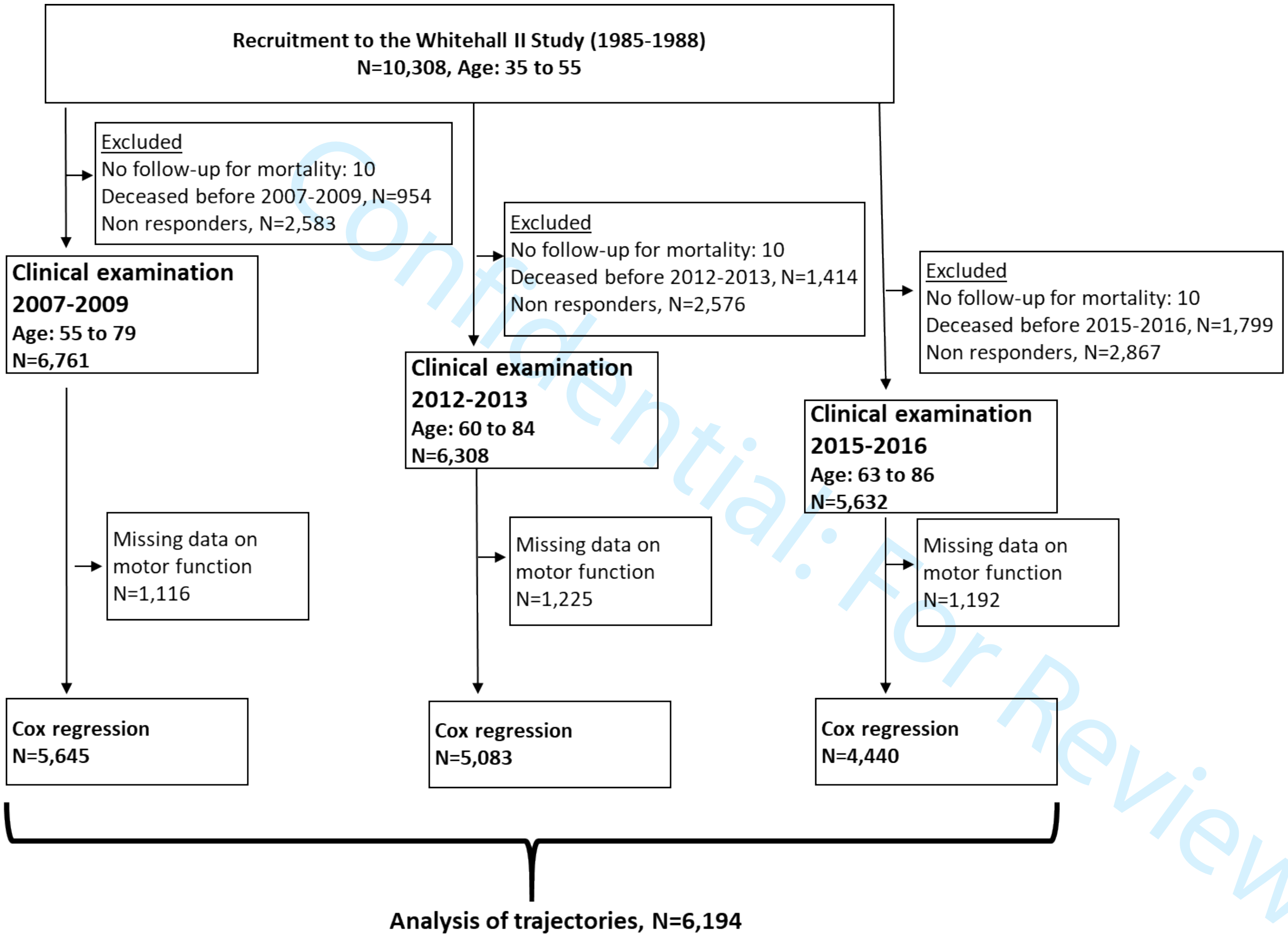
SUPPLEMENTAL DATA

eFigure 1. Flow-chart of the study.



eTable 1. Correlation matrix of measures of motor function.

