Independent and joint associations of grip strength and adiposity with all-cause and cardiovascular disease mortality in 403,199 adults: The UK Biobank study

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Abstract

Background—Higher grip strength (GS) is associated with lower mortality risk. However, whether this association is independent of adiposity is uncertain.

Objective—The purpose of this study was to examine the associations between GS, adiposity and mortality.

Design—The UK Biobank study is an ongoing prospective cohort of >0.5 million UK adults aged 40-69 years. Baseline data collection (2006-2010) included measurements of GS and adiposity indicators including body mass index (BMI). Age- and gender-specific GS quintiles were used. BMI was classified according to clinical cut-points.

Results—Data from 403,199 participants were included in analyses. Over a median 7.0-year follow-up, 8,287 all-cause deaths occurred. The highest GS quintile had 32% (95% confidence interval [CI]: 26%, 38%) and 25% (95% CI: 16%, 33%) lower all-cause mortality risks in men and women, respectively, compared with the lowest GS quintile, after adjustment for confounders and BMI. Obesity class II (BMI 35) was associated with greater all-cause mortality risks. Compared with the highest GS and normal weight category, the highest GS and Obesity class II category showed relatively higher all-cause mortality hazards (not statistically significant in men); however, the increased risk was relatively lower than the risk for the lowest GS and Obesity class II category. All-cause mortality risks were generally lower for obese but stronger individuals than for non-obese but weaker individuals. Similar patterns of associations were observed for cardiovascular mortality.

Conclusions—Lower grip strength and excess adiposity are both independent predictors of higher mortality risk. The higher mortality risk associated with excess adiposity is attenuated,

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although not completely attenuated, by greater GS. Interventions/polices should focus on improving muscular strength of the population regardless of their adiposity levels.

Keywords

grip strength; adiposity; muscle strength; obesity; mortality; UK Biobank

Introduction

Obesity is a global public health concern (1). Excess adiposity is known to be associated with greater risk of mortality as well as cardiovascular disease (CVD) such as heart failure, hypertension, and coronary heart disease (2). However, substantial evidence (3) suggests greater aerobic fitness can lower the risk of death and CVD associated with greater fatness.

Muscular fitness, a complementary aspect of fitness, has also been found to be a strong predictor of mortality (4). As such, grip strength (GS), as a simple inexpensive measure of overall muscular strength (5–7), has been recognized as a useful prognostic indicator of mortality (8, 9) as well as adverse health outcomes, such as sarcopenia and frailty (10). A few studies (11–14) have attempted to further explore the "fit-fat" paradigm in relation to mortality and muscle strength, suggesting that mortality risk may be reduced in individuals with higher muscle strength irrespective of weight status. However, the evidence on the associations of muscle strength and fatness with mortality has been predicated primarily upon data with a relatively small sample size (<8000) of men (11, 12) or older adults (13). So, findings from these studies provide limited evidence on the relative risk of mortality for the combination of muscle strength and fatness for general adult populations. Furthermore, the majority of the studies have used body mass index (BMI) as a sole crude adiposity indicator (12–14). Abdominal adiposity defined by waist circumference (WC) predicts mortality independently of general adiposity (i.e. BMI, percent body fat [%BF]) (15). Hence, it is critical to discern the interactions of different adiposity indicators and muscle strength with mortality in general populations of men and women. Therefore, the purpose of the present analysis is to examine the relative risk of all-cause and CVD mortality for GS, various clinical adiposity measures (BMI, WC, %BF) and their interactions in middle-aged and older men and women.

Subjects and Methods

Study design and participants

UK Biobank is an ongoing UK national cohort of over half a million adults aged 40-69 years at recruitment. Individuals were contacted who were registered with the National Health Service and living <25 miles away from one of 22 assessment centers across the UK. Of those, >500 000 individuals performed baseline data collection (2006-2010) that included a wide variety of physical measurements and biological samples, as well as questionnaires on socio-demographic factors, family history/early-life exposures, general health/disabilities, environmental/lifestyle factors, and psychological/cognitive state. The UK Biobank methodology is described in detail elsewhere (16). All participants signed informed written

consent prior to participation, and the protocol of the UK Biobank project was approved by the North West Multi-Centre Research Ethics Committee.

Exposures

Grip strength (GS)—GS was assessed once in each hand using a Jamar J00105 hydraulic hand dynamometer, which can measure isometric grip force up to 90 kilograms (calibrated by staff at the start of each measurement day) showing good reliability and reproducibility (17). The handle of the device was adjustable to five grip positions between 1-3/8 and 3-3/8 inches. Participants were allowed to choose a grip position that they felt most comfortable with. Each participant was asked to grasp the handle of the device in their right hand while sitting upright on a chair with their forearm on the armrest. They were required to maintain a 90° angle of their elbow adjacent to their side so that their thumb would face upwards while squeezing the handle as strongly as possible for about 3 seconds. The same protocol was undertaken with the left hand. For the current analysis, values from the two hands were averaged if available; otherwise, the value from a single hand was used in a small subsample (n=1,177).

Adiposity measures—BMI was calculated as measured weight (kg) divided by measured height (m) squared. WC was measured using a tape measure at the level of the umbilicus. Fat-free mass was assessed with the Tanita BC-418MA bio-impedance analyzer, from which %BF was calculated as 1 minus fat-free mass divided by body weight. BMI was categorized into normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), obesity class I (30.0-34.9 kg/m^2) and obesity class II (35.0 kg/m^2). The following sex-specific clinical cut-offs were applied to create three groups of WC and %BF: WC<94cm, 94-102cm or 102cm for men; WC<80cm, 80-88cm, or 88cm for women (1); %BF 20%, 20-25% or >25% for men; and %BF 30%, 30-33% or >33% for women (18).

Outcomes

Participants were followed up for mortality until February 15th 2016 through linkage with death records from the National Health Service Information Centre and the Scottish Morbidity Record. CVD mortality was defined as the International Classification of Diseases-10 codes F01 and I00-I99. The median follow-up period was 7 years (interquartile range: 6.3 and 7.6 years).

Covariates

The following variables that could confound GS-mortality associations were included as covariates in the analyses: ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index (a composite score of employment, car ownership, home ownership and household overcrowding, with higher values indicating a given area's higher degree of deprivation), statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently 3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity (MVPA) (minutes/day). MVPA time was estimated based on self-reported walking, transportation activities, occupational activities/

walking, strenuous/other exercise, and do-it-yourself activities by calibrating them to heart rate and accelerometry data (19) from 12 435 UK adults participating in the Fenland project (20).

Statistical analyses

Cox regression models (with age as the underlying time scale) were used to estimate associations of GS and adiposity with all-cause and CVD mortality. First, models were fit to estimate associations between GS and mortality, with adjustment for potential confounders (Model 1). Further adjustments for each of the three adiposity indicators (BMI, WC or %BF) were made in three separate models (Models 2a, 2b and 2c). In parallel with the models using GS as an exposure variable, models using each adiposity measure as an exposure variable were also fitted with adjustment for the same covariates (Model 1) and additional adjustments for GS (Model 2). Models using per-5kg increment in GS as an exposure were fitted by personal/lifestyle risk factor and disease status. GS-mortality associations were stratified by each adiposity variable. Gender- and age-specific quintiles of GS (Q1-Q5) and different adiposity categories were combined to examine joint associations with mortality. All analyses were performed for men and women separately. Subgroup analyses and tests of interaction between GS and age, weight status, waist circumference, %BF, MVPA, TV viewing, smoking, alcohol consumption, hypertension and diabetes were performed. Log-log plots provided support for the proportional hazards assumptions for all covariates. Sensitivity analyses were performed 1) using the maximum GS from either hand, 2) GS normalized for body weight or fat-free mass to account for variation by body size, 3) excluding the first 2-year mortality follow-up, and 4) excluding individuals who had chronic obstructive pulmonary disease or were 'current'/'previous' smokers at baseline when examining adiposity as exposure (the latter two to minimize the risk of reverse causality). All analyses were performed in STATA/SE Version 14 (StataCorp LP, College Station, TX).

