Mortality risk comparing walking pace to handgrip strength and a healthy lifestyle: a UK Biobank Study

Francesco Zaccardi[a], Paul W Franks[b,c], Frank Dudbridge[d], Melanie J Davies[a,e], Kamlesh Khunti[a,f], Thomas Yates[a,e]

[a] Diabetes Research Centre, University of Leicester, Leicester General Hospital, Gwendolen Rd, Leicester LE5 4PW, UK

[b] Department of Clinical Sciences, Lund University, Skane University Hospital, Malmö, Sweden, SE–221 00

[c] Umeå University, Umeå, Sweden

[d] Department of Health Sciences, University of Leicester, Leicester, UK

[e] NIHR Leicester Biomedical Research Centre, University of Leicester, Leicester LE1 7RH, UK

[f] NIHR Collaboration for Leadership in Applied Health Research and Care—East Midlands, University as Leicester, Leicester, LE1 7RH, UK

Corresponding author and request for reprints
Dr Francesco Zaccardi
Diabetes Research Centre
Leicester General Hospital
Gwendolen Rd, Leicester LE5 4PW, UK
Email: frazac@fastwebnet.it
Phone: 0044 0116 258 4322
ORCID: 0000-0002-2636-6487
Twitter: @LRWEUnit

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Declaration of Interests
PWF is a consultant for and has stock options in Zoe Global and has received research funding from Boehringer Ingelheim, Eli Lilly, Janssen, Novo Nordisk, Sanofi Aventis, and Servier.
KK is a consultant and speaker for Novartis, Novo Nordisk, Sanofi–Aventis, Lilly and Merck Sharp & Dohme. He has received grants in support of investigator and investigator initiated trials from Novartis, Novo Nordisk, Sanofi–Aventis, Lilly, Pfizer, Boehringer Ingelheim and Merck Sharp & Dohme.

MJD is a consultant, advisory board member and speaker for Novo Nordisk, Sanofi–Aventis, Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca and Janssen and as a speaker for Mitsubishi Tanabe Pharma Corporation. She has received grants in support of investigator and investigator initiated trials from Novo Nordisk, Sanofi–Aventis and Lilly.
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ABSTRACT

Aims

Brisk walking and a greater muscle strength have been associated with a longer life; whether these associations are influenced by other lifestyle behaviours, however, is less well known.

Methods

Information on usual walking pace (self–defined as slow, steady/average, or brisk), dynamometer–assessed handgrip strength, lifestyle behaviours (physical activity, TV viewing, diet, alcohol intake, sleep, and smoking), and body mass index was collected at baseline in 450 888 UK Biobank study participants. We estimated 10–year standardised survival for individual and combined lifestyle behaviours and body mass index across levels of walking pace and handgrip strength.

Results

Over a median follow–up of 7.0 years, 3808 (1.6%) deaths in women and 6783 (3.2%) in men occurred. Brisk walkers had a survival advantage over slow walkers, irrespective of the degree of engagement in other lifestyle behaviours, except for smoking. Estimated 10–year survival were higher in brisk walkers who otherwise engaged in an unhealthy lifestyle compared to slow walkers who engaged in an otherwise healthy lifestyle: 97.1% (95% confidence interval: 96.9, 97.3) vs 95.0% (94.6, 95.4) in women; 94.8% (94.7, 95.0) vs 93.7% (93.3, 94.2) in men. Body mass index modified the association between walking pace and survival in men, with the largest survival benefits of brisk walking observed in underweight participants. Compared to walking pace, for handgrip strength there was more overlap in 10–year survival across lifestyle behaviours.

Conclusion

Except for smoking, brisk walkers with an otherwise unhealthy lifestyle have a lower mortality risk than slow walkers with an otherwise healthy lifestyle.

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Keywords

Walking pace; grip strength; lifestyle; smoking; mortality; absolute risk

INTRODUCTION

Simple measures of physical fitness and function, such as walking pace and handgrip strength, are strong determinants of morbidity and mortality within the general population. Self–rated slow walkers are at roughly twice the risk of all–cause and cardiovascular disease (CVD) mortality than those who rate their walking pace as "brisk".[1] Studies in which walking pace was objectively assessed support these findings: 1 ms^{-1} faster pace was associated with around 12% mortality reduction and survival in fastest walkers was up to 20 years longer compared to slowest at age 65 years.[2, 3] Similarly, handgrip strength has been associated with lower all–cause and CVD mortality, particularly in men.[1, 4]