	Walking speed	Grip strength	Timed 5 chair-rises	SF-36 PCS score
Walking speed	x			
Grip strength	0.29	x		
Timed 5 chair-rises	-0.34	-0.22	x	
SF-36 PCS score	0.35	0.21	-0.35	x

Abbreviation: SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey.

eTable 2. Association between motor function and mortality in mutually adjusted models.

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Motor function in 2007-2009[a]			
Walking speed	0.86 (0.78 to 0.94)*	0.87 (0.79 to 0.95)*	0.88 (0.80 to 0.97)*
Grip strength	0.90 (0.82 to 0.98)*	0.90 (0.83 to 0.98)*	0.92 (0.84 to 1.00)
Timed 5 chair-rises[b]	1.09 (1.01 to 1.17)*	1.08 (1.00 to 1.17)*	1.07 (0.99 to 1.16)
SF-36 PCS score	0.85 (0.78 to 0.93)*	0.87 (0.79 to 0.94)*	0.92 (0.84 to 1.01)
Limitations in ADL or IADL[b]	1.09 (0.87 to 1.37)	1.08 (0.87 to 1.36)	1.07 (0.85 to 1.34)
Motor function in 2012-2013[a]			
Walking speed	0.79 (0.69 to 0.90)*	0.80 (0.70 to 0.91)*	0.80 (0.70 to 0.91)*
Grip strength	0.92 (0.83 to 1.03)	0.92 (0.82 to 1.03)	0.94 (0.84 to 1.05)
Timed 5 chair-rises[b]	1.14 (1.03 to 1.25)*	1.14 (1.03 to 1.25)*	1.12 (1.02 to 1.23)*
SF-36 PCS score	0.88 (0.79 to 0.99)*	0.91 (0.81 to 1.01)	0.95 (0.85 to 1.07)
Limitations in ADL or IADL[b]	1.11 (0.84 to 1.46)	1.10 (0.83 to 1.45)	1.06 (0.80 to 1.40)
Motor function in 2015-2016[a]			
Walking speed	0.76 (0.62 to 0.94)*	0.76 (0.61 to 0.94)*	0.78 (0.62 to 0.97)*
Grip strength	0.84 (0.70 to 1.00)*	0.83 (0.70 to 0.99)*	0.85 (0.71 to 1.01)
Timed 5 chair-rises[b]	1.10 (0.99 to 1.22)	1.10 (0.99 to 1.22)	1.07 (0.96 to 1.19)
SF-36 PCS score	0.88 (0.74 to 1.04)	0.88 (0.74 to 1.04)	0.96 (0.81 to 1.14)
Limitations in ADL or IADL[b]	1.28 (0.83 to 1.96)	1.29 (0.84 to 1.97)	1.20 (0.78 to 1.83)

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; HR: Hazard ratio; CI: Confidence interval.

[a]Standardized using mean and SD from 2007-2009, separately in men and women, for all tests except "limitations in ADL or IADL" which was dichotomized using 1 or more limitations.

[b]Higher values reflected poor motor function.

*p<0.05.

Model 1: adjusted for age, sex, ethnicity, marital status and occupational position.

Model 2: Model 1 + health behaviours.

Model 3: Model 2 + BMI categories and 9-point multimorbidity score.

eTable 3. Association between standardized measures of motor function and subsequent mortality, using inverse probability weighting to account for missing data.

