Association of accelerometer-measured physical activity patterns with cardiovascular diseases and mortality in people with osteoarthritis

Tianxiang Fan[1,2#]; Qiyu Xie[1,3#]; Jiawei Chen[1#]; Muhui Zeng[1,4]; Shibo Chen[1,5]; Hao Yang[1]; Guangfeng Ruan[1]; Qian Yang[6,7]; Yujie Zhang[8]; Ye Li[2]; Peihua Cao[1]; Kim L Bennell[9]; Siu Ngor Fu[2]; David J Hunter*[1,10]; Changhai Ding*[1,11,12]; Zhaohua Zhu*[1,10,11]

[1] Clinical Research Centre, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, China

[2] Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China

[3] The Second Clinical School, Southern Medical University, Guangzhou, Guangdong, China

[4] Department of Orthopedics, General Hospital of Southern Theater Command of PLA, Guangzhou, Guangdong, China

[5] Institute of Translational Genomics, Helmholtz Zentrum München, German Research Center for Environmental Health, 85764 Neuherberg, Germany

[6] MRC Integrative Epidemiology Unit at University of Bristol, Bristol, United Kingdom

[7] Population Health Sciences, Bristol Medical School, University of Bristol, United Kingdom

[8] Fujian Provincial Key Laboratory of Molecular Neurology, Institute of Neuroscience, Fujian Medical University, Fuzhou, China

[9] Centre for Health, Exercise and Sports Medicine, Department of Physiotherapy, School of Health Sciences, Faculty of Medicine Dentistry & Health Sciences, University of Melbourne, Melbourne, VIC, Australia.

[10] Royal North Shore Hospital and Sydney Musculoskeletal Health, Kolling Institute, University of Sydney, Sydney, Australia, 2065

[11] Orthopedic Centre, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, China

[12] Clinical Research Centre, Guangzhou First People's Hospital, School of Medicine, South China University of Technology, Guangzhou, China

Word Count: 3,180

 # Contributed equally

***Corresponding Authors:**

Zhaohua Zhu. Email: zhaohua.zhu@utas.edu.au; Address: Zhujiang Hospital, Southern Medical University, 253 Industrial Avenue Guangzhou, 510280 China; Telephone number/fax number: 020-61643039;

Changhai Ding. Email: changhai.ding@utas.edu.au; Address: Zhujiang Hospital, Southern Medical University, 253 Industrial Avenue Guangzhou, 510280 China; Telephone number/fax number: 020-62783252;

David J Hunter. Email: david.hunter@sydney.edu.au; Address: Royal North Shore Hospital and Sydney Musculoskeletal Health, Kolling Institute, University of Sydney, Sydney, Australia, 2065

Key Points

Question: What physical activity pattern can reduce the risks of cardiovascular diseases and mortality among people with osteoarthritis.

Findings: In this cohort study of 10,210 participants with osteoarthritis, weekend warriors reduced their risk of cardiovascular diseases by 27% and mortality by 45%, while the high level of light physical acivity reduced these risks by 15% and 64%, respectively.
Meaning: The weekend warrior pattern and high level of light physical activity might effectively lower CVD risk and mortality in people with ostearhritis.

Abstract

Bcakground: Individuals with osteoarthritis (OA) face a 1·7-fold increased risk of cardiovascular disease (CVD) and a 1·6 times higher mortality risk compared to those without OA. What physical activity pattern can reduce these risk is not clear. This study aimed to explore the associations between accelerometer-measured physical activity patterns and cardiovascular diseases (CVD), CVD-cause mortality, and all-cause mortality in people with osteoarthritis (OA).

Methods: We included participants with OA from the UK biobank with ≥36 hours of accelerometer data, collected over one-week. Moderate to vigorous physical activity (MVPA) patterns were classified as: 'weekend warriors' (≥150 min/week, >50% on 1-2 days), active regular (>150 min/week), or inactive (<150 min/week). Mean minutes per week of light physical activity (LPA) were categorized into quartiles based on the distribution in the analytical sample.

Findings: Among 10,210 study participants (mean age 58·1± 7·1 years; 64·5% female) followed for a median of 6·9 years, there were 1,538 incident cases of CVD, and 358 deaths, including 90 from CVD. Compared with inactive MVPA, both weekend warrior (adjusted hazard ratio, aHR (95% CIs); 0·73 (0·64-0·82)) and active regular MVPA (0·75 (0·65-0·87)) significantly lowered the risks of incident CVD. Notably, only the weekend warrior group showed significant reductions in CVD-cause mortality (0·55, 0·33-0·92), and all-cause mortality (0·75 (0·59-0·96)). Higher levels of LPA were linked to lower CVD, CVD-cause mortality, and all-cause mortality risks in a dose-response manner. Subgroup analysis indicated that more prominent associations were found in individuals with a body mass index greater than 30 or those aged over 60.

Interpretation: Engaging in a weekend warrior pattern may confer unique survival benefits for OA patients, especially among older adults and those with obesity. LPA may have dose-dependent protective effects for CVD and mortality risk in OA patients.

