Annals of Epidemiology 90 (2024) 21–27

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.sciencedirect.com/journal/annals-of-epidemiology

Original article

Walking pace and the time between the onset of noncommunicable diseases and mortality: a UK Biobank prospective cohort study

Joseph Henson, PhD [a,b,*], Thomas Yates, PhD [a,b], Atanu Bhattacharjee, PhD [b,c], Yogini V. Chudasama, PhD [b,c], Melanie J. Davies, MD [a,b], Paddy C. Dempsey, PhD [a,b], Jonathan Goldney, MBChB, BSc [a,b], Kamlesh Khunti, PhD [b,d], Jari A. Laukkanen, PhD [e,f], Cameron Razieh, PhD [a,b,c,g], Alex V. Rowlands, PhD [a,b,h], Francesco Zaccardi, PhD [b,c]

[a] NIHR Leicester Biomedical Research Centre (Lifestyle), Leicester, UK
[b] Diabetes Research Centre, College of Life Sciences, University of Leicester, Leicester, UK
[c] Leicester Real World Evidence Unit, University of Leicester, Leicester General Hospital, Leicester, UK
[d] NIHR Applied Health Research Collaboration–East Midlands (NIHR ARC-EM), Leicester Diabetes Centre, Leicester, UK
[e] Institute of Clinical Medicine and Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland
[f] Department of Medicine, Wellbeing Services County of Central Finland, Jyväskylä, Finland
[g] Office for National Statistics, Data & Analysis for Social Care and Health (DASCH) Division, Newport, UK
[h] Alliance for Research in Exercise, Nutrition and Activity (ARENA), UniSA Allied Health and Human Performance, University of South Australia, Adelaide, Australia

ARTICLE INFO

Keywords:
Walking
Cancer
Cardiovascular disease
Morbidity

ABSTRACT

Purpose: To estimate time spent in various cardiovascular disease (CVD) and cancer states, according to self-reported walking pace.
Methods: In total, 391,744 UK Biobank participants were included (median age = 57 years; 54.7% women). Data were collected 2006–2010, with follow-up collected in 2021. Usual walking pace was self-defined as slow, steady, average, or brisk. Multistate modeling determined the transition rate and mean sojourn time in and across three different states (healthy, CVD or cancer, and death) upon a time horizon of 10 years.
Results: The mean sojourn time in the healthy state was longer, while that in the CVD or cancer state was shorter in individuals reporting an average or brisk walking pace (vs. slow). A 75-year-old woman reporting a brisk walking pace spent, on average, 8.4 years of the next 10 years in a healthy state; an additional 8.0 (95% CI: 7.3, 8.7) months longer than a 75-year-old woman reporting a slow walking pace. This corresponded to 4.3 (3.7, 4.9) fewer months living with CVD or cancer. Similar results were seen in men.
Conclusions: Adults reporting an average or brisk walking pace at baseline displayed a lower transition to disease development and a greater proportion of life lived without CVD or cancer.
Availability of data and materials: Research was conducted using the UK Biobank resource under Application #33266. The UK Biobank resource can be accessed by researchers on application. Variables derived for this study have been returned to the UK Biobank for future applicants to request. No additional data are available.

Introduction

Noncommunicable diseases (NCDs) account for 41 million deaths globally (74% of all deaths), and 17 million NCD deaths occur before the age of 70 [1]. Cardiovascular diseases (CVD) and cancers account for 66% of all NCD deaths [1], reiterating the importance of modifiable risk behaviors for the prevention of morbidity and premature mortality.

Alongside smoking cessation, healthy diet, and moderate alcohol intake, physical activity is one of the most important modifiable risk factors for NCDs [2]. Indeed, physical activity may reduce the risk of CVD or cancer through preventing obesity, hypertension, dyslipidemia, and dysglycemia [3–6]. Walking pace, a strong indicator of overall health and cardiorespiratory fitness, and an important dimension of physical activity level, demonstrates inverse associations with all-cause, cardiovascular and cancer mortality and incident CVDs [7,8]. Moreover, self-reported walking pace is a stronger independent predictor of

* Corresponding author at: NIHR Leicester Biomedical Research Centre (Lifestyle), Leicester, UK.
E-mail address: jjh18@le.ac.uk (J. Henson).

https://doi.org/10.1016/j.annepidem.2023.10.001
Received 12 May 2023; Received in revised form 5 October 2023; Accepted 6 October 2023
Available online 4 January 2024

survival and cardiovascular mortality than other dimensions of physical activity or clinical risk factors, including serum cholesterol and blood pressure, with recent investigations also suggesting causal associations between self-reported walking pace, biological age, and health [9–13].

Previous studies have shown the association of walking pace with CVD and all-cause mortality by focusing on the risk of an event or overall life expectancy [7,10,14,15]. However, it is important to investigate how measures of lifestyle, functional capacity, and physical condition relate to years lived with and without serious disease (i.e., healthy years of life). Focusing on limiting the time horizon between the onset of chronic disease (diagnosis) and mortality is important because early onset of NCDs results in more years lived with the subsequent sequelae, including reduced quality of life, increased risk of frailty, loss of independence, greater rates of hospitalization and medication use, and higher health care expenditure [16–18]. Therefore, identifying factors that are associated with or predict greater compression of serious NCDs into later years of life may have important public health implications. In this respect, multistate modeling offers a flexible framework to describe the role of physical activity in clinical processes over time [19], whereby individuals fall under one of several states (e.g., healthy, CVD or cancer, death) and transition between these states over the course of their lifetime. Such population-based trajectories also allow the mean sojourn time in a given state to be determined.

