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Does the association between physical capability and mortality differ by deprivation?

Findings from the UK Biobank population-based cohort study.

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Conflict of interest

None to declare.

Abstract

Background: To investigate whether the higher risk of adverse health outcomes associated with a lower physical capability in adulthood differs by deprivation levels.

Methods: 279,030 participants from the UK Biobank were included. Handgrip strength and walking pace were the exposures. All-cause mortality, CVD mortality and incidence were the outcomes. Townsend deprivation index was treated as a potential effect modifier. The associations were investigated using Cox- regression models with years of follow-up as the time-varying covariate.

Results: A significant interaction effect between deprivation and handgrip strength was found for all-cause mortality ($p=0.024$), CVD mortality ($p=0.006$) and CVD incidence ($p=0.001$). The hazard for all-cause mortality was 1.18 [1.09; 1.29] per 1-tertile higher level of grip strength in the least deprived group, whereas the risk per tertile increment in grip strength was 1.30 [1.18; 1.43] in the most deprived individuals. Similar results were found for CVD mortality and incidence per tertile increment in hand grip strength in the least and most deprived quintiles, respectively. No significant interactions between deprivation and walking pace were found for any of the outcomes.

Conclusion

Low handgrip strength is a stronger predictor of morbidity and mortality in individuals living in more deprived areas.

Keywords: mortality; incidence; muscle strength; cardiovascular diseases.

INTRODUCTION

Recent observational studies have provided robust evidence that better physical capability (handgrip strength and walking speed) in older age (>60 years) is associated with lower incidence of cardiovascular (CVD) events and all-cause mortality

. Similarly, in middle-aged adults (40-69 years) from the UK Biobank cohort, walking pace (Celis-Morales, et al., 2019; T. Yates et al., 2017) and handgrip strength (Carlos A. Celis-Morales, Donald M. Lyall, et al., 2018; C. A. Celis-Morales et al., 2018; Pavasini, et al., 2018) were inversely associated with all-cause and CVD mortality, and a broad range of other health outcomes. Therefore, implementing these simple and low-cost tests of physical capability in clinical settings may have prognostic value in identifying people at higher risk of disease (Carlos A. Celis-Morales, Paul Welsh, et al., 2018).

Physical capability in adulthood is likely to be influenced by genetic factors (Willems et al., 2017) and lifetime exposure to lifestyle behaviours (physical activity, dietary patterns,

etc.)(McGrath, Kraemer, Snih, & Peterson, 2018), which could explain the strong associations between tests of physical capability and health outcomes. However, reverse causality (i.e. undetected pathology that leads to lower physical capability) could also explain the strong associations seen in observational studies.(Cooper, Strand, Hardy, Patel, & Kuh, 2014) Furthermore, socioeconomic factors shape the trajectories of physical capability during the ageing process. In 109,107 adults from 24 countries, lower occupational class was associated with the loss of four to seven years of good physical functioning at age 60 years compared to higher occupational class (Stringhini et al., 2018). The greater loss of physical capability observed among the lower occupational class may be due to worse environmental and behavioural factors compared with more socially advantaged groups. For example, in 2,093 middle-aged adults, unhealthy behavioural risk factors (obesity, physical inactivity and smoking) were associated with an increased risk of decline in physical capability (handgrip strength and chair rise speed) assessed at ages 53 and 60-64 years (Cooper, Muniz-Terrera, & Kuh, 2016). In addition, a differential susceptibility effect, where more deprived groups are more susceptible to the effects of harmful exposures, could help explain the poorer outcomes in these groups (Diderichsen, Hallqvist, & Whitehead, 2018; Foster et al., 2018). For example, a recent study conducted with UK Biobank data found a differential effect of a lifestyle score, including traditional and emerging risk factors such as sedentary behaviours and sleep duration, on all-cause mortality and cardiovascular disease risk for individuals with varying levels of deprivation (Foster, et al., 2018).

To our knowledge, there has been no previous examination of differential susceptibility effects of reduced physical capability across levels of socioeconomic deprivation. In the current study, using data from UK Biobank, we investigated whether the association of lower physical

capability (handgrip strength and walking pace) with mortality and cardiovascular diseases is modified by deprivation.

METHODS

Study design and participants

UK Biobank is a prospective, population-based cohort study involving participants aged 40-69 years, (n>502,000) recruited between 2006-2010 from centres across England, Scotland and Wales. Each participant provided information (self-reported questionnaires) about lifestyle factors, had a set of physical measurements and provided biological samples as described elsewhere (Palmer, 2007; Sudlow et al., 2015). Participants' data were linked to mortality and disease registries. Further information related to the linkage procedure is available at <http://www.ic.nhs.uk/services/medical-research-information-service>. For the purpose of the present study, participants with any self-reported non-communicable diseases (NCDs) at baseline were excluded from analyses (depression, bipolar disorder, schizophrenia, alcohol problems, substance abuse, eating disorders, cognitive impairment, dementia, Parkinson's disease, chronic pain syndrome, chronic obstructive pulmonary disease, chronic asthma, chronic liver disease, hypertension, heart disease, stroke, inflammatory diseases, arthritis and cancer).

Outcome variables

Participants' date of death was obtained from death certificates provided by the National Health Service (NHS) Information Centre in England and Wales; and the NHS Central Register Scotland (Palmer, 2007). Hospital admissions were measured using linkage to Health Episode Statistics (HES) and the Scottish Morbidity Records. CVD events were defined as hospital

admission or death based on ICD10 (International Classification of Diseases, 10th revision) codes I60, I61, I63, I64, I21, I21.4, and I21.9. The period at risk per participant began on the date of their first assessment. End of follow-up for each participant was recorded as the date of death or the date of end of follow-up for the assessment centre attended (censored at 31st of January 2016), or the first date of hospitalization for CVD (censored at 31st of January 2015), whichever came first. Mortality and incidence outcomes have different censor dates because of the difference in the linked data.

Exposure variables

Participants performed a maximal isometric contraction with each hand while seated upright with their elbow flexed at 90° and their forearm facing forward and resting on an armrest. For the current analysis, the average of the right and left side values in kilograms was used and age- and sex-specific tertiles of handgrip strength were generated (Age and sex specific cut-off points are shown in Table S1). Walking pace was self-reported by participants using a touch-screen questionnaire. Those who were able to walk, rated their usual walking pace as one of the following: slow pace (<3 miles /hour); average pace (3-4 miles/hour); and brisk pace (>4 miles/hour), as described elsewhere (Celis-Morales, et al., 2019).

Covariates

Sociodemographic factors (age, sex, and ethnicity, professional qualifications, current employment status), health behaviours (smoking status, time spent viewing TV, red meat intake, processed meat intake, fruits and vegetables intake, oily fish intake, alcohol consumption), body mass index (BMI), systolic blood pressure and diagnosis of hypertension and medication for CVDs were included as covariates in the current analyses. Dietary information was obtained by 24-hour recall questionnaire (OxfordWebQ), which was designed

to be administrated for large prospective studies (Liu et al., 2011). Age was calculated from dates of birth and baseline assessment. Smoking status was self-reported as: never, former or current smoking. Medical history (physician diagnosis of illness) was collected using a self-reported questionnaire. Height, body weight, waist circumference and total body fat percentage (bio-impedance) were measured by trained nurses as described in the online protocol (<http://www.ukbiobank.ac.uk>). Physical activity was self-reported using the *International Physical Activity Questionnaire* (IPAQ short-version). (Guo, Bradbury, Reeves, & Key, 2015) Total physical activity was calculated as time spent walking plus moderate and vigorous activities, in metabolic equivalents (MET/min/week). Body mass index was calculated as (weight/height²) and participants were categorized as: underweight <18.5, normal weight 18.5-24.9, overweight 25-29.9 and obese ≥ 30 kg/m². Deprivation was determined using the Townsend deprivation index, an area-level measure of material deprivation. (Adams, Ryan, & White, 2005) Townsend deprivation index scores are derived for postcodes of residence and use national census data for car ownership, household overcrowding and ownership and unemployment rate and for the purpose this study it was categorised into quintiles, where lowest represent the least deprived individuals and the highest quintile represent the most deprived individuals.