Introduction

Osteoarthritis (OA) is the most common musculoskeletal disorder that poses significant risks to individuals' long-term health[1-3]. Previous studies highlight an increased risk of cardiovascular diseases (CVD) and mortality in people with OA[4-6]. The prevalence of overall CVD was 38·4% in individuals with OA, compared to 9% in the non-OA people[3]. Excess mortality was observed for all disease-specific causes of mortality in patients with knee or hip OA but was particularly pronounced for CVD-caused mortality (standardized mortality ratio 1·71)[4].

Adhering to the World Health Organization's recommendation of engaging in at least 150 minutes of moderate to vigorous physical activity (MVPA) per week can significantly reduce the risks of CVD and mortality in the general population[7-9]. In recent years, the "weekend warrior of MVPA" has emerged as a new exercise pattern, characterized by individuals completing most of their MVPA within one to two days. Studies have shown that it can reduce CVD and mortality risks to a similar extent as more evenly distributed physical activity[10-13]. However, it is essential to investigate whether these findings can be extrapolated to individuals with OA for several reasons. First, individuals with OA face distinct challenges and potential limitations in engaging in regular physical activity, such as fear of exercise and pain aggravation, time management and doubt about the benefits and safety of workouts[14,15]. Theoretically, the "weekend warrior of MVPA" pattern can enhance exercise adherence by condensing activity into a schedule that accommodates physical conditions, providing flexibility, motivation, and the possibility of adapting to intermittent intense activity. Second, individuals with OA are predisposed to higher risks of CVD and mortality due to factors such as joint pain, chronic inflammation, and mobility limitations. This may lead to differences in the benefits derived from MVPA compared to the general population[16].

Although the American College of Rheumatology has advocated light physical activity (LPA) as suitable exercise for individuals with OA[17], it remains unclear whether longer durations of LPA provide greater benefits for reducing CVD and mortality risk in people with OA than shorter durations[18, 19]. Given the challenges of adherence to moderate to vigorous exercise among people with OA, it is also critical to explore the relationship between LPA duration and its impact on CVD and mortality risks.

To address these knowledge gaps, we examined the associations between accelerometer-measured MVPA physical activity patterns and CVD, CVD-cause mortality, and all-cause mortality over a 6·9-year period using data from the UK Biobank. In addition, we evaluated how the duration of LPA was related to the risks of CVD, CVD-cause mortality and all-cause mortality in individuals with OA.

Methods

Study design and participants

The UK Biobank is a prospective cohort study that recruited 502,411 participants between June 2013 and January 2016 in the UK[20]. Within the accelerometer sub-study, 103,660 participants submitted data from accelerometer worn for 1 week. We excluded participants who missed the data of daily MVPA or LPA (n=3,551), with insufficient wear-time (<36 h/week, n=3,142), with unrealistically high acceleration values (avg acceleration >100 mg, n=14), not sufficiently calibrated (error >10 mg, n=11)[10]. Participants who had not been diagnosed with OA before accelerometer wearing (n=79,554), had been diagnosed with CVD before OA (n=6,161), or had been diagnosed with CVD before accelerometer wearing were excluded (n=1,013). Finally, a total of 10,210 participants with OA were included in our analysis (Figure 1).

Assessment of physical activity

103,660 participants received an email invitation to inform them that they were required to wear a wrist-based accelerometer (Axivity AX3) for one week, recording the complete daily activities[21]. The accelerometers data process methods were published before[22].

To minimize the influence of outliers on the model, we trimmed observations below the 5th percentile and above the 95th percentile based on the distribution of the LPA and MVPA data from the lowest to the highest[23]. Based on accelerometer-measured MVPA, participants were classified as (1) Inactive: MVPA <150 min/week, (2) Active weekend warrior of MVPA: total MVPA ≥150 min/week & ≥50% of total MVPA over 1-2 days, (3) Active regular MVPA: total MVPA ≥150 min/week & not Active weekend warrior[10]. The participants were also separately grouped based on quartiles of their LPA duration into four categories: Low LPA Group (<1780 min/week), Moderate-Low LPA Group (>1780 & <2166 min/week), Moderate-High LPA Group (2166-2586 min/week), and High LPA Group (>2586 min/week).

Assessment of disease diagnosis

International Classification of Diseases, tenth Revision (ICD-10) codes were acquired through hospital inpatient records. Incident CVD was defined as ICD-10 codes (I20-I25, I50 and I60-I64)[24]. The ICD-10 codes for OA were shown in eTable 10.

Date and cause of death information were obtained from death certificates held within the National Health Service Information Centre (England and Wales) and the National Health Service Central Register (Scotland). Person time was calculated from baseline to the occurrence of death or the end of follow-up (England & Wales on 30 September 2021, Scotland on 31 October 2021), whichever came first. CVD-cause mortality was obtained in outcomes defined as ICD-10 codes I00-I99[25].

