



Original article

Joint associations of handgrip strength and physical activity with incident cardiovascular disease and overall mortality in the UK Biobank



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SUMMARY

Background & aims: Questions remain whether higher handgrip strength confers additional health advantages beyond adherence to current physical activity guidelines. We aimed to evaluate prospective associations of joint objectively measured handgrip strength and physical activity with incident cardiovascular disease (CVD) and all-cause mortality.

Methods: We analysed the UK Biobank study in a cohort of participants who wore accelerometers for one week, with follow-up based on hospital records until 2022. Patterns of physical activity were compared: participants who met current moderate-vigorous physical activity guidelines (150 min per week) and those who did not. Handgrip strength was classified into sex- and age-specific tertiles. CVD events were identified as primary or secondary by examination of inpatient records and data extracted from the death registry. CVD-related deaths were also identified from the death registry. We examined prospective associations of moderate-vigorous physical activity with incident CVD and all-cause mortality by level of handgrip using Cox regressions, adjusted for confounding factors.

Results: A total of 76 074 persons were included (mean 55.2 years). Meeting physical activity guidelines is necessary to reduce all-cause mortality in those at the lower and middle thirds of handgrip strength. However, meeting physical activity guidelines did not confer additional reduction of all-cause mortality of those with high handgrip strength. Those with the lowest handgrip strength showed the greatest benefit from meeting physical activity guidelines for reducing all-cause mortality (HR 0.74; 95 % CI 0.65–0.85).

Conclusion: Our results indicate that, while following physical activity guidelines does not reduce mortality in individuals with high handgrip strength, it is essential for preventing cardiovascular disease across all levels of handgrip strength. This underscores the importance of these guidelines for cardiovascular health.

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1. Introduction

Cardiovascular diseases (CVD) constitute the leading cause of global mortality and morbidity, accounting for over 17 million

deaths annually [1]. The etiology of these diseases is multifactorial [2], with physical inactivity identified as a primary modifiable factor [3]. Indeed, physical activity is fundamental for overall health and prevent CVD and mortality in the population [4–6]. Prominent public health guidelines for adults, such as those endorsed by the World Health Organization (WHO) and the American Heart Association, recommend engaging in at least 150 min of moderate-to-vigorous aerobic physical activity (MVPA) on a weekly basis [4,7].

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Beyond aerobic physical activity, muscle strength training for two or more days per week is recommended in public health guidelines to attain additional health benefits [4,8]. In this regard, handgrip strength is a good and reliable objective indicator of overall muscle strength [9,10]. Given its simple and cost-effective applicability and predictive capacity, this variable has emerged in the past decade as a reliable health biomarker in adults and older adults [9,11]. For instance, various studies have demonstrated an inverse association of handgrip strength with the incidence of CVD and all-cause mortality [12]. However, while the inverse association between handgrip strength and the incidence of CVD and all-cause mortality is clearer, questions remain whether higher handgrip strength confers additional health advantages beyond adherence to physical activity guidelines. According to recent global estimates, approximately 27.5 % of adults do not meet the physical activity recommendations [13]. While physical activity should still be promoted on a global scale, there is also a critical need to document alternatives to the recommended duration of MVPA that not only guarantee health benefits but are also achievable by a broader segment of the population. In this sense, investigating the interaction between two important health markers, such as handgrip strength and the adherence to physical activity guidelines, may offer new preventive strategies.

Hence, the aim of our study was to evaluate prospective associations of joint objectively measured handgrip and MVPA with incident cardiovascular disease and all-cause mortality in the UK Biobank sample.