Statistical analyses

We investigated the associations of handgrip strength and walking pace with cause specific incidence and mortality using Cox regression models with years of follow-up as the time-varying covariate. Results were reported as hazard ratios and 95% confidence intervals. No evidence of deviation from linearity was found between exposures and outcomes. Outcomes were: all-cause mortality, CVD mortality and CVD incidence (fatal and non-fatal events combined). To reduce the chance of reverse causality, all-analyses were landmark analyses

with follow-up commencing two years after recruitment thereby excluding participants with an event within two years of recruitment. In addition, participants with any self-reported non-communicable diseases (NCDs) at baseline (n=134,611) were excluded from analyses (depression, bipolar disorder, schizophrenia, alcohol problems, substance abuse, eating disorders, cognitive impairment, dementia, Parkinson's disease, chronic pain syndrome, chronic obstructive pulmonary disease, chronic asthma, chronic liver disease, hypertension, heart disease, stroke, inflammatory diseases, arthritis and cancer).

The primary exposures of interest were handgrip strength and walking pace. Grip strength was categorised in age- and sex-specific tertiles whereas walking pace was based on three self-reported categories (brisk, average, and slow). For the Townsend deprivation index scores, quintiles were derived, and the least deprived quintile (quintile 1) was used as the reference group, the highest quintile represent the most deprived individuals. Cox regression analyses were conducted to investigate the association of deprivation, handgrip strength and walking pace with health outcomes.

To investigate the associations between physical capability and health outcomes by deprivation quintiles, we tested for interactions by fitting a multiplicative interaction term between the exposure variables (i.e. grip strength tertile * area-level deprivation quintile). In addition, to illustrate the interaction effect we used ordinal coding with the reference group being those from the least deprived quintile with highest handgrip strength or brisk walking pace.

All analyses were adjusted for age, sex, ethnicity, professional qualifications, current employment status, smoking, body mass index, red meat intake, processed meat intake, fruits and vegetables intake, oil fish intake, alcohol consumption, TV viewing, month of assessment, systolic blood pressure, diagnosis of hypertension and medication for CVDs.

The proportional hazards assumption was checked visually, as well as based on Schoenfeld residuals, and no evidence of violation of the assumption was found. All analyses were performed using the statistical software STATA 14 (StataCorp LP).

RESULTS

Of the 502,628 participants recruited to UK Biobank, we excluded 134,611 participants who reported a NCDs diagnosis at baseline and 39,447 participants who developed an event within the first 2 years after recruitment. After also excluding participants with missing data for exposure variables or covariates 279,030 participants were included for analyses. The mean follow-up period was 4.9 years after the landmark period (ranging from 3.3 to 7.9) for all-cause and CVD mortality, and 4.1 years (ranging from 2.4 to 7.0) for CVD incidence.

Table 1 summarises cohort characteristics stratified by deprivation quintiles. In summary, people living in the most deprived areas had a higher prevalence of current smoking and obesity ($BMI \geq 30.0 \text{ kg/m}^2$), reported a higher amount of physical activity (MET-h/week) and a lower prevalence of daily alcohol intake compared with those living in the least deprived areas. The main characteristics of participants stratified by handgrip strength tertiles and walking pace categories are shown in Table S2 and S3, respectively.

Higher deprivation, low grip strength and slow walking were all associated with adverse health outcomes (Tables S4-S6). Compare to the least deprived quintile those who were classified in the highest deprivation quintile had a higher hazard for all-cause mortality (HR: 1.20 [95% CI: 1.08; 1.33]), CVD mortality (HR: 1.32 [95% CI: 1.09; 1.62]) and CVD incidence (HR: 1.20 [95% CI: 1.08; 1.33]) (Table S4). Similarly, individuals classified in the lowest tertile for grip strength had a higher hazard for all-cause mortality (HR: 1.60 [95% CI: 1.49; 1.73]), CVD

mortality (HR: 1.75 [95% CI: 1.51; 2.02]) and CVD incidence (HR: 1.35 [95% CI: 1.29; 1.40]) compared to the highest tertile for strength (Table S5). Compare to brisk walkers those who reported a slow walking pace had a higher hazard for all-cause mortality (HR: 1.80 [95% CI: 1.50; 2.03]), CVD mortality (HR: 2.28 [95% CI: 1.83; 2.82]) and CVD incidence (HR: 1.51 [95% CI: 1.40; 1.62]) (table S6).

Handgrip strength, area-level deprivation and health outcomes

As shown in Figure 1 and Table S7, there were interactions between handgrip strength and deprivation for all-cause mortality (P=0.024), CVD mortality (P=0.006) and CVD incidence (P=0.001).

In the most deprived quintile, the hazard trend for all-cause mortality per tertile lower strength was 1.30 [95% CI: 1.18; 1.43], whereas the hazard trend was 1.18 [95% CI: 1.09; 1.29] per tertile lower strength in those individuals who belong to the least deprived quintile (Figure 1). Similar interactions, between deprivation and tertiles of grip strength, were found for CVD mortality (hazard trend for the most deprived 1.43 [95% CI: 1.09; 1.29] vs least deprived 1.15 [95% CI: 0.98; 1.36]) and CVD incidence (hazard trend for the most deprived 1.20 [95% CI: 1.14; 1.26] vs least deprived 1.11 [95% CI: 1.06; 1.16]) (Figure 1 and Table S7).

Walking pace, area-level deprivation and health outcomes

As shown in Figure 2 and Table S8, although there was no significant interaction between walking pace and deprivation for any of the outcomes of interest (all-cause mortality p= 0.666, CVD mortality p=0.062 and CVD incidence p=0.195) the hazard for all-cause mortality, CVD incidence and mortality was higher on slow-walkers from the most deprived quintiles compare to those in the least deprived category. Overall, regardless of deprivation levels those individuals who reported a slow walking pace compare to brisk and average pace walkers had

a higher hazard for all-cause mortality (hazard ranging from 1.69 to 2.03), CVD mortality (hazard ranging from 1.49 to 3.11) and CVD incidence (hazard ranging from 1.37 to 1.71).

DISCUSSION

The results obtained in this study support the differential influence of deprivation on the association of physical capability, specially handgrip strength, with CVD incidence and mortality (Diderichsen, et al., 2018); whereby individuals from more socioeconomically disadvantaged areas with low handgrip strength have a disproportionately high risk of morbidity (CVD incidence) and mortality (all-cause and CVD) compared with their more affluent counterparts with low grip strength. To illustrate the magnitude of the differences, individuals with lower levels of handgrip strength and who belong to the most deprived sector of the population had almost three-times higher risk of dying from CVD compared to those individuals with similar levels of grip strength but who belong to the least deprived group (hazard for CVD mortality in individuals with low strength was 43% and 15% higher in the most vs. least deprived areas, respectively). If these associations are causal, this suggests that the population subgroups with the lowest levels of strength and who belongs to the most deprived sector of the population, could potentially obtain the greatest benefit from interventions aimed at improving strength levels. Conversely, in those with high levels of handgrip strength, the adverse association of deprivation on health outcomes were completely abolished.

The findings from our study conflict with previous studies on this topic which have been conducted mainly in older adults (Gu, Yang, & Sautter, 2016). For example in 13,731 older adults (age 65 years and older) Gu et al. (Gu, et al., 2016) examined the moderating role of deprivation (using a socioeconomic vulnerability index) in the association between frailty

(scored based on 38 items reflecting dimensions of health) and all-cause mortality. The higher mortality risk associated with frailty was weaker among the most deprived group, which is in direct contrast to our findings. This paradox, a lower mortality risk in the most vulnerable social groups, may be an endogenous selection bias caused by oversampling of older individuals (almost 75% were 80 years and older) (Infante-Rivard and Cusson, 2018). In support of our findings are the data obtained by Singh-Manoux et al. (Singh-Manoux et al., 2007), from middle aged French workers (n= 20,404, average age= 44.2 years), where the association between self-rated health (considered a valid measure of health status, although not a marker of physical capability) and mortality risk weakened with increasing socioeconomic status (based on occupational position and income).