The relative importance of these measures may vary by other lifestyle behaviours or risk factors, which have been associated to mortality to a different extent, and across levels of the same risk factor. For example, body mass index (BMI) modifies the association of walking pace and cardiorespiratory fitness with all–cause and CVD mortality.[1, 5, 6] Such heterogeneous effects are likely present because cardiorespiratory fitness could differentiate healthy and unhealthy status more at low than high BMI levels.[1] There is also evidence that the health attributes of physical activity or sedentary behaviours are greatest in people with low fitness or strength.[7] However, these finding have not been replicated in all studies.[8, 9]

It is therefore plausible that the benefit of brisk walking and muscle strength on longevity is conditional on other lifestyle behaviours; if true, it might be possible to optimise public health strategies by targeting those who stand to benefit most from strength and conditioning interventions. However, providing such recommendations requires a solid evidence–base that investigates multiple, rather than single, lifestyle behaviours and quantifies the absolute rather than relative risk of adverse health outcomes.

This study systematically investigates the association of self–reported walking pace and objectively–measured handgrip strength with survival across levels of 16 different lifestyle behaviours and risk factors. The aim is to elucidate the relative importance and interaction of walking pace and handgrip strength with other lifestyle behaviours and risk factors.

METHODS

Cohort definition

Participants were from UK Biobank, an ongoing cohort study with data collected between March 2006–July 2010 in women and men aged between 40–70 years recruited in England, Wales, and Scotland. From the initial sample of 502 599 participants, we excluded people who withdrew consent, pregnant women, participants self–reporting cancer at the baseline visit, or those whose date of death preceded study entry, leaving 460 696 participants (Electronic Supplementary Material (ESM) Table 1). In UK Biobank, date of death is obtained with data linkage; patients were followed–up between study entry until date of death or censoring (31/1/2016 for England and Wales; 30/11/2015 for Scotland).

Physical fitness variables

The UK Biobank self–reported touchscreen questionnaire was used to capture usual walking pace at baseline. Participants were asked to answer: "How would you describe your usual walking pace: slow; steady/average; brisk?" Objectively–measured handgrip strength was assessed using a hydraulic hand dynamometer (Jamar J00105) while seated. Left– and right–hand strengths were measured and sex–specific thirds of the mean value used for all analyses, to facilitate comparisons with the three groups of walking pace.

Lifestyle behaviours and risk factors

We derived the following continuous variables (details reported in ESM Table 2): beef, lamb/mutton, pork, white meat, and processed meat intake; alcohol intake; time spent viewing television; time spent using a computer during leisure time; sleep duration; total time spent walking and in other forms of physical activity; time spent walking for pleasure; time spent exercising; and smoking status. BMI was calculated at baseline visit.

Healthy lifestyle score

We created an overall lifestyle score ranging from 0 to 7 (the greater the healthier) that summed key evidence–based lifestyle behaviours (details reported in ESM Table 2). Smoking and BMI were not included in the score and considered separately, as we aimed to assess their effect modification compared to other lifestyle factors.[1, 10]

Confounding variables

Data were captured for the following confounding variables which are strongly associated with mortality: age, sex, ethnicity, social deprivation (Townsend Deprivation Index), and self–reported number of treatments/medications (ESM Table 3).

Statistical analysis

From the initial dataset of 460 696 participants, we excluded participants with missing data on main exposures (walking pace or handgrip strength), smoking status, or any confounding variables, leaving a sample of 450 888 individuals (ESM Table 3); smoking and all other confounders were included in all models.

Where necessary, the distributions of variables were normalized using log–transformation. Given the highly–skewed distribution of physical activity variables, sex–specific thirds were defined and used in all analyses. Descriptive values are shown as median (interquartile range) and number (percentage). The Royston–Parmar–Lambert survival model, with study entry to all–cause death as time scale, was used.[11] Associations of walking pace and handgrip strength with survival across levels of each lifestyle behaviour and risk factor were firstly analysed by adding or removing an interaction (categorical or spline–transformed continuous variable with knots at 33th and 66th centile of distribution): if models were different (likelihood ratio test $p<0.0029$ to account for multiple testing, i.e. 0.05/17 - 16 lifestyle behaviours and risk factors and 1 healthy score), then the model with the lower Akaike's Information Criterion was selected. Secondly, to standardise (adjust) survival probabilities for confounding variables, 10-year individual survival estimates were averaged across levels of the main exposures.[11]

Two sensitivity analyses were performed: 1) To understand the relationship between walking pace and handgrip strength, we estimated 10–year standardised survival for handgrip strength across categories of walking pace; 2) To test the impact of confounding variables, we estimated hazard ratios and survivals in models progressively adjusted for confounders.