2. Materials and methods

2.1. Participants and design

The UK Biobank study is a large cohort of around 500 000 participants aged 40–69 years enrolled between 2006 and 2010 [14]. During the aforementioned timeframe, the participants provided informed consent and performed physical examination by trained staff, which also included the baseline handgrip measurement, and answered touchscreen questionnaires at 22 assessment centers across the UK. The baseline assessment (2006–2010) was used when a first follow-up assessment (2009–2013) was not available. Priority was given to first follow-up data when available given closer temporal proximity before accelerometry. Ethical approval was obtained from the UK's National Health Service, National Research Ethics Service (Ethics Committee reference number: 11/NW/0382). The study is reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

2.2. Accelerometer-measured physical activity

Data were obtained from a cohort comprising 103 666 participants, constituting the subsample equipped with accelerometers. These individuals utilized Axivity AX3 wrist-based triaxial accelerometers for one week to evaluate MVPA. After calibrating the acceleration signals, the accelerometers captured continuous acceleration data at a sampling rate of 100 Hz, featuring a dynamic range of ± 8 g and segmented into 5-s epochs. Participants lacking sufficient wear time with the accelerometer or incomplete covariate information were excluded from the study (Fig. 1). Adequate wear time was defined as wearing the device for more than 16 h daily. Furthermore, to ensure measurement robustness and representativeness, only participants with a minimum of three valid measurement days, including at least one weekend day, were included in subsequent analyses [15]. MVPA was categorized into

those participants who met current MVPA guidelines (i.e., 150 weekly minutes of MVPA per week) and those who did not [4].

2.3. Handgrip strength

Handgrip strength was evaluated utilizing a Jamar J00105 hydraulic hand dynamometer, measuring grip force isometrically. The

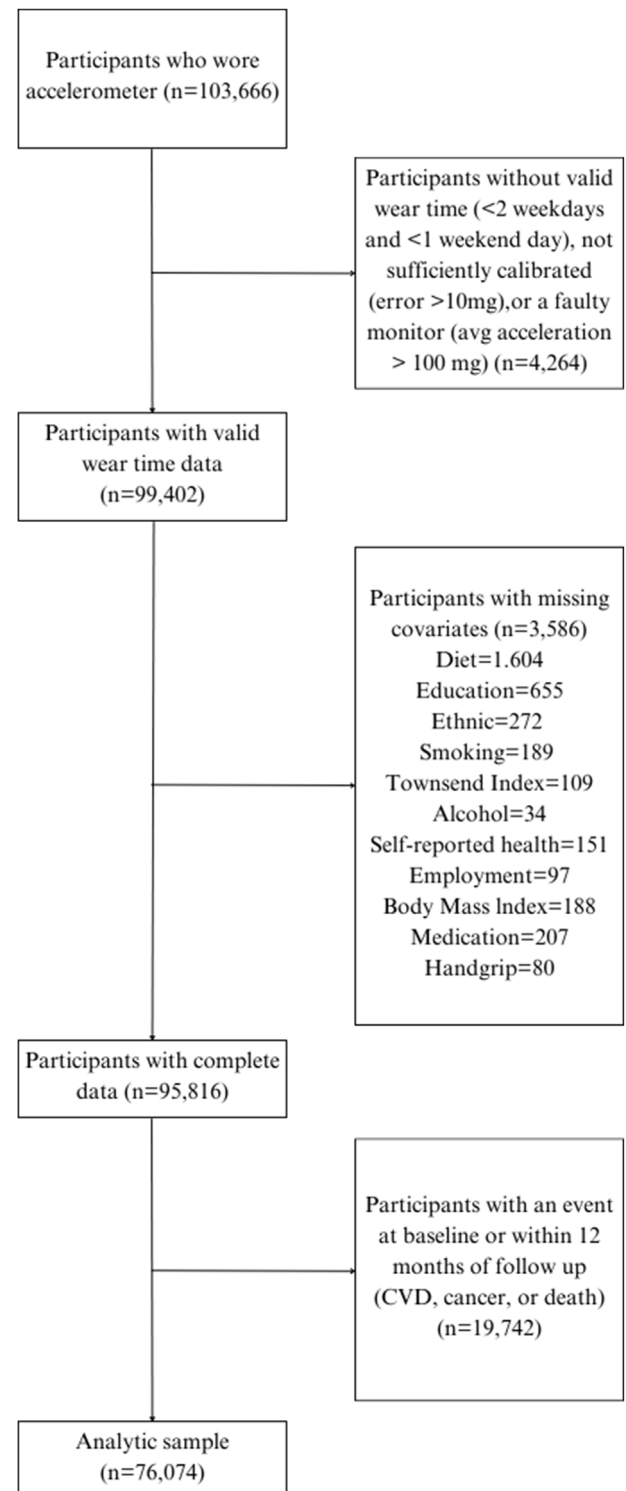


Fig. 1. Flowchart of the study sample.

