Original Article

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Intensity of Physical Activity and Cardiovascular Events in Adults: A Systematic Review and Meta-Analysis

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Abstract:

Objective: To determine whether the cardiovascular protective effects of physical activity (PA) differ between moderate and vigorous intensities in adults without pre-existing cardiovascular disease (CVD).

Material and Methods: A systematic search was performed in PubMed, Scopus, and Web of Science for studies published between 1990 and 2024. Eligible studies were prospective cohorts that examined the association between PA intensity—expressed in metabolic equivalent tasks (METs)—and incident CVD outcomes. PA was categorized as moderate (3–5.9 METs) or vigorous (≥6 METs). Studies included adult populations without prior CVD. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using a random-effects model. Heterogeneity was assessed using the I^2 statistic, and sensitivity analyses were conducted to evaluate result robustness.

Results: A total of 1,057,895 participants were included, with a mean follow-up of 10.4 years. Moderate-intensity PA was associated with a pooled HR of 0.84 (95% CI: 0.73–0.98), while vigorous-intensity PA had a pooled HR of 0.84 (95% CI: 0.78–0.91), suggesting similar cardiovascular benefits. Moderate heterogeneity was present (I^2=66.4%), potentially

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due to varying definitions of intensity and adjustment factors across studies. Sensitivity analyses supported the stability of results, and publication bias was minimal.

Conclusion: Both moderate and vigorous physical activity are associated with comparable reductions in CVD risk. These findings reinforce the current public health guidelines recommending either 150–300 minutes of moderate or 75–150 minutes of vigorous PA per week for cardiovascular prevention.

Keywords: cardiovascular disease, physical activity, exercise intensity, meta-analysis, mortality reduction

Introduction

As of 2024, cardiovascular disease (CVD) remains the largest contributor to global mortality[1]. Although the array of treatment options for CVD is continuously expanding, one of the main pillars of reducing CVD is prevention. Physical activity (PA) is an essential pillar of a healthy lifestyle, important for both primary CVD prevention and slowing/reversing CVD progression[2]. There is an inverse relationship between moderate-to-vigorous PA and all-cause mortality, cardiovascular (CVD) morbidity and mortality, as well as incidence of type 2 diabetes mellitus, an important CVD precursor[3]. Therefore, the role of PA in the prevention of CVD is well established. Current World Health Organization (WHO), American Heart Association (AHA), and European Society of Cardiology guidelines recommend that adults of all age groups should achieve a weekly total of 150-300 minutes of moderate-intensity or 75 - 150 minutes of vigorous-intensity aerobic PA, or a balanced combination of both[3–5].

While PA has clear benefits, the ideal PA prescription is uncertain, and there are a wide variety of possible exercise methods, intensities, and durations. When considering whether moderate or vigorous-intensity exercise is superior, there is presently no definitive answer. PA can be expressed in absolute or relative terms. Absolute intensity gauges the amount of energy expended per minute during activity, typically measured by oxygen uptake per unit of time (in mL/min or L/min) or by metabolic equivalent of task (MET) values. This measure does not account for individual variables like body weight, sex, and physical fitness level. Conversely, relative intensity is established based on an individual's maximum effort, such as a percentage of cardiorespiratory fitness (maximum oxygen consumption - $\%VO_{2max}$), percentage of maximum heart rate ($\%\,HR_{max}$), etc. While relative intensity is important in making individualized training plans and goals, absolute measures allow for more generalizable recommendations[3].

Regular aerobic exercise training produces numerous cardiovascular adaptations that contribute to these protective effects. These adaptations include improved cardiac output, reduced resting heart rate and blood pressure, improved endothelial function, favorable changes in lipid profiles, and enhanced insulin sensitivity. Exercise also decreases myocardial oxygen demand while improving myocardial perfusion through the increased diameter of the epicardial coronary arteries and their favorable effects on microcirculation[4].

A 2020 meta-analysis of prospective studies suggested that for the same total physical activity both moderate-intensity and vigorous-intensity physical activities reduce all-cause mortality to the same extent[6]. Among subsequent articles published studying the relationship between PA and CVD[7–10], there also remains a lack of clear consensus on the relative benefits between low-moderate versus vigorous exercise as defined by MET values. Hence, the aim of this review was to provide further insights into the effect of exercise intensity in absolute terms, on cardiovascular events by synthesizing evidence from the existing literature on the effects of high-intensity versus moderate-to-low intensity exercise on the incidence of cardiovascular events in adults through a systematic review and meta-analysis.

Material and Methods

This review was registered on the International Registry of Systematic Reviews (PROSPERO) (registration number: CRD42024572810). The review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Eligibility criteria

The eligibility criteria included human adults (18+ years of age) without cardiovascular disease (CVD), defined as no history of infarction, angina, bypass, angioplasty, stroke, or genetic cardiovascular disease.