Although slow walking pace has been associated with adverse health outcomes (Celis-Morales, et al., 2019; Thomas Yates, et al., 2017), our analyses did not reveal any interaction effect with deprivation. Those individuals who reported being slow walkers were at higher risk of all-cause mortality, CVD mortality and incidence regardless their deprivation levels. This may be explained partially by the self-reported nature of the data as interaction analyses depend on some critical assumptions such as a dose-response relationship between exposure and disease risk, which are sensitive to misclassification of exposures. To our knowledge, the criterion validity of self-reported measurements of walking pace has never been studied in the UK Biobank data. Within the UK Biobank cohorts those individuals who reported a brisk walking pace were younger, active, fitter and leaner than those who reported a slow walking pace (Celis-Morales, et al., 2019; Thomas Yates, et al., 2017). However, there was no evidence of walking pace and age interaction, suggesting that the association of walking pace with health outcomes is not explained by frailty or ageing (Celis-Morales, et al., 2019; Thomas Yates, et al., 2017).

Clinical and policy implications

As previously stated, the adoption and maintenance of healthy behaviours in adulthood (e.g. physical activity, the intake of nutrient-dense foods)(McGrath, et al., 2018), as well as early life developmental factors (birthweight) (Sayer et al., 2008) or socioeconomic circumstances (Cheval et al., 2018) shape the trajectory of physical capability throughout the life course. A key question is what type of health strategies should be prioritized to maximize the levels of physical capability in the population. Some population health strategies- those reaching the whole population- (i.e. increases in taxes for highly processed foods or large investments in infrastructure to favour active transport in cities) may be especially effective in the most socially deprived groups (Diderichsen, et al., 2018). Targeting “vulnerable individuals” (socially deprived) or “high-risk individuals” (with impaired physical capabilities) may produce substantial short-term health benefits in some communities. However, empowering individuals to make healthy behavioural change in socially deprived areas may not succeed long-term, as individual-level interventions do not modify the wider economic, social and cultural factors that shape health behaviours.

Strengths and limitations of the study

The large sample size of UK Biobank alongside with a 2-years landmark analyses and exclusion of participants with comorbidities at baseline may contribute to reduce the influence of reverse causality, however, these does not guaranty its fully exclusion. Compared with the general population from UK, the UK Biobank cohort is comprised of a more affluent and healthy population. However, a recent study reported similar effect sizes in the risk factor associations in UK Biobank against UK population representative studies and concluded the associations found in UK Biobank are generalisable (Batty, Gale, Kivimäki, Deary, & Bell, 2020). Despite the richness of data that UK Biobank offers, we restricted our analyses to area-

level deprivation. Education, another marker of socio-economic status was not included in our analyses because this socioeconomic variable was not appropriately captured by questionnaires in the UK Biobank. Moreover, household gross income, is another marker of deprivation available in UK Biobank but was not included in this study was. Income was self-reported while area-level deprivation was obtained from objective sources (postcodes based on preceding national census data). Therefore, it is likely that misclassification errors might be more common for self-reported income compared with data collected from a UK census (employment status, number of household members, household ownership, car ownership) which may be less susceptible to social desirability biases. In addition, Townsend deprivation scores may provide a more stable measure of socioeconomic position whereas household income may fluctuate more over the life course of individuals and could be influenced by other incomes from the family or partners of the participants which were not reported.

Conclusions

Low handgrip strength is a stronger predictor of morbidity and mortality in individuals living in more deprived areas. Low physical capability could be used to identify populations with the highest risk for poor health. Preventive interventions could then be targeted at and tailored for those at highest risk. Nonetheless, population health strategies (reaching the whole population) are also required to modify the harmful environmental and lifestyle factors that influence physical capability.

Supplementary Data

Supplementary data are available at JSS online.

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doi:10.1093/eurheartj/ehx449

Table 1. Cohort characteristics by Townsend deprivation quintiles

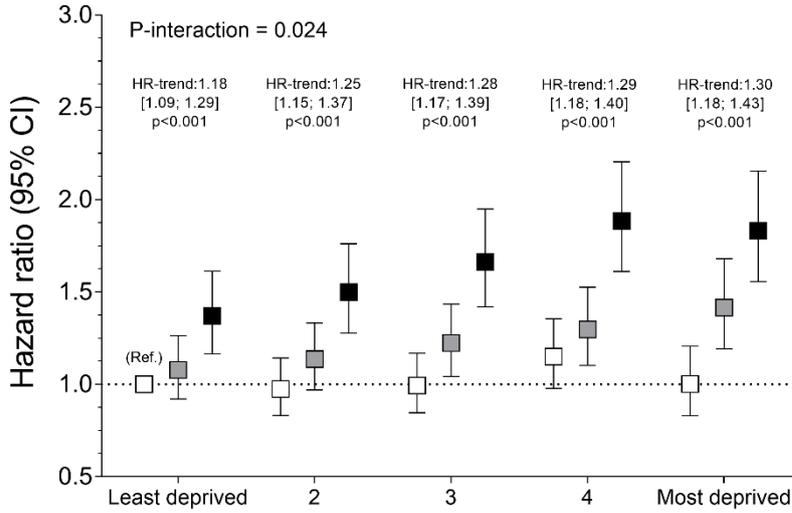
Variables	Townsend index				
	Least deprived	2	3	4	Most deprived
Socio-demographics					
Total, n	62,020	59,757	57,291	54,880	45,305
Women, n (%)	33,123 (53.4)	32,423 (54.3)	31,584 (55.1)	30,461 (55.5)	24,780 (54.7)
Men, n (%)	28,897 (46.6)	27,334 (45.7)	25,707 (44.9)	24,419 (44.5)	20,525 (45.3)
Age, (years)	55.9 (7.88)	55.7 (7.93)	55.1 (8.03)	54.20 (8.08)	53.13 (8.11)
Professional qualifications, n (%)	25,620 (41.3)	23,304 (39.0)	22,123 (38.6)	23,155 (42.2)	19,090 (42.1)
College or University degree	9,184 (14.8)	8,473 (14.2)	7,865 (13.7)	7,045 (12.8)	5,317 (11.7)
A levels/AS levels or equivalent	16,150 (26.1)	16,370 (27.4)	15,377 (26.8)	13,490 (24.6)	10,272 (22.7)
O levels/GCSEs or equivalent	3,201 (5.2)	3,589 (6.0)	4,115 (7.2)	4,107 (7.5)	4,093 (9.0)
CSEs or equivalent	4,076 (6.6)	4,340 (7.3)	4,317 (7.5)	4,054 (7.4)	4,142 (9.1)
NVQ or HND or HNC or equivalent	3,789 (6.1)	3,681 (6.2)	3,494 (6.1)	3,029 (5.5)	2,391 (5.3)
Other professional qualifications					
Townsend deprivation index, mean [range]	-4.69 (-6.25, -3.94)	-3.34 (-3.93, -2.75)	-2.10 (-2.74, -1.29)	-0.10 (-1.28, 1.35)	3.74 (1.36, 11.0)
Current employment status, n (%)	39,548 (63.8)	38,755 (64.8)	38,648 (67.5)	39,169 (71.4)	32,850 (72.5)
In paid employment or self-employed	19,480 (31.4)	18,028 (30.2)	15,652 (27.3)	12,406 (22.6)	7,871 (17.4)
Retired	1,866 (3.0)	1,745 (2.9)	1,520 (2.6)	1,491 (2.7)	1,307 (2.9)
Looking after home and/or family	304 (0.5)	342 (0.6)	444 (0.8)	531 (1.0)	1,085 (2.4)
Unable to work (sickness or disability)	474 (0.8)	511 (0.9)	640 (1.1)	819 (1.5)	1,557 (3.4)
Unemployed	254 (0.4)	259 (0.4)	258 (0.4)	270 (0.5)	316 (0.7)
Doing unpaid or voluntary work	94 (0.1)	117 (0.2)	129 (0.2)	194 (0.3)	319 (0.7)
Full or part time student					
Income categories, n (%)					
More than £100,000	4,699 (8.5)	3,740 (7.0)	3,115 (6.1)	3,258 (6.6)	2,736 (6.7)
£52,000 to £100,000	17,218 (31.3)	14,933 (28.1)	13,125 (25.6)	11,311 (22.9)	6,966 (17.1)
£30,000 to £51,999	16,672 (30.3)	16,185 (30.5)	15,757 (30.7)	14,740 (29.8)	10,131 (24.8)
£18,000 to £29,999	11,792 (21.4)	12,446 (23.4)	12,573 (24.5)	12,288 (24.8)	10,630 (26.1)
Less than £ 18,000	4,585 (8.3)	5,796 (10.9)	6,723 (13.1)	7,867 (15.9)	10,326 (25.3)
Ethnicity, n (%)					
White	60,721 (97.9)	58,306 (97.6)	55,326 (96.6)	51,141 (93.2)	39,110 (86.3)
Mixed background	220 (0.3)	230 (0.4)	288 (0.5)	422 (0.8)	629 (1.4)
South Asian	526 (0.8)	569 (0.9)	778 (1.4)	1,438 (2.6)	1,475 (3.3)
Black	165 (0.3)	237 (0.4)	446 (0.8)	1,041 (1.9)	2,718 (6.0)
Chinese	153 (0.2)	160 (0.3)	163 (0.3)	263 (0.5)	255 (0.6)
Other	235 (0.4)	255 (0.4)	290 (0.5)	575 (1.1)	1,118 (2.5)
Smoking status, n (%)					
Never	39,288 (63.3)	36,767 (61.5)	34,206 (59.7)	31,125 (56.7)	23,469 (51.8)
Previous	19,106 (30.8)	19,010 (31.8)	18,522 (32.3)	18,048 (32.9)	14,740 (32.5)
Current	3,626 (5.9)	3,626 (6.7)	4,563 (8.0)	5,707 (10.4)	7,096 (15.7)
Body composition					
Weight in kg, mean (SD)	76.82 (14.82)	76.94 (14.95)	77.11 (15.20)	77.27 (15.65)	77.84 (16.13)
Height in cm, mean (SD)	169.63 (9.24)	169.31 (9.20)	169.12 (9.20)	169.01 (15.65)	168.64 (9.23)
BMI, mean (SD)	26.6 (4.11)	26.7 (4.2)	26.9 (4.4)	26.97 (4.60)	27.31 (5.01)
BMI Categories, n (%)					
Under weight (<18.5 kg/m ²)	289 (0.5)	278 (0.5)	251 (0.4)	294 (0.5)	308 (0.7)
Normal weight (18.5-24.9 kg/m ²)	23,421 (37.8)	22,003 (36.8)	20,675 (36.1)	19,905 (36.3)	15,807 (34.9)
Overweight (25.0 to 29.9 kg/m ²)	27,319 (44.1)	26,114 (43.7)	24,838 (43.4)	22,945 (41.8)	18,119 (40.0)
Obese (≥30.0 kg/m ²)	10,991 (17.7)	11,362 (19.0)	11,527 (20.1)	11,736 (21.4)	11,071 (24.4)
Waist Circumference (cm)	88.23 (12.49)	88.40 (12.57)	88.62 (12.74)	88.89 (12.99)	89.59 (13.33)