Covariates

The following potential covariates were selected by referring to previous relevant studies: age, sex, body mass index (BMI), ethnic background, Townsend deprivation index (TDI), education level, employment status, smoking status, alcohol drinking status, diet score, metabolic syndrome and self-reported health status[10, 26, 27]. Ethnic background was classified as white and non-white. Education includes college or university degrees and others. For employment, we set two groups: employed (including individuals who were self-employed or in paid employment, retired, engaged in unpaid or voluntary work, and full or part-time students) and unemployed. Smoking status was classified as never, former and current smoker. Alcohol drinking status was classified as abstainer, former drinker, and current drinker. TDI was chosen to assess socio-economic deprivation within a particular geographic area and reflect health inequalities and social determinants of health. A diet score for ten diet components from questionnaires was used1. BMI was calculated from height and weight (kg/m^2). Self-reported health was identified through the question: "In general, how would you rate your overall health?" and the answers from participants were sorted into excellent, good, fair, and poor. Metabolic health score was constructed referring to the National Cholesterol Education Program's report, Adult Treatment Panel-III (ATP3), to identify patients with metabolic syndrome, including five components of the metabolic syndrome relating to: abdominal obesity, triglycerides, high-density lipoprotein cholesterol, blood pressure and fasting glucose. Each component that did not meet the criteria received one point in the healthy metabolic score (eTable 1). All missing covariates were imputed using multiple imputation by the 'mice' package in R software, and subsequently used in the regression analysis.

Statistical Analysis

Descriptive analyses used the means with standard deviation (SD) to portray continuous variables. The categorical variables were characterized as frequency and proportion. The associations between MVPA and incident CVD, CVD-caused mortality, and all-cause mortality were estimated with Cox proportional hazards regression, yielding hazard ratios (HRs) and 95% confidence intervals (CIs). Model 1 adjusted for age, sex, BMI, ethnic background, TDI, education, and employment; Model 2 further adjusted for smoking, alcohol use, and diet score; Model 3, building on Model 2, further adjusted for self-reported health status and metabolic syndrome. Inactive MVPA was set as the reference group. Analyses of the association between duration of LPA and incident CVD, CVD-cause mortality, and all-cause mortality used the same models as MVPA. We also used a non-linear test to determine whether there was a linear relationship between the duration of LPA and CVD or mortality risks. Meanwhile, we tested the influence of different durations of LPA on the risk of CVD and mortality in OA, with the first quartile of duration set as the reference.

Several sensitivity and subgroup analyses were conducted. First, as age, sex and BMI may influence the risks of CVD and mortality, we performed subgroup analyses according to age (⩾60 years and <60 years), sex, and BMI categories (<25, 25-30, >30 kg/m^2) (eTable 2-4). Multiplicative interactions and additive interactions were tested between age, sex or BMI terms and MVPA on incident CVD, CVD-cause mortality, and all-cause mortality in the multivariable Cox models. Second, to assess whether MVPA was associated with CVD, CVD-cause mortality, or all-cause mortality for the same amount of LPA, we included LPA in the model (eTable 5). Similarly, we included MVPA in the models to examine associations between LPA and CVD, CVD-cause mortality, and all-cause mortality (eTable 6).

All analyses were performed using R software (version 4·1·3), and all statistically significance tests were two-sided with an alpha level of 0·05.

Results

Population characteristics

A total of 10,210 participants (mean age 58·1, SD 7·1 years; 6,581 female (64·5%); 9,976 white (97·7%)) were followed during a median of 6·9 years after wearing the accelerometer (Figure 1). There were 1,538 incidents of CVD, and 358 deaths, including 90 from CVD documented (Table 1). Compared with active regular MVPA, weekend warriors of MVPA were older, more likely to be female, never smokers, employed, have higher BMI, lower educational attainment and lower TDI. In both groups, no discernible differences in ethnic background, diet score and self-reported health were observed. Active regular MVPA were younger and more likely to be male, college graduates, never or former smokers, had a higher rate of paid employment or self-employed, had a higher education level, lower TDI, and better self-reported health status compared with physically inactive participants.

Associations between MVPA and risks of CVD or mortality in participants with OA

In multivariable-adjusted analyses, weekend warrior of MVPA had a lower risk of incident CVD in OA participants (adjusted HR 0·73, 95% CI 0·64 to 0·82), and active regular MVPA pattern had a lower risk of incident CVD (adjusted HR 0·75, 95% CI 0·65 to 0·87) after adjustment for age, sex, BMI, ethnic background, TDI, education, employment (Table 2, Figure 2). Similarly, weekend warrior of MVPA was significantly associated with a lower risk of CVD-cause mortality (P for model 1&2 <·05) and all-cause mortality ($P_{\text{model 1}}$ =·02, $P_{\text{model 2}}$ =·03), while active regular MVPA showed significant

associations for these outcomes. All results remained similar after adjusting for smoking status, alcohol drinking status and diet score into the models. The associations between weekend warrior of MVPA for CVD-cause mortality, and all-cause mortality became of borderline significance after adding self-reported health status and metabolic syndrome in the models.