Information sources, search strategy, and data extraction

The information sources consisted of electronic databases, specifically PubMed, Scopus, and Web of Science, which were systematically searched in July 2024. Additionally, references from cited texts within the full-text studies were also searched. Only texts published between 1990 and 2024 were considered. The search strategy was developed in conjunction with university librarians, incorporating key terms related to cardiovascular events, physical exercise, and the metabolic equivalent of task (Full search strategy can be requested). Only articles in English and Spanish were included.

The selection process focused on studies containing data about the incidence of CV events and physical activity (PA) intensity levels as determined by METs. Studies involving patients with pre-existing CVD, populations with chronic diseases (e.g., chronic kidney disease, diabetes), paediatric populations, or those not reporting on exercise intensity were excluded. Eligible study designs included prospective and other cohort studies, while individual case reports, case series, editorials, cross-sectional studies, and reviews were excluded.

During the data collection process, two authors independently (AF, EL) reviewed each article through title and abstract screening, full-text review, data extraction, and quality assessment using the Covidence© platform (https://www.covidence.org). Covidence© is a web-based tool used to manage references and data from systematic reviews, allowing reviewers' decisions to be blinded until consensus is required. Data were exported to Microsoft Excel for final quality analysis. Studies were selected based on predefined inclusion/exclusion criteria, and data extraction included relevant information on participants, interventions, outcomes, and study design, recorded in a structured format. All discrepancies between the two independent primary reviewers were resolved by one of the senior investigators (AFM).

Figure 1 PRISMA Flowchart illustrating the selection process for studies included in the systematic review and meta - analysis. The flowchart details the number of records identified through PubMed, Scopus, and Web of Science, the number of records screened, the number of full - text articles assessed for eligibility, and the number of studies included in the final analysis.

Data items collected included the measure of intensity used, activity types measured, adjusted model variables, population and sex, measures of effect, and outcomes (total CVD, stroke, heart failure, coronary heart disease).

Risk-of-bias assessment

Two independent reviewers (AF, EL) conducted a bias assessment using the National Heart, Lung, and Blood