Body fat, mean (SD)	30.24 (8.14)	30.47 (8.26)	30.67 (8.35)	30.70 (8.52)	30.90 (8.90)
Physical activity and sedentary behaviour					
Total PA (MET-h/week), mean (SD)	41.74 (53.64)	43.70 (57.67)	45.14 (59.90)	46.07 (62.88)	48.48 (69.24)
TV viewing (h/day), mean (SD)	2.47 (1.35)	2.51 (1.38)	2.51 (1.42)	2.47 (1.47)	2.54 (1.69)
Dietary intakes					
Alcohol intake frequency					
Never	2,598 (4.2)	2,819 (4.7)	2,980 (5.2)	3,467 (6.3)	4,318 (9.5)
Special occasions only	4,618 (7.4)	5,021 (8.4)	5,124 (8.9)	5,557 (10.1)	6,188 (13.6)
One to three times a month	6,179 (10.0)	6,334 (10.6)	6,462 (11.3)	6,222 (11.3)	5,552 (12.3)
Once or twice a week	16,589 (26.7)	15,776 (26.4)	15,284 (26.7)	14,161 (25.8)	10,959 (24.2)
Three or four times a week	17,661 (28.5)	16,218 (27.1)	14,868 (25.9)	13,454 (24.5)	9,105 (20.1)
Daily or almost daily	14,375 (23.2)	13,589 (22.8)	12,573 (22.0)	12,019 (21.9)	14,375 (20.3)
Fruit and vegetables intake (g/day), mean (SD)	330.4 (176.4)	328.7 (175.3)	329.51 (182.4)	330.6 (191.9)	332.3 (215.1)
Processed meat intake					
Never	4,762 (7.7)	4,805 (8.0)	5,224 (9.1)	5,981 (10.9)	5,764 (12.7)
Less than 3 portions/week	38,421 (61.9)	36,740 (61.5)	34,549 (60.3)	32,250 (58.8)	25,621 (56.6)
3 or more portions/week	18,837 (30.4)	18,212 (30.5)	17,518 (30.6)	16,649 (30.3)	13,920 (30.7)
Red meat					
Never	3,444 (5.6)	3,596 (6.0)	3,950 (6.9)	4,893 (8.9)	4,445 (9.8)
Less than 3 portions/week	50,011 (80.6)	48,149 (80.6)	45,728 (79.8)	42,746 (77.9)	34,003 (75.0)
3 or more portions/week	8,565 (13.8)	8,012 (13.4)	7,613 (13.3)	7,241 (13.2)	6,857 (15.2)
Oily fish					
Never	4,917 (7.9)	5,240 (8.8)	5,611 (9.8)	6,117 (11.1)	5,724 (12.6)
Less than 1 a week	46,617 (75.2)	44,286 (74.1)	42,052 (73.4)	39,244 (71.5)	31,016 (68.5)
2 or more a week	10,486 (16.9)	10,231 (17.1)	9,628 (16.8)	9,519 (17.3)	8,565 (18.9)
Health status					
Systolic blood pressure in mmHg, mean (SD)	139.53 (19.40)	139.54 (19.44)	138.89 (19.43)	137.81 (19.26)	136.46 (19.32)
Medications					
Cholesterol lowering	2,109 (3.4)	2,146 (3.6)	2,108 (3.7)	2,053 (3.7)	1,795 (4.0)
Blood pressure lowering	2,901 (4.7)	2,932 (4.9)	2,834 (4.9)	2,633 (4.8)	2,226 (4.9)
None of the above medication	57,010 (91.9)	54,679 (91.5)	52,349 (91.4)	50,194 (91.5)	41,284 (91.1)

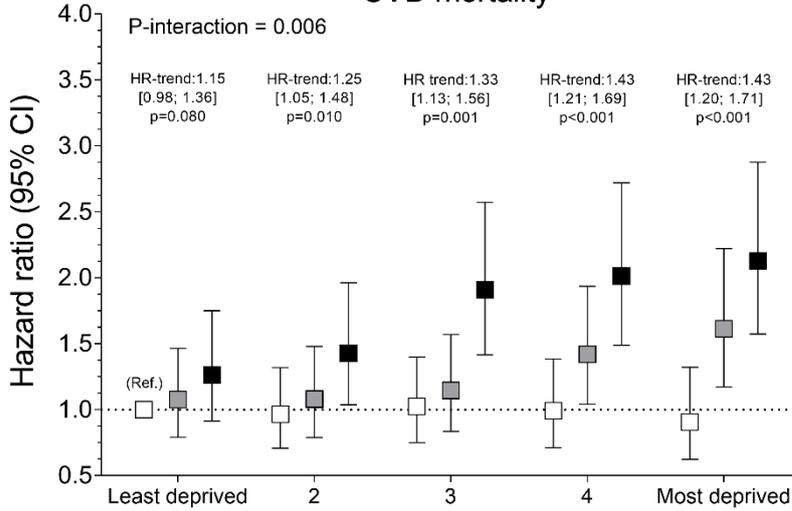
Data presented as mean (SD) or % (n) for continuous and categorical variables as appropriate. % given as row totals. TE: total energy intake–SD: standard deviation–TV: television–BMI: body mass index–PA: physical activity–MET: metabolic equivalent.