Some early studies have started to apply multistate models to health behaviors, demonstrating that a clustering of healthy lifestyle factors (e.g., not smoking, regular physical activity, healthy diet and/or body weight, moderate alcohol consumption) is associated with a delayed transition from a healthy state to a single chronic disease or from a single chronic disease to multimorbidity, with different etiologies [20,21]. However, because of the complexity of these models and the need for suitably large study populations, research in this area is still in its infancy. As self-reported walking pace has previously been shown to be a strong predictor of survival and CVD risk, we hypothesize that this simple composite measure of physical activity, fitness, and function will be associated with compression of morbidity, defined here as the transition to disease development (diagnosis) and the proportion of life lived without chronic disease. Therefore, the aim of this study was to estimate the trajectories of time spent in various CVD and cancer states, according to self-reported walking pace in the UK Biobank population.

Materials and methods

Cohort definition

During the baseline visits (March 2006–July 2010) of the ongoing UK Biobank cohort study, clinical, demographic, and lifestyle information were collected in more than 500,000 women and men recruited from family practices close to the 22 UK Biobank assessment centers in England, Wales, and Scotland; at baseline, participants were aged between 38 and 73 years old. In total, ~9.2 million invitations were sent to potential participants, yielding a 5.5% response rate. The UK Biobank complies with the Declaration of Helsinki and written consent was obtained from all participants. UK Biobank ethical approval was obtained from the North West Center for Research Ethics Committee (MREC, 11/NW/0382) and, in Scotland, from the Community Health Index Advisory Group. The protocol of this study has been registered with the UK Biobank (application number 33266). This study has been conducted and reported following the STROBE guidelines for cohort studies (checklist and details are reported in the Supplementary Material).

In our investigation, from the initial sample of 502,413 individuals, we excluded 150 (0.03%) participants who were pregnant at the baseline visit; 47,381 with missing data on the main exposure or confounder (s); and 63,138 self-reporting a previous doctor diagnosis of cancer or CVD, leaving 391,744 participants for the analyses. The flowchart of study participants and details on confounders and UK Biobank data-field codes used to identify cancer or CVD are shown in Supplementary Figure S1.

Self-reported walking pace

The main exposure was the usual walking pace (UK Biobank Data Field 924), which has been collected at baseline. Participants were asked to answer the following question via a touchscreen questionnaire: "How would you describe your usual walking pace: slow; steady/average; brisk; none of the above; prefer not to answer?" Further information was available to participants to define a slow pace as less than 3 miles per hour (mph); a steady or average pace as 3–4 mph; and a brisk pace as greater than 4 mph. We excluded from the analyses participants who did not answer or answered "none of the above" or "prefer not to answer." Self-reported walking speed is strongly associated with directly measured walking speed [22] and cardiorespiratory fitness, the latter of which is also considered a vital sign for cardiovascular risk assessment [23]. Moreover, self-reported walking pace is associated with accelerometer-assessed physical activity, with both exposures having similar associations with all-cause mortality [24].

Transition states: hospitalization and death

We obtained information on the date of death through the linkage of the UK Biobank with NHS Digital (England and Wales) and NHS Central Register (Scotland). Information on date and reasons for hospital admission (primary and secondary, coded using the International Classification of Diseases [ICD] 9th and 10th revisions) was available in three databases linked to UK Biobank: the Hospital Episode Statistics, the Scottish Morbidity Record, and the Patient Episode Database for Wales. Participants were followed up from their study entry date until the occurrence of hospitalization, death, or censoring. As censoring dates for hospitalization and death differed (Wales: March 31, 2016 and September 30, 2021, respectively; Scotland: July 31, 2021 and October 31, 2021), we censored the observation at the minimum of these two dates for each devolved nation; for England, the right-censoring date was the same (September 30, 2021) across the two linked records of hospitalization and death. The first hospital record reporting a primary or secondary ICD code (i.e., in any position) relating to CVD or cancer following the baseline visit was extracted.

Each individual could therefore move across three states, with three transitions (Fig. 1, *S2*): transition 1, from the initial "healthy" state (baseline UK Biobank visit) to the "CVD or cancer" state, if the patient was admitted to the hospital with records reporting ICD codes for CVD or cancer; transition 2, from the initial "healthy" state to the "dead" state, if the patient died; transition 3, from the "CVD or cancer" to "dead" state, if the patient died. In this multistate model, commonly defined as "illness-death" model [25], the "dead" state is defined as "absorbing"—as no further transitions are possible once reached—while "healthy" and "CVD or cancer" as "transient" or "nonabsorbing."

Confounding variables

We extracted baseline information on the following plausible confounders of the association between walking pace with hospitalization for CVD or cancer and death: age, sex, social deprivation (Townsend deprivation index, with higher values indicating a greater deprivation), systolic blood pressure, smoking status (current/former/never), body mass index (BMI), serum low-density lipoprotein (LDL) cholesterol, and leisure-time physical activity volume (metabolic equivalent of task-minutes/week), which was estimated combining the duration and frequency of self-reported leisure-time physical activity as previously reported [26].