Results

Of an initial sample of 502,639 participants who undertook baseline data collection, individuals were excluded if they had a history of heart attack, stroke or cancer at baseline (n=55,401) to minimize the risk for reverse causality (8, 21), their censoring date was before the date of baseline data collection (n=3) or they had missing values on any of the variables (n=44,036), leaving 403,199 participants in the final analytic sample (Supplemental Figure 1).

Table 1 shows participants' characteristics across quintiles of GS. The specific cut-points to create the gender- and age-specific quintiles of GS are shown in Supplemental Table 1. A total of 8,081 all-cause deaths occurred during 1,268,314 person-years of follow-up for men and 1,533,538 person-years for women. Differences in BMI, WC, and %BF across quintiles of GS and the correlations between these variables (Supplemental Table 2) were minimal.

Table 2 summarizes associations between GS and all-cause mortality. Compared with the lowest quintile of GS, the highest quintile of GS had considerably lower risks of all-cause mortality in both men and women (except for Q2) after adjusting for confounders (Model 1) plus additional adjustments for each adiposity measure (Model 2): p-values for trends

<0.0001. Specifically, hazards of all-cause mortality were approximately 32% (95% confidence interval [CI]: 26%, 38%) and 25% (95%CI: 16%, 33%) lower for men and women in Q5 of GS, respectively, compared with Q1 of GS after adjusting for confounders and BMI (Model 2a). The hazard ratios (HR) for per-5kg increase in GS was 0.92 for both men (95%CI: 0.90, 0.93) and women (95%CI: 0.89, 0.95) after adjusting for all confounders and BMI (Model 2a). Sensitivity analyses found similar associations with the maximal GS from either hand, and GS unnormalized or normalized for body weight or fat-free mass (Supplemental Figure 2). Another sensitivity analysis removing the first 2 years of follow-up yielded similar results (Supplemental Table 3). The pattern of associations of GS with CVD mortality was similar to the associations with all-cause mortality for men (Table 2). While the HRs were not statistically significant in women, p-values for linear trends were all less than 0.05. The associations of per-5kg increase in GS with all-cause and CVD mortality were significant (p-values<0.05) within almost all of the subgroups examined in both men and women (Figure 1), with some exceptions particularly for women.

Associations of adiposity measures with all-cause and CVD mortality after adjusting for confounders (Model 1) and GS (Model 2) are shown in Supplemental Table 4. There were 'J-shaped' associations between BMI and mortality risk (i.e. substantially lower all-cause mortality only in overweight men compared with normal weight men), which persisted even after excluding individuals who had chronic obstructive pulmonary disease and/or were 'current'/'previous' smokers at baseline (Supplemental Table 5). The highest categories of BMI (i.e. obesity class II) and WC (i.e. abdominal obesity in men) were associated with increased hazards of all-cause and CVD mortality.

Figure 2 shows joint associations of GS quintiles and adiposity categories with all-cause mortality. Compared with normal weight men with the highest level of GS, more obese men with lower GS had higher risks of all-cause mortality. For example, men with the highest level of BMI (i.e. Obesity class II) and lowest level of GS had a 89% higher risk of all-cause mortality (HR: 1.89; 95%CI: 1.50, 2.39) compared with the normal weight men with the highest GS. A notable observation was the relatively higher mortality risks for normal weight men with lower GS in comparison with more obese men with higher GS. Similar trends of findings were observed with WC and %BF as adiposity indicators.

Similarly, more obese women with lower GS had generally higher all-cause mortality risks compared with normal weight women with higher GS. The HR for women with the highest BMI level (i.e. Obesity class II) and lowest GS was 1.69 (95%CI: 1.32, 2.16) compared with normal weight women with the highest GS. The higher GS quintiles in the Obesity class II category were associated with significantly higher risks of all-cause mortality compared with the reference group. Joint analyses with WC and %BF as adiposity indicators found more obese women with higher GS to have lower all-cause mortality risks compared with non-obese women with lower GS. This pattern of associations was, in general, similar to the associations observed for CVD mortality (Figure 3).

The lower GS quintiles had relatively higher all-cause (Supplemental Figure 3) and CVD mortality (Supplemental Figure 4) risks compared with the highest GS quintile within each adiposity stratum in both men and women.

Discussion

This study investigated the complex interplay of GS and various clinical adiposity measures with mortality from all causes and CVD in middle-aged and older men and women. Overall, greater GS was strongly associated with lower all-cause mortality risks, independently of adiposity measures. Moreover, every 5kg increment in GS was associated with about 8% lower hazard of mortality across nearly all subgroups defined by demographic and lifestyle risk factors or disease status. In contrast, adiposity measures had non-significant and/or inconsistent associations with mortality, although obesity class II and abdominal obesity were strong predictors of mortality, independent of GS. The mortality risk was highest for men and women with the lowest level of GS and the highest level of adiposity in the combined analyses. More importantly, obese individuals with greater GS had lower or similar mortality risks compared with non-obese individuals with lower GS. The pattern of associations between GS and CVD mortality was comparable to the findings for all-cause mortality. Overall, our findings provide compelling rationales for developing interventions and policies to improve muscular strength and reduce excess adiposity to minimize mortality risk.

The findings of this study are consistent with previous research by Leong at al. (9), which also demonstrated the high prognostic value of GS for various mortality and adverse health outcomes in 139,691 adults from 17 countries of different economic status. The HR of all-cause mortality for every 5kg reduction was 1.16 in Leong et al. study (9) but 1.08 (i.e. 1/0.92) in the present study. Some potential reasons for the difference are the use of gender- and age-specific quintiles of GS to take into account the inherent variation of GS by gender and age since GS is higher in men and younger individuals, and the exclusion of baseline medical conditions to minimize potential bias due to underlying subclinical conditions on GS and mortality in the present study. Furthermore, the use of a substantially larger sample allowed for comprehensive subgroup analyses by a number of lifestyle risk factors as well as disease status.

The present study is generally consistent with the previous studies (11–14) in terms of the independent and joint associations of GS and adiposity with mortality outcomes. For instance, greater muscle strength predicted mortality independent of adiposity (11–14). In addition, the highest mortality risk was observed in individuals with the lowest muscle strength level and the highest adiposity level, implying the interactive impacts of muscle strength and adiposity on mortality (11, 12, 14). However, a novel observation of the present study is that strong obese individuals had relatively lower mortality risks compared with weak non-obese individuals. This suggests that improving muscle strength may be a more important public health priority than reducing adiposity levels in decreasing mortality risks, although excessive adiposity itself is a strong risk factor for mortality (15). Another novel aspect of this study over the previous studies (11–14) is the use of a large cohort dataset, which enabled to create multiple sub-groups of GS and various clinical adiposity indicators in examining the joint associations with mortality in men and women separately.

The present study found that men had more consistent associations between GS and mortality (independent of adiposity) than women, which is in line with previous research

(13). There is also evidence on the weaker associations of GS with all-cause mortality for women (22). In this regard, convincing evidence suggests an age-related decline in muscle strength in women (particularly after menopause) can be prevented through estrogen-hormone replacement therapy (23). However, none of the previous studies (13, 22) included estrogen-hormone replacement therapy as a potential confounder in the models for women whereas the present study did. Our study clearly demonstrated lower mortality rates for both men and women with greater GS. Moreover, given that current public health guidelines (24) recommend that both men and women do muscle-strengthening activities at least twice a week, interventions and policies should be designed and implemented in a way to encourage both genders to engage in regular muscle-strengthening activities, regardless of their adiposity levels.

Compelling evidence suggests that resistance exercise can result in improvements in muscle strength (including GS) and neuromotor functions in healthy and clinical adult populations (25). It appears that muscle strength gained through resistance exercise can diminish rapidly after the termination of training, but its effects on neuromotor functions can be sustained for a relatively long period of time even with a weekly session of moderate-to-vigorous intensity resistance exercise (25). We observed weak relationships between GS and adiposity measures, suggesting greater GS is determined based on better neuromotor functions rather than higher adiposity itself. Nonetheless, it is important to point out that the effects of resistance training are typically site-specific (26), so training solely GS may not necessarily yield favorable effects on other parts of the body. Thus, efforts should be placed on improving whole-body muscle strength as well as neuromuscular functions.