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Motor function in 2007-2009[a]			
Walking speed	0.73 (0.66 to 0.80)*	0.75 (0.68 to 0.82)*	0.79 (0.72 to 0.87)*
Grip strength	0.81 (0.74 to 0.88)*	0.83 (0.76 to 0.91)*	0.85 (0.78 to 0.93)*
Timed 5 chair-rises[b]	1.20 (1.12 to 1.29)*	1.18 (1.10 to 1.27)*	1.13 (1.05 to 1.22)*
SF-36 PCS score	0.77 (0.72 to 0.83)*	0.80 (0.74 to 0.86)*	0.86 (0.79 to 0.93)*
Limitations in ADL or IADL[b]	1.63 (1.34 to 1.98)*	1.54 (1.27 to 1.87)*	1.36 (1.11 to 1.66)*
Motor function in 2012-2013[a]			
Walking speed	0.66 (0.57 to 0.75)*	0.68 (0.60 to 0.78)*	0.72 (0.62 to 0.82)*
Grip strength	0.83 (0.74 to 0.94)*	0.85 (0.76 to 0.96)*	0.88 (0.78 to 0.99)*
Timed 5 chair-rises[b]	1.27 (1.18 to 1.36)*	1.25 (1.16 to 1.34)*	1.20 (1.12 to 1.30)*
SF-36 PCS score	0.77 (0.71 to 0.85)*	0.80 (0.73 to 0.88)*	0.87 (0.78 to 0.96)*
Limitations in ADL or IADL[b]	1.73 (1.36 to 2.19)*	1.61 (1.27 to 2.04)*	1.39 (1.10 to 1.76)*
Motor function in 2015-2016[a]			
Walking speed	0.56 (0.46 to 0.67)*	0.56 (0.46 to 0.67)*	0.63 (0.52 to 0.76)*
Grip strength	0.73 (0.60 to 0.88)*	0.73 (0.60 to 0.89)*	0.76 (0.63 to 0.92)*
Timed 5 chair-rises[b]	1.24 (1.15 to 1.34)*	1.24 (1.14 to 1.34)*	1.17 (1.06 to 1.28)*
SF-36 PCS score	0.71 (0.63 to 0.81)*	0.72 (0.63 to 0.82)*	0.82 (0.71 to 0.95)*
Limitations in ADL or IADL[b]	2.01 (1.41 to 2.87)*	1.97 (1.38 to 2.82)*	1.47 (1.02 to 2.13)*

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; HR: Hazard ratio; CI: Confidence interval.
[a]Standardized using mean and SD from 2007-2009, separately in men and women, for all tests except "limitations in ADL or IADL" which was dichotomized using 1 or more limitations.
[b]Higher values reflected poor motor function.
*p<0.05.
Model 1: adjusted for age, sex, ethnicity, marital status and occupational position.
Model 2: Model 1 + health behaviours.
Model 3: Model 2 + BMI categories and 9-point multimorbidity score.

eTable 4. Association between standardized measures of motor function and subsequent mortality as a function of multimorbidity status at assessment of motor function.

	Participants without multimorbidity[c] HR (95% CI)	**Participants with multimorbidity[c]** HR (95% CI)
Motor function in 2007-2009[a]		
N mortality/N total	444/4869	166/776
Walking speed	0.81 (0.73 to 0.90)*	0.81 (0.68 to 0.96)*
Grip strength	0.91 (0.79 to 1.04)	0.83 (0.71 to 0.98)*
Timed 5 chair-rises[b]	1.20 (1.10 to 1.30)*	1.10 (0.95 to 1.27)
SF-36 PCS score	0.80 (0.73 to 0.87)*	0.89 (0.78 to 1.01)
Limitations in ADL or IADL[b]	1.23 (0.96 to 1.57)	1.62 (1.16 to 2.25)*
Motor function in 2012-2013[a]		
N mortality/N total	228/4204	131/879
Walking speed	0.73 (0.63 to 0.85)*	0.69 (0.56 to 0.83)*
Grip strength	0.87 (0.79 to 0.96)*	0.81 (0.67 to 0.96)*
Timed 5 chair-rises[b]	1.26 (1.12 to 1.43)*	1.19 (1.06 to 1.34)*
SF-36 PCS score	0.83 (0.73 to 0.94)*	0.85 (0.73 to 0.98)*
Limitations in ADL or IADL[b]	1.37 (1.00 to 1.87)*	1.55 (1.08 to 2.22)*
Motor function in 2015-2016[a]		
N mortality/N total	74/3569	76/871
Walking speed	0.78 (0.59 to 1.03)	0.57 (0.44 to 0.73)*
Grip strength	0.78 (0.61 to 1.00)	0.75 (0.59 to 0.96)*
Timed 5 chair-rises[b]	1.34 (1.14 to 1.58)*	1.15 (1.02 to 1.29)*
SF-36 PCS score	0.79 (0.64 to 0.97)*	0.79 (0.66 to 0.95)*
Limitations in ADL or IADL[b]	1.37 (0.77 to 2.42)	1.97 (1.21 to 3.20)*