Statistical analysis

All analyses were stratified by sex. Descriptive data are reported as

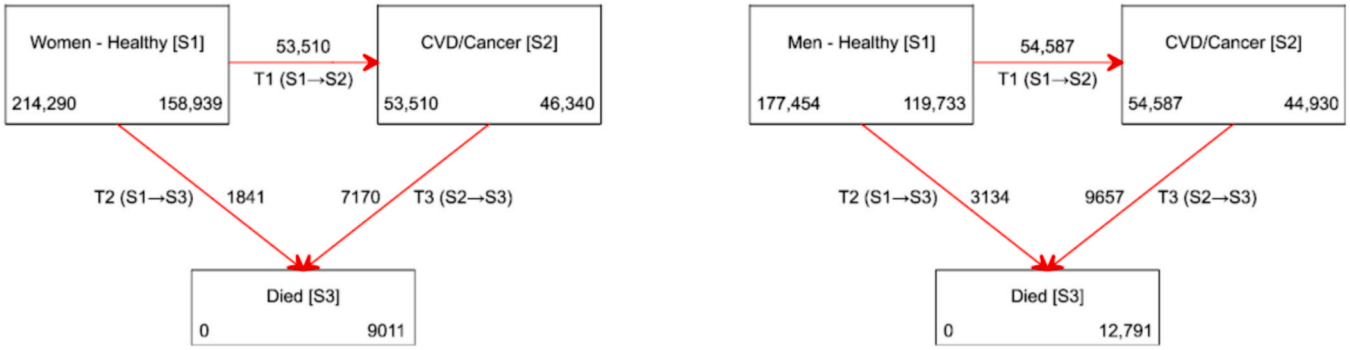

Fig. 1. Transition diagram (illness-death model). In women (left panel), from the initial cohort of 214,290 participants, 53,510 had a diagnosis of CVD or cancer (ICD codes in any position in the hospital records), and 1841 died during the follow-up; thus, 158,939 remained in the state "healthy" by the end of the observation. Of those who developed CVD or cancer, 7170 subsequently died and 46,340 terminated the study observation in the CVD or cancer state. The number of deaths was therefore 1841 from "healthy" and 7170 from "CVD or cancer" state, equating to a total of 9011 deaths. "Died" is an absorbing state; "healthy" and "CVD or cancer" are defined as transient or nonabsorbing states. Transitions further stratified by walking pace are reported in Table 2. S = state; T = transition.

median and interquartile range (IQR) or number and percentage, as appropriate.

The multistate modeling approach followed the analytical strategy described in Crowther et al. [27]. We firstly modeled each of the three transitions (Fig. 1) using three distinct Royston–Parmar models with three internal knots placed at the 25th, 50th, and 75th centiles of the event times and boundary knots at the minimum and maximum event times. The estimates from the survival regressions were then used to obtain the length of stay in each state upon a time horizon of 10 years (i.e., the sojourn time, which corresponds to the integral of the probability across follow-up time) using the same timescale from the baseline visit [28]. To account for confounding, we considered two models: [1] In the base model, we adjusted only for age (continuous); [2] in the adjusted model, we further included continuous measures of systolic blood pressure, serum LDL cholesterol, Townsend deprivation index, in-person interview assessed leisure-time physical activity volume, BMI, and categorical smoking status. Using the first model, we estimated the sojourn times for an individual at 55, 65, and 75 years old across the three levels of walking pace, as well as the differences in the sojourn times comparing brisk and average versus slow pace (reference). In the second model, we estimated the sojourn times at the mean values of each confounder and at the most common smoking status (never smoker). In a sensitivity analysis, we reestimated the sojourn times including only first hospitalizations reporting a CVD or cancer as the primary cause of admission.

Data were prepared, summarized, and modeled using Stata routine commands, *stmerlin*, and the *multistate* package in Stata/BE version 17.0 ; results are reported with a 95% confidence interval (CI) and graphs prepared in Stata (*schemepack* version 1.3) and Inkscape version 1.2.1. The statistical code is available at GitHub (frazac82).

Results

Cohort characteristics

The baseline characteristics of the 214,290 (54.7%) women and 177,454 (45.3%) men included in the analysis are shown in Table 1. Both sexes displayed similar ages (women, 57.2 [IQR: 49.8–62.9] years; men, 57.4 [49.6–63.2] years) and levels of deprivation. Overall, more than half of the participants reported an average walking pace (n = 206,178; 52.3%), with slow and brisk pace making up the remaining 6.6% (n = 25,739) and 41.1% (n = 159,827) of the cohort, respectively; this distribution was similar across women and men. Women were less likely to smoke (8.7% vs. 12.4%), have a lower BMI (26.0 [23.4–29.5] vs. 27.2 [24.9–29.9] kg/m^2), and engage in less leisure-time physical activity (450 [149–1040] vs. 668 [210–1505] metabolic equivalent of task-min/week).

Table 1
Baseline characteristics by sex

	Women	Men	Total
No. of people	214,290	177,454	391,744
Age, years	57.2 (49.8, 62.9)	57.4 (49.6, 63.2)	57.3 (49.8, 63.0)
Systolic blood pressure, mmHg	133 (121, 147)	140 (129, 152)	136 (125, 149)
Low-density lipoprotein cholesterol, mmol/L	3.6 (3.0, 4.2)	3.5 (3.0, 4.1)	3.6 (3.0, 4.1)
Body mass index, kg/m^2	26.0 (23.4, 29.5)	27.2 (24.9, 29.9)	26.6 (24.1, 29.7)
Townsend deprivation index	−2.2 (−3.7, 0.4)	−2.2 (−3.7, 0.5)	−2.2 (−3.7, 0.4)
Leisure-time physical activity volume, MET-min/wk	450.0 (148.5, 1039.5)	668.3 (210.0, 1504.7)	535.3 (158.8, 1216.9)
Smoking status			
Never	129,618 (60.5)	90,354 (50.9)	219,972 (56.2)
Former	66,055 (30.8)	65,139 (36.7)	131,194 (33.5)
Current	18,617 (8.7)	21,961 (12.4)	40,578 (10.4)
Usual walking pace			
Slow pace	15,115 (7.1)	10,624 (6.0)	25,739 (6.6)
Steady average pace	113,339 (52.9)	92,839 (52.3)	206,178 (52.6)
Brisk pace	85,836 (40.1)	73,991 (41.7)	159,827 (40.8)

Data are reported as median (interquartile range) or number (%).
A greater Townsend index indicates a greater degree of deprivation.
MET = metabolic equivalent of task.

The characteristics stratified by walking pace are shown in Supplementary Table S1: when compared to slow walkers, those who reported being average and brisk walkers were marginally younger, were more likely to have never smoked, engaged in more physical activity, and had a lower deprivation index and BMI.

