Comparative relevance of physical fitness and adiposity on life expectancy: A UK Biobank observational study

Short Title: Fitness, fatness and mortality

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ABSTRACT

Objective

To investigate the extent to which two measures of physical fitness, walking pace and handgrip strength, are associated with life expectancy across different levels of adiposity, as the relative importance of physical fitness and adiposity on health outcomes is still debated.

Patients and Methods

Usual walking pace (self-defined as slow, steady/average, brisk), dynamometer assessed handgrip strength, body mass index (BMI), waist circumference and body fat percentage were determined at baseline in the UK Biobank prospective cohort study (March 13, 2006 – January 31, 2016). Life expectancy was estimated at 45 years old.

Results

The median age and BMI of the 474 919 participants included in this analysis were 58.2 years and 26.7 kg/m^2, respectively; over a median follow-up of 6.97 years, 12823 deaths occurred. Participants reporting brisk walking pace had longer life expectancy across all levels of BMI, ranging from 86.7 to 87.8 years in women and from 85.2 to 86.8 years in men. Conversely, subjects reporting slow walking pace had a shorter life expectancy, being the lowest observed in slow walkers with a BMI less than 20 kg/m^2 (women: 72.4 years; men: 64.8 years). Smaller, less consistent differences in life expectancy were observed between participants with high and low handgrip strength, particularly in women. The same pattern of results was observed for waist circumference or body fat percentage.

Conclusion

Brisk walkers were found to have a longer life expectancy which was constant across different levels and indices of adiposity. These findings could help clarify the relative importance of physical fitness and adiposity on mortality.

Keywords: life expectancy; fitness; fatness; physical activity; obesity; mortality

Abbreviations

BMI: Body mass index; **CI**: Confidence interval; **HR**: Hazard ratio; **IQR**: Interquartile range; **NHS**: National Health Service

INTRODUCTION

Poor physical fitness, encompassing low cardiorespiratory fitness and muscle strength, and high levels of adiposity are fundamental characteristics of an unhealthy lifestyle and important predictors of excess morbidity and mortality. The relative importance of measures of physical fitness and adiposity in relation to each other, however, is debated.[1] Thirty years ago, data from the Aerobics Center Longitudinal Study suggested that fitness, but not obesity, was independently associated with mortality outcomes when one was adjusted for the other.[2] These early findings have been extended and confirmed in meta-analyses concluding that, compared with normal-weight individuals, there was no evidence of an increased mortality risk among those who were fit and overweight or fit and obese;[3, 4] these results suggest that high levels of fitness may protect against the deleterious consequences of obesity.[5-8]

These studies, however, have limitations which have hampered the understanding of the interplay between fitness and body mass index (BMI). Some studies used only a single BMI threshold (e.g. ≥ 30 kg/m^2) and do not investigate associations at low levels of BMI, which are common in patients with sarcopenia and frailty;[9, 10] most studies only adjusted associations for fitness or physical activity, rather than exploring interactions between these factors and BMI;[11] and the large majority reported exclusively hazard ratio as a measure of association. Hazard ratio lacks a relationship with survival probabilities and makes direct comparison of the importance of one factor in relation to another difficult to interpret;[12-14] its use also implies a constant relative hazard at all times during follow-up.[15] As the absolute risk of death and virtually of all chronic diseases is largely dependent on age, reporting only a single relative metric does not allow quantifying absolute risk differences across increasing ages. A better metric to report associations and compare the relative importance of fitness and obesity is the estimation of residual life expectancy across levels of fitness and BMI. Study outcomes that focus on life expectancy are also more likely to be understood by wider audiences and convey more intuitive risk messages to the general public.[16] To date, the literature on the association of fitness or obesity with life expectancy is sparse. In a cohort of patients with an average age of 60 years, those with high compared to low self-reported physical fitness lived on average 5 years longer,[17] a finding supported by studies comparing high versus low levels of physical activity.[18, 19] In another study, at 60 years participants with class II and III obesity live for as much as 7 years less that those with normal weight[20]; an earlier study reported similar findings.[21] However, to our knowledge only one study has investigated the relative importance of physical activity and BMI on life expectancy,[19] whilst none have compared the relative importance and interaction of physical fitness and obesity or quantified it using different measures of adiposity.

The aim of this study was to investigate how walking pace and handgrip strength, two easily captured measures of physical fitness, are associated with life expectancy across different levels and measures of adiposity.

METHODS

UK Biobank

UK Biobank is a large prospective cohort of middle-aged adults recruited between March 2006 and July 2010 in 22 assessment centres located throughout England, Scotland and Wales.[22] Participants registered with a family physician were invited to take part. All participants provided written informed consent; the study was approved by the NHS National Research Ethics Service.