□ High strength ■ Middle strength ■ Low strength

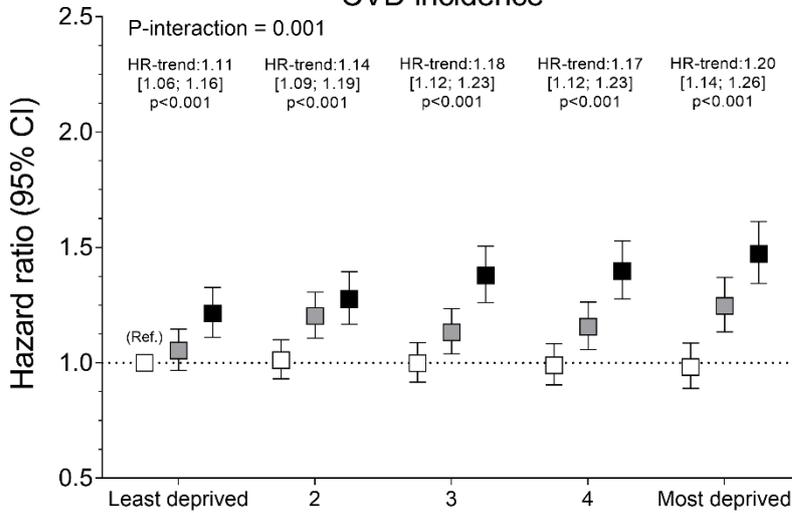
All-cause mortality



CVD mortality



CVD incidence



Townsend deprivation quintiles

Figure 1. Cox proportional hazard models of the association of handgrip strength with all-cause mortality, CVD mortality and incidence and deprivation strata.

Data presented as adjusted hazard ratio (HR) (95%CI) per categories of handgrip strength and area-level deprivation quintiles. The highest category of handgrip strength (tertile 3) and lowest quintile for deprivation were used as the reference category. The HR for trend indicates the change in the HR by one tertile lower handgrip strength. All analyses were restricted to participants with at least 2 years of follow-up. All analyses were adjusted for age, sex, ethnicity, professional qualifications, current employment status, smoking, body mass index, red meat intake, processed meat intake, fruits and vegetables intake, oil fish intake, alcohol consumption, time spent viewing TV, month of assessment, systolic blood pressure, diagnosis of hypertension and medication for CVDs.

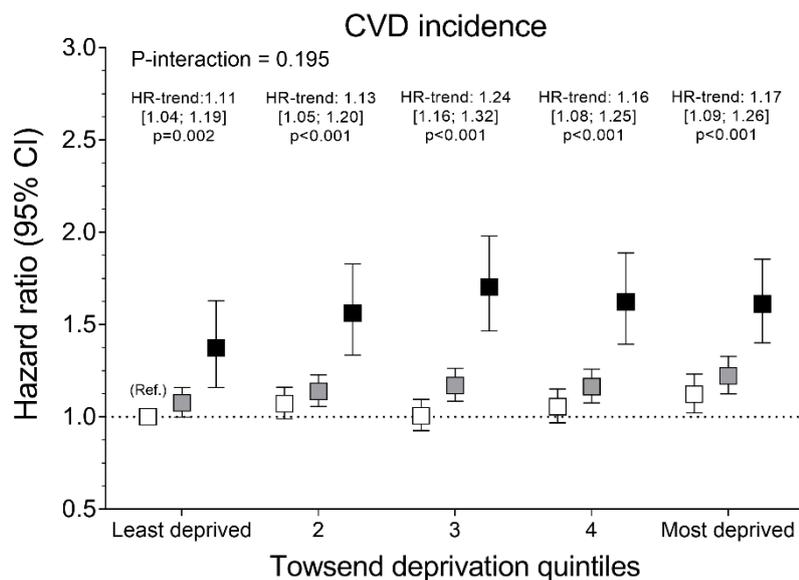
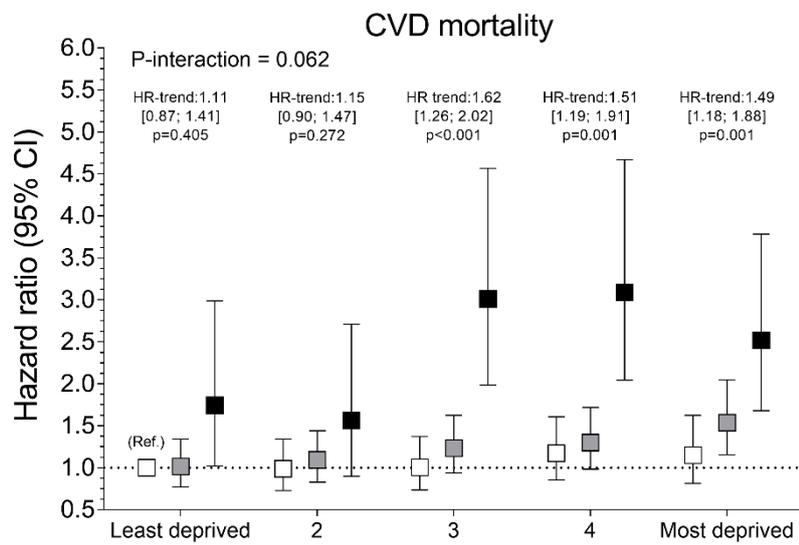
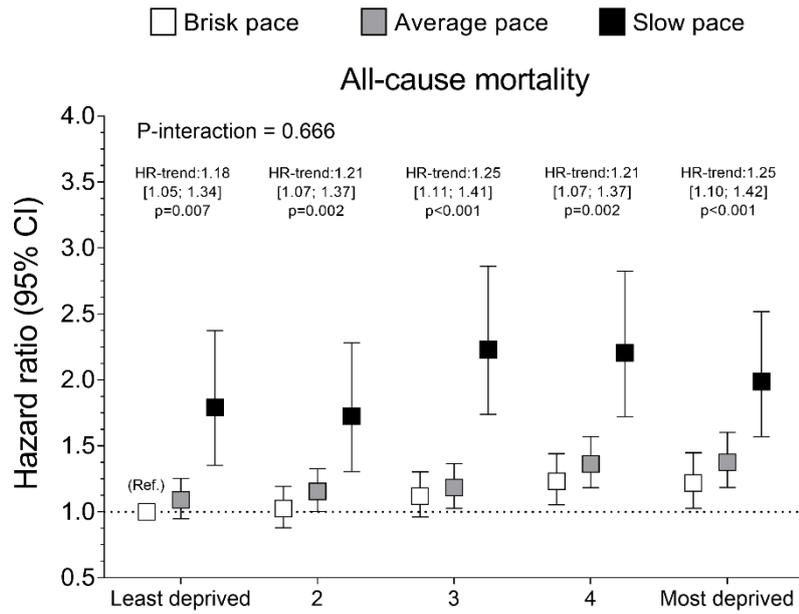


Figure 2. Cox proportional hazard models of the association of self-reported walking pace with all-cause mortality, CVD mortality and incidence and deprivation strata.

Data presented as adjusted hazard ratio (HR) (95%CI) per categories of handgrip strength and area-level deprivation quintiles. Brisk pace walkers and the lowest quintile for deprivation were used as the reference category. The HR for trend indicates the change in the HR by one category lower walking pace. All analyses were restricted to participants with at least 2 years of follow-up. All analyses were adjusted for age, sex, ethnicity, professional qualifications, current employment status, smoking, body mass index, red meat intake, processed meat intake, fruits and vegetables intake, oil fish intake, alcohol consumption, time spent viewing TV, month of assessment, systolic blood pressure, diagnosis of hypertension and medication for CVDs.

Supplementary Online Material

Table S1. Cut-off points for age and sex-specific grip strength tertiles.

Sex	Age group	Low strength	Middle strength	High strength
Women	<56 years	<23	23 – 28	>28
	56 to 65 years	<20	20 – 25	>25
	>65 years	<18	18 – 23	>23
Men	<56 years	<38	38 – 46	>46
	56 to 65 years	<35	35 – 42	>42
	>65 years	<33	33 – 39	>39

Data presented as kg.

Table S2. Cohort general characteristics by handgrip strength levels.