Transition rates

The overall median follow-up was 12.5 years (IQR: 11.8–13.2). In total, 108,097 individuals (27.6%) experienced a hospitalization for CVD or cancer during the study; 4975 (1.3%) deaths occurred without a previous hospitalization; and 16,827 (4.3%) individuals died following a previous hospitalization for CVD or cancer. Among women, 53,510 (25.0%) had a hospitalization for CVD or cancer and 1841 (0.9%) died without a previous hospitalization; 7170 (3.3%) deaths occurred in women who had a previous hospitalization for CVD or cancer; the

corresponding figures in men were 54,587 (30.8%), 3134 (1.8%), and 9657 (5.4%), respectively (Fig. 1).

The rates of transitions across the three states, stratified by walking pace, are shown in Table 2. The transition rates from healthy to CVD or cancer or from CVD or cancer to death were higher than transitions from a healthy state to death; this was consistent across all walking paces and sex, with those reporting an average or brisk walking pace displaying lower rates across all transitions compared to slow walkers. For example, for women who reported an average or brisk walking pace, the progression rates from healthy to CVD or cancer were considerably lower (2.4 events per 100 person years [95% CI: 2.4, 2.4] and 1.9 [1.9, 2.0], respectively) compared to those that reported a slower walking pace (3.7 [3.6, 3.8]). Moving from CVD or cancer to death yielded similar pattern, where the transition rates for brisk, average, and slow pace were 2.0 (95% CI: 1.9, 2.1), 2.4 (2.3, 2.5), and 3.6 (3.4, 3.8), respectively. In men who reported an average or brisk walking pace, the progression rates from healthy to CVD or cancer were considerably lower (3.2 events per 100 person years [95% CI: 3.1, 3.2] and 2.4 [2.4, 2.4], respectively) compared to those reporting a slower walking pace (5.1 [4.9, 5.2]). Moving from CVD or cancer to death yielded transition rates of 2.7 (95% CI: 2.6, 2.9), 3.4 (3.3, 3.5), and 5.6 (5.4, 5.9) for brisk, average, and slow, respectively.

Sojourn times

The sojourn times (i.e., the length of stay) in the healthy or CVD or cancer state and their differences across walking pace are presented in Figures 2 and 3, respectively, for the adjusted model; corresponding results for the base model are shown in Supplementary Figs. S2 and S3. Regardless of age or sex, the sojourn time in the healthy state (i.e., the disease-free survival) was longer while that in the CVD or cancer state was shorter in individuals reporting an average or brisk walking pace compared to those that reporting a low walking pace. For example, a 75-year-old woman reporting a brisk walking pace spent, on average, 8.4 years of the next 10 years in a healthy state (Fig. 2), which is an additional 8.0 (95% CI: 7.3, 8.7) months longer compared to a 75-year-old woman reporting a slow walking pace (Fig. 3) and spent 4.3 (3.7, 4.9) fewer months living with CVD or cancer. In addition, brisk walking was associated with 3.7 (95% CI: 3.2, 4.2) additional months in the overall life expectancy compared to slow walkers. Similarly, a 75-year-old man reporting brisk walking spent 7.4 years of the next 10 years in the healthy state (Fig. 2); this corresponded to 12.3 (95% CI: 11.4, 13.3) additional months in a healthy state, 5.4 (4.5, 6.3) fewer months living with CVD or cancer, and 6.9 (6.2, 7.6) months longer life expectancy compared to a 75-year-old man reporting a slow walking pace (Fig. 3). This pattern across walking pace was also observed in 55- or 65-year-old individuals, yet the differences were smaller for living in a healthy state or in the overall life expectancy and more similar for living with CVD or cancer (Fig. 3).

Table 2
Transition rates across the three states

Sex	Transition	From state to state	Walking pace	Events	Rate (95% CI)
Women	T1	Healthy [S1] to CVD/cancer [S2]	Slow pace	5591	3.7 (3.6, 3.8)
			Steady average pace	29,452	2.4 (2.4, 2.4)
			Brisk pace	18,467	1.9 (1.9, 2.0)
	T2	Healthy [S1] to died [S3]	Slow pace	356	0.2 (0.2, 0.3)
			Steady average pace	995	0.1 (0.1, 0.1)
			Brisk pace	490	0.1 (0.1, 0.1)
	T3	CVD/cancer [S2] to died [S3]	Slow pace	1120	3.6 (3.4, 3.8)
			Steady average pace	3958	2.4 (2.3, 2.5)
			Brisk pace	2092	2.0 (1.9, 2.1)
Men	T1	Healthy [S1] to CVD/cancer [S2]	Slow pace	4891	5.1 (4.9, 5.2)
			Steady average pace	30,429	3.2 (3.1, 3.2)
			Brisk pace	19,267	2.4 (2.4, 2.4)
	T2	Healthy [S1] to died [S3]	Slow pace	473	0.5 (0.5, 0.5)
			Steady average pace	1694	0.2 (0.2, 0.2)
			Brisk pace	967	0.1 (0.1, 0.1)
	T3	CVD/cancer [S2] to died [S3]	Slow pace	1466	5.6 (5.4, 5.9)
			Steady average pace	5476	3.4 (3.3, 3.5)
			Brisk pace	2715	2.7 (2.6, 2.9)

Rate is reported per 100 person years.
CI = confidence interval; CVD = cardiovascular disease; S = state; T = transition to another state.

The base model results mirrored those obtained from the adjusted model. Yet, across ages, walking paces, and sexes the sojourn times were shorter for the healthy state (compared to the adjusted model, from 0.3 to 5.5 months in women and from 0.6 to 8.1 in men) and longer in the CVD or cancer state (0.2–3.0 months in women and 0.5–3.1 in men; Supplementary Fig. S2). This translated into larger differences across walking pace compared to the adjusted model (Supplementary Fig. S3): in a 75-year-old woman, brisk walking was associated with 13.0 (95% CI: 12.3, 13.7) additional months spent in a healthy state, 6.8 (6.2, 7.4) fewer months living with CVD or cancer, and 6.2 (5.7, 6.8) months longer life expectancy compared to slow walking; corresponding estimates in men were 18.9 (18.0, 19.9), 6.0 (5.1, 6.9), and 12.9 (12.1, 13.8) months.