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; HR: Hazard ratio; CI: Confidence interval.
[a]Standardized using mean and SD from 2007-2009, separately in men and women, for all tests except “limitations in ADL or IADL” which was dichotomized using 1 or more limitations.
[b]Higher values reflected poor motor function.
[c]Chronic conditions considered were: diabetes, coronary heart disease, stroke, cancer, dementia, Parkinson’s disease, chronic obstructive pulmonary disease, depression, and arthritis; analyses adjusted for age, sex, ethnicity, marital status and occupational position, health behaviours, and BMI categories.
*p<0.05.

eTable 5. Association between standardized measures of motor function and subsequent mortality, with additional adjustment for global cognition (Mini Mental State Examination).

	Adjusted for all covariates[C] HR (95% CI)
Motor function in 2007-2009[a]	
N mortality/N total = 591/5,501; Mean (SD) age, 65.6 (5.9) years; Mean (SD) follow-up, 10.6 (1.8) years	
Walking speed	0.83 (0.76 to 0.91)*
Grip strength	0.87 (0.80 to 0.95)*
Timed 5 chair-rises[b]	1.15 (1.07 to 1.23)*
SF-36 PCS score	0.86 (0.79 to 0.93)*
Limitations in ADL or IADL[b]	1.31 (1.07 to 1.59)*
Motor function in 2012-2013[a]	
N mortality/N total = 349/4,956; Mean (SD) age, 69.4 (5.8) years; Mean (SD) follow-up, 6.8 (1.0) years	
Walking speed	0.73 (0.64 to 0.82)*
Grip strength	0.88 (0.79 to 0.98)*
Timed 5 chair-rises[b]	1.19 (1.09 to 1.29)*
SF-36 PCS score	0.85 (0.78 to 0.94)*
Limitations in ADL or IADL[b]	1.35 (1.07 to 1.72)*
Motor function in 2015-2016[a]	
N mortality/N total = 145/4,405; Mean (SD) age, 72.1 (5.6) years; Mean (SD) follow-up, 3.7 (0.6) years	
Walking speed	0.74 (0.61 to 0.89)*
Grip strength	0.82 (0.68 to 0.98)*
Timed 5 chair-rises[b]	1.13 (1.02 to 1.25)*
SF-36 PCS score	0.84 (0.73 to 0.96)*
Limitations in ADL or IADL[b]	1.40 (0.96 to 2.03)

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; HR: Hazard ratio; CI: Confidence interval.
[a]Standardized using mean and SD from 2007-2009, separately in men and women, for all tests except "limitations in ADL or IADL" which was dichotomized using 1 or more limitations.
[b]Higher values reflected poor motor function.
[C]Models adjusted for age, sex, ethnicity, marital status and occupational position, health behaviours, BMI categories, 9-point multimorbidity score, and the Mini Mental State Examination score.
*p<0.05.

eTable 6. Association of change in motor function between 2007-2009 and 2012-2013[a] and subsequent mortality.