Variables	Handgrip strength tertiles		
	High	Middle	Low
Socio-demographics			
Total, n	97,366	95,960	85,712
Women, n (%)	53,889 (55.4)	51,152 (53.3)	47,205 (55.1)
Men, n (%)	43,477 (44.6)	44,808 (46.7)	38,507 (45.0)
Age, (years)	54.6 (8.1)	54.9 (8.0)	55.1 (8.0)
Professional qualifications, n (%)			
College or University degree	40,842 (42.0)	39,091 (40.7)	33,291 (38.9)
A levels/AS levels or equivalent	13,348 (13.5)	12,940 (13.5)	11,568 (13.5)
O levels/GCSEs or equivalent	23,981 (24.6)	24,811 (25.9)	22,806 (26.6)
CSEs or equivalent	6,124 (6.3)	6,394 (6.7)	6,566 (7.7)
NVQ or HND or HNC or equivalent	7,328 (7.5)	7,181 (7.5)	6,397 (7.5)
Other professional qualifications	5,743 (5.9)	5,543 (5.8)	5,084 (5.9)
Current employment status, n (%)			
In paid employment or self-employed	66,931 (68.7)	65,429 (68.1)	56,503 (66.0)
Retired	25,092 (25.8)	25,151 (26.2)	23,109 (27.0)
Looking after home and/or family	2,926 (3.0)	2,650 (2.8)	2,350 (2.7)
Unable to work (sickness or disability)	551 (0.6)	654 (0.7)	1,483 (1.7)
Unemployed	1,066 (1.1)	1,365 (1.4)	1,570 (1.8)
Doing unpaid or voluntary work	490 (0.5)	433 (0.5)	432 (0.5)
Full or part time student	310 (0.3)	278 (0.3)	265 (0.3)
Income categories, n (%)			
More than £100,000	6,812 (7.8)	6,167 (7.2)	4,562 (6.0)
£52,000 to £100,000	23,953 (27.3)	22,208 (25.8)	17,358 (22.9)
£30,000 to £51,999	26,459 (30.2)	25,391 (29.5)	21,584 (28.5)
£18,000 to £29,999	19,860 (22.7)	20,515 (23.9)	19,301 (25.5)
Less than £18,000	10,536 (12.0)	11,714 (13.7)	12,975 (17.1)
Deprivation index, n (%)			
Lowest	23,209 (23.8)	21,640 (22.6)	17,127 (20.0)
2	21,830 (22.4)	20,761 (21.6)	17,119 (20.0)
3	20,187 (20.7)	19,741 (20.6)	17,327 (20.2)
4	18,272 (18.8)	14,994 (15.6)	17,745 (20.7)
Highest	13,868 (14.2)	14,994 (15.6)	16,394 (19.1)
Ethnicity, n (%)			
White	93,634 (96.2)	91,601 (95.5)	79,161 (92.4)
Mixed background	652 (0.7)	577 (0.6)	559 (0.7)
South Asian	571 (0.6)	1,292 (1.5)	2,923 (3.4)
Black	1,753 (1.8)	1,402 (1.5)	1,449 (1.7)
Chinese	190 (0.2)	338 (0.4)	466 (0.5)
Other	566 (0.6)	750 (0.8)	1,154 (1.4)
Body composition			
Weight in kg, mean (SD)	79.4 (15.6)	76.7 (15.0)	75.1 (15.1)
Height in cm, mean (SD)	171.0 (9.1)	169.1 (9.0)	167.1 (9.2)
BMI Categories, n (%)			
Under weight (<18.5 kg/m ²)	324 (0.3)	490 (0.5)	603 (0.7)
Normal weight (18.5;24.9 kg/m ²)	33,431 (34.3)	36,225 (37.8)	32,075 (37.4)
Overweight (25.0 to 29.9 kg/m ²)	42,915 (44.1)	40,858 (42.6)	35,440 (41.4)
Obese (≥30.0 kg/m ²)	20,696 (21.3)	18,347 (19.1)	17,594 (20.5)
Waist Circumference (cm)	89.0 (12.8)	88.4 (12.7)	88.7 (13.0)
Body fat, mean (SD)	30.4 (8.4)	30.3 (8.3)	31.1 (8.5)
Physical activity and sedentary behaviour			
Total PA (MET-h/week), mean (SD)	47.6 (62.2)	44.6 (59.8)	41.8 (58.8)
TV viewing (h/day), mean (SD)	2.4 (1.4)	2.5 (1.4)	2.6 (1.5)
Dietary intakes			
Alcohol intake frequency			
Never	4,540 (4.7)	5,103 (5.3)	6,522 (7.6)
Special occasions only	8,311 (8.5)	8,811 (9.2)	9,358 (10.9)
One to three times a month	10,528 (10.8)	10,419 (10.9)	9,788 (11.4)
Once or twice a week	25,364 (26.1)	25,028 (26.1)	22,317 (26.0)
Three or four times a week	25,923 (26.6)	24,879 (25.9)	20,454 (23.9)
Daily or almost daily	22,700 (23.3)	21,720 (22.6)	17,273 (20.2)

Fruit and vegetables intake (g/day), Mean (SD)	335.8 (185.9)	328.0 (185.9)	325.5 (190.2)
Processed meat intake			
Never	8,634 (8.9)	9,024 (9.4)	8,858 (10.3)
Less than 1 portion/week	59,617 (61.2)	57,551 (60.0)	50,293 (58.7)
2 or more portions/week	29,115 (29.9)	29,385 (30.6)	26,561 (31.0)
Red meat			
Never	6,478 (6.7)	6,876 (7.2)	6,959 (8.1)
Less than 1 portions/week	77,141 (79.2)	76,193 (79.4)	67,137 (78.3)
3 or more portions/week	13,747 (14.1)	12,891 (13.4)	11,616 (13.6)
Oily fish			
Never	8,306 (8.5)	9,379 (9.8)	9,896 (11.6)
Less than 1 a week	71,669 (73.6)	70,088 (73.0)	61,311 (71.5)
2 or more a week	17,391 (17.9)	16,493 (17.2)	14,505 (16.9)
Health status			
Systolic blood pressure in mmHg, Mean (SD)	139.8 (19.4)	138.5 (19.4)	137.3 (19.4)
Medications			
Cholesterol lowering	3,374 (3.5)	3,268 (3.4)	3,559 (4.2)
Blood pressure lowering	4,557 (4.7)	4,393 (4.6)	4,557 (5.3)
None of the above medication	89,435 (91.9)	88,299 (92.0)	77,596 (90.5)

High: Tertile 3; Middle: Tertile 2; Low: Tertile 1. Data presented as mean (SD) or % (n) for continuous and categorical variables as appropriate. % given as row totals. TE: total energy intake-SD: standard deviation-TV: television-BMI: body mass index-PA: physical activity-MET: metabolic equivalent.

Table S3. Cohort characteristics by walking pace categories.