Effects of resistance training on reducing metabolic risk are also well-documented. Specifically, glucose metabolisms and insulin sensitivity can be enhanced in response to resistance exercise (27). In the present study, the prevalence of diabetes was lower in both men and women across incremental GS quintiles. It may be that participation in resistance training was higher in those with greater GS since people use their hands in most upper-body resistance training. This suggests individuals with greater muscle strength may sustain metabolically healthier lives.

Furthermore, a meta-analysis of randomized-controlled trials concluded that resistance training programs reduced levels of lipids and lipoproteins circulating in the blood stream (28). However, high-intensity resistance training may increase arterial stiffness (29), which may then increase the risk of mortality and CVD (30). More evidence is needed to determine the specific dose-response relationship between resistance training and health outcomes.

This study is not without limitations. First, the use of data from an observational prospective study cannot fully determine causal relationships between GS and mortality. However, we excluded individuals with critical medical conditions at baseline in the primary analysis, and further excluded individuals who died in the first 2 years of follow-up and individuals who had respiratory disease or were current or previous smokers at baseline in the sensitivity analysis, in order to minimize the risk for reverse causality. Second, due to the lack of sampling strategies for recruiting samples in UK Biobank, results of this study may only be generalizable to those of similar characteristics to the sample analyzed here. Another

limitation is the measurement method for aerobic fitness, a strong mortality predictor (31). Ideally, this is measured as oxygen consumption during maximal exercise tests. We adjusted for resting pulse rate instead, which is strongly associated with maximal oxygen consumption (32). The relatively low number of death cases in the analysis for CVD mortality is another limitation. Finally, the use of self-reported data for some of the covariates may have increased the risk of residual confounding.

Conclusions

Men and women with greater GS had lower risks of all-cause and CVD mortality, independent of adiposity. While excess adiposity *per se* presents substantial risk of mortality, the risk associated with excess adiposity was reduced, although not completely eliminated, through greater GS. Public health efforts should aim to improve muscle strength of the population in all adiposity levels.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

Abbreviations

BMI	body mass index
CVD	cardiovascular disease
GS	grip strength
HR	hazard ratio
MVPA	moderate-to-vigorous physical activity
%BF	percent body fat
WC	waist circumference

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A. All-cause mortality

Men

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Age groups					
<50yrs	0.90 (0.85, 0.95)	46175	391	120.7	0.016
50-59yrs	0.90 (0.87, 0.93)	60330	1210	287.1	
≥60yrs	0.92 (0.90, 0.94)	76501	3448	659.4	
Weight Status					
Normal Weight (18.5≤BMI<25)	0.89 (0.86, 0.92)	45623	1203	380.2	0.005
Overweight (25≤BMI<30)	0.92 (0.90, 0.95)	91493	2277	358.7	
Obesity class I (30≤BMI<35)	0.94 (0.91, 0.98)	35495	1103	449.0	
Obesity class II (BMI≥35)	0.92 (0.87, 0.98)	9989	411	596.9	
Waist Circumference					
<94cm(M) or <80(W)	0.89 (0.86, 0.91)	82862	1877	326.5	0.005
94-102cm(M) or 80-88(W)	0.92 (0.89, 0.96)	46394	1224	379.5	
≥102cm(M) or ≥88(W)	0.93 (0.90, 0.95)	53750	1948	525.0	
Percent Body Fat					
≤20%(M) or ≤30%(W)	0.86 (0.83, 0.90)	33532	773	331.3	<0.0001
20-25%(M) or 30-33%(W)	0.91 (0.88, 0.94)	56487	1272	324.2	
>25%(M) or >33%(W)	0.93 (0.91, 0.95)	92987	3004	467.4	
MVPA					
Lower 50%	0.90 (0.88, 0.92)	91503	3468	551.4	0.049
Upper 50%	0.94 (0.91, 0.97)	91503	1581	247.3	
TV					
≤2hours/day	0.90 (0.87, 0.92)	87964	1825	298.4	0.193
>2hours/day	0.92 (0.90, 0.94)	94074	3180	489.1	
Meat consumption					
≤5times/week	0.91 (0.89, 0.94)	96661	2390	356.7	0.455
>5times/week	0.91 (0.89, 0.93)	86345	2659	444.5	
Smoking					
Never	0.91 (0.88, 0.94)	92302	1675	261.0	0.270
Previous	0.92 (0.90, 0.95)	68260	2209	468.3	
Current	0.91 (0.88, 0.94)	22444	1165	752.2	
Alcohol consumption					
Never	0.82 (0.74, 0.91)	4855	116	346.9	0.790
Previous	0.90 (0.84, 0.96)	5941	300	738.6	
Current, <3times a week	0.93 (0.91, 0.96)	76530	1998	377.0	
Current, ≥3times a week	0.90 (0.88, 0.93)	95680	2635	396.7	
Hypertension					
No	0.90 (0.87, 0.93)	71205	1309	264.7	0.058
Yes	0.92 (0.90, 0.94)	111800	3740	483.4	
Diabetes					
No	0.92 (0.90, 0.94)	171235	4359	366.8	0.289
Yes	0.89 (0.85, 0.93)	11197	661	869.2	
Overall	0.91 (0.91, 0.92)				

Women

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Age groups					
<50yrs	0.91 (0.83, 1.00)	55106	301	77.9	0.955
50-59yrs	0.93 (0.88, 0.98)	76749	841	156.7	
≥60yrs	0.90 (0.87, 0.94)	88338	2096	343.3	
Weight Status					
Normal Weight (18.5≤BMI<25)	0.91 (0.86, 0.96)	85682	1090	182.6	0.310
Overweight (25≤BMI<30)	0.92 (0.88, 0.97)	81582	1199	210.9	
Obesity class I (30≤BMI<35)	0.88 (0.82, 0.95)	34426	540	225.3	
Obesity class II (BMI≥35)	0.98 (0.90, 1.06)	16806	369	315.8	
Waist Circumference					
<94cm(M) or <80(W)	0.92 (0.87, 0.97)	93490	1119	171.7	0.501
94-102cm(M) or 80-88(W)	0.90 (0.84, 0.96)	48220	637	189.5	
≥102cm(M) or ≥88(W)	0.92 (0.88, 0.96)	78483	1482	271.6	
Percent Body Fat					
≤20%(M) or ≤30%(W)	0.86 (0.80, 0.94)	38723	459	169.9	0.158
20-25%(M) or 30-33%(W)	0.97 (0.88, 1.06)	28259	352	178.8	
>25%(M) or >33%(W)	0.92 (0.89, 0.95)	153211	2427	227.6	
MVPA					
Lower 50%	0.91 (0.87, 0.94)	110095	2127	277.9	0.168
Upper 50%	0.94 (0.89, 0.99)	110098	1111	144.6	
TV					
≤2hours/day	0.95 (0.91, 1.00)	105765	1180	160.0	0.044
>2hours/day	0.90 (0.87, 0.93)	112542	2013	257.1	
Meat consumption					
≤5times/week	0.92 (0.89, 0.96)	161828	2303	204.4	0.315
>5times/week	0.89 (0.84, 0.94)	58365	935	229.9	
Smoking					
Never	0.92 (0.88, 0.96)	132794	1534	165.7	0.057
Previous	0.94 (0.89, 0.99)	68252	1139	240.0	
Current	0.87 (0.82, 0.94)	19147	565	423.5	
Alcohol consumption					
Never	0.82 (0.73, 0.91)	12385	225	263.5	0.201
Previous	0.86 (0.65, 1.08)	7522	203	390.7	
Current, <3times a week	0.94 (0.90, 0.97)	118342	1748	212.1	
Current, ≥3times a week	0.91 (0.87, 0.96)	81944	1062	185.6	
Hypertension					
No	0.90 (0.86, 0.95)	115096	1213	151.1	0.262
Yes	0.92 (0.89, 0.96)	105096	2025	277.0	
Diabetes					
No	0.92 (0.89, 0.95)	212212	2977	201.3	0.534
Yes	0.88 (0.80, 0.98)	7553	257	496.5	
Overall	0.91 (0.91, 0.92)				