After additional adjustment for LPA, both the weekend warrior and active MVPA groups exhibited similar lower risks for incident CVD (eTable 5). However, only the weekend warrior MVPA group had a significantly lower risk for CVD-cause mortality and all-cause mortality, while these reductions were not significant in the active MVPA group. In stratified analyses by age, sex, and BMI, both weekend warrior of MVPA and active regular MVPA groups demonstrated similar lower risks of incident CVD across subgroups (eTable 2-4). Significant additive interactions were found between MVPA patterns and age/ BMI for incident CVD, and between age and MVPA patterns for all-cause mortality. Weekend warrior of MVPA showed lower risks of CVD-cause mortality and all-cause mortality only in individuals with obesity (BMI >30) or older age (aged ≥60) (eTable 4 and 6). The lower risk of CVD-cause mortality and all-cause mortality for weekend warriors was only found in males (eTable 3). The sensitivity analyses based on different OA sites (knee, hip, and hand) found that the significant associations between weekend warrior MVPA and reduced CVD risk were only observed in individuals with knee OA and hand OA. For hip OA, these associations were not significant (eTable 8).

Associations between LPA and CVD or mortality risks in participants with OA

In the non-linear test, LPA and CVD demonstrated a significant linear association ($P_{\text{non-linear}}$=0·46) (Figure 3). Therefore, we divided LPA into four groups according to its duration quantile. Higher levels of LPA resulted in a dramatic decline in CVD-cause mortality (adjusted HR 0·34, 95% CI 0·16 to 0·72) in participants with OA. We also found that higher duration of LPA was significantly associated with lower risk of all-cause mortality in participants with OA in a dose-response manner (moderate-low LPA: adjusted HR 0·73, 95% CI 0·55 to 0·96; moderate-high LPA: adjusted HR 0·66, 95% CI 0·49 to 0·88; high LPA: adjusted HR 0·59, 95% CI 0·43 to 0·80) and CVD-cause mortality (moderate-low LPA: adjusted HR 0·86, 95% CI 0·52 to 1·44; moderate-high LPA: adjusted HR 0·62, 95% CI 0·34 to 1·11; high LPA: adjusted HR 0·34, 95% CI 0·16 to 0·72). After additional adjustment for MVPA, significant linear associations were still observed between LPA and both CVD-cause mortality and all-cause mortality, but not for incident CVD (eTable 6). In our sensitivity analyses by different OA sites (knee, hip, and hand), none of the results for LPA were statistically significant (eTable 9). When LPA was analyzed as a continuous variable, the effect sizes were very low (eTable 7).

Discussion

This is the first study using accelerometer-measured physical activity data to assess the impact of different physical activity patterns on risks of CVD and mortality in individuals with OA. We found that compared with inactive regular MVPA participants, weekend warrior MVPA participants were exposed to similar or even greater reductions in the risks of incident CVD, all-cause mortality, and CVD-cause mortality, especially in people aged ⩾60 years or with obesity. A dose-response relationship was identified between duration of LPA and both CVD-cause mortality and all-cause mortality. These findings suggest that among individuals with OA, engaging in MVPA as a “weekend warrior”, active regular MVPA, or maintaining a higher amount of LPA are associated with lower risks of incident CVD, all-cause mortality, and CVD-cause mortality.

Exercise therapy is considered one of the core treatments for OA, with demonstrated safety and positive therapeutic effects[28]. The concept of the weekend warrior of MVPA has attracted attention in recent years, as lack of time has emerged as a major barrier to exercise in modern society. Several cohort studies supported that the weekend warrior of MVPA had the same effect on the risk of CVD as the active regular MVPA in the general population[10, 12, 13], the effect sizes of which were similar.[10] Our findings in individuals with OA mirror this trend. Moreover, we found significant associations between the weekend warrior of MVPA and reduced risks of CVD-caused mortality, and all-cause mortality, whereas active regular MVPA did not exhibit significant associations with these outcomes.

Conversely, a previous study in the general population demonstrated that active regular engagement in MVPA significantly reduced the risk of CVD-cause mortality and all-cause mortality, while weekend warrior of MVPA did not[12]. The difference may be attributed to several possible reasons. First, while prolonged sedentary behavior and lower levels of physical activity are concerns shared by both the general population and OA patients, individuals with OA face additional challenges that make them more vulnerable to the negative health effects of inactivity. Unlike the general population, OA patients often experience joint pain, stiffness, and reduced mobility, which further hinders their ability to engage in active regular physical activity throughout the week. These functional limitations mean that for many OA patients, achieving the recommended amount of physical activity consistently is particularly difficult. Second, OA is associated with increased levels of systemic inflammation, which are associated with increased cardiovascular risk and risk of mortality[29]. MVPA has been shown to help reduce levels of systemic inflammation, which may offer dual benefits for patients with OA[30]. Third, patients with OA may require a longer recovery time following exercise. Therefore, a concentrated exercise regimen on weekends gives them more days to recover and alleviate the symptoms of OA after fatigue. Finally, participating in focused weekend activities with others can also help improve social connection and mental health, both of which are very important for reducing mortality risk. We also found significant interactions between age, BMI and MVPA pattern for incident CVD, which suggested that OA patients aged ≥60 years or those with obesity could benefit more from a 'weekend warrior' pattern of MVPA than an activeregular pattern of MVPA. The possible reasons may due to both obesity and older age OA population are associated with higher risks of CVD. Additionally, these groups usually have lower levels of physical activity, making the "weekend warrior" pattern a significant improvement over their generally inactive lifestyles. Moreover, obesity and aging are connected to ongoing inflammation and metabolic problems, which can increase the risk of CVD and death. Physical activity, even in short bursts, can help reduce inflammation and improve overall health. Therefore, the "weekend warrior" approach may be especially beneficial for these high-risk groups, providing a practical way to lessen the negative health effects of obesity and aging OA people. Taken together, our findings suggest that the weekend warrior of MVPA may be a more beneficial exercise pattern for cardiovascular health and longevity than active regular MVPA for individuals with OA, particularly those 60 years of age or older, or those with obese.