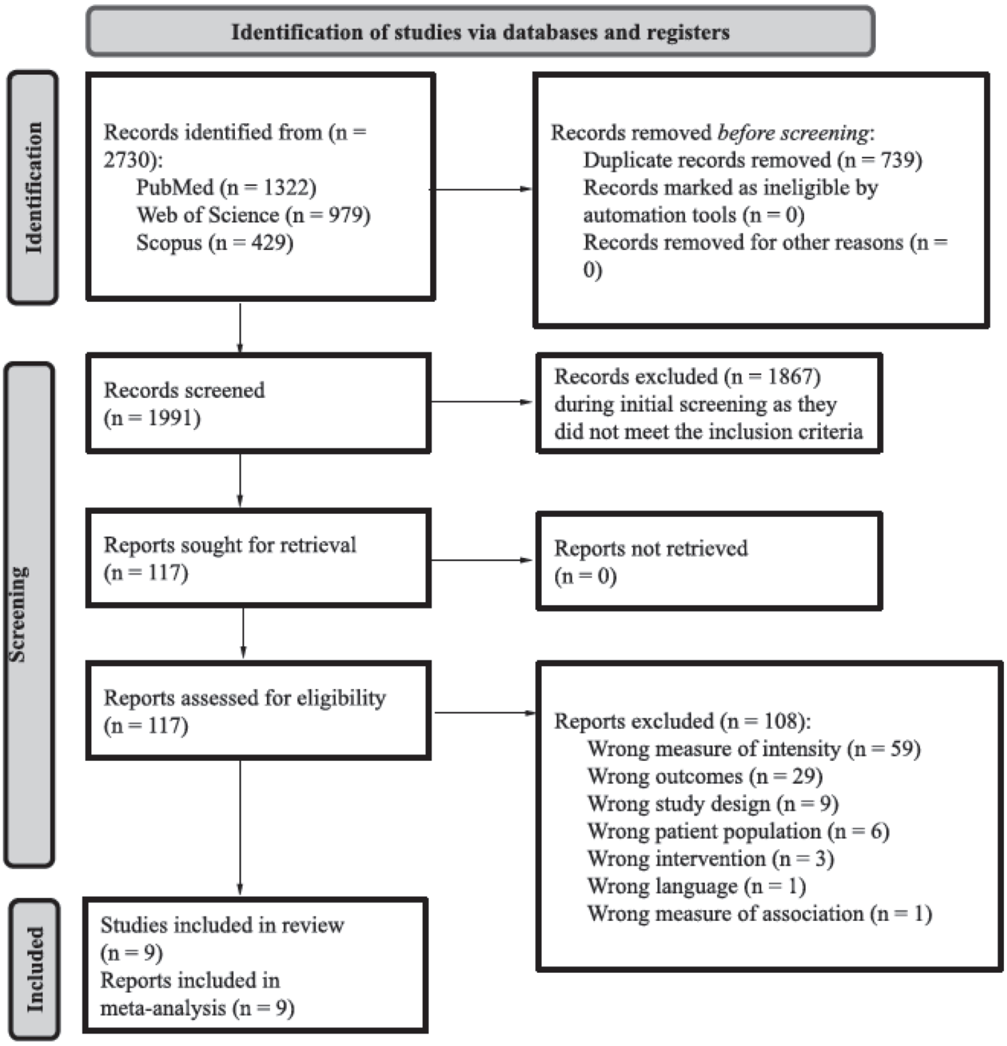

Figure 1 Flowchart showing study selection process

Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Each question had to be answered "yes" or "no", and if no, then further classified as CD, cannot determine; NA, not applicable; NR, not reported. A consensus was reached and can be found in Supplementary Table 1.

Data extraction

In this study, we defined physical activity (PA) intensities based on established thresholds for moderate and vigorous activities[4]. Moderate-intensity PA (MPA) was classified as activity performed at an intensity equivalent to 3–5.9 metabolic equivalents (METs). Vigorous-intensity PA (VPA) was defined as activity performed at an intensity equal to or exceeding 6 METs, or 6 or more times the intensity of the resting metabolic rate. For this review, we included studies that explicitly presented data on the average intensity of PA performed. It was essential to confirm that the majority of the exercise in these studies fell within the specified moderate or vigorous intensity ranges to ensure consistency with the defined thresholds and accurate classification of PA levels.

Statistical analysis

The effect measure used in the analysis was the hazard ratio (HR). A random-effects inverse variance model was applied for the meta-analysis using the Paule and Mandel estimator. Inconsistency was assessed using the I^2 statistic. A subgroup analysis was conducted to examine differences according to intensity levels, and a sensitivity analysis was performed by systematically excluding individual studies. Publication bias was evaluated through funnel plots and the trim-and-fill method. All analyses were conducted using RStudio Version 2023.12.1+402 with R version 4.3.3.

Results

Characteristics of the studies

Study designs

The main characteristics and results of the selected studies are summarized in Table 1. The nine studies analyzed in this review cover a wide range of populations, with sample sizes ranging from 4672 to 403,681 participants, and male participants ranging from 17% to 100%. All studies employed a longitudinal design, following participants over time to assess the incidence of cardiovascular disease (CVD) outcomes. These outcomes included fatal and nonfatal myocardial infarction (MI), stroke, heart failure, and overall CVD mortality. Each study accounted for key confounding factors such as age, sex, BMI, smoking status, comorbidities (e.g., diabetes, hypertension), socioeconomic status, and dietary habits. Some studies offered more nuanced adjustments by including additional factors like exercise intensity and duration.

Physical activity assessment

In the majority of studies reviewed, leisure-time physical activity (LTPA) was measured using self-reported methods. Participants typically reported the type, duration, and frequency of their activities. Based on this information, activity levels were estimated in terms of metabolic equivalent tasks (METs). The papers generally predetermined a MET value for each type of physical activity, using standard compendiums or established MET guidelines. Some studies provided further detail on intensity, dividing activity levels into moderate and vigorous physical activity categories. Two studies, Hidalgo-Santamaria[8] and Mu[11], specifically adjusted for MET-hours per week (MET-h/wk) in their models. This allowed for a more precise quantification of the relationship between physical activity dose and cardiovascular outcomes, reflecting both the intensity and duration of exercise. Notably, only the studies by Hidalgo-Santamaria and Mu explored the relationship between exercise intensity and sub-outcomes, such as stroke, as opposed to focusing solely on overall CVD risk.

Another notable methodological difference was observed in Lacey[12], which used different cut-offs for physical activity intensity compared to other studies. Lacey assigned a MET value of three to non-vigorous activity and five to vigorous activity. This variation in intensity definitions may impact the comparability of results, as exercise intensity thresholds differed between studies.

A subset of papers—Wang[13], Mu[11], Liu[14], and Shiroma[15]—used the proportion of vigorous physical activity (VPA) relative to total moderate-to-vigorous physical activity (MVPA) as their primary metric, rather than focusing on the mean intensity of total exercise. This approach allowed these studies to explore how varying intensities within the total volume of exercise influenced CVD outcomes.