B. CVD mortality

Men

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Age groups					
<50yrs	0.85 (0.76, 0.95)	46175	98	30.3	0.476
50-59yrs	0.88 (0.82, 0.93)	60330	312	74.0	
≥60yrs	0.88 (0.85, 0.92)	76501	846	161.8	
Weight Status					
Normal Weight (18.5≤BMI<25)	0.85 (0.78, 0.92)	45623	248	78.4	0.075
Overweight (25≤BMI<30)	0.88 (0.84, 0.93)	91493	557	87.8	
Obesity class I (30≤BMI<35)	0.92 (0.86, 0.98)	35495	289	117.6	
Obesity class II (BMI≥35)	0.89 (0.82, 0.98)	9989	152	220.8	
Waist Circumference					
<94cm(M) or <80(W)	0.82 (0.77, 0.87)	82862	411	71.5	0.001
94-102cm(M) or 80-88(W)	0.90 (0.84, 0.97)	46394	298	92.4	
≥102cm(M) or ≥88(W)	0.91 (0.87, 0.96)	53750	547	147.4	
Percent Body Fat					
≤20%(M) or ≤30%(W)	0.82 (0.75, 0.91)	33532	160	68.6	0.017
20-25%(M) or 30-33%(W)	0.88 (0.82, 0.94)	56487	276	70.4	
>25%(M) or >33%(W)	0.90 (0.86, 0.94)	92987	820	127.6	
MVPA					
Lower 50%	0.87 (0.84, 0.91)	91503	887	141.0	0.520
Upper 50%	0.91 (0.85, 0.97)	91503	369	57.7	
TV					
≤2hours/day	0.88 (0.83, 0.93)	87964	467	76.4	0.894
>2hours/day	0.88 (0.84, 0.92)	94074	783	120.4	
Meat consumption					
≤5times/week	0.90 (0.85, 0.94)	96661	592	88.3	0.153
>5times/week	0.86 (0.83, 0.90)	86345	664	111.0	
Smoking					
Never	0.89 (0.84, 0.94)	92302	418	65.1	0.234
Previous	0.89 (0.85, 0.94)	68260	545	115.5	
Current	0.86 (0.80, 0.92)	22444	293	189.2	
Alcohol consumption					
Never	0.99 (0.79, 1.25)	4855	26	77.7	0.027
Previous	0.91 (0.80, 1.03)	5941	76	187.1	
Current, <3times a week	0.89 (0.85, 0.94)	76530	534	100.7	
Current, ≥3times a week	0.86 (0.82, 0.90)	95680	620	93.3	
Hypertension					
No	0.86 (0.80, 0.93)	71205	240	48.5	0.294
Yes	0.88 (0.85, 0.91)	111800	1016	131.3	
Diabetes					
No	0.88 (0.85, 0.91)	171235	1036	87.2	0.363
Yes	0.90 (0.83, 0.97)	11197	217	285.3	
Overall	0.88 (0.87, 0.89)				

Women

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Age groups					
<50yrs	1.06 (0.84, 1.34)	55106	44	11.4	0.386
50-59yrs	0.93 (0.79, 1.09)	76749	100	18.6	
≥60yrs	0.92 (0.84, 1.01)	88338	341	55.9	
Weight Status					
Normal Weight (18.5≤BMI<25)	0.87 (0.75, 1.00)	85682	148	24.8	0.045
Overweight (25≤BMI<30)	0.93 (0.81, 1.05)	81582	175	30.8	
Obesity class I (30≤BMI<35)	0.92 (0.76, 1.11)	34426	78	32.5	
Obesity class II (BMI≥35)	1.09 (0.92, 1.30)	16806	78	66.8	
Waist Circumference					
<94cm(M) or <80(W)	0.96 (0.83, 1.12)	93490	144	22.1	0.534
94-102cm(M) or 80-88(W)	0.81 (0.67, 0.98)	48220	79	23.5	
≥102cm(M) or ≥88(W)	0.97 (0.88, 1.08)	78483	262	48.0	
Percent Body Fat					
≤20%(M) or ≤30%(W)	1.00 (0.81, 1.25)	38723	65	24.1	0.705
20-25%(M) or 30-33%(W)	0.84 (0.65, 1.08)	28259	45	22.9	
>25%(M) or >33%(W)	0.95 (0.87, 1.03)	153211	375	35.2	
MVPA					
Lower 50%	1.00 (0.91, 1.09)	110095	339	44.3	0.009
Upper 50%	0.80 (0.69, 0.92)	110098	146	19.0	
TV					
≤2hours/day	0.91 (0.79, 1.04)	105765	150	20.3	0.658
>2hours/day	0.97 (0.88, 1.06)	112542	322	41.1	
Meat consumption					
≤5times/week	0.94 (0.85, 1.03)	161828	326	28.9	0.626
>5times/week	0.94 (0.83, 1.08)	58365	159	39.1	
Smoking					
Never	0.89 (0.79, 0.99)	132794	238	25.7	0.066
Previous	0.97 (0.84, 1.11)	68252	152	32.0	
Current	1.04 (0.87, 1.23)	19147	95	71.2	
Alcohol consumption					
Never	0.81 (0.64, 1.02)	12385	49	57.4	0.424
Previous	0.92 (0.71, 1.19)	7522	34	65.4	
Current, <3times a week	0.98 (0.88, 1.08)	118342	272	33.0	
Current, ≥3times a week	0.92 (0.79, 1.08)	81944	130	22.7	
Hypertension					
No	0.96 (0.83, 1.10)	115096	139	17.3	0.965
Yes	0.93 (0.85, 1.02)	105096	346	47.3	
Diabetes					
No	0.95 (0.87, 1.03)	212212	421	28.5	0.834
Yes	0.93 (0.76, 1.15)	7553	64	123.7	
Overall	0.94 (0.91, 0.96)				

Figure 1.

Associations of per-5kg increment of grip strength with all-cause and cardiovascular disease (CVD) mortality for men and women. Models (using age as the underlying time variable) were adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current; except for models stratified by smoking status), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently ≥3times/week; except for models stratified by alcohol

consumption), processed/red meat consumption (days/week; except for models stratified by processed/red meat consumption), resting pulse rate (beats/min), moderate-to-vigorous physical activity (MVPA) time (minutes/day; except for models stratified by MVPA), and body mass index (BMI) (except for models stratified by BMI, waist circumference and percent body fat). Hypertension was defined as systolic/diastolic blood pressure   140/90mm Hg, reported physician diagnosis of hypertension, or reported medication use to regulate blood pressure. Participants were considered to have diabetes if they reported a physician diagnosis of diabetes, or taking glucose-lowering treatment. Mortality rate is crude mortality rate per 100,000-person years. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded in the BMI-stratified models. Abbreviations: HR – hazard ratio; CI – confidence interval; M – men; W– Women.