LPA was considered a protective behavior on mortality and CVD risks in the general population. Accelerometer-measured LPA showed an inverse association with risks of CVD and all-cause mortality in Swedish adults[31]. LPA was shown to improve adult cardiometabolic health and reduce mortality risk[32]. The dose-response relationships of LPA and the risk of CVD, CVD-cause mortality, and all-cause mortality in our study were in line with the findings of the general population. Notably, another study emphasized that individuals with OA tend to primarily engage in LPA[33]. Our findings reinforce the importance of encouraging greater LPA among individuals with OA to reduce CVD risk and extend the

lifespan. The results for LPA for CVD, CVD-cause mortality and all-cause mortality were non-significant across different OA sites, possibly reflecting insufficient sample size and a relatively weak relationship between LPA, CVD, and mortality risk.

Limitations

Our study also has limitations. First, The UK Biobank samples are predominantly composed of individuals of European ancestry, which may limit the generalizability of the findings to populations with different ethnic backgrounds. Second, because physical activity was only measured for 1 week at baseline, we did not have information on how changes in physical activity contribute to the risk of CVD and mortality. Third, the awareness of wearing the accelerometer could lead participants to increase their activity levels, a phenomenon known as the Hawthorne effect[34]. This change in behavior could lead to potential misclassification, where individuals who are normally inactive might be mistakenly identified as active. Fourth, as we used hospital diagnoses, the prevalence of OA and CVD may be underestimated, particularly since OA patients often seek hospital care only when experiencing severe symptoms. Fifth, our results for the associations of MVPA with mortality had wide 95% CIs, suggesting insufficient statistical power and potentially inflated HRs. Finally, being a cohort study, our findings are limited to associations rather than causation. Future clinical trials are needed to confirm these findings.

Conclusions

This large cohort study shows that compared with inactive MVPA, individuals with OA who engage in a "weekend warrior" MVPA pattern have similar or even lower risks of CVD-cause mortality and all-cause mortality than those who follow active regular MVPA, especially for those aged over 60 or with obesity. Furthermore, this study suggests a potential dose-response relationship between amount of LPA and lower risks of CVD, CVD-cause mortality, and all-cause mortality for individuals with OA.

Contributors: TF and ZZ conceived the study. TF, JC, QX, YZ, CD, and ZZ contributed to the study design. JC, TF, MZ, and SC processed the data and conducted the main analysis, TF, QX, JC and ZZ wrote the original manuscript draft. TF, XF, SC, and HY undertook simulation and sensitivity analyses. All authors revised the manuscript for important intellectual content and approved its final version. TF is the guarantor and attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. We thank the UK Biobank participants and the UK Biobank team for generating an important research data resource.

Competing interests: Hunter DJ Provides consulting advice on scientific advisory boards for Pfizer, Lilly, TLCBio, and Novartis. QY works in a unit that receives core funding from the University of Bristol and UK Medical Research Council (MM_UU_00011/6). There is no competing interests of other authors.

Ethical approval: UK Biobank has received ethical approval from the UK national health service's National Research Ethics Service (16/NW/0274). The present analyses were conducted under UK Biobank application number 67654.

Funding: The present study was supported by the National Natural Science Foundation of China (82372428), and Clinical Research Startup Program of Southern Medical University (LC2019ZD015).

Data availability: The data on which this study is based (application number 67654) are available for bona fide researchers from the UKBB Resource (http://www.ukbiobank.ac.uk/about-biobank-uk/), on filing an application to the UK Biobank. Relevant additional data will be available from the authors on request.

Patient and public involvement: The analyses were based on existing data from the UK Biobank. No patients or participants were involved in the study design, recruitment, or conduct. No patients were asked to advise on the interpretation or writing up of results.

References

1 Martel-Pelletier J, Barr AJ, Cicuttini FM, et al. Osteoarthritis. *Nat Rev Dis Primers* 2016; **2**(1): 16072.

2 Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *Jama : The Journal of the American Medical Association* 2021; **325**(6): 568-78.