In summary, while the studies shared a common focus on physical activity and CVD risk, the diversity in methodologies—including adjustments by MET-h/wk, the

Table 1 Characteristics of studies included

Author (year)	Number of participants (% men), Follow up period	Intensity measure	Outcome	Activity type	Adjusted modes (16)
Autenrieth 2011 et al.	4, 672 (50.7), Median 17.8 years	Moderate 3-6 MET, Vigorous >6 MET	ICD-9: 390-459	LTPA	Adjusted for sex, BMI, systolic blood pressure, total-to-HDL cholesterol ratio, education, smoking status, alcohol consumption, myocardial infarction, stroke, diabetes, cancer, self-reported limited physical activity due to health problems, and other domains of physical activity. No adjustments for other types of physical activity in total activity.
Chomistek 2012 et al.	44, 551 (100), Total 22 years	Moderate 3-6 MET, Vigorous >6 MET	Total CVD included fatal or nonfatal myocardial infarction and fatal or nonfatal stroke	LTPA	The multivariable model is adjusted for age, adjusts for parental history of MI at or before the age of 60 yr, parental history of cancer at or before the age of 60 yr, smoking, aspirin, vitamin E supplement use, intake of polyunsaturated fat, trans fat, eicosapentaenoic acid and docosahexaenoic acid, and fiber, as well as alcohol intake and preexisting disease including a diagnosis of diabetes, hypertension, or hypercholesterolemia.
Hidalgo-Santamaria 2018 et al.	18, 737 (39), Median 10.3 years	Moderate 3-6 MET, Vigorous >6 MET	CVD (myocardial infarction, stroke, and death due to cardiovascular causes)	LTPA	Adjusted for sex, baseline body mass index, total energy intake, adherence to the Mediterranean Diet, alcohol intake, smoking pack years, educational level, elevated triglycerides, low high density lipoproteins, hypertension, diabetes mellitus, cancer, antiaggregant treatment, anticoagulant treatment, family history of coronary heart disease, weekly energy expenditure in leisure time physical activity (MET-h/week) and changes in physical activity in the 2th and 4th year follow-up, with age and year of entering the cohort as stratification variables.
Lacey 2015 et al.	7564 (100), Mean 11.4 years	Non-vigorous activity was assigned a MET value of three and vigorous activity a MET value of five	ICD-10: I00-I99	LTPA	Hazard ratios were adjusted for age at risk, education and smoking. Participants reporting no recreational physical activity were referent.

Table 1 Continued

Author (year)	Number of participants (% men), Follow up period	Intensity measure	Outcome	Activity type	Adjusted modes (16)
Liu 2020 et al.	100, 560 (40), Median 7.3 years	Moderate 3-6 MET, Vigorous >6 MET. Stratified by Proportion of MVPA by VPA . 0% >0% to <50% ≥50%	stroke (fatal or non-fatal stroke events, ICD-10 I60 to I69), CHD (fatal or non-fatal CHD events, ICD-10 I20 to I25), heart failure (fatal or non-fatal heart failure events, ICD-10 I50), and CVD death (ICD-10 I00 to I99)	LTPA	Models were adjusted for age, sex, geographic region, urbanization, education, family history of CVD, current smoking status, alcohol consumption, light physical activity, total volume of MVPA, and cohort sources.
Mu 2022 et al.	366566 (46), Median 11.8 years	Moderate 3-6 MET, Vigorous >6 MET. Stratified by Proportion of MVPA by VPA . 0%, ≥30%	CVD (ICD-10: I00-I99), its main subtypes including CHD (I20-25), heart failure (HF; I50, I500, I501, I509), and stroke (I60, I61, I63, I64)	LTPA	Adjusted for education (college/university or below college), income (<18,000 or 18,000–52,000 or≥52,000 £/year), race (white or others), Townsend index, smoking status (never or current or former), alcohol consumption (0 or 0.1–30 or≥30 g/day), sedentary behaviour (hours/day), MVPA (MET-hours/ week), BMI (kg/m2), diet quality score and family history of CVD.
Rey Lopez 2019 et al.	64913 (44), Mean 9.0 years	Moderate 3-6 MET, Vigorous >6 MET. Stratified by Proportion of MVPA by VPA . 0% >0% to <60% ≥60%	I01 to I99 for ICD-10	LTPA	For CVD mortality values were adjusted for alcohol, total weighted volume of MVPA, longstanding illness, CVD diagnosis at baseline, BMI and psychological distress.
Shiroma 2014 et al.	46, 650 (17), Mean 17.3 years Men Mean 16.4 years Women	Moderate 3-6 MET, Vigorous >6 MET. Stratified by Proportion of MVPA by VPA . 0% >25%to <50% ≥75%	CVD	TPA volume was calculated from walking, climbing stairs, and participating in LTPA	Adjusted for age, MVPA, for smoking status, dietary factors, and alcohol consumption. Additionally adjusted for body mass index, high cholesterol, and hypertension, clinical trial randomization, smoking status, dietary factors, alcohol consumption, postmenopausal status, hormone therapy, and parental history of myocardial infarction.
Wang 2021 et al.	403681 (44), Median 10.1 years	Moderate 3-6 MET, Vigorous >6 MET. Stratified by Proportion of MVPA by VPA . 0% >25%to <50%, 100%	CVD mortality (codes I00-I09, I11, I13, I20-I51, and I60-I69)	LTPA	Adjusted for age, sex, race/ethnicity, educational level, income, marital status, body mass index, smoking status, alcohol consumption, and MVPA.