All-cause mortality

Men

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Normal Weight: 18.5≤BMI<25					
Q5 (Reference)	1.00 (1.00, 1.00)	7554	158	294.0	.080
Q4	0.97 (0.79, 1.20)	9330	202	309.2	
Q3	1.00 (0.82, 1.23)	9449	214	325.4	
Q2	1.25 (1.03, 1.53)	9357	249	387.1	
Q1	1.63 (1.35, 1.96)	9933	380	565.3	
Overweight: 25≤BMI<30					
Q5	0.92 (0.76, 1.10)	20432	407	281.1	
Q4	1.02 (0.85, 1.23)	19865	484	349.1	
Q3	0.96 (0.80, 1.15)	18424	423	331.0	
Q2	1.05 (0.88, 1.27)	16374	400	355.2	
Q1	1.33 (1.11, 1.58)	16398	563	507.6	
Obesity class I: 30≤BMI<35					
Q5	1.10 (0.90, 1.36)	8500	213	355.1	
Q4	1.13 (0.92, 1.39)	7419	217	420.8	
Q3	1.16 (0.94, 1.43)	6742	206	442.1	
Q2	1.24 (1.00, 1.53)	6049	196	471.6	
Q1	1.35 (1.11, 1.65)	6785	271	589.5	
Obesity class II: BMI≥35					
Q5	1.11 (0.82, 1.51)	2106	56	376.3	
Q4	1.31 (0.98, 1.75)	1812	65	519.5	
Q3	1.42 (1.07, 1.88)	1813	71	568.5	
Q2	1.54 (1.18, 2.02)	1893	84	644.0	
Q1	1.89 (1.50, 2.39)	2365	135	847.4	
WC: <94cm(M) or <80(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	16148	280	244.2	.051
Q4	1.07 (0.92, 1.26)	17693	357	288.5	
Q3	1.02 (0.87, 1.20)	17006	335	283.6	
Q2	1.25 (1.07, 1.47)	16022	366	332.5	
Q1	1.65 (1.43, 1.91)	15993	539	498.3	
WC: 94-102cm(M) or 80-88(W)					
Q5	1.06 (0.89, 1.27)	10514	223	298.8	
Q4	1.12 (0.94, 1.32)	9889	249	360.0	
Q3	1.13 (0.95, 1.35)	9281	234	363.1	
Q2	1.18 (0.99, 1.42)	8259	215	377.5	
Q1	1.48 (1.25, 1.74)	8451	303	528.8	
WC: ≥102cm(M) or ≥88(W)					
Q5	1.22 (1.04, 1.43)	11943	332	394.5	
Q4	1.32 (1.13, 1.54)	10873	366	485.7	
Q3	1.32 (1.13, 1.55)	10210	351	497.7	
Q2	1.44 (1.23, 1.68)	9478	352	540.7	
Q1	1.72 (1.48, 1.99)	11246	547	720.7	
% BF: ≤20%(M) or ≤30%(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	7308	122	234.8	<0.0001
Q4	0.97 (0.76, 1.25)	7349	129	250.4	
Q3	1.16 (0.91, 1.47)	6856	145	303.9	
Q2	1.37 (1.08, 1.75)	6139	149	352.2	
Q1	1.89 (1.52, 2.36)	5880	228	572.2	
% BF: 20-25%(M) or 30-33%(W)					
Q5	0.94 (0.75, 1.17)	12791	231	254.6	
Q4	1.01 (0.81, 1.25)	12331	265	307.6	
Q3	0.93 (0.74, 1.16)	11304	227	289.0	
Q2	1.04 (0.83, 1.30)	10242	219	311.2	
Q1	1.49 (1.21, 1.84)	9819	330	496.2	
% BF: >25%(M) or >33%(W)					
Q5	1.02 (0.84, 1.25)	18506	482	368.6	
Q4	1.10 (0.91, 1.34)	18775	578	442.6	
Q3	1.07 (0.88, 1.30)	18337	548	432.0	
Q2	1.19 (0.98, 1.45)	17378	565	473.0	
Q1	1.39 (1.14, 1.68)	19991	831	615.5	

Women

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Normal Weight: 18.5≤BMI<25					
Q5 (Reference)	1.00 (1.00, 1.00)	19034	198	145.8	.340
Q4	1.04 (0.85, 1.26)	18776	203	154.4	
Q3	1.10 (0.91, 1.33)	18380	231	181.4	
Q2	1.31 (1.08, 1.58)	15779	226	207.8	
Q1	1.40 (1.16, 1.69)	13713	232	248.1	
Overweight: 25≤BMI<30					
Q5	0.97 (0.80, 1.17)	18359	228	174.9	
Q4	1.03 (0.85, 1.24)	17178	224	186.0	
Q3	1.05 (0.87, 1.27)	16885	244	207.7	
Q2	1.26 (1.04, 1.52)	14650	243	241.0	
Q1	1.25 (1.04, 1.51)	14510	260	261.9	
Obesity class I: 30≤BMI<35					
Q5	0.88 (0.68, 1.13)	7553	90	167.8	
Q4	1.05 (0.82, 1.34)	6785	97	204.2	
Q3	1.00 (0.79, 1.27)	6873	102	213.8	
Q2	1.29 (1.02, 1.63)	6196	113	264.6	
Q1	1.28 (1.02, 1.59)	7019	138	286.8	
Obesity class II: BMI≥35					
Q5	1.49 (1.13, 1.95)	3699	73	279.1	
Q4	1.50 (1.12, 2.00)	3090	63	290.6	
Q3	1.57 (1.19, 2.07)	3117	71	328.6	
Q2	1.49 (1.11, 1.98)	2930	62	307.5	
Q1	1.69 (1.32, 2.16)	3970	100	367.1	
WC: <94cm(M) or <80(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	20592	215	146.2	.808
Q4	0.97 (0.80, 1.17)	20518	206	143.1	
Q3	0.98 (0.81, 1.18)	20132	227	162.7	
Q2	1.23 (1.02, 1.48)	17259	234	196.7	
Q1	1.32 (1.09, 1.58)	14989	237	231.9	
WC: 94-102cm(M) or 80-88(W)					
Q5	0.81 (0.64, 1.01)	10875	113	146.3	
Q4	0.94 (0.75, 1.17)	10181	123	172.6	
Q3	0.91 (0.73, 1.14)	10015	126	180.6	
Q2	1.17 (0.95, 1.46)	8714	136	226.8	
Q1	1.13 (0.91, 1.40)	8435	139	240.2	
WC: ≥102cm(M) or ≥88(W)					
Q5	1.05 (0.87, 1.26)	17394	264	214.2	
Q4	1.16 (0.97, 1.39)	15475	263	242.8	
Q3	1.24 (1.04, 1.48)	15502	303	281.8	
Q2	1.33 (1.11, 1.60)	13951	292	293.6	
Q1	1.41 (1.19, 1.68)	16161	370	334.6	
% BF: ≤20%(M) or ≤30%(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	9536	88	129.1	.181
Q4	0.87 (0.63, 1.18)	8620	72	119.1	
Q3	1.23 (0.93, 1.63)	8007	104	187.9	
Q2	1.29 (0.96, 1.74)	6872	90	189.8	
Q1	1.60 (1.20, 2.13)	5688	105	270.6	
% BF: 20-25%(M) or 30-33%(W)					
Q5	1.08 (0.79, 1.46)	6547	78	167.5	
Q4	0.99 (0.72, 1.36)	6246	67	153.0	
Q3	0.91 (0.66, 1.26)	5847	64	157.8	
Q2	1.25 (0.92, 1.70)	5189	75	209.9	
Q1	1.22 (0.89, 1.67)	4430	68	224.8	
% BF: >25%(M) or >33%(W)					
Q5	0.92 (0.73, 1.16)	32778	426	182.9	
Q4	1.04 (0.83, 1.31)	31308	453	206.6	
Q3	1.02 (0.81, 1.29)	31795	488	220.9	
Q2	1.21 (0.96, 1.52)	27863	487	253.9	
Q1	1.24 (0.99, 1.56)	29467	573	284.2	

(Men x-axis: 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0; Women x-axis: 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0)

Figure 2.

Joint associations of grip strength and body mass index, waist circumference or percent body fat with all-cause mortality for men and women. All Cox regression models (using age as the underlying time variable) were adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently 3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity time (minutes/day). The quintiles of grip strength were gender- and age-specific. Mortality rate is crude mortality rate per 100,000-person years. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded in the models with BMI. Abbreviations: HR – hazard ratio; CI – confidence interval; M– men; W– Women.
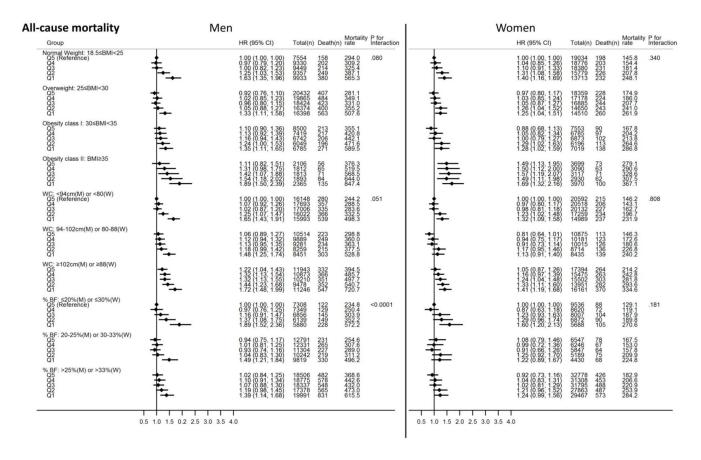
CVD mortality