	Model 1 HR (95% CI)	**Model 2** HR (95% CI)	**Model 3** HR (95% CI)
N mortality/N total = 316/4,606; Mean (SD) age, 68.4 (5.7) years; Mean (SD) follow-up, 7.0 (1.0) years			
Walking speed	1.20 (1.06 to 1.34)*	1.19 (1.06 to 1.34)*	1.18 (1.05 to 1.32)*
Grip strength	1.24 (1.06 to 1.45)*	1.24 (1.06 to 1.45)*	1.22 (1.04 to 1.42)*
Timed 5 chair-rises[b]	0.90 (0.81 to 1.00)*	0.91 (0.81 to 1.01)	0.93 (0.84 to 1.03)
SF-36 PCS score	1.19 (1.06 to 1.33)*	1.16 (1.04 to 1.30)*	1.16 (1.03 to 1.29)*
Limitations in ADL or IADL			
No limitations at both waves (N mortality/N total = 202/3,567)	Ref.	Ref.	Ref.
No limitations to 1 or more limitations (N mortality/N total = 50/406)	1.62 (1.19 to 2.21)*	1.52 (1.11 to 2.08)*	1.37 (1.00 to 1.87)*
1 or more limitations to no limitations (N mortality/N total = 46/353)	1.18 (0.73 to 1.92)	1.13 (0.70 to 1.84)	0.99 (0.61 to 1.61)
1 or more limitations at both waves (N mortality/N total = 18/280)	1.74 (1.26 to 2.40)*	1.61 (1.16 to 2.24)*	1.32 (0.95 to 1.85)

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; HR: Hazard ratio; CI: Confidence interval.

[a]Both 2007-2009 and 2013-2013 measures were standardized using mean and SD from 2007-2009, separately in men and women, so that estimates represent HRs associated with decrease between 2007-2009 and 2012-2013 of 1SD of the respective motor function measures for all tests except "limitations in ADL or IADL" which was dichotomized using 1 or more limitations.

[b]Higher values reflected lower decline in motor function.

*p<0.05.

Model 1: adjusted for age, sex, ethnicity, marital status and occupational position.

Model 2: Model 1 + health behaviours.

Model 3: Model 2 + BMI categories and 9-point multimorbidity score.

eTable 7. Population characteristics in 2007-2009 by survival status at time 0 in the retrospective time scale in the analysis (date of death or 31st of December 2017).

		Vital status, 31st December 2017	
	Total (N= 5,645)	**Decedents** (N = 458)	**Survivors** (N = 5,187)
Age, M (SD)	65.6 (5.9)	69.7 (6.0)	65.3 (5.7)
Women	1,539 (27.3)	111 (24.2)	1,428 (27.5)
White ethnicity	5,244 (92.9)	430 (93.9)	4,814 (92.8)
Living in couple	4,263 (75.5)	311 (67.9)	3,952 (76.2)
High socioeconomic position	2,476 (43.9)	177 (38.6)	2,299 (44.3)
Moderate alcohol consumption	2,901 (51.4)	212 (46.3)	2,689 (51.8)
Never smoker	2,722 (48.2)	198 (43.2)	2,524 (48.7)
Daily fruit & vegetable consumption	2,267 (40.2)	183 (40.0)	2,084 (40.2)
Physical activity at recommended levels	3,236 (57.3)	226 (49.3)	3.010 (58.0)
Motor function[a]			
Walking speed (cm/s), M (SD)	110.6 (26.7)	101.2 (28.2)	111.5 (26.3)
Grip strength (kg), M (SD)	38.0 (10.6)	35.1 (10.5)	38.3 (10.6)
Timed 5 chair-rises (s), M (SD)	11.3 (3.4)	12.5 (4.3)	11.2 (3.3)
SF-36 PCS score	48.8 (8.7)	45.2 (10.1)	49.1 (8.5)
Limitations in ADL or IADL	860 (15.2)	109 (23.8)	751 (14.5)
Chronic conditions			
Diabetes	541 (9.6)	58 (12.7)	483 (9.3)
Coronary Heart Disease	1,167 (20.7)	136 (29.7)	1,031 (19.9)
Stroke	216 (3.8)	45 (9.8)	171 (3.3)
Cancer	436 (7.7)	89 (19.4)	347 (6.7)
Dementia	7 (0.1)	2 (0.4)	5 (0.1)
Parkinson's disease	20 (0.4)	6 (1.3)	14 (0.3)
Chronic Obstructive Pulmonary Disease	47 (0.8)	14 (3.1)	33 (0.6)
Depression	561 (9.9)	54 (11.8)	507 (9.8)
Arthritis	496 (8.8)	48 (10.5)	448 (8.6)
BMI, M (SD)	26.7 (4.4)	26.7 (4.7)	26.7 (4.4)
Multimorbidity score[b]			
0	3,098 (54.9)	153 (33.4)	2,945 (56.8)
1	1,771 (31.4)	181 (39.5)	1,590 (30.7)
2 or more	776 (13.8)	124 (27.1)	652 (12.3)