For each variable reported here, the UK Biobank Data-Field (DF) number is provided (Supplementary Material Table S1); DFs are linked to detailed information on measurement procedures through the UK Biobank website.[23]

Measures of physical function and adiposity

Walking pace, handgrip strength, BMI, waist circumference and body fat percentage were measured within the full UK Biobank cohort. Walking pace was assessed by a single item question: "How would you describe your usual walking pace? 1) Slow pace, 2) Steady/average pace, 3) Brisk pace". Handgrip strength was assessed in both hands by a hydraulic hand dynamometer whilst sitting. The elbow of the arm holding the dynamometer was placed against the side of the body and bent at a 90° angle with the forearm placed on an armrest. Participants squeezed the handle of the dynamometer as hard as they could for 3 seconds. The average value for the right and left hand were used for this analysis. Waist circumference and BMI (kg/m^2) were also measured. Body mass and body fat percentage were measures by electronic bio-impedance scales and height was measured by stadiometer.

Potential confounders

This study utilised demographic (age, sex, ethnicity, social deprivation [Townsend index] and employment); health (number of medications); and lifestyle (smoking, alcohol, diet and TV viewing time) factors as confounders. Alcohol and diet were assessed through a questionnaire; the diet variable included were fresh fruit and salad/raw vegetable intake. Details for each variable are available on the UK Biobank website.[24]

Mortality

Details on linkage procedures are available online.[24] Date and cause of death were obtained from the NHS Information Centre (England and Wales) and the NHS Central Register (Scotland). Linkage captured all deaths occurring until 31st January 2016 for England and 30th November 2015 for Scotland.

Statistical analysis

From the initial sample of 502 614 participants, 474 919 (94.6%) with complete data on covariates were included in the analyses, with missing information in less than 2% for included covariates (Table S1 and Table S2).

Characteristics of participants were summarised as median and interquartile range (IQR) for continuous variables and number and percentage for categorical ones. To describe the shape of the associations of walking pace, handgrip strength, BMI, waist circumference and body fat percentage with all-cause mortality, Cox-regression hazard ratios (HRs) adjusted for potential confounders were estimated for average and brisk walking pace versus slow pace (reference group), for the second and third tertile of grip strength versus first tertile (reference), for eight ordered BMI groups (<20 kg/m^2; ≥20–<22.5; ≥22.5–<25.0 [reference]; ≥25.0–<27.5; ≥27.5–<30.0; ≥30.0–<35.0; ≥35.0–<40.0; ≥40 kg/m^2) and for octiles (eight ordered categories, first as reference) of waist circumference and body fat percentage; 95% confidence intervals (95% CI) were estimated for all HRs, including the reference group.[25, 26] We opted to categorise BMI in eight groups, instead of the six defined by the World Health Organization,[27] to better characterise the shape of the association for the majority of the population (i.e., BMI <30.0 kg/m^2).

The calculation of residual life involved a three-step process. First, participants' follow-up (risk time and death) was split into intervals of 24 months by current age; mortality rates were then modelled using a Poisson regression including current age as a natural spline, BMI (eight levels), walking pace (three groups), BMI x walking pace interaction and time-to-death as person-time (exposure). Second, model estimates were used to predict age-specific mortality rates within each combination of BMI and walking pace group (overall 24 groups, eight for BMI and 3 for walking pace). Third, survival curves were obtained from predicted cumulative mortality rates and residual life calculated as the area under the survival curve up to 90 years old conditional on surviving at age 45. These three steps were repeated for grip strength.

The above analysis was also repeated using waist circumference and body fat percentage to investigate whether the association with life expectancy were consistent across different measures of adiposity. In order to make the analysis consistent with BMI, data for waist circumference and body fat percentage were categorised into the same number of groups (i.e., octiles).

To reduce the risk of reverse causation, in a sensitivity analysis we repeated the estimations excluding patients with prevalent cardiovascular disease or cancer at baseline.

Analyses were performed with Stata v.15 and R v.3.3.1 (Epi package[28]) and stratified by sex.

RESULTS

Participants and events

The median age and BMI of the included 474 919 participants (259 752 women; 215 167 men) was 58.2 (IQR 50.5, 63.6) years and 26.7 (24.1, 29.9) kg/m^2, respectively; the characteristics of the participants across categories of walking pace and handgrip strength or levels BMI are reported in Table 1 and Table 2, respectively, and across octiles of waist circumference and body fat percentage in Table S3 and Table S4, respectively. Participants reporting brisk walking pace and higher handgrip strength were younger; BMI, waist circumference and body fat percentage were progressively lower as walking pace and handgrip strength increased.

Over a median (IQR) follow-up of 6.97 (6.28, 7.64) years and 3 292 051 person-years, there were 12823 deaths (5153 in women and 7670 in men), corresponding to mortality rates of 2.85 (95% CI: 2.78 to 2.93) and 5.16 (95% CI: 5.05 to 5.28) per 1000 person-years, respectively.