Men

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Normal Weight: 18.5≤BMI<25					
Q5 (Reference)	1.00 (1.00, 1.00)	7554	23	42.8	.397
Q4	1.48 (0.90, 2.45)	9330	45	68.9	
Q3	1.47 (0.89, 2.42)	9449	46	69.9	
Q2	1.69 (1.03, 2.78)	9357	50	77.7	
Q1	2.34 (1.47, 3.72)	9933	84	125.0	
Overweight: 25≤BMI<30					
Q5	1.28 (0.81, 2.03)	20432	84	58.0	
Q4	1.61 (1.03, 2.52)	19865	113	81.5	
Q3	1.52 (0.96, 2.39)	18424	100	78.3	
Q2	1.89 (1.20, 2.96)	16374	108	95.9	
Q1	2.31 (1.49, 3.59)	16398	152	137.0	
Obesity class I: 30≤BMI<35					
Q5	1.93 (1.18, 3.14)	8500	56	93.4	
Q4	1.97 (1.21, 3.20)	7419	57	110.5	
Q3	1.75 (1.06, 2.89)	6742	48	103.0	
Q2	1.97 (1.19, 3.25)	6049	48	115.5	
Q1	2.55 (1.60, 4.07)	6785	80	174.0	
Obesity class II: BMI≥35					
Q5	2.21 (1.17, 4.14)	2106	17	114.2	
Q4	2.59 (1.42, 4.73)	1812	20	159.9	
Q3	3.28 (1.86, 5.78)	1813	26	208.2	
Q2	4.63 (2.76, 7.78)	1893	40	306.7	
Q1	4.17 (2.52, 6.90)	2365	49	307.6	
WC: <94cm(M) or <80(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	16148	45	39.2	.008
Q4	1.47 (1.02, 2.12)	17693	79	63.8	
Q3	1.19 (0.81, 1.74)	17006	63	53.3	
Q2	1.66 (1.15, 2.39)	16022	79	71.8	
Q1	2.64 (1.89, 3.70)	15993	145	134.1	
WC: 94-102cm(M) or 80-88(W)					
Q5	1.36 (0.90, 2.05)	10514	46	61.6	
Q4	1.59 (1.07, 2.35)	9889	57	82.4	
Q3	2.04 (1.40, 2.98)	9281	69	107.1	
Q2	1.81 (1.22, 2.69)	8259	54	94.8	
Q1	2.08 (1.43, 3.03)	8451	72	125.7	
WC: ≥102cm(M) or ≥88(W)					
Q5	1.99 (1.39, 2.85)	11943	89	105.8	
Q4	2.16 (1.51, 3.08)	10873	99	131.4	
Q3	2.02 (1.41, 2.90)	10210	90	127.6	
Q2	2.73 (1.93, 3.88)	9478	113	173.6	
Q1	2.82 (2.01, 3.96)	11246	156	205.5	
% BF: ≤20%(M) or ≤30%(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	7308	21	40.4	.055
Q4	1.18 (0.67, 2.09)	7349	27	52.4	
Q3	1.38 (0.79, 2.42)	6856	30	62.9	
Q2	1.53 (0.87, 2.68)	6139	29	68.5	
Q1	2.45 (1.47, 4.06)	5880	53	133.0	
% BF: 20-25%(M) or 30-33%(W)					
Q5	1.00 (0.59, 1.69)	12791	43	47.4	
Q4	1.27 (0.77, 2.10)	12331	58	67.3	
Q3	1.10 (0.66, 1.84)	11304	47	59.8	
Q2	1.27 (0.76, 2.12)	10242	47	66.8	
Q1	2.02 (1.25, 3.27)	9819	81	121.8	
% BF: >25%(M) or >33%(W)					
Q5	1.40 (0.88, 2.23)	18506	116	88.7	
Q4	1.62 (1.02, 2.59)	18775	150	114.9	
Q3	1.58 (1.00, 2.50)	18337	145	114.3	
Q2	1.99 (1.26, 3.14)	17378	170	142.3	
Q1	2.16 (1.37, 3.39)	19991	239	177.0	

Women

Group	HR (95% CI)	Total(n)	Death(n)	Mortality rate	P for Interaction
Normal Weight: 18.5≤BMI<25					
Q5 (Reference)	1.00 (1.00, 1.00)	19034	27	19.9	.049
Q4	0.74 (0.41, 1.31)	18776	20	15.2	
Q3	1.02 (0.61, 1.71)	18380	31	24.3	
Q2	1.06 (0.62, 1.81)	15779	27	24.8	
Q1	1.67 (1.03, 2.71)	13713	43	46.0	
Overweight: 25≤BMI<30					
Q5	0.84 (0.50, 1.42)	18359	29	22.2	
Q4	1.14 (0.69, 1.87)	17178	37	30.7	
Q3	0.87 (0.52, 1.46)	16885	31	26.4	
Q2	1.31 (0.80, 2.15)	14650	40	39.7	
Q1	1.11 (0.67, 1.83)	14510	38	38.3	
Obesity class I: 30≤BMI<35					
Q5	0.88 (0.46, 1.69)	7553	14	26.1	
Q4	0.96 (0.50, 1.84)	6785	14	29.5	
Q3	0.66 (0.33, 1.34)	6873	11	23.1	
Q2	1.04 (0.55, 1.96)	6196	15	35.1	
Q1	1.28 (0.73, 2.24)	7019	24	49.9	
Obesity class II: BMI≥35					
Q5	1.76 (0.91, 3.38)	3699	14	53.5	
Q4	2.74 (1.51, 4.98)	3090	19	87.6	
Q3	1.81 (0.94, 3.49)	3117	14	64.8	
Q2	1.92 (1.00, 3.71)	2930	14	69.4	
Q1	1.59 (0.85, 2.96)	3970	17	62.4	
WC: <94cm(M) or <80(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	20592	28	19.0	.615
Q4	0.78 (0.45, 1.36)	20518	22	15.3	
Q3	1.06 (0.64, 1.75)	20132	34	24.4	
Q2	0.98 (0.62, 1.81)	17259	26	21.9	
Q1	1.28 (0.77, 2.12)	14989	34	33.3	
WC: 94-102cm(M) or 80-88(W)					
Q5	0.63 (0.32, 1.23)	10875	12	15.5	
Q4	0.82 (0.44, 1.55)	10181	15	21.0	
Q3	0.56 (0.28, 1.12)	10015	11	15.8	
Q2	1.17 (0.66, 2.08)	8714	20	33.4	
Q1	1.12 (0.63, 1.98)	8435	21	36.3	
WC: ≥102cm(M) or ≥88(W)					
Q5	1.19 (0.74, 1.93)	17394	44	35.7	
Q4	1.63 (1.03, 2.58)	15475	55	50.8	
Q3	1.17 (0.73, 1.90)	15502	44	40.9	
Q2	1.57 (0.98, 2.50)	13951	52	54.1	
Q1	1.55 (0.98, 2.44)	16161	67	60.6	
% BF: ≤20%(M) or ≤30%(W)					
Q5 (Reference)	1.00 (1.00, 1.00)	9536	12	17.6	.644
Q4	0.94 (0.41, 2.13)	8620	11	18.2	
Q3	1.21 (0.56, 2.58)	8007	15	27.1	
Q2	1.34 (0.62, 2.90)	6872	14	29.5	
Q1	1.23 (0.56, 2.70)	5688	13	33.5	
% BF: 20-25%(M) or 30-33%(W)					
Q5	0.88 (0.37, 2.09)	6547	9	19.3	
Q4	0.51 (0.18, 1.46)	6246	5	11.4	
Q3	0.66 (0.26, 1.69)	5847	7	17.3	
Q2	1.29 (0.58, 2.87)	5189	12	33.6	
Q1	1.33 (0.59, 2.97)	4430	12	39.7	
% BF: >25%(M) or >33%(W)					
Q5	0.87 (0.47, 1.62)	32778	63	27.1	
Q4	1.10 (0.60, 2.04)	31308	76	34.7	
Q3	0.86 (0.46, 1.59)	31795	67	30.3	
Q2	1.06 (0.57, 1.97)	27863	72	37.5	
Q1	1.18 (0.64, 2.17)	29467	97	48.1	

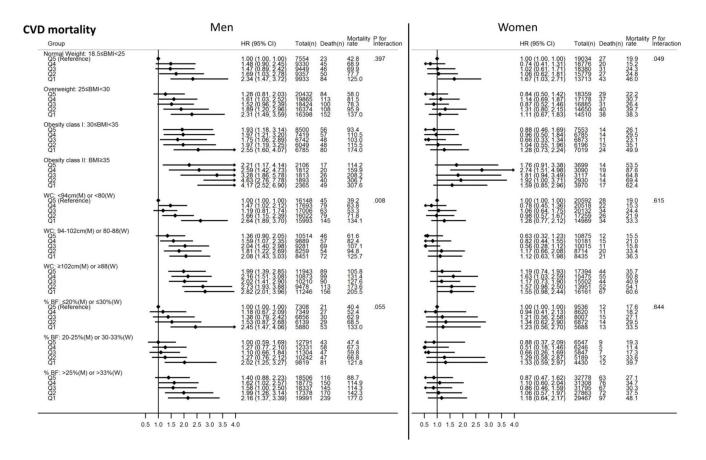*(X-axis scale for both panels: 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0)*

Figure 3.