dynamometer, adjustable for hand size in five half-inch increments, featured a dual-scale readout indicating isometric grip force from 0 to 90 kg. A ‘peak-hold’ needle remained in place once the grip was released. Calibration of the dynamometer occurred before each measurement day. Participants were seated upright in a chair, placing their forearms on armrests. The arm holding the dynamometer had the elbow against the side, bent at a 90° angle, and the forearm pointing forward with the thumb uppermost. The wrist was maintained straight, either pointing forwards or slightly bent outwards. Participants were instructed to exert maximum force on the dynamometer handle for approximately 3 s, with encouragement provided. Measurements were recorded for both the right and left hands. Previous analysis of UK Biobank data suggested comparable predictive ability of handgrip strength for mortality and health-related outcomes in absolute or relative terms, recommending the use of absolute units (kilograms) for clinical utility [16]. As such, the maximum value of either hand in kilograms was used for subsequent analysis. Given the strong differences concerning sex and age, handgrip strength was categorized into sex-age-specific thirds (i.e., accounting for sex and the median of the age [56 years] to create specific categories concerning handgrip).

2.4. Outcome measures

CVD events were identified as either primary or secondary diagnoses through the examination of inpatient hospital records and data extracted from the death registry, all retrieved from the UK Biobank. In this study, CVD encompassed coronary heart disease, stroke, heart failure, and atrial fibrillation. Coronary heart disease was defined in accordance with the International Classification of Diseases (ICD) 9th edition codes 410 to 411 and 10th edition codes I20.0, I21, and I22. Additionally, surgical codes related to percutaneous transluminal coronary angioplasty and coronary artery bypass graft (codes K40–K46, K49–K50, and K75) were included. Stroke was classified as either ischemic (ICD-9: 433–434; ICD-10: I63) or haemorrhagic (ICD-9: 430–432; ICD-10: I60–I62). Heart failure was defined using ICD-9 code 428 and ICD-10 code I50, while atrial fibrillation was denoted by ICD-9 code 427.3 and ICD-10 code I48, along with surgical codes K50.1 and K62.2–K62.4.

The hospital registry-based follow-up was completed on October 31, 2022, in England; August 31, 2022, in Scotland; and May 31, 2022, in Wales. CVD-related deaths were identified using the same ICD-10 codes for different endpoints, as outlined in the death registry. The death registry included all fatalities occurring before November 30, 2022, in England, Scotland, and Wales. Participants were censored at these specified dates, upon experiencing the event of interest, or at the time of their demise, whichever transpired first.

2.5. Statistical analysis

We examined the prospective associations of MVPA with incident CVD and all-cause mortality by level of handgrip through Cox regressions. Based on prior literature, the crude model was adjusted for age (continuous) and sex (categorical), whereas the fully adjusted model was additionally adjusted for racial and ethnic background (categorical), tobacco use (categorical), Townsend Deprivation Index (continuous), alcohol consumption (categorical), educational attainment (continuous), employment status (categorical), self-reported health (categorical), diet quality (categorical), family history of CVD and cancer (categorical), body mass index (continuous), medication use (categorical), and handgrip (continuous). Detailed information on these covariates has been detailed in the Supplement (eTable 1) and published elsewhere [17]. A Wald test showed no interaction between MVPA and each of

the aforementioned covariates by level of handgrip ($p > 0.10$). The proportional hazards assumption tested through Schoenfeld residuals showed no evidence of violation ($p > 0.10$). To avoid reverse causation bias, participants experiencing death, CVD or cancer at baseline or within the first twelve months of the study follow-up were removed from the analytical sample. We used complete case analysis. We also conducted additional analyses on the individual association between MVPA and handgrip strength with CVD and all-cause mortality. Estimations are shown with 95 % CIs if not otherwise stated. Analyses were conducted from October to November 2023 using Stata version 16.1 (StataCorp).