3 Hall AJ, Stubbs B, Mamas MA, Myint PK, Smith TO. Association between osteoarthritis and cardiovascular disease: Systematic review and meta-analysis. *Eur J Prev Cardiol* 2016; **23**(9): 938-46.

4 Nüesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Jüni P. All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *Bmj-Brit Med J* 2011; **342**: d1165.

5 Swain S, Coupland C, Sarmanova A, et al. Healthcare utilisation and mortality in people with osteoarthritis in the UK: findings from a national primary care database. *Brit J Gen Pract* 2023; **73**(733): e615-22.

6 Veronese N, Trevisan C, De Rui M, et al. Association of Osteoarthritis With Increased Risk of Cardiovascular Diseases in the Elderly: Findings From the Progetto Veneto Anziano Study Cohort. *Arthritis Rheumatol* 2016; **68**(5): 1136-44.

7 Saint-Maurice PF, Troiano RP, Matthews CE, Kraus WE. Moderate-to-Vigorous Physical Activity and All-Cause Mortality: Do Bouts Matter? *J Am Heart Assoc* 2018; **7**(6).

8 Liu Q, Liu FC, Huang KY, et al. Beneficial effects of moderate to vigorous physical activity on cardiovascular disease among Chinese adults. *J Geriatr Cardiol* 2020; **17**(2): 85-95.

9 WHO Guidelines on Physical Activity and Sedentary Behaviour. Geneva: World Health Organization; 2020.

10 Khurshid S, Al-Alusi MA, Churchill TW, Guseh JS, Ellinor PT. Accelerometer-Derived "Weekend Warrior" Physical Activity and Incident Cardiovascular Disease. *Jama-J Am Med Assoc* 2023; **330**(3): 247-52.

11 Dempsey PC, Rowlands AV, Strain T, et al. Physical activity volume, intensity, and incident cardiovascular disease. *Eur Heart J* 2022; **43**(46): 4789-800.

12 Dos SM, Ferrari G, Lee DH, et al. Association of the "Weekend Warrior" and Other Leisure-time Physical Activity Patterns With All-Cause and Cause-Specific Mortality: A Nationwide Cohort Study. *Jama Intern Med* 2022; **182**(8): 840-8.

13 O'Donovan G, Lee IM, Hamer M, Stamatakis E. Association of "Weekend Warrior" and Other Leisure Time Physical Activity Patterns With Risks for All-Cause, Cardiovascular Disease, and Cancer Mortality. *Jama Intern Med* 2017; **177**(3): 335-42.

14 Jordan JL, Holden MA, Mason EE, Foster NE. Interventions to improve adherence to exercise for chronic musculoskeletal pain in adults. *Cochrane Db Syst Rev* 2010; **2010**(1): CD005956.

15 Dobson F, Bennell KL, French SD, et al. Barriers and Facilitators to Exercise Participation in People with Hip and/or Knee Osteoarthritis: Synthesis of the Literature Using Behavior Change Theory. *Am J Phys Med Rehab* 2016; **95**(5): 372-89.

16 Fernandes GS, Valdes AM. Cardiovascular disease and osteoarthritis: common pathways and patient outcomes. *Eur J Clin Invest* 2015; **45**(4): 405-14.

17 Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Rheumatol* 2020; **72**(2): 220-33.