Abbreviations: M, mean; SD, standard deviation; SF-36: SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.
Data are N (%) unless stated otherwise.
[a]Higher scores on walking speed, grip strength, and the SF-36 PCS score reflect better motor function, the contrary is true for timed 5 chair-rises and ADL/IADL limitations.
[b]The score is composed of the nine chronic conditions listed above at the exception of obesity.

eTable 8. Differences in motor function between survivors and decedents in the 10 years preceding death in analysis adjusted only for sociodemographic variables, N mortality/N total = 484/6,194.[a,b]

	OBJECTIVE MEASURES						**SELF-REPORTED MEASURES**			
	Walking speed		**Grip strength**		**Timed 5 chair-rises**		**SF-36 PCS score**		**ADL/IADL limitations**	
Years preceding death	**Difference in mean (95% CI)**	***p***	**Difference in mean (95% CI)**	***p***	**Difference in mean (95% CI)**	***p***	**Difference in mean (95% CI)**	***p***	**Difference in probabilities (95% CI)**	***P***
-10	0.21 (-0.01 to 0.44)	0.063	0.03 (-0.17 to 0.24)	0.76	-0.41 (-0.64 to -0.17)	0.001	0.12 (-0.11 to 0.34)	0.307	-0.04 (-0.12 to 0.05)	0.39
-9	0.26 (0.10 to 0.42)	0.001	0.07 (-0.08 to 0.22)	0.36	-0.36 (-0.52 to -0.19)	< 0.001	0.16 (0.00 to 0.31)	0.054	-0.03 (-0.09 to 0.02)	0.25
-8	0.30 (0.19 to 0.42)	< 0.001	0.10 (-0.01 to 0.21)	0.09	-0.33 (-0.45 to -0.21)	< 0.001	0.20 (0.08 to 0.32)	0.001	-0.04 (-0.08 to 0.01)	0.11
-7	0.34 (0.24 to 0.44)	< 0.001	0.12 (0.02 to 0.22)	0.02	-0.32 (-0.42 to -0.22)	< 0.001	0.24 (0.14 to 0.35)	< 0.001	-0.04 (-0.08 to 0.00)	0.04
-6	0.37 (0.28 to 0.47)	< 0.001	0.14 (0.04 to 0.23)	0.007	-0.34 (-0.44 to -0.23)	< 0.001	0.29 (0.19 to 0.39)	< 0.001	-0.05 (-0.09 to -0.01)	0.02
-5	0.40 (0.30 to 0.49)	< 0.001	0.14 (0.04 to 0.24)	0.005	-0.37 (-0.48 to -0.27)	< 0.001	0.34 (0.24 to 0.45)	< 0.001	-0.06 (-0.10 to -0.02)	0.006
-4	0.41 (0.32 to 0.50)	< 0.001	0.14 (0.04 to 0.23)	0.004	-0.43 (-0.53 to -0.33)	< 0.001	0.40 (0.29 to 0.50)	< 0.001	-0.07 (-0.11 to -0.03)	0.001
-3	0.43 (0.34 to 0.51)	< 0.001	0.13 (0.04 to 0.22)	0.006	-0.51 (-0.61 to -0.41)	< 0.001	0.45 (0.35 to 0.55)	< 0.001	-0.09 (-0.13 to -0.05)	< 0.001
-2	0.43 (0.34 to 0.52)	< 0.001	0.11 (0.01 to 0.20)	0.03	-0.61 (-0.73 to -0.50)	< 0.001	0.51 (0.41 to 0.62)	< 0.001	-0.12 (-0.17 to -0.07)	< 0.001
-1	0.43 (0.31 to 0.55)	< 0.001	0.08 (-0.04 to 0.20)	0.19	-0.74 (-0.89 to -0.59)	< 0.001	0.58 (0.44 to 0.72)	< 0.001	-0.15 (-0.22 to -0.08)	< 0.001
0	0.42 (0.24 to 0.60)	< 0.001	0.05 (-0.13 to 0.22)	0.61	-0.88 (-1.10 to -0.67)	< 0.001	0.64 (0.44 to 0.84)	< 0.001	-0.19 (-0.30 to -0.08)	0.001
Difference in trajectories	**0.15**		**0.56**		**< 0.001**		**< 0.001**		**0.04**	