LTPA=Leisure-Time Physical Activity, MVPA=Moderate-To-Vigorous Physical Activity, BMI=Body Mass Index, ICD=International Classification of Diseases, HDL=High-Density Lipoprotein use of RRs versus HRs, and variations in exercise intensity definitions—highlights both the strengths and limitations of the current literature. Importantly, all studies employed longitudinal designs and accounted for major confounders like age, BMI, smoking status, and socioeconomic factors, enhancing the robustness of their findings.

Quantitative meta-analysis

Figure 2 Forest plot showing the hazard ratios (HR) for engaging in vigorous and moderate-intensity physical activity (VPA and MPA, respectively), presented as a subgroup analysis. The overall pooled HR for vigorous-intensity activity from the random effects model was 0.84 (95% CI: 0.73 to 0.98), while for moderate-intensity activity, the pooled HR was 0.84 (95% CI: 0.78 to 0.91). There was moderate heterogeneity across studies for both intensity categories, with I^2 values of 71% for vigorous-intensity and 40% for moderate-intensity exercise. The tau-squared (τ^2) values, representing the between-study variance, were 0.0462 and 0.0044 for vigorous and moderate intensity, respectively.

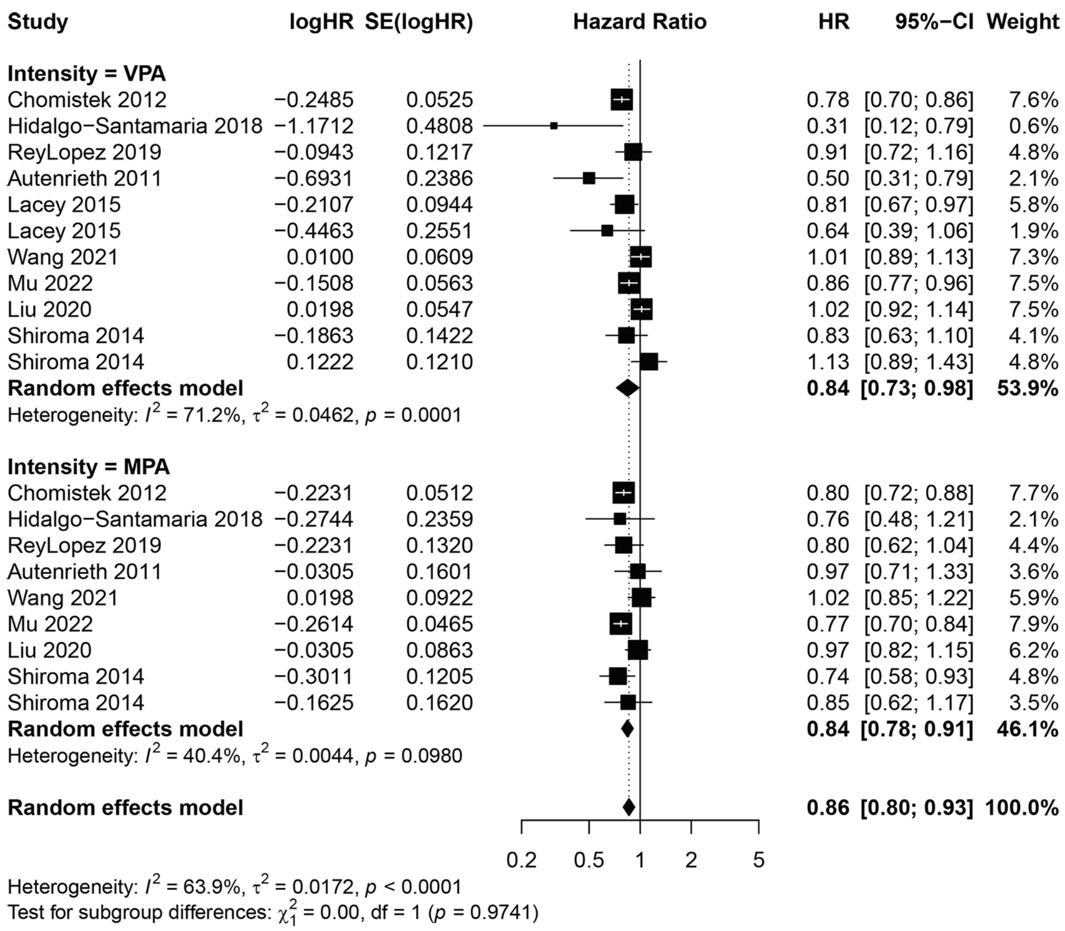

Figure 2 Forest Plot showing the Hazard Ratios (HR) for Engaging in Vigorous and Moderate-intensity Physical Activity (VPA and MPA, respectively), Presented as a Subgroup Analysis

Discussion

The results of our meta-analysis indicate that there is no significant difference in the associated cardiovascular protective benefits for reducing CVD risk between vigorous and moderate-intensity exercise. With essentially equivalent composite hazard ratios for both vigorous (0.84) and moderate (0.84) intensity exercise, our findings suggest that similar cardiovascular outcomes can be achieved regardless of exercise intensity level. The p-value for subgroup differences (0.97) further supports this conclusion, indicating that the variation between vigorous and moderate intensities is likely due to chance, rather than to a true difference in their protective effects. This does not imply that engaging in less intense physical activity is preferable; rather, it highlights that substantial cardiovascular benefits can be achieved even without high-intensity exercise. This is a crucial point, as it underscores that moderate-intensity exercise, which may be more accessible and sustainable for many individuals, is still highly effective for cardiovascular protection.