3. Results

We analyzed a cohort of 76 074 individuals (mean [SD] age, 55.2 [7.8] years; 57 % women) who utilized accelerometers for a duration of one week, spanning from any timepoint between June 1, 2013, and December 23, 2015. The median follow-up time was 8.0 years (interquartile range [IQR] 7.5–8.5). During the follow-up period, there were 5239 (6.9 %) cases of incident CVD and 2208 (2.9%) deaths due to all-causes. Table 1 provides information on the characteristics of the study sample categorized by levels of handgrip strength. Figure 1 shows flowchart of the study sample. Figure 2 shows the prospective association between meeting moderate to vigorous physical activity guidelines and all-cause mortality by handgrip level while Figure 3 shows the prospective association between meeting moderate to vigorous physical activity guidelines and incident cardiovascular disease by handgrip level. Meeting physical activity guidelines reduced all-cause mortality among individuals with lower (HR 0.74; 95 % CI 0.65–0.85), to middle (HR 0.78; 95 % CI 0.66–0.92) third levels of handgrip strength. However, meeting physical activity guidelines did not confer additional reduction (HR 0.83; 95 % CI 0.66–1.06) of all-cause mortality among individuals with high handgrip strength. Those with the lowest handgrip strength exhibited the most pronounced benefits from adhering to MVPA guidelines in relation to all-cause mortality (HR 0.74; 95 % CI 0.65–0.85). Conversely, higher levels of handgrip strength gradually diminished these benefits. Additional analyses showed significant inverse associations between meeting MVPA guidelines with CVD and all-cause mortality solely (eTable 2, eTable 3, eTable 4, eTable 5).

For incident CVD, meeting physical activity guidelines conferred protective benefits independently of the handgrip strength level.

4. Discussion

The primary findings of our study indicate that adherence to physical activity guidelines does not confer additional protective benefits for the risk of overall mortality among individuals with high handgrip strength. Notably, individuals with the lowest handgrip strength exhibit the most significant advantages in terms of reducing all-cause mortality through compliance with MVPA guidelines. Conversely, as handgrip strength levels increase, the magnitude of this benefit diminishes progressively. Therefore, handgrip strength could provide valuable information for identifying individuals who benefit most from adhering to physical activity recommendations, enabling targeted promotion efforts towards them to reduce all-cause mortality. By contrast, adhering to physical activity guidelines is imperative for CVD prevention regardless of the level of muscle strength.

Two cohort studies conducted in Europe support the findings of the present research regarding the incidence of mortality from any cause [18,19]. The study by Celis-Morales [18], which included 498 135 participants from the UK-Biobank, revealed an inverse association between physical activity and mortality from any cause

Table 1
Characteristics of study sample by levels of handgrip.