Associations and estimated life expectancy

The shape of association of BMI, waist circumference, body fat percentage, walking pace, and handgrip strength with all-cause mortality are displayed in Figure 1. BMI, waist circumference and body fat percentage displayed U-shaped associations with mortality. For BMI, underweight women and men with a value of less than 20 kg/m^2 had the highest risk of mortality compared to the reference group (HR women: 1.62; 95% CI: 1.42 to 1.86; HR men: 2.17; 1.86 to 2.52). Walking pace and handgrip strength showed graded associations: compared to slow walkers, the HR for mortality in the brisk walking pace group were 0.48 (95% CI: 0.46 to 0.51) and 0.47 (0.45 to 0.49) for women and men, respectively. Compared to participants in the lowest quintile of handgrip strength, the HR for mortality in those in the highest quintile were 0.67 (95% CI: 0.61 to 0.73) and 0.68 (0.63 to 0.73) for men and women, respectively.

The estimated mean life expectancy at age 45 years across categories of walking pace or handgrip strength and BMI is shown in Figure 2. Subjects with brisk walking pace had a longer life expectancy across all categories of BMI, ranging from 86.7 to 87.8 years in women and 85.2 to 86.8 years in men. Conversely, subjects with slow walking pace had shorter life expectancy across all categories of BMI, ranging from 72.4 to 85.0 years in women and 64.8 to 81.2 years in men. For both walking pace and handgrip strength, the shortest life expectancy was observed in those with a BMI of less than 20 kg/m^2, both in women and men. Compared to slow walkers with a low BMI, brisk walkers with a low BMI had a longer life expectancy of 14.9 (women) and 21.4 (men) years (Figure 3). Absolute differences in life expectancy were negligible between average and brisk walking pace in women across all levels of BMI and only became evident in men at low (<20 kg/m^2) and high (>40 kg/m^2) BMI, with approximately 5 years difference between brisk and average walking pace within these BMI categories. Compared to slow pace, differences in life expectancy for average and brisk pace were progressively lower from 45 years old onwards but still evident up to 80 years old, both in women and men (Figure S1).

Although the pattern for handgrip strength was similar to that of walking pace, differences in life expectancy were small, particularly in women (Figure 2 and Figure 3; Figure S1). Furthermore, in men an inverse U-shaped relationship was found between BMI and life expectancy for all three tertiles of handgrip strength (Figure 2). The greatest difference in life expectancy between participants in the lowest and highest tertile of handgrip strength were observed in those with a BMI of less than 20 kg/m^2, with values of 2.9 years for women and 6.3 years for men (Figure 3).

The associations for walking pace and handgrip strength were not changed if waist circumference or body fat percentage were used. In both cases, the lowest life expectancy was observed in participants in the lowest category of adiposity when combined with slow walking pace (Figure S2 and Figure S3).

The pattern of results was unchanged restricting the analysis to 411 400 participants (8289 deaths; Table S5) who did not report prevalent cardiovascular disease or cancer at baseline (Figures S4-S6).

DISCUSSION

Within a cohort of adults, self-reported walking pace was a powerful predictor of life expectancy across all levels of BMI and other indices of adiposity. Ranging from a BMI of less than 20 kg/m^2 to 40 kg/m^2 or higher, women and men reporting a brisk walking pace had a life expectancy of over 86 and 85 years, respectively. Women and men with low BMI and slow walking pace had the lowest life expectancy estimated at 72 and 65 years, respectively. The association between handgrip strength and life expectancy was less pronounced, particularly for women. The results were similar when waist circumference or body fat percentage where used as indices of adiposity.

Previous studies have consistently reported an association between indices of physical fitness and all-cause and cardiovascular mortality,[29-31] including a UK Biobank analysis which showed that the association between walking pace and handgrip strength is modified by BMI.[32] Interestingly, the 50% reduction of all-cause mortality in brisk walkers is within the ranges reported in other cohorts and consistent since initial observations from the 1950s in the studies of Morris.[33] However, as far as we are aware, this is the first study to quantify how the associations between indices of physical fitness and all-cause mortality translate into life expectancy across categories of adiposity measured by BMI, waist circumference and body fat percentage. A novel finding was the observation that participants reporting brisk walking pace had a longer life expectancy regardless of their adiposity category compared to slow walkers, whose shorter life expectancy was particularly pronounced at the lowest levels of adiposity. Indeed, the difference in life expectancy between brisk and slow walker at BMI levels of less than 20 kg/m^2 was 15 years for women and over 21 years for men. It has previously been reported that self-reported walking pace within UK Biobank is closely associated with objectively assessed cardiorespiratory fitness,[32] while a slow walking pace is an established marker of frailty.[32, 34, 35] Conversely, a low BMI is associated with an elevated risk of sarcopenia and a poor nutritional status.[9, 10] Therefore, it is likely that the interaction between low BMI and slow walking pace is identifying those with pronounced frailty and poor nutritional status with low resilience in responding to threats such as infectious, chronic disease or falls.