Joint associations of grip strength and body mass index, waist circumference or percent body fat with cardiovascular disease (CVD) mortality for men and women. All Cox regression models (using age as the underlying time variable) were adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently 3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity time (minutes/day). The quintiles of grip strength were gender- and age-specific. Mortality rate is crude mortality rate per 100,000-person years. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded in the models with BMI. Abbreviations: HR – hazard ratio; CI – confidence interval; M– men; W– Women.

Table 1

Participants' characteristics

Variables	Men (n=183,006)						Women (n=220,193)					
	All	Quintiles of grip strength					All	Quintiles of grip strength				
		Q1	Q2	Q3	Q4	Q5		Q1	Q2	Q3	Q4	Q5
Grip strength, kg	39.7 (8.8)	27.7 (4.9)	35.3 (26)	39.3 (2.7)	43.6 (2.9)	51.2 (4.9)	23.5 (6.2)	14.7 (3.6)	20.2 (2.1)	22.9 (2.1)	26.2 (2.1)	31.2 (3.5)
Age, years	56.2 (8.2)	56.4 (8.4)	55.8 (8.3)	56.5 (8.1)	56.5 (8.2)	55.6 (8.1)	56.0 (8.0)	56.7 (8.0)	55.8 (8.2)	56.5 (8.0)	55.7 (7.7)	55.4 (8.1)
Ethnicity, %												
White	94.4%	89.6%	93.7%	95.5%	96.3%	96.6%	94.4%	90.9%	94.0%	95.1%	95.9%	95.6%
Mixed	0.5%	0.5%	0.6%	0.5%	0.5%	0.5%	0.7%	0.7%	0.7%	0.6%	0.7%	0.8%
Asian/Asian British	2.6%	6.3%	3.2%	2.0%	1.2%	0.7%	2.1%	5.0%	2.5%	1.7%	1.2%	0.6%
Black/Black British	1.6%	2.0%	1.5%	1.4%	1.4%	1.7%	1.8%	1.8%	1.6%	1.7%	1.5%	2.4%
Others	0.9%	1.6%	1.0%	0.7%	0.7%	0.5%	1.0%	1.6%	1.1%	0.9%	0.8%	0.6%
Smoking status, %												
Never	50.4%	51.4%	50.9%	50.7%	49.6%	49.7%	60.3%	61.6%	61.4%	60.5%	59.6%	58.8%
Previous	37.3%	35.0%	36.5%	37.1%	38.7%	38.9%	31.0%	29.2%	29.9%	31.3%	31.7%	32.5%
Current	12.3%	13.6%	12.6%	12.1%	11.7%	11.4%	8.7%	9.2%	8.7%	8.2%	8.7%	8.7%
Employment, %												
Unemployed	35.9%	42.2%	35.3%	36.0%	35.6%	30.9%	43.0%	50.2%	42.4%	44.4%	39.3%	39.9%
Townsend deprivation index	-1.33 (3.1)	-0.58 (3.4)	-1.16 (3.1)	-1.44 (3.0)	-1.62 (2.9)	-1.79 (2.8)	-1.39 (3.0)	-0.95 (3.2)	-1.28 (3.0)	-1.47 (3.0)	-1.57 (2.9)	-1.59 (2.9)
Statin use, %	19.7%	23.6%	19.7%	19.8%	18.9%	16.8%	11.7%	15.4%	12.1%	11.5%	10.3%	10.0%
Hormone replacement therapy (W), %	(N/A)	(N/A)	(N/A)	(N/A)	(N/A)	(N/A)	7.5%	7.4%	7.2%	7.2%	7.7%	7.9%
Alcohol Consumption, %												
Never	2.7%	4.7%	2.8%	2.4%	1.9%	1.6%	5.6%	9.1%	6.1%	5.1%	4.4%	4.1%
Previous	3.3%	5.0%	3.4%	2.9%	2.7%	2.3%	3.4%	4.8%	3.7%	3.2%	2.9%	2.7%
Current (<3times/week)	41.8%	44.3%	42.7%	41.3%	40.3%	40.7%	53.7%	56.4%	55.1%	53.4%	52.9%	51.5%
Current (≥3times/week)	52.3%	45.9%	51.0%	53.5%	55.1%	55.3%	37.2%	29.8%	35.2%	38.2%	39.7%	41.7%
Processed/red meat consumption, days/week	1.04 (0.60)	1.05 (0.64)	1.04 (0.61)	1.04 (0.59)	1.03 (0.58)	1.05 (0.58)	0.78 (0.50)	0.79 (0.53)	0.78 (0.50)	0.78 (0.50)	0.78 (0.49)	0.78 (0.49)
Resting pulse rate, beats/min	68.3 (11.7)	69.5 (12.3)	68.4 (11.8)	68.0 (11.6)	67.9 (11.6)	67.9 (11.5)	70.1 (10.5)	70.8 (10.7)	70.1 (10.5)	69.9 (10.4)	69.8 (10.4)	69.9 (10.6)
Self-reported MVPA time, min/day	82.3 (22.9)	78.4 (20.7)	81.8 (22.2)	82.4 (24.0)	83.1 (23.0)	85.3 (23.6)	51.6 (19.5)	49.2 (16.1)	51.0 (18.8)	51.3 (18.8)	52.5 (19.5)	53.5 (22.9)

Variables	Men (n=183,006)						Women (n=220,193)					
	All	Quintiles of grip strength					All	Quintiles of grip strength				
		Q1	Q2	Q3	Q4	Q5		Q1	Q2	Q3	Q4	Q5
BMI, kg/m²	27.7 (4.2)	27.7 (4.6)	27.6 (4.3)	27.6 (4.1)	27.7 (3.9)	28.2 (3.9)	27.0 (5.1)	27.6 (5.5)	26.9 (5.1)	26.8 (5.0)	26.8 (4.9)	27.0 (5.0)
Normal weight, %	25.0%	28.0%	27.8%	25.9%	24.3%	19.6%	39.2%	35.0%	39.9%	40.6%	41.0%	39.1%
Overweight, %	50.1%	46.2%	48.6%	50.6%	51.7%	52.9%	37.3%	37.0%	37.0%	37.3%	37.5%	37.7%
Obesity class I, %	19.4%	19.1%	18.0%	18.5%	19.3%	22.0%	15.8%	17.9%	15.7%	15.2%	14.8%	15.5%
Obesity class II, %	5.5%	6.7%	5.6%	5.0%	4.7%	5.5%	7.7%	10.1%	7.4%	6.9%	6.7%	7.6%
WC, cm	96.6 (11.1)	97.0 (12.0)	96.2 (11.4)	96.2 (11.0)	96.4 (10.7)	97.3 (10.5)	84.5 (12.4)	86.0 (13.1)	84.2 (12.3)	83.9 (12.1)	83.8 (12.1)	84.6 (12.2)
<94cm(M); <80cm(W)	45.3%	44.8%	47.5%	46.6%	46.0%	41.8%	42.5%	37.9%	43.2%	44.1%	44.4%	42.1%
94-102cm(M); 80-88cm(W)	25.4%	23.7%	24.5%	25.4%	25.7%	27.2%	21.9%	21.3%	21.8%	21.9%	22.1%	22.3%
102cm(M); 88cm(W)	29.4%	31.5%	28.1%	28.0%	28.3%	30.9%	35.6%	40.8%	34.9%	34.0%	33.5%	35.6%
%BF	25.1 (5.8)	25.8 (6.1)	25.2 (5.9)	25.0 (5.7)	24.8 (5.6)	24.7 (5.5)	36.4 (6.9)	37.5 (7.0)	36.5 (6.9)	36.4 (6.8)	36.1 (6.8)	36.0 (6.9)
20%(M); 30%(W)	18.3%	16.5%	18.2%	18.8%	19.1%	18.9%	17.6%	14.4%	17.2%	17.5%	18.7%	19.5%
20-25%(M); 30-33%(W)	30.9%	27.5%	30.3%	31.0%	32.1%	33.1%	12.8%	11.2%	13.0%	12.8%	13.5%	13.4%
>25%(M); >33%(W)	50.8%	56.0%	51.5%	50.2%	48.8%	47.9%	69.6%	74.4%	69.8%	69.7%	67.8%	67.1%
Fat free mass, kg	63.8 (7.8)	61.0 (8.0)	62.3 (7.5)	63.3 (7.3)	64.5 (7.1)	67.3 (7.4)	44.5 (5.0)	43.4 (5.2)	43.7 (4.8)	44.0 (4.7)	44.8 (4.7)	46.3 (4.9)
Systolic blood pressure, mm Hg	140.9 (17.3)	139.2 (17.7)	139.8 (17.2)	141.1 (17.4)	142.0 (17.2)	142.3 (16.9)	135.0 (19.2)	134.3 (19.2)	133.8 (19.2)	135.2 (19.3)	135.1 (19.0)	136.1 (19.1)
Diastolic blood pressure, mm Hg	84.3 (9.9)	83.2 (10.1)	83.8 (10.0)	84.3 (9.9)	84.8 (9.9)	85.4 (9.8)	80.7 (10.0)	80.2 (10.0)	80.1 (10.0)	80.5 (9.9)	80.8 (9.9)	81.5 (9.9)
Hypertension, %	61.1%	60.3%	58.7%	60.9%	62.4%	62.8%	47.7%	49.3%	46.0%	47.9%	46.8%	48.6%
Diabetes, %	6.1%	9.7%	6.5%	5.8%	4.9%	4.1%	3.4%	5.4%	3.6%	3.1%	2.8%	2.6%