Our findings support the need for individualized exercise prescriptions rather than universal recommendations. Given that both moderate and vigorous exercise appear to confer similar cardiovascular protection, exercise intensity should be tailored to individual circumstances, including health status, physical capabilities, and personal preferences. While vigorous exercise may achieve comparable cardiovascular benefits in less time, offering greater time efficiency for those with busy schedules, moderate-intensity exercise may be more sustainable and accessible for certain individuals, particularly those with cardiovascular conditions, sedentary lifestyles, or lower baseline fitness levels. Factors such as age, existing comorbidities, readiness for lifestyle change, and individual time constraints should inform these decisions. The equivalent protective effects we observed between intensity levels provide clinicians with greater flexibility in developing realistic, person-centered exercise programs that individuals are more likely to adhere to long-term, supporting a flexible and personalized approach to cardiovascular risk reduction.

These findings have important implications for meeting WHO energy expenditure recommendations. The WHO guidelines translate to approximately 450-750 MET-minutes per week (150-300 minutes of moderate activity at ~3 METs) or 450-900 MET-minutes per week (75-150 minutes of vigorous activity at ~6 METs)[4]. Our results demonstrate that individuals can achieve equivalent cardiovascular protection regardless of which pathway they choose to reach these energy expenditure targets. This flexibility is particularly relevant for public health implementation, as it acknowledges that vigorous exercise may offer similar benefits in less time, while moderate-intensity exercise may be more sustainable for certain populations. Our findings suggest that populations with different physical capabilities, time constraints, or preferences can all achieve a similar cardiovascular risk reduction by meeting WHO energy expenditure thresholds through their preferred intensity level. The equivalent protective effects we observed (HR 0.84 for both intensities) support the WHO's flexible approach of allowing either moderate or vigorous activity to meet weekly recommendations, providing evidence that both pathways are equally valid for cardiovascular protection.

Initially, we expected vigorous exercise to confer a stronger protective effect than moderate exercise, particularly based on studies like Hidalgo et al.[8], which suggested a greater reduction in CVD risk with higher-intensity exercise. Physiologically, both vigorous and moderate-intensity exercise improve cardiovascular health through mechanisms such as increased cardiorespiratory fitness, better endothelial function, reduced blood pressure, and improved lipid profiles[3,17]. However, vigorous exercise may not offer additional benefits beyond those achieved with moderate exercise due to factors such as the body's maximal capacity for cardiovascular adaptations. However, much of the current literature on the topic is skewed towards post-stroke populations[18], special populations[19], or looking at other outcomes[20]. It is possible that moderate exercise elicits sufficient protective effects, such that additional intensity does not further decrease CVD risk in a meaningful way.

While vigorous exercise is beneficial, its additional benefit over moderate-intensity exercise may not be as substantial as previously thought. This emphasizes the need for further research to clarify the specific physiological mechanisms at play and to explore whether certain populations might derive more benefit from vigorous exercise than others. Future studies should also aim to address the inconsistencies in how exercise intensity is measured and reported, as these variations may have contributed to the inconsistency observed in our analysis. Overall, although our results suggest that moderate exercise is just as effective as vigorous exercise in protecting against CVD, the findings exhibited a high level of inconsistency across studies. Therefore, this study cannot lead to any definitive conclusions regarding average exercise intensity and its association with CVD outcomes.

In our meta-analysis, several key factors emerged that contributed to the inconsistency in the methodologies of the included studies. One major area of variation was how different studies classified physical activity intensity. Some studies calculated MET-h/week and divided by time to determine average METs, while others used a vigorous-to-moderate physical activity (VPA/MVPA) ratio, splitting it into groups based on percentages. A notable example is a study that used a cut-off of 5 METs to define vigorous activity. Across the literature search, there remains a lack of consensus on how to best retrieve and measure exercise intensity. Many studies rely solely on MET-h/week, which does not account for the average intensity level at which exercise is performed.

In terms of health outcomes, the majority of studies in this analysis focused on cardiovascular disease (CVD), often as defined by the International Classification of Diseases (ICD) or by specific outcomes like stroke, myocardial infarction (MI), and cardiovascular death. While this broad definition of CVD is not a significant source of confusion, it did limit our ability to perform meaningful subgroup analyses for the sub-outcomes within CVD, such as stroke or coronary heart disease (CHD). For instance, only two studies (Hidalgo and Mu) provided hazard ratios (HRs) specifically related to the association between exercise intensity and stroke. This lack of sufficient data prevented us from conducting more detailed subgroup analyses, highlighting a need for more focused studies examining distinct CVD subtypes.