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; CI: Confidence interval.

[a]Higher scores on walking speed, grip strength, and the SF-36 PCS score reflect better motor function, the contrary is true for timed 5 chair-rises and ADL/IADL limitations.

[b]Estimated from linear mixed models except ADL/IADL limitations where logistic regression with generalized estimated equation models were used; analyses adjusted for age at year 0, sex, ethnicity, marital status, occupational position, vital status, time terms (time & time^2), interactions of sociodemographic covariates with time terms.

eTable 9. Difference in the probability of limitations in ADL and IADL, examined separately, between survivors and decedents in the 10 years preceding death, N mortality/N total = 484/6,194.[a]

	ADL limitations		IADL limitations	
Years preceding death	**Difference in probability (%) (95% CI)**	**p**	**Difference in probability (%) (95% CI)**	**p**
-10	0.00 (-0.03 to 0.02)	0.69	0.01 (-0.02 to 0.03)	0.57
-9	0.00 (-0.02 to 0.01)	0.55	0.00 (-0.02 to 0.02)	0.82
-8	-0.01 (-0.02 to 0.01)	0.36	0.00 (-0.02 to 0.01)	0.73
-7	-0.01 (-0.02 to 0.00)	0.20	-0.01 (-0.02 to 0.01)	0.28
-6	-0.01 (-0.02 to 0.00)	0.11	-0.01 (-0.03 to 0.00)	0.11
-5	-0.01 (-0.02 to 0.00)	0.06	-0.02 (-0.04 to 0.00)	0.06
-4	-0.02 (-0.03 to 0.00)	0.02	-0.02 (-0.04 to 0.00)	0.03
-3	-0.02 (-0.04 to -0.01)	0.002	-0.03 (-0.04 to -0.01)	0.01
-2	-0.03 (-0.05 to -0.01)	< 0.001	-0.03 (-0.05 to -0.01)	0.01
-1	-0.04 (-0.07 to -0.01)	0.003	-0.03 (-0.06 to 0.00)	0.08
0	-0.05 (-0.10 to -0.01)	0.03	-0.02 (-0.07 to 0.02)	0.31
Difference in trajectories	**0.07**		**0.30**	

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; CI: Confidence interval.
[a] Estimates from logistic regression with generalized estimated equation; analyses adjusted for age, sex, ethnicity, marital status, occupational position, vital status, time terms (time, time²), interactions of these covariates with time terms, and health behaviours, BMI categories and 9-point multimorbidity score assessed at motor function measurement.

eTable 10. Difference in motor function between survivors and decedents in the 10 years preceding death with additional adjustment for global cognition (Mini Mental State Examination), N mortality/N total = 477/6,149.[a,b]