Variables	Walking pace		
	Brisk	Average	Slow
Socio-demographics			
Total, n	126,469	141,284	11,500
Women, n (%)	67,370 (53.3)	77,902 (55.1)	7,099 (61.7)
Men, n (%)	59,099 (46.7)	63,382 (44.9)	4,401 (38.3)
Age, (years)	54.1 (8.0)	55.5 (8.1)	56.8 (7.9)
Professional qualifications, n (%)			
College or University degree	57,630 (45.6)	51,960 (36.8)	3,702 (32.2)
A levels/AS levels or equivalent	17,834 (14.1)	18,585 (13.2)	1,465 (12.7)
O levels/GCSEs or equivalent	29,190 (23.1)	39,114 (27.7)	3,355 (29.2)
CSEs or equivalent	7,170 (5.7)	11,020 (7.8)	915 (8.0)
NVQ or HND or HNC or equivalent	7,991 (6.3)	11,813 (8.4)	1,125 (9.8)
Other professional qualifications	6,654 (5.3)	8,792 (6.2)	938 (8.2)
Current employment status, n (%)			
In paid employment or self-employed	90,990 (72.0)	92,498 (65.5)	5,482 (47.7)
Retired	28,985 (22.9)	40,404 (28.6)	4,048 (35.2)
Looking after home and/or family	3,546 (2.8)	4,037 (2.9)	346 (3.0)
Unable to work (sickness or disability)	354 (0.3)	1,072 (0.8)	1,280 (11.1)
Unemployed	1,569 (1.2)	2,179 (1.5)	253 (2.2)
Doing unpaid or voluntary work	623 (0.5)	688 (0.5)	46 (0.4)
Full or part time student	402 (0.3)	406 (0.3)	45 (0.4)
Income categories, n (%)			
More than £100,000	10,360 (9.0)	6,902 (5.5)	286 (2.9)
£52,000 to £100,000	33,264 (29.0)	28,858 (23.1)	1,431 (14.6)
£30,000 to £51,999	34,002 (29.7)	37,079 (29.6)	2,404 (24.6)
£18,000 to £29,999	24,424 (21.3)	32,588 (26.0)	2,717 (27.8)
Less than £18,000	12,622 (11.0)	19,729 (15.8)	2,946 (30.1)
Deprivation index, n (%)			
Lowest	29,144 (23.0)	30,995 (21.9)	1,881 (16.4)
2	27,556 (21.8)	30,106 (21.3)	2,095 (18.2)
3	25,986 (20.6)	29,076 (20.6)	2,229 (19.4)
4	24,613 (19.5)	27,875 (19.7)	2,392 (20.8)
Highest	19,170 (15.2)	23,232 (16.4)	2,903 (25.2)
Ethnicity, n (%)			
White	122,079 (96.5)	132,390 (93.7)	10,135 (88.1)
Mixed background	798 (0.6)	878 (0.6)	113 (1.0)
South Asian	1,217 (1.0)	3,076 (2.2)	493 (4.3)
Black	1,435 (1.1)	2,767 (2.0)	405 (3.5)
Chinese	235 (0.2)	660 (0.5)	99 (0.9)
Other	705 (0.6)	1,513 (1.1)	255 (2.2)
Smoking status, n (%)			
Never	76,568 (60.5)	82,072 (58.1)	6,215 (54.0)
Previous	39,762 (31.4)	45,883 (32.5)	3,781 (32.9)
Current	10,139 (8.0)	13,329 (9.4)	1,504 (13.1)
Body composition			
Weight in kg, mean (SD)	74.5 (14.1)	78.9 (15.5)	85.1 (19.3)
Height in cm, mean (SD)	170.1 (9.2)	168.6 (9.1)	166.2 (9.3)
BMI, mean (SD)	25.6 (3.7)	27.7 (4.5)	30.8 (6.4)
BMI Categories, n (%)			
Under weight (<18.5 kg/m ²)	915 (0.7)	462 (0.3)	43 (0.4)
Normal weight (18.5-24.9 kg/m ²)	58,663 (46.4)	41,183 (29.2)	1,965 (17.1)
Overweight (25.0 to 29.9 kg/m ²)	52,243 (41.3)	63,219 (44.8)	3,873 (33.7)
Obese (≥30.0 kg/m ²)	14,648 (11.6)	36,420 (25.8)	5,619 (58.9)
Waist Circumference (cm)	85.8 (11.8)	90.6 (12.8)	97.1 (15.0)
Body fat, mean (SD)	28.6 (7.8)	31.9 (8.4)	36.2 (9.3)
Physical activity and sedentary behaviour			
Total PA (MET-h/week), mean (SD)	49.3 (62.3)	42.4 (59.2)	25.8 (45.1)
TV viewing (h/day), mean (SD)	2.3 (1.4)	2.7 (1.5)	3.17 (1.9)
Dietary intakes			
Alcohol intake frequency			
Never	5,873 (4.6)	8,774 (6.2)	1,535 (13.4)
Special occasions only	9,655 (7.6)	14,843 (10.5)	2,010 (17.5)
One to three times a month	12,863 (10.2)	16,430 (11.6)	1,456 (12.7)

Once or twice a week	32,646 (25.8)	37,487 (26.5)	2,636 (22.9)
Three or four times a week	35,332 (27.9)	34,026 (24.1)	1,948 (16.9)
Daily or almost daily	30,100 (23.8)	29,724 (21.0)	1,915 (16.7)
Fruit and vegetables intake (g/day), mean (SD)	344.4 (187.3)	318.7 (184.8)	315.4 (205.0)
Processed meat intake			
Never	13,964 (11.0)	11,473 (8.1)	1,099 (9.6)
Less than 3 portions/week	76,932 (60.8)	84,229 (59.6)	6,420 (55.8)
3 or more portions/week	35,573 (28.1)	45,582 (32.3)	3,981 (34.6)
Red meat			
Never	10,708 (8.5)	8,794 (6.2)	826 (7.2)
Less than 3 portions/week	100,096 (79.2)	111,997 (79.3)	8,544 (74.3)
3 or more portions/week	15,665 (12.4)	20,493 (14.5)	2,130 (18.5)
Oily fish			
Never	11,327 (9.0)	14,755 (10.4)	1,527 (13.3)
Less than 1 a week	91,271 (72.2)	103,922 (73.6)	8,022 (69.8)
2 or more a week	23,871 (18.9)	22,607 (16.0)	1,951 (17.0)
Health status			
Systolic blood pressure in mmHg, mean (SD)	137.0	139.7	141.6
Medications			
Cholesterol lowering	3,187 (2.5)	6,070 (4.3)	954 (8.3)
Blood pressure lowering	4,352 (3.4)	7,928 (5.6)	1,246 (10.8)
None of the above medication	118,930 (94.0)	127,286 (90.1)	9,300 (80.9)

Data presented as mean (SD) or % (n) for continuous and categorical variables as appropriate. % given as row totals. TE: total energy intake-SD: standard deviation-TV: television-BMI: body mass index-PA: physical activity-MET: metabolic equivalent.

1 **Table S4.** Hazard ratios for the association of deprivation with all-cause mortality CVD mortality and incidence.

Outcomes	Total N	Number of events	1 (Least deprived)	2	3	4	5 (Most deprived)
All-cause mortality	279245	4087	1.00 (Ref.)	1.03 (0.94; 1.14)	1.10 (1.00; 1.21)	1.23 (1.12; 1.35)	1.20 (1.08; 1.33)
CVD mortality	279245	1090	1.00 (Ref.)	1.02 (0.85; 1.23)	1.17 (0.97; 1.41)	1.26 (1.05; 1.53)	1.32 (1.09; 1.62)
CVD incidence	279245	13,466	1.00 (Ref.)	1.06 (1.01; 1.21)	1.06 (1.01; 1.12)	1.08 (1.03; 1.14)	1.14 (1.08; 1.21)

2 Data presented as adjusted hazard ratio (HR) (95%CI) per categories of deprivation quintiles. The lowest category of deprivation was used as the reference category. All analyses were restricted
 3 to participants with at least 2 years of follow-up and lack of comorbidities at baseline. All analyses were adjusted for age, sex, ethnicity, professional qualifications, current employment status,
 4 smoking, body mass index, red meat intake, processed meat intake, fruits and vegetables intake, oil fish intake, alcohol consumption, TV viewing, handgrip strength, walking pace, month of
 5 assessment, systolic blood pressure, diagnosis of hypertension and medication for CVDs.

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 7 **Table S5.** Hazard ratios for the association of handgrip strength with all-cause mortality CVD mortality and incidence.

Outcomes	Total N	Number of events	1 (Highest)	2	3 (Lowest)
All-cause mortality	279245	4087	1.00 (Ref.)	1.18 (1.10; 1.28)	1.60 (1.49; 1.73)
CVD mortality	279245	1090	1.00 (Ref.)	1.25 (1.08; 1.45)	1.75 (1.51; 2.02)
CVD incidence	279245	13,466	1.00 (Ref.)	1.15 (1.11; 1.20)	1.35 (1.29; 1.40)

8 Data presented as adjusted hazard ratio (HR) (95%CI) per age- and sex-specific tertiles of handgrip strength. The highest tertile of strength was used as the reference category. All analyses were
 9 restricted to participants with at least 2 years of follow-up and lack of comorbidities at baseline. All analyses were adjusted for age, sex, ethnicity, professional qualifications, current
 10 employment status, smoking, body mass index, red meat intake, processed meat intake, fruits and vegetables intake, oil fish intake, alcohol consumption, TV viewing, month of assessment,
 11 systolic blood pressure, diagnosis of hypertension and medication for CVDs.

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 13 **Table S6.** Hazard ratios for the association of walking pace with all-cause mortality CVD mortality and incidence.