Moreover, another source of inconsistency arose from the different types of physical activity evaluated across studies. Most studies looked at leisure-time physical activity (LTPA), but one study[15] also considered total physical activity volume, which included walking, climbing stairs, and other activities beyond LTPA. This distinction is important because it introduces variability in how physical activity is defined and measured. Future research should aim to clearly delineate exercise-related energy expenditure from non-exercise energy expenditure to ensure more accurate and consistent comparisons across studies.

Another factor contributing to variability was how models were adjusted. Adjustment for sex and age, which are critical variables for cardiovascular outcomes, was common across the studies. However, there was considerable inconsistency regarding the inclusion of other confounders such as alcohol consumption, smoking status, biomarkers, and pre-existing health conditions. Interestingly, only two studies[8,11], specifically adjusted MET-h/week to account for exercise volume, which is essential for accurately showing the relationship between exercise intensity and health outcomes.

In the sensitivity analysis presented (Supplementary Table 2), each study was excluded one at a time to assess its influence on the overall HR estimates and inconsistency. The results showed that the exclusion of any individual study did not significantly alter the overall effect size. The pooled hazard ratios remained consistent, indicating a protective effect of physical activity on cardiovascular outcomes, with HRs hovering around 0.84-0.87 across all iterations. This suggests the findings are robust and not heavily influenced by any single study. The 95% confidence intervals also remained fairly narrow and consistent, indicating stable estimates. The inconsistency, as measured by the I^2 statistic, showed minor fluctuations but remained moderate throughout (ranging from around 57% to 65%), indicating some variation between studies but not enough to undermine the overall conclusions. The Tau^2 statistic, which measures the between-study variance, was relatively small across all iterations, showing that no individual study was causing significant between-study inconsistency. Similarly, the p-values consistently remained below 0.01, confirming that the overall findings were statistically significant, regardless of which study was excluded.

The publication bias analysis presented (Supplementary Figure 1), shows some asymmetry, indicating potential publication bias, with smaller studies reporting protective effects (HR <1) more likely to be published. After applying the trim-and-fill method, two imputed studies were added to correct for this asymmetry. Despite the adjustments, the overall effect remained stable. The random-effects inverse variance model, using the Paule and Mandel estimator, reported a hazard ratio (HR) of 0.8723 (95% CI: 0.7914–0.9614), indicating a significant protective effect of physical activity on cardiovascular disease (CVD) outcomes (p=0.0054). Moderate heterogeneity was observed (I^2=66.4%), which is typical in meta-analyses of observational studies.

Lastly, while our meta-analysis provides evidence that moderate-intensity exercise may be just as effective as vigorous exercise in reducing cardiovascular disease (CVD) risk, there are several important limitations to consider. One notable issue is the high degree of inconsistency observed across studies, which can be attributed to variations in how exercise intensity was measured and reported. The lack of consistency in categorizing and quantifying physical activity introduces variability that complicates direct comparisons between studies. For instance, some studies used MET-h/week as a standard measure, while others used ratios of vigorous to moderate activity or set different thresholds for defining intensity levels.

Additionally, many studies failed to adjust for key confounders, such as alcohol consumption, smoking status, and pre-existing health conditions, which could influence CVD outcomes. Moreover, although the majority of studies focused on CVD broadly, there was insufficient data to conduct subgroup analyses on more specific cardiovascular conditions, such as stroke or coronary heart disease (CHD). This limits the ability to draw more detailed conclusions about the relationship between exercise intensity and particular CVD subtypes.

The sensitivity analysis confirmed that our findings are robust, as excluding any single study did not significantly alter the overall results. However, the trim-and-fill method indicated potential publication bias, as smaller studies with non-significant results may be underreported. The persistent asymmetry in the funnel plot, despite adjustment attempts, raises important concerns about the representativeness of our included studies and suggests that our observed protective effects of physical activity may represent an overestimation of the true effect size. This potential overestimation should be considered when interpreting our findings, particularly the magnitude of cardiovascular risk reduction we report. While publication bias assessment in meta-analysis faces inherent methodological limitations, and we applied the accepted standard approaches, the possibility that unpublished null or negative results could alter our conclusions cannot be dismissed. Therefore, our results should be interpreted with the appropriate caution, acknowledging that the true protective effects of physical activity, while likely present, may be more modest than our analysis suggests. Despite these limitations, the large sample size (485,687 men and 572,208 women) provides substantial statistical power, though this does not eliminate concerns about systematic bias in the literature. Future research should focus on standardizing exercise measurement methods, collecting more granular data on CVD subtypes, and encouraging publication of null results to enhance the precision and reduce bias in meta-analyses like this one.