Sensitivity analysis

We reestimated the sojourn times including only hospitalizations that reported a CVD or cancer ICD code as the primary cause of admission. This resulted in 16,079 less CVD or cancer hospitalizations (8222 in women and 7857 in men; transition diagrams are presented in Supplementary Fig. S4). Although the differences across walking pace were marginally attenuated, they did not materially change (Supplementary Fig. S5). For example, in a 75-year-old woman, brisk walking pace was associated with an additional 6.2 months (95% CI: 5.5, 6.8) in the healthy state and 2.4 (1.9, 2.9) fewer months in the CVD or cancer state compared to a 75-year-old woman reporting a slow walking pace; this also corresponded to an additional 3.7 (95% CI: 3.2, 4.2) months lived. Similarly, a 75-year-old man reporting a brisk walking pace could expect to spend an additional 9.6 months (95% CI: 8.7, 10.5) in the healthy state, 2.9 (2.1, 3.7) fewer months in the CVD or cancer state, and an additional 6.7 (6.0, 7.4) months lived compared to a 75-year-old man reporting a slow walking pace.

Discussion

In this large study of more than 390,000 UK adults, those that reported an average (3–4 mph) or brisk walking (greater than 4 mph) pace at baseline displayed a lower transition to disease development and a greater proportion of life lived without CVD or cancer morbidity (i.e., healthy life years) compared with adults reporting a slow walking pace (less than 3 mph). The patterns of results remained significant after adjustment for potential confounders and were consistent across different age categories, subgroups of the cohort (women and men), and those with and without CVD or cancer as a primary cause of hospital admission. Previous research examining the association of walking pace with specific CVDs, cancer, and all-cause mortality has provided clear evidence for exposure-disease associations [7,8,10]. However, the present study allows for greater insight into what these associations could mean at a population level for delaying the onset of CVD or cancer and

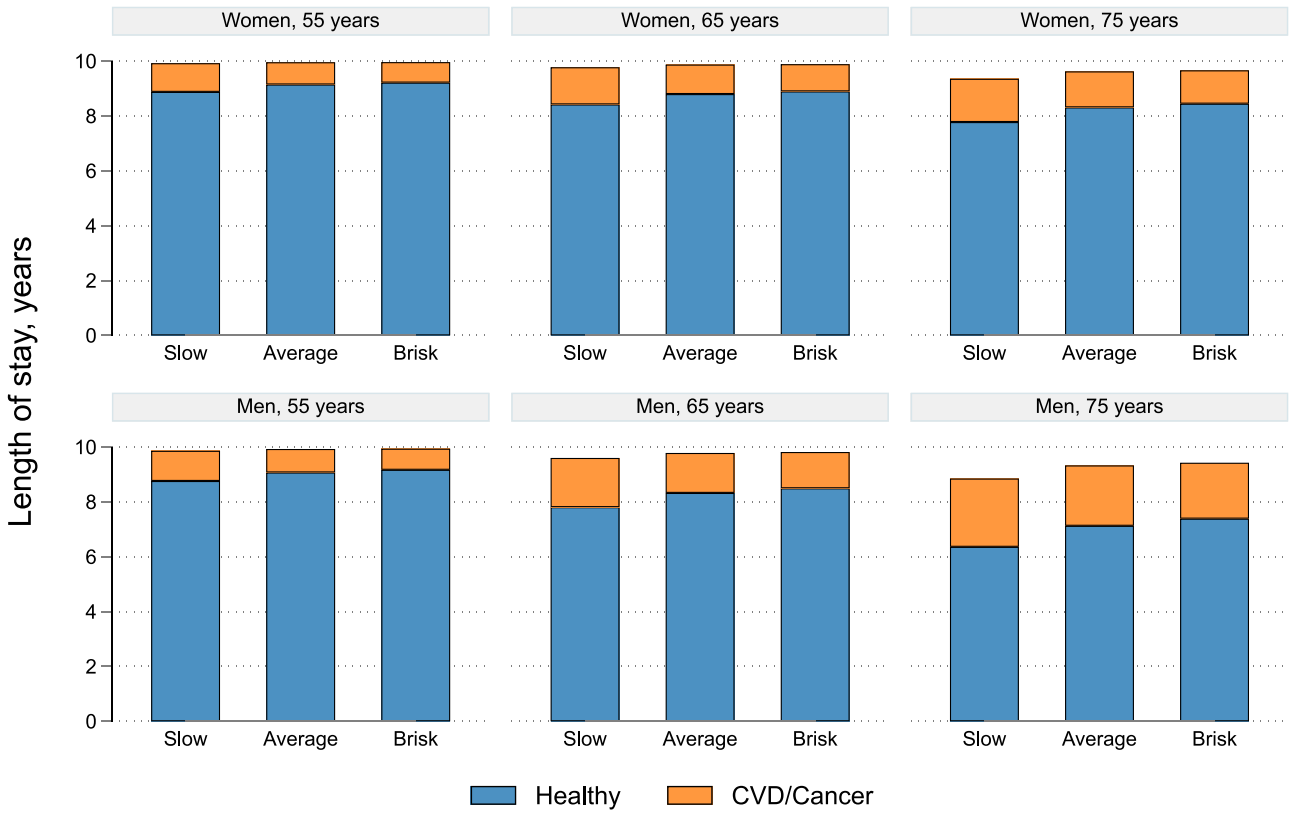

Fig. 2. Sojourn times in each state. The plot shows the time spent in each state upon a time horizon of 10 years. Adjusted estimates to the mean of the confounding variables (systolic blood pressure, LDL cholesterol, Townsend score, leisure-time physical activity volume, body mass index) and the most frequent category for smoking (never smoker).