While this study focused on indices of physical fitness, a previous one investigated the association between physical activity, BMI and life expectancy.[19] Our findings are somewhat in contrast with the previous study which showed that, although physical activity was associated with a longer life expectancy across BMI categories, life years were lost with increasing BMI even in those who were active. This discrepancy, however, is consistent with the wider literature where fitness has been shown to be a stronger predictor of cardiovascular events than self-reported physical activity.[36] Physical activity is the single strongest determinant of cardiorespiratory fitness,[36] yet other environmental and genetic factors influence fitness and may therefore contribute to the strength of association with health.

Although the elevated risk of all-mortality at high and low BMI is well-established, the identification of optimal BMI levels defined by the nadir of the U-shaped curve is debated.[37] Our study supports an earlier meta-analysis evidencing that BMI is associated with an elevated risk mortality only after 35 kg/m^2,[38] but in contrast to another recent individual participant meta-analyses where BMI was incrementally associated with all-cause mortality above 25 kg/m^2.[39] However, regardless of where the nadir of the curve is located, it has been suggested that high levels of cardiorespiratory fitness may be protective against the deleterious associations of high BMI on cardiovascular and mortality risk,[1, 3, 40, 41] consistent with our findings indicating that those with good cardiorespiratory fitness and functional status as measured by walking pace have a prolonged life expectancy across the spectrum of BMI status.

This study suggests that self-reported walking pace is a stronger predictor of life expectancy than objectively assessed handgrip strength. Whilst walking pace largely reflects cardiorespiratory fitness and functional status, handgrip strength is a measure of whole body muscle strength.[32] Handgrip strength has been associated with reduced cardiovascular mortality,[29] particularly in men,[32] yet a counterintuitive positive association with cancer mortality has also been shown,[29] including in UK

Biobank.[32] Therefore, the overall value of handgrip strength as a predictor of health status requires further investigation and may have less utility than a simple measure of self-reported walking pace.

The large, contemporary and well-phenotyped nature of the UK Biobank cohort, along with robust mortality linkage, are important strengths of this study. Moreover, we estimated survival curves and their differences directly from our data without any comparison with synthetic population mortality rates and used complementary indices of obesity.[42] The main limitations include the study design and generalisability. The observational nature means that casualty cannot be inferred or, even if assumed, the direction cannot be established: for example, low BMI and slow walking pace may result from the development of infectious or chronic disease. Furthermore, faster walking pace (especially in older adults) might be linked to lack of frailty or orthopaedic issues, which should be consider as possible confounders. Generalisability may be lowered by the recruitment method which was not specifically designed to include participants representative of UK population.

CONCLUSION

In conclusion, this study suggests that subjects with a brisk self-reported walking pace have a longer and similar life expectancy across the spectrum of BMI or other adiposity indices, providing further evidence that walking pace is an important marker of overall health status. In contrast, the coexistence of a low BMI and a slow walking pace was associated with the lowest lifestyle expectancy. Further research is needed to investigate the phenotype of this high risk group and the effectiveness of targeted interventions to increase cardiorespiratory fitness and physical function in those with low BMI.

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Author contributions: TY and FZ conceived the study question and design. FZ undertook the statistical analysis. TY drafted the manuscript. FZ, KK and MJD revised the manuscript for important intellectual content.

Data source: This research has been conducted using the UK Biobank Resource under Application Number 18815. Statistical codes are available from the corresponding author (FZ).

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FIGURES LEGEND

Figure 1: Associations of adiposity indices, walking pace, and grip strength with all-cause mortality

Legend: Associations adjusted for age, Townsend score, ethnicity, employment, number of medications, smoking, alcohol, fruit, salad and vegetable intake, TV viewing. References (Hazard Ratio 1, dash lines) are 22.5-25.0 kg/m^2 for body mass index, the lowest group for waist circumference, body fat percentage, grip strength, and slow pace for walking pace. Bars indicate 95% confidence intervals.

Figure 2: Life expectancy at the age of 45 years old, by body mass index group

Legend: Estimated mean life expectancy for slow (red), average (yellow), and brisk (green) walking pace and first (red), second (yellow), and third (green) tertile of grip strength.

Figure 3: Differences in life expectancy at the age of 45 years old, by body mass index group

Legend: Years of life gained for average (yellow lines) and brisk (green lines) walking pace and second (yellow lines) and third (green lines) tertiles of grip strength. Life expectancy references (points with zero value) are those for body mass index <20 kg/m^2 and the first tertile for grip strength or slow pace for walking pace.