Baseline Characteristic	no. (%)		
	Lower third of handgrip (n = 26 494)	Middle third of handgrip (n = 26 235)	Upper third of handgrip (n = 23 345)
Age, mean (SD), y	57.7 (7.4)	55.4 (7.7)	52.3 (7.5)
Sex			
Female	15 374 (58.0)	14 473 (55.2)	13 816 (59.2)
Male	11 120 (42.0)	11 762 (44.8)	9529 (40.8)
Ethnic background ^a			
Asian	532 (2.0)	257 (1.0)	146 (0.6)
Black	67 (0.3)	78 (0.3)	103 (0.4)
Other	416 (1.6)	424 (1.6)	470 (2.0)
White	25 479 (96.2)	25 476 (97.1)	22 626 (96.9)
Tobacco use			
Never	15 567 (58.8)	15 214 (58.0)	13 752 (58.9)
Former	9327 (35.2)	9241 (35.2)	7856 (33.7)
Current	1600 (6.0)	1780 (6.8)	1737 (7.4)
Townsend deprivation index ^b	−1.6 (2.9)	−1.7 (2.8)	−1.8 (2.8)
Alcohol consumption			
Never	951 (4.0)	693 (2.6)	557 (2.4)
Former	872 (3.3)	645 (2.5)	556 (2.4)
Current	24 671 (93.1)	24 897 (94.9)	22 232 (95.2)
Educational attainment, mean (SD),y	14.2 (5.4)	14.6 (5.3)	15.0 (5.2)
Employed	14 087 (53.2)	16 987 (64.8)	17 654 (75.6)
Self-reported health			
Excellent	4972 (18.8)	6206 (23.7)	6226 (26.7)
Good	16 120 (60.8)	16 001 (61.0)	13 817 (59.2)
Fair	4545 (17.2)	3579 (13.6)	2964 (12.7)
Poor	857 (3.2)	449 (1.7)	338 (1.5)
Diet quality			
Good	6083 (23.0)	6041 (23.0)	5268 (22.6)
Intermediate	14 190 (53.6)	14 019 (53.4)	12 611 (22.6)
Poor	6221 (23.5)	6175 (23.5)	5466 (23.4)
Family history of cardiovascular disease	18 972 (71.6)	18 668 (71.2)	16 362 (70.1)
Family history of cancer	8120 (30.7)	7856 (29.9)	6945 (29.8)
Body mass index, mean (SD), kg/m ²	26.6 (4.6)	26.5 (4.4)	26.7 (4.5)
Medication use			
Blood pressure	4774 (18.0)	3745 (14.3)	2541 (10.9)
Cholesterol	4059 (15.3)	3017 (11.5)	1895 (8.1)
Insulin	225 (0.9)	147 (0.6)	89 (0.4)
Handgrip, mean (SD), kg	24.8 (8.0)	33.5 (8.5)	40.8 (10.5)
Meeting MVPA guidelines ^c	17 074 (64.4)	18 087 (68.9)	16 332 (70.0)
MVPA (min/week), mean (SD)	276.6 (238.2)	299.5 (245.2)	306.9 (248.9)

SD = standard deviation.

^a Represents self-reported “ethnic background.” Race classification of “Other” defined as self-report of a race other than Asian, Black, or White.^b The Townsend Deprivation Index is a way to measure material deprivation standardized by geographic area. Greater values indicate more deprivation. The sample range is −6.3 to 10.6, with values around −2 and −1 indicating somewhat less deprivation compared to average based on geographic location.^c Moderate to Vigorous Physical Activity physical activity current guidelines (150 min per week or more).

across all levels of handgrip strength, with a stronger effect observed in individuals with low strength. On the other hand, Karlsen et al. [19] conducted a 15-year study of 2529 Norwegian women, observing that those with low handgrip strength had a higher risk of mortality from any cause, regardless of their adherence to physical activity recommendations. However, the latter study did not incorporate the incidence of cardiovascular disease, unlike the Celis-Morales study, whose results differ from ours in that the significant increase in risk associated with decreased physical activity is evident only in individuals with lower handgrip strength [18]. Moreover, it is important to note that both studies substantially differ from the present research in two relevant aspects. First, in the previous studies, physical activity was self-reported through questionnaires, which are susceptible to bias and measurement error [20–22], and may not be suitable for capturing all physical activity throughout the day [23]. In contrast, our study employs accelerometers, which validly capture all components of physical activity, including frequency, intensity, and duration [23]. Second, the objectives of the aforementioned studies differ from ours, as they do not assess the prospective associations between objectively measured handgrip strength and physical activity with mortality from all causes and the incidence of CVD.