Outcomes	Total N	Number of events	1 (Highest)	2	3 (Lowest)
All-cause mortality	279245	4087	1.00 (Ref.)	1.10 (1.03; 1.18)	1.80 (1.59; 2.03)
CVD mortality	279245	1090	1.00 (Ref.)	1.15 (1.01; 1.31)	2.28 (1.83; 2.82)
CVD incidence	279245	13,409	1.00 (Ref.)	1.10 (1.06; 1.14)	1.51 (1.40; 1.62)

14 Data presented as adjusted hazard ratio (HR) (95%CI) per categories of walking pace. Brisk walkers were used as the reference category. All analyses were restricted to participants with at least
 15 2 years of follow-up and lack of comorbidities at baseline. All analyses were adjusted for age, sex, ethnicity, professional qualifications, current employment status, smoking, body mass index,
 16 red meat intake, processed meat intake, fruits and vegetables intake, oil fish intake, alcohol consumption, TV viewing, month of assessment, systolic blood pressure, diagnosis of hypertension
 17 and medication for CVDs.

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19 **Table S7.** Hazard ratios for the association of handgrip strength with all-cause mortality, CVD mortality and incidence by deprivation strata.

Outcomes	Total N	Number of events	Exposure (categories)			HR for trend	P-value	P-interaction
			Tertile 3	Tertile 2	Tertile 1			
All-cause mortality	279030	4083						
Least deprived	61975	880	1.00 (Ref.)	1.10 (0.94; 1.29)	1.41 (1.20; 1.66)	1.18 (1.09; 1.29)	<0.001	0.024
2	59708	847	1.00 (Ref.)	1.18 (1.00; 1.39)	1.58 (1.33; 1.86)	1.25 (1.15; 1.37)	<0.001	
3	57254	843	1.00 (Ref.)	1.22 (1.03; 1.45)	1.63 (1.38; 1.93)	1.28 (1.17; 1.39)	<0.001	
4	54839	833	1.00 (Ref.)	1.14 (0.96; 1.36)	1.64 (1.39; 1.94)	1.29 (1.18; 1.40)	<0.001	
Most deprived	45254	680	1.00 (Ref.)	1.35 (1.10; 1.64)	1.69 (1.40; 2.05)	1.30 (1.18; 1.43)	<0.001	
CVD mortality	279030	1089						
Least deprived	61975	225	1.00 (Ref.)	1.12 (0.82; 1.52)	1.33 (0.96; 1.85)	1.15 (0.98; 1.36)	0.080	0.006
2	59708	213	1.00 (Ref.)	1.16 (0.83; 1.60)	1.56 (1.12; 2.18)	1.25 (1.05; 1.48)	0.010	
3	57254	230	1.00 (Ref.)	1.09 (0.78; 1.51)	1.75 (1.27; 2.39)	1.33 (1.13; 1.56)	0.001	
4	54839	220	1.00 (Ref.)	1.43 (1.01; 2.02)	2.04 (1.46; 2.86)	1.43 (1.21; 1.69)	<0.001	
Most deprived	45254	201	1.00 (Ref.)	1.70 (1.16; 2.51)	2.14 (1.47; 3.12)	1.43 (1.20; 1.71)	<0.001	
CVD incidence	279030	13409						
Least deprived	61975	3000	1.00 (Ref.)	1.06 (0.98; 1.16)	1.24 (1.13; 1.36)	1.11 (1.06; 1.16)	<0.001	0.001
2	59708	2994	1.00 (Ref.)	1.20 (1.10; 1.30)	1.29 (1.18; 1.41)	1.14 (1.09; 1.19)	<0.001	
3	57254	2777	1.00 (Ref.)	1.14 (1.04; 1.24)	1.39 (1.26; 1.52)	1.18 (1.12; 1.23)	<0.001	
4	54839	2496	1.00 (Ref.)	1.16 (1.05; 1.27)	1.38 (1.25; 1.52)	1.17 (1.12; 1.23)	<0.001	
Most deprived	45254	2142	1.00 (Ref.)	1.24 (1.11; 1.38)	1.44 (1.30; 1.61)	1.20 (1.14; 1.26)	<0.001	

20 Data presented as adjusted hazard ratio (HR) (95%CI) per categories of handgrip strength and area level deprivation quintiles. The highest category of handgrip strength (tertile 3) was used as
21 the reference category. The HR for trend indicates the change in the HR by one category lower handgrip strength. All analyses were restricted to participants with at least 2 years of follow-up.
22 All analyses were adjusted for age, sex, ethnicity, professional qualifications, current employment status, smoking, body mass index, red meat intake, processed meat intake, fruits and
23 vegetables intake, oil fish intake, alcohol consumption, time spent viewing TV, month of assessment, systolic blood pressure, diagnosis of hypertension and medication for CVDs.

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31 **Table S8.** Hazard ratios for the association of self-reported walking pace with all-cause mortality, CVD mortality and incidence by deprivation strata.

Outcomes	Total N	Number of events	Exposure (categories)			HR for trend	P-value	P-interaction
			Brisk pace	Average pace	Slow pace			
All-cause mortality	279245	4087						
Least deprived	62019	880	1.00 (Ref.)	1.08 (0.93; 1.24)	1.75 (1.31; 2.34)	1.18 (1.05; 1.34)	0.007	0.666
2	59755	847	1.00 (Ref.)	1.14 (0.98; 1.32)	1.69 (1.27; 2.26)	1.21 (1.07; 1.37)	0.002	
3	57290	843	1.00 (Ref.)	1.06 (0.91; 1.23)	2.03 (1.57; 2.64)	1.25 (1.11; 1.41)	<0.001	
4	54878	833	1.00 (Ref.)	1.07 (0.92; 1.25)	1.73 (1.33; 2.25)	1.21 (1.07; 1.37)	0.002	
Most deprived	45303	684	1.00 (Ref.)	1.16 (0.98; 1.38)	1.64 (1.26; 2.13)	1.25 (1.10; 1.42)	0.001	
CVD mortality	279245	1090						
Least deprived	62019	225	1.00 (Ref.)	0.98 (0.74; 1.31)	1.61 (0.92; 2.80)	1.11 (0.87; 1.41)	0.405	0.062
2	59755	213	1.00 (Ref.)	1.08 (0.81; 1.45)	1.49 (0.84; 2.65)	1.15 (0.90; 1.47)	0.272	
3	57290	230	1.00 (Ref.)	1.25 (0.92; 1.68)	3.11 (1.98; 4.88)	1.60 (1.26; 2.02)	<0.001	
4	54878	220	1.00 (Ref.)	1.12 (0.82; 1.51)	2.85 (1.81; 4.47)	1.51 (1.19; 1.91)	0.001	
Most deprived	45303	202	1.00 (Ref.)	1.39 (0.99; 1.95)	2.27 (1.42; 3.61)	1.49 (1.18; 1.88)	0.001	
CVD incidence	279245	13416						
Least deprived	62019	3001	1.00 (Ref.)	1.07 (0.99; 1.16)	1.37 (1.15; 1.63)	1.11 (1.04; 1.19)	0.002	0.195
2	59755	2994	1.00 (Ref.)	1.06 (0.98; 1.15)	1.48 (1.26; 1.74)	1.13 (1.05; 1.20)	<0.001	
3	57290	2777	1.00 (Ref.)	1.17 (1.08; 1.27)	1.71 (1.46; 2.00)	1.24 (1.16; 1.32)	<0.001	
4	54878	2498	1.00 (Ref.)	1.09 (1.00; 1.19)	1.51 (1.29; 1.78)	1.16 (1.08; 1.25)	<0.001	
Most deprived	45303	2146	1.00 (Ref.)	1.10 (1.00; 1.21)	1.45 (1.24; 1.69)	1.17 (1.09; 1.26)	<0.001	

32 Data presented as adjusted hazard ratio (HR) (95%CI) per categories of walking pace and area-level deprivation quintiles. The highest category of walking pace (brisk) was used as the reference
33 category. The HR for trend indicate the change in the HR by one category lower in walking pace. All analyses were restricted to participants with at least 2 years of follow-up. All analyses were
34 adjusted for age, sex, ethnicity, professional qualifications, current employment status, smoking, body mass index, red meat intake, processed meat intake, fruits and vegetables intake, oil fish
35 intake, alcohol consumption, time spent viewing TV, month of assessment, systolic blood pressure, diagnosis of hypertension and medication for CVDs.

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