Analyses were complete-case and conducted with Stata MP 14.2 routines, stpm2, and stpm2_standsurv;[11] results are reported with 95% confidence intervals (CI). Aggregate results and statistical codes are available at [*GitHub/UK-BB*].

RESULTS

ESM Table 4 shows the characteristics of the 241 390 women and 209 498 men without missing data on main exposures, smoking, or confounders. For women, median handgrip strength was 23.5 kg, with 8.0% self–identifying as slow and 39.1% as brisk walkers. Corresponding values for men were: 39.5 kg, 7.7%, and 39.8%. Over a median (range) of 7.0 (0.01–9.9) years and 3 133 035 person–years, 3808 (1.6%) and 6783 (3.2%) deaths occurred in women and men, respectively. Characteristics of participants stratified by main exposures are shown in ESM Table 5-6; levels of physical activity in ESM Table 7; and number of participants and deaths for each lifestyle behaviour analysis in ESM Table 8.

For walking pace, in both men and women there was a clear differentiation in survival comparing slow and brisk walkers across all considered lifestyle behaviours and risk factors. In brisk walkers, estimated 10–year survival was persistently greater than slow walkers, with values above 97% in women and 95% in men across all levels of diet, sedentary behaviour, sleep, or BMI (Figure 1; ESM Figure 1); alcohol intake (Figure 2; ESM Figure 2); or physical activity (Figure 3; ESM Figure 3). The exception was smoking status, with a strong impact of current smoking: women and men who were brisk walkers had a 10–year survival of 94.8% (95% CI: 94.6, 95.1) and 91.9% (91.6, 92.2), respectively (Figure 2). These estimates indicated that current smoking nullified the benefit of being brisk walkers, as the respective 10–year survival in slow walkers who were non–smoker resulted 96.0% (95.8, 96.2) and 92.9% (92.6, 93.1) (Figure 2).

Slow walkers had comparatively low levels of survival, particularly in men. Ten–year survival below 90% were observed in slow walkers across contrasting behaviours or risk factors, for example no fruit and vegetables intake or cereal intake; normal BMI (18.5–25 kg/m^2); current smoking; or no alcohol intake (Figures 1–3). These survival estimates translated into differences of at least 5 fewer deaths per 1000 person per year in brisk walkers compared to slow walkers across these factors (ESM Figures 1–3). For women, smaller survival difference of at least 2.5 less deaths per 1000 person per year were observed in brisk walkers compared to slow walkers across the same risk factors (ESM Figures 1–3).

The results for individual lifestyle factors were maintained when considering the overall healthy lifestyle score (Figure 4). In women, 10–year survival in brisk walkers with the lowest healthy lifestyle score (i.e., 2, indicating poor compliance with health behaviours) was 97.1% (96.9, 97.3); in contrast, 10–year survival in slow walkers who reported the highest healthy lifestyle score (i.e., 7) was 95.0% (94.6, 95.4). Corresponding values for men were 94.8% (94.7, 95.0) and 93.7% (93.3, 94.2). For the median lifestyle score within this population (women, 5; men, 4), survival differences between brisk and slow walkers were 2.3 (2.1, 2.5) and 4.1 (3.8, 4.4) less deaths per 1000 person per year in women and men, respectively (ESM Figure 4).

An interaction between walking pace and BMI was observed in men (p<0.001), with a greater difference in survival between slow and brisk walkers at lower levels of BMI. At a BMI of 21 kg/m^2, there were 11 (9, 13) more deaths per 1000 person per year between slow and brisk walkers compared to 3 (2, 4) more at a BMI of 35 kg/m^2 (Figure 1; ESM Figure 1).

Compared to walking pace, there was more overlap in 10–year survival across levels of handgrip strength (Figures 1–4), with consistently greater survival differences between brisk and slow walkers than between those with a weak and strong handgrip (ESM Figures 1–4). In women with a strong handgrip and the lowest lifestyle score, the 10–year survival was 96.8% (96.6, 97.1), identical to the survival in those with a weak handgrip and the highest lifestyle score (96.9%; 96.6, 97.1) (Figure 4). In contrast, men with a strong handgrip and the lowest lifestyle score had survival (94.1%; 93.9, 94.3) lower than those with a weak handgrip and the highest lifestyle score (95.7%; 95.4, 96.0) (Figure 4).