18 Matthews CE, Keadle SK, Troiano RP, et al. Accelerometer-measured dose-response for physical activity, sedentary time, and mortality in US adults. *Am J Clin Nutr* 2016; **104**(5): 1424-32.
19 LaCroix AZ, Bellettiere J, Rillamas-Sun E, et al. Association of Light Physical Activity Measured by Accelerometry and Incidence of Coronary Heart Disease and Cardiovascular Disease in Older Women. *Jama Netw Open* 2019; **2**(3): e190419.
20 Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *Plos Med* 2015; **12**(3): e1001779.
21 Doherty A, Jackson D, Hammerla N, et al. Large Scale Population Assessment of Physical Activity Using Wrist Worn Accelerometers: The UK Biobank Study. *Plos One* 2017; **12**(2): e0169649.
22 Walmsley R, Chan S, Smith-Byrne K, et al. Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease. *Brit J Sport Med* 2021; **56**(18): 1008-17.
23 Zhang X, Liu YM, Lei F, et al. Association between questionnaire-based and accelerometer-based physical activity and the incidence of chronic kidney disease using data from UK Biobank: a prospective cohort study. *Eclinicalmedicine* 2023; **66**: 102323.
24 Ramakrishnan R, Doherty A, Smith-Byrne K, et al. Accelerometer measured physical activity and the incidence of cardiovascular disease: Evidence from the UK Biobank cohort study. *Plos Med* 2021; **18**(1): e1003487.
25 Sanchez-Lastra MA, Ding D, Del PCB, et al. Joint associations of device-measured physical activity and abdominal obesity with incident cardiovascular disease: a prospective cohort study. *Brit J Sport Med* 2023.
26 Inoue K, Tsugawa Y, Mayeda ER, Ritz B. Association of Daily Step Patterns With Mortality in US Adults. *Jama Netw Open* 2023; **6**(3): e235174.
27 Grundy SM, Brewer HJ, Cleeman JI, Smith SJ, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation* 2004; **109**(3): 433-8.
28 Bowden JL, Hunter DJ, Deveza LA, et al. Core and adjunctive interventions for osteoarthritis: efficacy and models for implementation. *Nat Rev Rheumatol* 2020; **16**(8): 434-47.
29 Motta F, Barone E, Sica A, Selmi C. Inflammaging and Osteoarthritis. *Clin Rev Allerg Immu* 2023; **64**(2): 222-38.
30 Wang Y, Han Q, Han X, et al. Objectively-measured movement behaviors, systemic low-grade inflammation, and plasma neurofilament light chain in older adults: a population-based study. *Immun Ageing* 2023; **20**(1): 36.
31 Ekblom-Bak E, Halldin M, Vikström M, et al. Physical activity attenuates cardiovascular risk and mortality in men and women with and without the metabolic syndrome - a 20-year follow-up of a population-based cohort of 60-year-olds. *Eur J Prev Cardiol* 2021; **28**(12): 1376-85.
32 Chastin S, De Craemer M, De Cocker K, et al. How does light-intensity physical activity associate with adult cardiometabolic health and mortality? Systematic review with meta-analysis of experimental and observational studies. *Brit J Sport Med* 2019; **53**(6): 370-6.
33 Liu SH, Driban JB, Eaton CB, McAlindon TE, Harrold LR, Lapane KL. Objectively Measured Physical Activity and Symptoms Change in Knee Osteoarthritis. *Am J Med* 2016; **129**(5): 497-505.
34 Sedgwick P, Greenwood N. Understanding the Hawthorne effect. *Bmj-Brit Med J* 2015; **351**.

Figure 1. Flow chart

Figure 2. Lower cardiovascular diseases and mortality risks by moderate-to-vigorous physical activity patterns among individuals with osteoarthritis
Abbreviations: CVD, cardiovascular diseases

Figure 3. Cox proportional hazards models of the association between light physical activity and cardiovascular diseases, cardiovascular-disease-cause mortality and all-cause mortality in patients with osteoarthritis
Restricted cubic spline models fitted for Cox proportional hazards models with three knots were used. Adjustment for age, sex, economic status, ethnic background and education; Abbreviations: CVD, cardiovascular diseases

Table 1. Baseline Characteristics of Participants

Baseline Characteristics	Inactive (N=3,965)	Weekend warrior (N=3,915)	Active regular (N=2,330)	Overall (N=10,210)
Age, mean (SD), year	58.74 (7.06)	58.25 (7.05)	57.40 (7.34)	58.25 (7.14)
Sex (Female)	3,036 (76.6%)	2,226 (56.9%)	1,319 (56.5%)	6,581 (64.5%)
Ethnic background (White)	3,874 (97.8%)	3,843 (98.2%)	2,257 (96.9%)	9,976 (97.7%)
BMI, mean (SD)	28.50 (5.10)	26.56 (3.91)	26.36 (4.08)	27.27 (4.55)
Townsend Deprivation Index, mean (SD)	-1.76 (2.78)	-2.03 (2.65)	-1.32 (3.06)	-1.76 (2.81)
Education (College/university degree or above)	398 (10.0%)	521 (13.3%)	334 (14.3%)	1253 (12.3%)
Employment (In paid employment or self-employed)	1,986 (50.1%)	2,129 (54.4%)	1,405 (60.3%)	5,520 (54.1%)
Diet score sum, mean (SD)	3.27 (1.28)	3.33 (1.34)	3.33 (1.35)	3.31 (1.32)
Smoking				
Never	2,105 (53.1%)	2,100 (53.6%)	1,262 (54.2%)	5,467 (53.5%)
Previous	1,512 (38.1%)	1,563 (39.9%)	919 (39.4%)	3,994 (39.1%)
Current	348 (8.8%)	252 (6.4%)	149 (6.4%)	749 (7.3%)
Alcohol drinker status				
Never	137 (3.5%)	88 (2.2%)	62 (2.7%)	287 (2.8%)
Previous	132 (3.3%)	88 (2.2%)	64 (2.7%)	284 (2.8%)
Current	3,696 (93.2%)	3,739 (95.5%)	2,204 (94.6%)	9,639 (94.4%)
Incident CVD	734 (18.5%)	501 (12.8%)	303 (13.0%)	1,538 (15.1%)
All-Cause mortality	163 (4.1%)	120 (3.1%)	75 (3.2%)	358 (3.5%)
CVD mortality	45 (1.1%)	24 (0.6%)	21 (0.9%)	90 (0.9%)