	OBJECTIVE MEASURES						SELF-REPORTED MEASURES			
	Walking speed		Grip strength		Timed 5 chair-rises		SF-36 PCS score		ADL/IADL limitations	
Years preceding death	**Difference in mean (95% CI)**	***p***	**Difference in mean (95% CI)**	***p***	**Difference in mean (95% CI)**	***p***	**Difference in mean (95% CI)**	***p***	**Difference in probabilities (95% CI)**	***P***
-10	0.15 (-0.07 to 0.37)	0.19	0.00 (-0.21 to 0.20)	0.99	-0.36 (-0.60 to -0.12)	0.003	0.00 (-0.22 to 0.22)	0.99	-0.01 (-0.05 to 0.03)	0.69
-9	0.21 (0.05 to 0.36)	0.01	0.04 (-0.11 to 0.19)	0.61	-0.31 (-0.48 to -0.15)	< 0.001	0.05 (-0.10 to 0.21)	0.49	-0.01 (-0.03 to 0.02)	0.61
-8	0.25 (0.14 to 0.37)	< 0.001	0.07 (-0.04 to 0.18)	0.23	-0.28 (-0.40 to -0.16)	< 0.001	0.11 (-0.01 to 0.22)	0.07	-0.01 (-0.03 to 0.01)	0.48
-7	0.29 (0.19 to 0.39)	< 0.001	0.09 (-0.01 to 0.19)	0.07	-0.27 (-0.38 to -0.17)	< 0.001	0.16 (0.06 to 0.26)	0.002	-0.01 (-0.02 to 0.01)	0.34
-6	0.32 (0.23 to 0.41)	< 0.001	0.10 (0.01 to 0.20)	0.04	-0.28 (-0.39 to -0.18)	< 0.001	0.21 (0.11 to 0.31)	< 0.001	-0.01 (-0.03 to 0.01)	0.22
-5	0.34 (0.25 to 0.43)	< 0.001	0.11 (0.01 to 0.21)	0.03	-0.31 (-0.42 to -0.21)	< 0.001	0.25 (0.15 to 0.35)	< 0.001	-0.01 (-0.03 to 0.00)	0.12
-4	0.35 (0.26 to 0.44)	< 0.001	0.10 (0.01 to 0.20)	0.03	-0.37 (-0.47 to -0.26)	< 0.001	0.30 (0.20 to 0.40)	< 0.001	-0.02 (-0.04 to 0.00)	0.04
-3	0.35 (0.27 to 0.43)	< 0.001	0.09 (0.00 to 0.18)	0.05	-0.44 (-0.54 to -0.34)	< 0.001	0.35 (0.25 to 0.44)	< 0.001	-0.03 (-0.05 to -0.01)	0.004
-2	0.34 (0.25 to 0.43)	< 0.001	0.07 (-0.03 to 0.16)	0.17	-0.53 (-0.64 to -0.42)	< 0.001	0.39 (0.29 to 0.50)	< 0.001	-0.04 (-0.06 to -0.02)	0.001
-1	0.32 (0.20 to 0.45)	< 0.001	0.04 (-0.09 to 0.16)	0.57	-0.64 (-0.78 to -0.49)	< 0.001	0.44 (0.30 to 0.57)	< 0.001	-0.05 (-0.09 to -0.02)	0.004
0	0.30 (0.12 to 0.48)	0.001	-0.01 (-0.18 to 0.17)	0.95	-0.77 (-0.98 to -0.56)	< 0.001	0.48 (0.28 to 0.68)	< 0.001	-0.08 (-0.14 to -0.01)	0.03
Difference in trajectories	**0.28**		**0.47**		**< 0.001**		**< 0.001**		**0.09**	

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SF-36 PCS score: Physical Component Summary score of the Short Form 36 General Health Survey; CI: Confidence interval.

[a]Higher scores on walking speed, grip strength, and the SF-36 PCS score reflect better motor function, the contrary is true for timed 5 chair-rises and ADL/IADL limitations.

[b]Estimated from linear mixed models except ADL/IADL limitations where logistic regression with generalized estimated equation models were used; analyses adjusted for age at year 0, sex, ethnicity, marital status, occupational position, vital status, time terms (time & time^2), interactions of sociodemographic covariates with time terms, and health behaviours, BMI categories, 9-point multimorbidity score and the Mini Mental State Examination score assessed at motor function measurement.