Physical inactivity is closely associated with sarcopenia, characterized by the progressive loss of muscle mass and function [24]. Handgrip strength is a key marker for sarcopenia, and sarcopenia is intricately linked to major cardiovascular diseases such as hypertension, heart failure, atherosclerosis, and coronary heart disease, all of which have been correlated with a decline in muscle function [25]. In fact, a previous systematic review with meta-analysis [11] identified robust associations of lower levels of handgrip strength with higher risk for all-cause and cardiovascular mortality risk, and weaker associations for higher risk of cancer mortality. Thus, individuals with high grip strength might not gain further benefits from following the WHO's physical activity recommendations, as they likely need more intense or higher levels of physical activity to achieve additional health benefits. However, regarding the necessity of adhering to MVPA guidelines regardless of the level of handgrip strength to prevent risk of CVD, this may be explained by different factors. First, we need to consider that individuals failing to meet aerobic physical activity guidelines also show a lower likelihood of participating in resistance training compared to those who engage in aerobic activities [26]. In addition, regarding those who adhere to MVPA guidelines, different physiological adaptations can be expected depending on the case they practice

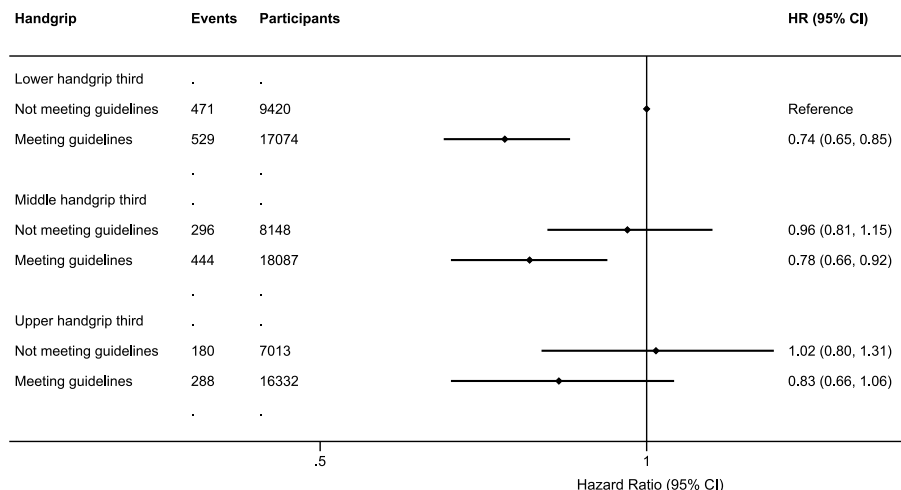


Fig. 2. Prospective association between meeting moderate to vigorous physical activity guidelines and all-cause mortality by handgrip level. Reference: Lower handgrip third and <150 weekly minutes of moderate to vigorous physical activity (not meeting MVPA guidelines). Model adjusted for age, sex, racial and ethnic background, tobacco use, Townsend Deprivation Index, alcohol consumption, educational attainment, employment status, self-reported health, diet quality, family history of cardiovascular disease and cancer, body mass index, medication use, and handgrip.