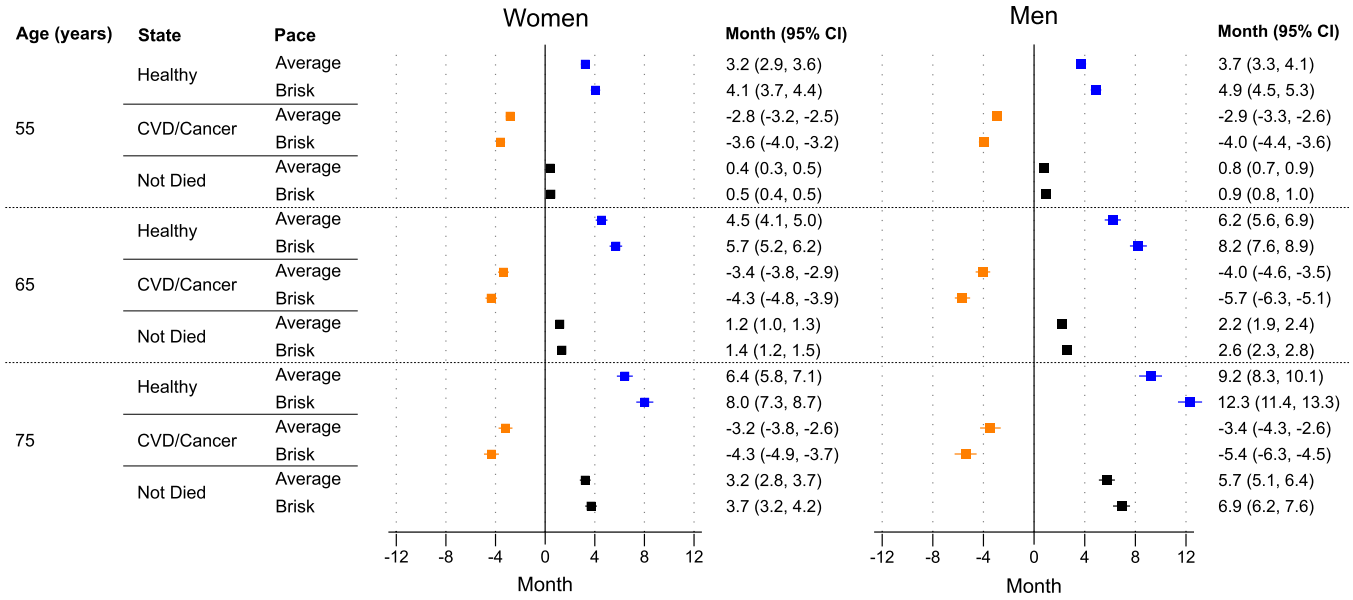

Fig. 3. Adjusted differences in sojourn times and survival. Adjusted estimates to the mean of the confounding variables systolic blood pressure, LDL cholesterol, Townsend score, leisure-time physical activity volume, body mass index, and the most frequent category for smoking (never smoker). Estimates, obtained upon a time horizon of 10 years, indicate how longer (positive) or shorter (negative) is the sojourn time or length of stay in the healthy (blue squares) or CVD or cancer (orange squares) state for average or brisk versus slow walking pace (reference); for the state "not died," the estimates (black squares) represent the extra time (months) lived.

the subsequent compression of living with morbidity over a 10-year time horizon. For example, a 75-year-old man, with a brisk walking speed, on average spent over a year longer in a healthy state compared to a slow walker, with the time spent living with CVD or cancer compressed by over 5 months.

Our findings also corroborate previous research demonstrating that

healthy lifestyle behaviors can delay the onset of disease and/or compress morbidity [20,21,29–32]. For instance, individuals with favorable lifestyle risk factors (overweight but not obese, light/-moderate drinker, nonsmoker, and undertaking some form of vigorous physical activity) lived between 15.7 (women) and 7.4 (men) years longer than those with unfavorable lifestyle risk factors, with a large proportion of the extra life years being disease-free (greater than 90%) [33]. Although these cohort studies highlight the preventive potential of healthy lifestyle habits, the challenges of yielding multiple lifestyle changes should not be underestimated. As such, our decision to focus on a simple, practical, subjective measure of fitness (self-reported walking pace) is important in assessing overall physical condition. Not only are physical capability measures, such as walking speeds, predictors of institutionalization, disability, falls, hospitalization, and mortality, but they are also closely associated with frailty and physical function [7,34,35]. Therefore, modifiable behavioral factors that can reduce the duration of morbidity as a fraction of remaining life (i.e., compress morbidity) are prime goals of both clinical medicine and public health, as well as healthy aging research. Indeed, previous research has suggested that behavioral factors determine progression to the onset of NCDs and prediction of mortality to a greater extent than clinical risk factors (e.g., overweight and obesity and family history of CVD) [28,29].

Despite increases in life expectancy (the number of people aged greater than 60 years will double by 2050 [36]), healthy life expectancy has not increased at the same rate. For example, in 2013–2015 in England the period lived in poor health was 19 years for women and 16.1 years for men [18]. These results, coupled with higher transition rates from healthy to CVD or cancer and CVD or cancer to death for participants reporting a slow walking speed (roughly two times higher than those reporting a brisk walking pace), reiterate the importance of prevention and management of NCDs at both an individual and population level. For instance, living a relatively longer and healthier life free of major morbidity can yield multiple physiological (e.g., delayed acceleration in functional decline or preservation of quality of life) [37], psychological (e.g., delayed cognitive impairment) [38], and societal benefits (reducing the burden of care) [39]. Understanding how effective interventions on modifiable risk behaviors (i.e., walking pace) can maximize time lived without major disease will help focus initiatives to prolong independence, improve quality of life, and diminish the health care costs associated with aging populations. Indeed, as walking provides a safe, easy-to-understand metric of ambulation, the findings of this study add to the multitude of accessible interventional options across the age and fitness spectrum.