Sensitivity analyses demonstrated that: 1) there was no interaction between handgrip strength and walking pace (P=0.666 for women and 0.894 for men; ESM Figure 5); 2) the association between walking pace and mortality (both relative and absolute risk) was not meaningfully affected by further adjustment for multiple lifestyle factors once age, ethnicity, social deprivation, smoking status, and treatments/medications were considered (ESM Figure 6).

DISCUSSION

In this study, we found that brisk walkers had a longer survival regardless of the degree to which they adhered to other lifestyle behaviours or levels of several risk factors, with the relevant exception of smoking. In contrast, slow walkers had substantially lower survival across all levels of other lifestyle behaviours and risk factors. In brisk walkers who had the lowest lifestyle score, indicating poor adherence to other lifestyle behaviours, 10–year survival was higher than slow walkers who adhered to multiple healthy lifestyle behaviours. BMI was the only factor found to modify the relationship of walking pace with survival, whereby the difference in survival between brisk and slow walkers was most pronounced in those with low BMI, particularly in men. Survival differences between strong and weak handgrip strength across all lifestyle factors were lower than those observed for categories of walking pace.

This study extends previous research investigating the association of walking pace or handgrip strength with mortality.[1, 2, 4, 8, 12] However, as far as we are aware, it is the first to consider the combined and comparative effects of multiple other lifestyle factors; moreover, we estimated the absolute risk of death because this measure facilitates a better understanding of the role of each factors compared to relative measures (i.e., hazard ratio). Two previous studies using UK Biobank showed that handgrip strength modifies the association between physical activity or sedentary behaviours and mortality.[13, 14] Using the same data, we were not able to replicate these interactions. This may be because, unlike previous publications, our analysis accounted for a more flexible non–linear associations between lifestyle factors and mortality and for multiple testing. A previous study also reported that walking pace modifies the association between BMI and mortality,[1] while another showed that slow walkers with low BMI have the lowest life expectancy,[10] in line with these findings. This interaction may reflect the importance of walking pace in differentiating healthy from unhealthy forms of low BMI, particularly in relation to frailty and undernutrition.[1]

The lower 10–year survival observed in slow walkers is clinically important. In men who ate no fruit and vegetables or cereal, had a normal BMI, never drank alcohol, were smokers, or who engaged in a minimal number of healthy lifestyle behaviours, being a slow walker was associated with a 10–year survival between 80%–90%, which is comparable to the survival probabilities observed after diagnosis of several cancers, including prostate, melanoma, and Hodgkin lymphoma.[15] The inferred effect of walking pace is likely to reflect the fact that walking is a complex functional activity, with many factors combining to influence pace (i.e., motor control; musculoskeletal condition; sensory and perceptual function; cardiorespiratory fitness; habitual activity levels; cognition, motivation and mental health; environment where walking occurs).[16-18] Therefore, walking pace reflects multiple processes that combine to make it an indicator of whole–body reserve and resilience. This finding supports the continued focus within physical activity guidelines on moderate–to–vigorous forms of physical activity, which are exemplified by brisk walking.[19] Yet our result did not disprove the importance of each risk factor, they also indicated that the potential impact of physical fitness and smoking on the risk of death is greater compared to other modifiable lifestyle behaviours. From a public health perspective our findings would suggest that, rather than focusing on difficult-to-implement and costly interventions on multiple risk factors or lifestyle behaviours, more feasible public health policies should be directed to improve few risk factors which have a stronger absolute impact on longevity, particularly physical fitness and smoking.

Although handgrip strength was associated with longer survival, differences between strong and weak handgrip were persistently lower than those between brisk and slow walkers. This observation is in line with previous research and suggests that, even though it was objectively measured, handgrip strength is a weaker measure of overall functional status than walking pace, particularly in women.[1] Of note, low dose of resistance exercise, which could improve handgrip strength, has been associated with a lower risk of death;[20] at the same time, previous research has also suggested that higher handgrip strength may actually be associated with an increased risk of cancer mortality.[1, 4]

This study has several limitations. Walking pace was self–reported, which is both a strength and limitation. It suggests that a simple single item question is strongly associated with survival which could have utility in risk stratification. In contrast, the self–reported nature of the question makes it possible that sources of error inherent to self–reporting any health behaviour may bias the results. However, previous research has shown that self–reported walking pace corresponds reasonably well to objectively–measure walking pace and is associated with cardiorespiratory fitness assessed through a sub–maximal test.[1, 21, 22] The UK Biobank cohort is overrepresented by participants healthier than the general population,[23] which may limit generalizability. The strength of association between walking pace and mortality may be due to unmeasured or poorly measured confounding variables. However, this study and others have shown that adjusting for factors beyond age, ethnicity, social deprivation, smoking status and number of medications does not further meaningfully attenuate the association between walking pace and mortality in UK Biobank.[1]