Metabolically healthy score ATP3, mean (SD)	3.13 (1.22)	3.52 (1.10)	3.55 (1.12)	3.38 (1.17)
Self-report health status				
Excellent	486 (12.3%)	794 (20.3%)	494 (21.2%)	1,774 (17.4%)
Good	2,330 (58.8%)	2,519 (64.3%)	1,448 (62.1%)	6,297 (61.7%)
Fair	910 (23.0%)	536 (13.7%)	349 (15.0%)	1,795 (17.6%)
Poor	239 (6.0%)	66 (1.7%)	39 (1.7%)	344 (3.4%)
All Osotearthritis	3,965	3,915	2,330	10,210
Knee Osotearthritis	1,399	1,417	855	3,671
Hip Osotearthritis	1,009	1,000	586	2,595
Hand Osotearthritis	302	238	134	674

Abbreviations: SD, Standard Deviation; BMI: body mass index; CVD: cardiovascular diseases; ATP3, Adult Treatment Panel-III.

Table 2. Associations Between Moderate to Vigorous Physical Activity (MVPA) Pattern and Incident Cardiovascular Diseases and Mortality in people with osteoarthritis.

	Model 1			**Model 2**			**Model 3**		
Outcome and Exposure	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Incident CVD									
Inactive	1			1			1		
Weekend warrior	0.73	0.64 – 0.82	**<0.001**	0.73	0.65 – 0.82	**<0.001**	0.79	0.70 – 0.89	**<0.001**
Active regular	0.75	0.65 – 0.87	**<0.001**	0.76	0.66 – 0.87	**<0.001**	0.81	0.70 – 0.93	**0.003**
CVD-cause mortality									

Inactive	1			1			1		
Weekend warrior	0.55	0.33 – 0.92	**0.02**	0.56	0.34 – 0.95	**0.03**	0.63	0.37 – 1.06	0.08
Active regular	0.88	0.51 – 1.52	0.65	0.92	0.53 – 1.58	0.75	0.98	0.57 – 1.68	0.93
All-cause mortality									
Inactive	1			1			1		
Weekend warrior	0.75	0.59 – 0.96	**0.02**	0.76	0.60 – 0.98	**0.03**	0.79	0.62 – 1.02	0.07
Active regular	0.84	0.63 – 1.11	0.23	0.86	0.64 – 1.14	0.29	0.88	0.66 – 1.17	0.38

Abbreviations: CVD: cardiovascular diseases; HR, hazard ratio; 95% CI, 95% confidence interval.

Weekend warrior of MVPA was defined as ⩾150 min of MVPA/week with ⩾50% over 1-2 days

Model 1: adjustment for age, sex, BMI, ethnic background, Townsend deprivation index, education, employment

Model 2: Model1 + smoking status, alcohol drinking status, and diet score

Model 3: Model2 + self-reported health status and metabolic syndrome

Table 3. Associations Between Light Physical Activity and Incident Cardiovascular Diseases and Mortality.

	Model 1			**Model 2**			**Model 3**		
Outcome and Exposure	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Incident CVD									
Low LPA	1			1			1		
Moderate-Low LPA	0.89	0.77 – 1.02	0.09	0.89	0.78 – 1.02	0.11	0.92	0.80 – 1.06	0.24
Moderate-High LPA	0.91	0.79 – 1.04	**0.017**	0.91	0.79 – 1.05	0.19	0.94	0.82 – 1.09	**0.04**
High LPA	0.85	0.74 – 0.98	**0.003**	0.85	0.74 – 0.98	**0.003**	0.89	0.77 – 1.02	0.10

P for trend			**0.04**			**0.04**			0.13
CVD-cause mortality									
Low LPA	1			1			1		
Moderate-Low LPA	0.86	0.52 – 1.44	0.57	0.87	0.53 – 1.45	0.60	0.92	0.55 – 1.54	0.76
Moderate-High LPA	0.62	0.34 – 1.11	0.11	0.62	0.35 – 1.12	0.11	0.66	0.37 – 1.19	0.17
High LPA	0.34	0.16 – 0.72	**0.004**	0.34	0.16 – 0.72	**0.005**	0.36	0.17 – 0.76	**0.007**
P for trend			**0.002**			**0.003**			**0.005**
All-cause mortality									
Low LPA	1			1			1		
Moderate-Low LPA	0.73	0.55 – 0.96	**0.02**	0.73	0.56 – 0.97	**0.03**	1.07	0.81 – 1.41	0.65
Moderate-High LPA	0.66	0.49 – 0.88	**0.005**	0.66	0.49 – 0.89	**<0.01**	0.82	0.61 – 1.12	0.21
High LPA	0.59	0.43 – 0.80	**<0.001**	0.59	0.44 – 0.80	**<0.01**	0.73	0.52 – 1.01	0.06
P for trend			**<0.001**			**<0.01**			**<0.001**

Abbreviations: CVD: cardiovascular diseases; HR, hazard ratio; 95% CI, 95% confidence interval, LPA: light physical activity

Model 1: adjustment for age, sex, BMI, ethnic background, Townsend deprivation index, education, employment

Model 2: Model1 + smoking status, alcohol drinking status, and diet score

Model 3: Model2 + self-reported health status and metabolic syndrome