Strengths of the present study include the large, contemporary, well-phenotyped cohort, as well as the longer-term follow-up, larger number of events, and robust outcomes coded in hospital records. Furthermore, we used the Royston–Parmar model as it allowed us to model each transition separately, without assuming a specific distribution for all transitions, and to obtain sojourn times in each state upon a time horizon of 10 years for specific patterns of risk factor (i.e., age) [27]. Despite these strengths, several limitations of our study need to be considered. Firstly, residual bias may also have occurred via some unmeasured factors and/or included variables measured with substantial error. In order to address this, we ran a sensitivity analysis with CVD or cancer as the primary cause of admission, which did not materially change the relationships between walking pace and sojourn times. Similarly, the trajectories across disease states for levels of walking pace may differ between CVD and cancer and within different types of CVD and cancer. Secondly, walking pace and key covariates (e.g., systolic blood pressure, serum LDL cholesterol, BMI) were only obtained at baseline, and changes over time were not accounted for in this study. However, with regard to walking pace, in the absence of a specific intervention, individuals are unlikely to change their lifestyle behaviors [40], highlighting the potential of exploring whether a simple measure like self-reported walking pace has value as a future behavioral intervention. Finally, we may have underestimated the time spent in disease states as the UK Biobank is not a representative population-based cohort and arguably has a more favorable health profile than the general population [41]. This may have been further compounded by the fact that diagnoses were taken from hospitalizations (and not primary care). Nevertheless, it has served to strengthen our ability to draw inferences from the multistate group comparisons. Future research should investigate whether these findings are exhibited in younger age groups and those at increased risk of NCDs.

Our analysis shows self-reported walking pace to be a key indicator of the incidence of a first NCD, in this study CVD or cancer, and an important modifiable risk factor in the compression of morbidity. Individuals who report a faster walking pace (greater than 4 mph) may not only live a longer life but also a healthier life. Given the increasing prevalence of NCDs, the compression of morbidity related to modifiable health behaviors (i.e., walking pace) will continue to be of great importance.

CRediT authorship contribution statement

FZ, AR, PCD, CR, JH, JG, and TY formed the core working group and developed the research question. FZ developed the analysis code. JH and FZ drafted the manuscript. All authors contributed to the interpretation and revised the manuscript for important intellectual content.

Declaration of Competing Interest

The authors declare no competing interests

Acknowledgments

This research is funded by the National Institute for Health and Care Research Leicester Biomedical Research Center and the National Institute for Health Research Applied Research Collaboration–East Midlands. The views expressed are those of the author(s) and not necessarily those of the National Institute for Health and Care Research or the Department of Health and Social Care. We are grateful to the participants of the UK Biobank study and those who collected and managed the data.

Disclaimers

The authors had financial support from the funders listed above for the submitted work. The authors declare that they have no competing interests.

Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.annepidem.2023.10.001.

References

[1] World Health Organisation. United Force Nations InterAgency on the prevention and of noncommunicable task control diseases. 2022–25 strategy. ⟨https://apps.who.int/iris/bitstream/handle/10665/362066/9789240051409-eng.pdf?sequence=1⟩; 2022. accessed 17/11/2022.
[2] Katzmarzyk PT, Friedenreich C, Shiroma EJ, Lee IM. Physical inactivity and non-communicable disease burden in low-income, middle-income and high-income countries. Br J Sports Med 2021;56(2):101–6.
[3] Jayedi A, Emadi A, Shab-Bidar S. Dose-dependent effect of supervised aerobic exercise on HbA(1c) in patients with type 2 diabetes: a meta-analysis of randomized controlled trials. Sports Med 2022;52(8):1919–38.
[4] Jakicic JM, Powell KE, Campbell WW, Dipietro L, Pate RR, Pescatello LS, et al. Physical activity and the prevention of weight gain in adults: a systematic review. Med Sci Sports Exerc 2019;51(6):1262–9.
[5] Moore SC, Lee IM, Weiderpass E, Campbell PT, Sampson JN, Kitahara CM, et al. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. JAMA Intern Med 2016;176(6):816–25.
[6] Mora S, Cook N, Buring JE, Ridker PM, Lee IM. Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. Circulation 2007;116(19):2110–8.