Finally, the degree to which a slow walking pace is simply a marker of mortality risk or has potential to causally affect mortality cannot be addressed, given the observational nature of the study. However, it is important to note that exercise–based rehabilitation programmes aimed at returning frail individuals to good physical function result in an increased functional fitness, including walking pace, and a reduced risk of death.[24-26] This observation provides evidence of causation beyond simple association and supports the potential public health relevance of this research.

In conclusion, this study found that those with a brisk walking pace had longer survival regardless of the degree to which they adhered to non–smoking lifestyle behaviours. In contrast, slow walkers had a substantially lower survival, even when adhering to multiple healthy lifestyle behaviours. This study therefore highlights the potential primacy of self–reported walking pace at identifying individuals with a high risk of mortality compared to other self–reported non–smoking lifestyle behaviours, as well the potential public health importance of maintaining or reversing poor physical function and fitness within the general population.[27, 28] Interventional research is needed to investigate whether rehabilitation–type exercise programmes, already developed in the context of chronic disease management, can be optimised for use within the minority of the general population that have functional limitations, such as slow walking pace, with the aim of increasing physical function and life expectancy.[29]

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MJD is a consultant, advisory board member and speaker for Novo Nordisk, Sanofi–Aventis, Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca and Janssen and as a speaker for Mitsubishi Tanabe Pharma Corporation. She has received grants in support of investigator and investigator initiated trials from Novo Nordisk, Sanofi–Aventis and Lilly.
FZ, FD, TY: no conflicts of interests relevant to this paper.

Data access and sharing
Statistical codes are available at [GitHub link, if accepted] and UK Biobank.

Ethical approval
Ethical approval for the UK Biobank study was obtained from the North West Centre for Research Ethics Committee (MREC, 11/NW/0382). In Scotland, UK Biobank has approval from the Community Health Index Advisory Group (CHIAG).

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UK Biobank Application Number 33266.

Author Contribution
TY, FZ, PWF, FD contributed to study idea and design
TY, FZ contributed to literature search
FZ contributed to data preparation and analysis
TY, FZ contributed to first draft
FZ, PWF, FD, MJD, KK, TY contributed to study critical revision and manuscript draft
All authors provided final approval of the version to publish. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit it for publication.

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FIGURES TITLE AND LEGEND

Figure 1: Association of diet and sedentary behaviour with survival, by levels of walking pace and grip strength

Legend: 10–year adjusted (age, ethnicity, Townsend score, smoking status, number of treatments/medications) survival for slow (red), average (orange), and brisk (green) walking pace and first (red), second (orange), and third (green) third of grip strength. Areas indicate 95% confidence interval; values for x–axes range from 5^{th} to 95^{th} percentile of variable distribution. Please note the different y–axis for body mass index and walking pace in men.

Figure 2: Association of alcohol consumption and smoking status with survival, by levels of walking pace and grip strength

Legend: 10–year adjusted (age, ethnicity, Townsend score, smoking status, number of treatments/medications) survival for slow (red), average (orange), and brisk (green) walking pace and first (red), second (orange), and third (green) third of grip strength. Spikes indicate 95% confidence interval.

Figure 3: Association of physical activity with survival, by levels of walking pace and grip strength

Legend: 10–year adjusted (age, ethnicity, Townsend score, smoking status, number of treatments/medications) survival for slow (red), average (orange), and brisk (green) walking pace and first (red), second (orange), and third (green) third of grip strength. Estimates are evaluated within thirds of total (i.e., minutes of activity/week) walking, moderate and vigorous physical activity and of total walking and exercise for pleasure. Spikes indicate 95% confidence interval.

Figure 4: Association of lifestyle score with survival, by levels of walking pace and grip strength

Legend: 10–year adjusted (age, ethnicity, Townsend score, smoking status, number of treatments/medications) survival for slow (red), average (orange), and brisk (green) walking pace and first (red), second (orange), and third (green) third of grip strength across levels of lifestyle score. Areas indicate 95% confidence interval; values for x–axes range from the minimum (2; less healthy) to the maximum (7; healthier) value of lifestyle score distribution.