Note: The quintiles of grip strength were gender- and age-specific. Body Mass Index (BMI) was used to categorize participants into normal weight (18.5kg/m² BMI<25kg/m², overweight (25kg/m² BMI<30kg/m², obesity class I (30kg/m² BMI<35kg/m² and obesity class II (BMI 35kg/m². Hypertension was defined as systolic/diastolic blood pressure 140/90mm Hg, reported physician diagnosis of hypertension, or reported medication use to regulate blood pressure. Participants were considered to have diabetes if they reported a physician diagnosis of diabetes, or taking glucose-lowering treatment.

Table 2

Independent associations of grip strength with all-cause and cardiovascular disease (CVD) mortality.

Mortality outcome	Gender	Comparisons	Number of deaths	Person-years of follow-up	Mortality rate	Hazard ratios (95% confidence interval) for mortality			
						Model 1	Model 2a	Model 2b	Model 2c
All-cause	Men		5,049	1,268,314	398.1				
		Quintiles of grip strength							
		Q1 (Reference)	1,389	241,358	575.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
		Q2	933	232,139	401.9	0.80 (0.73, 0.87)	0.81 (0.75, 0.88)	0.80 (0.73, 0.87)	0.80 (0.73, 0.87)
		Q3	920	253,118	363.5	0.71 (0.65, 0.77)	0.72 (0.66, 0.78)	0.70 (0.65, 0.77)	0.71 (0.65, 0.77)
		Q4	972	268,240	362.4	0.72 (0.66, 0.78)	0.73 (0.67, 0.79)	0.72 (0.66, 0.78)	0.72 (0.66, 0.78)
		Q5	835	273,460	305.3	0.67 (0.62, 0.73)	0.68 (0.62, 0.74)	0.67 (0.61, 0.73)	0.67 (0.62, 0.74)
		P for linear trend				<0.0001	<0.0001	<0.0001	<0.0001
		Per 5kg increment in grip strength				0.91 (0.90, 0.93)	0.92 (0.90, 0.93)	0.91 (0.90, 0.93)	0.91 (0.90, 0.93)
	Women		3,238	1,533,538	211.1				
		Quintiles of grip strength							
		Q1 (Reference)	746	270,638	275.6	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
		Q2	652	274,981	237.1	0.96 (0.86, 1.06)	0.97 (0.87, 1.08)	0.97 (0.87, 1.07)	0.96 (0.86, 1.06)
		Q3	656	316,838	207.0	0.81 (0.73, 0.90)	0.82 (0.74, 0.91)	0.82 (0.74, 0.91)	0.81 (0.73, 0.90)
		Q4	592	323,506	182.0	0.79 (0.71, 0.88)	0.80 (0.72, 0.89)	0.80 (0.71, 0.89)	0.79 (0.71, 0.88)
		Q5	592	347,576	170.3	0.74 (0.67, 0.83)	0.75 (0.67, 0.84)	0.74 (0.67, 0.83)	0.74 (0.67, 0.83)
		P for linear trend				<0.0001	<0.0001	<0.0001	<.0001
		Per 5kg increment in grip strength				0.91 (0.89, 0.94)	0.92 (0.89, 0.95)	0.91 (0.89, 0.94)	0.91 (0.89, 0.94)
CVD	Men		1,256	1,268,314	99.0				
		Quintiles of grip strength							
		Q1 (Reference)	373	241,358	154.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)

Mortality outcome	Gender	Comparisons	Number of deaths	Person-years of follow-up	Mortality rate	Hazard ratios (95% confidence interval) for mortality			
						Model 1	Model 2a	Model 2b	Model 2c
		Q2	246	232,139	106.0	0.81 (0.69, 0.96)	0.82 (0.70, 0.97)	0.81 (0.69, 0.95)	0.81 (0.69, 0.96)
		Q3	222	253,118	87.7	0.66 (0.56, 0.78)	0.67 (0.56, 0.79)	0.67 (0.56, 0.79)	0.67 (0.57, 0.79)
		Q4	235	268,240	87.6	0.68 (0.58, 0.81)	0.69 (0.58, 0.81)	0.68 (0.58, 0.81)	0.69 (0.58, 0.82)
		Q5	180	273,460	65.8	0.58 (0.48, 0.69)	0.57 (0.47, 0.68)	0.57 (0.47, 0.68)	0.58 (0.48, 0.70)
		P for linear trend				<0.0001	<0.0001	<0.0001	<0.0001
		Per 5kg increment in grip strength				0.88 (0.84, 0.91)	0.88 (0.85, 0.91)	0.88 (0.85, 0.91)	0.88 (0.86, 0.92)
	Women		485	1,533,538	31.6				
		Quintiles of grip strength							
		Q1 (Reference)	122	270,638	45.1	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
		Q2	98	274,981	35.6	0.93 (0.72, 1.22)	0.93 (0.71, 1.21)	0.95 (0.73, 1.24)	0.94 (0.72, 1.23)
		Q3	89	316,838	28.1	0.73 (0.56, 0.97)	0.72 (0.55, 0.95)	0.75 (0.57, 0.99)	0.74 (0.56, 0.97)
		Q4	92	323,506	28.4	0.85 (0.65, 1.12)	0.83 (0.63, 1.10)	0.86 (0.65, 1.13)	0.85 (0.65, 1.12)
		Q5	84	347,576	24.2	0.74 (0.56, 0.98)	0.73 (0.55, 0.97)	0.74 (0.56, 0.98)	0.74 (0.56, 0.98)
		P for linear trend				0.028	0.021	0.021	0.027
		Per 5kg increment in grip strength				0.93 (0.87, 0.99)	0.93 (0.86, 1.01)	0.94 (0.87, 1.01)	0.94 (0.87, 1.01)

Note: All Cox regression models used age as the underlying time variable. The quintiles of grip strength were gender- and age-specific. Mortality rate is crude mortality rate per 100,000-person years

Model 1: Adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently 3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity time (minutes/day).

Model 2a: Adjusted for all confounders included in Model 1 plus body mass index. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded.

Model 2b: Adjusted for all confounders included in Model 1 plus waist circumference.

Model 2c: Adjusted for all confounders included in Model 1 plus percent body fat.