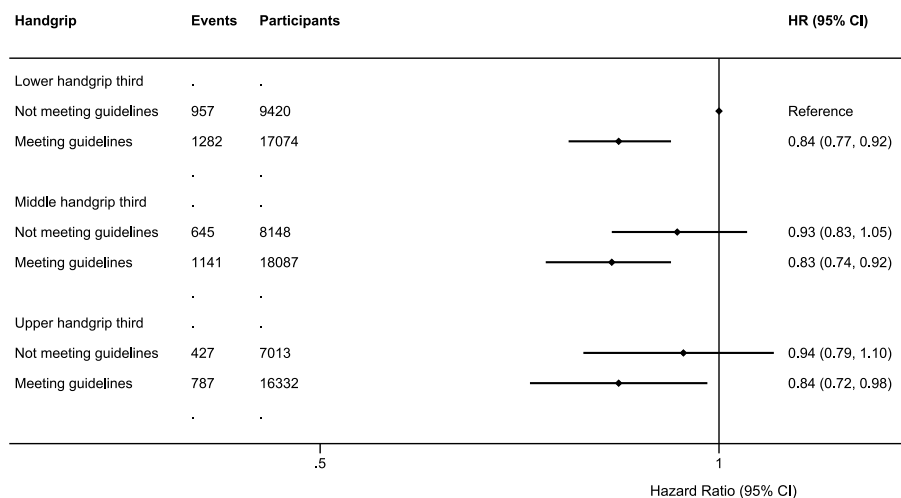


Fig. 3. Prospective association between meeting moderate to vigorous physical activity guidelines and incident cardiovascular disease by handgrip level. Reference: Lower handgrip third and <150 weekly minutes of moderate to vigorous physical activity (not meeting MVPA guidelines). Model adjusted for age, sex, racial and ethnic background, tobacco use, Townsend Deprivation Index, alcohol consumption, educational attainment, employment status, self-reported health, diet quality, family history of cardiovascular disease and cancer, body mass index, medication use, and handgrip.

resistance training. For instance, while resistance training, aerobic training, and combined training exhibit comparable benefits in enhancing blood pressure and lipid profiles, aerobic training and, particularly, combined training appear to be more effective in enhancing other CVD risk factors such as glycemic control and reducing weight loss and fat mass [27]. Nevertheless, it is important to consider that some participants in our study could have shown high handgrip strength without engaging in resistance training, since factors such as body weight and height [28] or the type of job [29] may influence this outcome.

The significance of our findings lies in their potential practical application. A previous study [13], which included 1.9 million adults aged 18 and older from 168 countries, representing 96 % of the world’s population, revealed that 27.5 % of adults did not engage in sufficient physical activity. According to that study, in the year 2016, the prevalence of physical inactivity in the United Kingdom

was over 30 % in men and over 40 % in women, and in Europe, it exceeded 20 % in men and 30 % in women. Therefore, it is imperative to explore more efficient alternatives to the recommended time of MVPA that still ensure health benefits, something that would apply to a larger segment of the population. In line with the results of our study and since handgrip is a marker of general muscular strength [9,10], it is suggested that a strategy to address the issue could be to increase the level of muscular strength in individuals with low performance in this test. In this sense, high-intensity resistance exercise with ≥80 % of one-repetition maximum, or ≤7 maximum repetitions has proved to be the most effective and efficient way of achieving this goal [30]. This approach could presumably provide significant benefits avoiding the strict adherence to the recommended 150 weekly minutes of MVPA. Interestingly, a recent meta-analysis reported that the maximum risk reduction for all-cause mortality, CVD, and total

cancer was achieved at only 30–60 min per week of muscle-strengthening activities [31].

4.1. Limitations

This study should be interpreted in the light of several limitations. First, although a wide set of confounders were used to adjust our models, there is a possibility for both residual and time-varying confounding concerning specific neurological disorders such as Alzheimer not considered in the analyses. Second, individuals may have modified their behavior during the period wearing accelerometers. Third, since the UK Biobank is not a representative sample of the UK adult population, generalizations over other populations should be cautiously made. Fourth, most of the information on covariates were collected several years prior to accelerometry, which may increase the risk of misclassification bias and time-varying confounding. For example, the handgrip strength may vary if this was measured in a quite distant timeframe concerning the accelerometer measurement. Lastly, MVPA measured through accelerometry does not account for stationary exercise such as yoga, resistance training or similar, which should be considered when interpreting the findings of the present study.

5. Conclusion

Our results suggest a nuanced relationship between handgrip strength and physical activity in relation to different types of health outcomes. Meeting physical activity guidelines do not confer additional protection from all-cause mortality for individuals with high handgrip strength. For incident CVD, the necessity of meeting physical activity guidelines holds true across all handgrip strength levels, emphasizing the broad applicability of such guidelines in cardiovascular health promotion.

Statement of authorship

APL, JC and RLB contributed to the study conception and design. Material preparation and data collection were performed by RLB. Data analysis was performed by RLB. The first draft of the manuscript was written by APL, and all authors commented on previous versions of the manuscript. All the authors have read and approved the final manuscript.

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Conflict of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnu.2024.10.022>.

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