[7] Yates T, Zaccardi F, Dhalwani NN, Davies MJ, Bakrania K, Celis-Morales CA, et al. Association of walking pace and handgrip strength with all-cause, cardiovascular, and cancer mortality: a UK Biobank observational study. Eur Heart J 2017;38(43):3232–40.
[8] Del Pozo Cruz B, Ahmadi MN, Lee IM, Stamatakis E. Prospective associations of daily step counts and intensity with cancer and cardiovascular disease incidence and mortality and all-cause mortality. JAMA Intern Med 2022;182(11):1139–48.
[9] Dempsey PC, Musicha C, Rowlands AV, Davies M, Khunti K, Razieh C, et al. Investigation of a UK biobank cohort reveals causal associations of self-reported walking pace with telomere length. Commun Biol 2022;5(1):381.
[10] Argyridou S, Zaccardi F, Davies MJ, Khunti K, Yates T. Walking pace improves all-cause and cardiovascular mortality risk prediction: a UK Biobank prognostic study. Eur J Prev Cardiol 2020;27(10):1036–44.
[11] Ganna A, Ingelsson E. 5 year mortality predictors in 498,103 UK Biobank participants: a prospective population-based study. Lancet (London, England) 2015;386(9993):533–40.
[12] Cigarroa I, Bravo-Leal M, Petermann-Rocha F, Parra-Soto S, Concha-Cisternas Y, Matus-Castillo C, et al. Brisk walking pace is associated with better cardiometabolic health in adults: findings from the Chilean National Health Survey 2016-2017. Int J Environ Res Public Health 2023;20(8):5490. https://doi.org/10.3390/ijerph20085490.
[13] Stamatakis E, Kelly P, Strain T, Murtagh EM, Ding D, Murphy MH. Self-rated walking pace and all-cause, cardiovascular disease and cancer mortality: individual participant pooled analysis of 50 225 walkers from 11 population British cohorts. Br J Sports Med 2018;52(12):761–8.
[14] Zaccardi F, Franks PW, Dudbridge F, Davies MJ, Khunti K, Yates T. Mortality risk comparing walking pace to handgrip strength and a healthy lifestyle: a UK Biobank study. Eur J Prev Cardiol 2021;28(7):704–12.
[15] Zaccardi F, Davies MJ, Khunti K, Yates T. Comparative relevance of physical fitness and adiposity on life expectancy: a UK Biobank observational study. Mayo Clin Proc 2019;94(6):985–94.
[16] Muka T, Imo D, Jaspers L, Colpani V, Chaker L, van der Lee SJ, et al. The global impact of non-communicable diseases on healthcare spending and national income: a systematic review. Eur J Epidemiol 2015;30(4):251–77.
[17] Orkaby AR. Moving beyond chronological age: frailty as an important risk factor for cardiovascular disease. Eur Heart J 2021;42(37):3866–8.
[18] Public Health England. Life expectancy and healthy life expectancy. ⟨https://www.gov.uk/government/publications/health-profile-for-england/chapter-1-life-expectancy-and-healthy-life-expectancy⟩; 2017. accessed 08/11/2022.
[19] Hougaard P. Multi-state models: a review. Lifetime Data Anal 1999;5(3):239–64.
[20] Freisling H, Viallon V, Lennon H, Bagnardi V, Ricci C, Butterworth AS, et al. Lifestyle factors and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study. BMC Med 2020;18(1):5–7.
[21] Cao Z, Xu C, Yang H, Li S, Wang Y. The role of healthy lifestyle in cancer incidence and temporal transitions to cardiometabolic disease. Cardio Oncol 2021;3(5):663–74.
[22] Syddall HE, Westbury LD, Cooper C, Sayer AA. Self-reported walking speed: a useful marker of physical performance among community-dwelling older people? J Am Med Dir Assoc 2015;16(4):323–8.
[23] Kondamudi N, Mehta A, Thangada ND, Pandey A. Physical activity and cardiorespiratory fitness: vital signs for cardiovascular risk assessment. Curr Cardiol Rep 2021;23(11):172.
[24] Rowlands AV, Dempsey PC, Maylor B, Razieh C, Zaccardi F, Davies MJ, et al. Self-reported walking pace: a simple screening tool with lowest risk of all-cause mortality in those that 'walk the talk'. J Sports Sci 2023;41(4):333–41.
[25] Touraine C, Helmer C, Joly P. Predictions in an illness-death model. Stat Methods Med Res 2016;25(4):1452–70.
[26] Jetté M, Sidney K, Blümchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. Clin Cardiol 1990;13(8):555–65.
[27] Crowther MJ, Lambert PC. Parametric multistate survival models: flexible modelling allowing transition-specific distributions with application to estimating clinically useful measures of effect differences. Stat Med 2017;36(29):4719–42.
[28] Weibull CE, Lambert PC, Eloranta S, Andersson TML, Dickman PW, Crowther MJ. A multistate model incorporating estimation of excess hazards and multiple time scales. Stat Med 2021;40(9):2139–54.
[29] Li D, Wang L, Zhou Z, Song L, Chen S, Yang Y, et al. Role of socioeconomic, lifestyle, and clinical factors in the progression of cardiometabolic multimorbidity in China: a 10-year prospective cohort study. Nutr Metab Cardiovasc Dis 2022;32(10):2383–91.
[30] Licher S, Heshmatollah A, van der Willik KD, Stricker BHC, Ruiter R, de Roos EW, et al. Lifetime risk and multimorbidity of non-communicable diseases and disease-free life expectancy in the general population: a population-based cohort study. PLoS Med 2019;16(2):e1002741.
[31] Singh-Manoux A, Fayosse A, Sabia S, Tabak A, Shipley M, Dugravot A, et al. Clinical, socioeconomic, and behavioural factors at age 50 years and risk of cardiometabolic multimorbidity and mortality: a cohort study. PLoS Med 2018;15(5):e1002571.
[32] Xie H, Li J, Zhu X, Li J, Yin J, Ma T, et al. Association between healthy lifestyle and the occurrence of cardiometabolic multimorbidity in hypertensive patients: a prospective cohort study of UK Biobank. Cardiovasc Diabetol 2022;21(1):1–12.
[33] O'Doherty MG, Cairns K, O'Neill V, Lamrock F, Jørgensen T, Brenner H, et al. Effect of major lifestyle risk factors, independent and jointly, on life expectancy with and without cardiovascular disease: results from the Consortium on Health and Ageing Network of Cohorts in Europe and the United States (CHANCES). Eur J Epidemiol 2016;31(5):455–68.
[34] Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49(2):85.
[35] Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. JAMA 2011;305(1):50–8.
[36] World Health Organisation. Ageing and health, ⟨https://www.who.int/news-room/fact-sheets/detail/ageing-and-health⟩; 2022. accessed 17/11/2022.
[37] Crimmins EM. Lifespan and healthspan: past, present, and promise. Gerontologist 2015;55(6):901–11.
[38] Marioni RE, Valenzuela MJ, Hout Avd, Brayne C, Matthews FE, Function MC, et al. Active cognitive lifestyle is associated with positive cognitive health transitions and compression of morbidity from age sixty-five. PloS One 2012;7(12):e50940.
[39] Allen NB, Zhao L, Liu L, Daviglus M, Liu K, Fries J, et al. Favorable cardiovascular health, compression of morbidity, and healthcare costs: forty-year follow-up of the CHA study (Chicago Heart Association Detection Project in Industry). Circulation 2017;135(18):1693–701.
[40] Newsom JT, Huguet N, McCarthy MJ, Ramage-Morin P, Kaplan MS, Bernier J, et al. Health behavior change following chronic illness in middle and later life. J Gerontol Series B Psychol Sci Soc Sci 2012;67(3):279–88.
[41] Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with those of the general population. Am J Epidemiol 2017;186(9):1026–34.