Conclusion

In conclusion, this meta-analysis successfully synthesized the existing evidence on the effects of high-intensity versus moderate-to-low intensity exercise on the incidence of cardiovascular events in adults. The findings suggest that both vigorous and moderate-intensity physical activity offer similar cardiovascular protective benefits, with little to no difference between the two in reducing the risk of cardiovascular disease (CVD). This meta-analysis highlights several areas where further research is necessary, including the standardization of physical activity intensity measurements, the collection of more specific sub-outcome data, and the refinement of model adjustments. These improvements would provide deeper insights into the relationship between physical activity and cardiovascular health, ultimately allowing for more effective public health recommendations.

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Conflict of interest

The authors have no industry affiliations or relationships with any entities to disclose.

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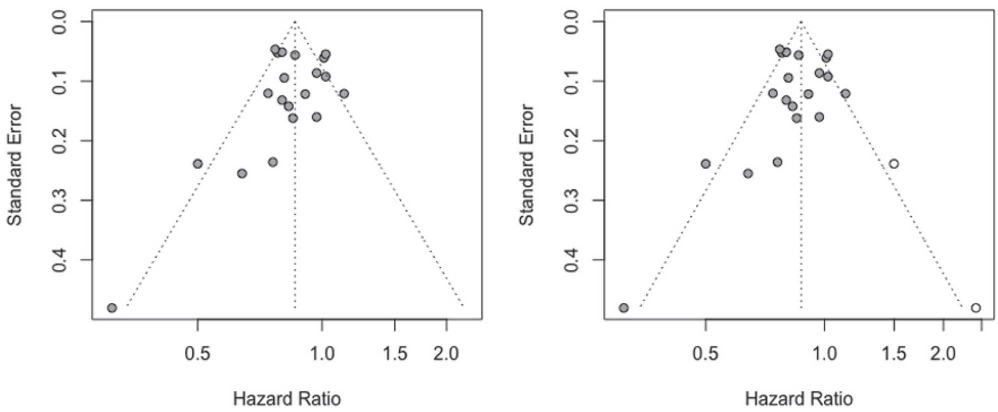
Supplementary Table 1 Bias assessment based on quality assessment tool for observational cohort and cross-sectional studies

Criteria	Autenrieth 2011	Chomistek 2012	Hidalgo-Santamaria 2018	Lacey 2015	Liu 2020	Mu 2022	Rey Lopez 2019	Shiroma 2014	Wang 2021
Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was a sample size justification, power description, or variance and effect estimates provided?	NR	NR	NR	NR	NR	NR	NR	NR	NR
For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the exposure(s) assessed more than once over time?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcome assessors blinded to the exposure status of participants?	NA	NA	NA	NA	NA	NA	NA	NA	NA
Was loss to follow-up after baseline 20% or less?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Supplementary Table 2 Sensitivity analysis

Study_Removed	TE_Estimate	Lower_CI	Upper_CI	Tau2	I2	p-value
Chomistek 2012	0.865468857	0.79313252	0.94440251	0.01840469	0.62924983	0.00268566
Hidalgo-Santamaria 2018	0.86683506	0.80620426	0.93202561	0.01162664	0.62594155	0.00061429
ReyLopez 2019	0.855700047	0.78408874	0.93385165	0.01927276	0.65676667	0.00147883
Autenrieth 2011	0.870826721	0.80971577	0.93654984	0.01153218	0.62038885	0.00085162
Lacey 2015	0.861364061	0.78897227	0.94039813	0.01922218	0.65519383	0.00218063
Lacey 2015	0.864197331	0.79567681	0.93861857	0.01710338	0.64900394	0.00159556
Wang 2021	0.848887159	0.78055274	0.923204	0.01642578	0.60137837	0.00067037
Mu 2022	0.857962806	0.78492552	0.93779621	0.01953188	0.65810339	0.00196933
Liu 2020	0.848005061	0.78035502	0.92151977	0.01588869	0.57049774	0.00058007
Shiroma 2014	0.859398557	0.78748449	0.93787991	0.01946014	0.65765405	0.00186142
Shiroma 2014	0.849752319	0.78550084	0.91925937	0.01407914	0.62109361	0.00038545
Chomistek 2012	0.863386889	0.79055939	0.94292337	0.01892643	0.64167088	0.00254503
Hidalgo-Santamaria 2018	0.860711682	0.78990616	0.93786407	0.01903795	0.65625167	0.0017484
ReyLopez 2019	0.86113415	0.78930041	0.93950543	0.01918579	0.65600379	0.00201986
Autenrieth 2011	0.854609592	0.78422542	0.93131074	0.01869206	0.65447044	0.00119844
Wang 2021	0.850364514	0.78196731	0.9247443	0.01678485	0.63383883	0.00073287
Mu 2022	0.866886754	0.79483333	0.94547198	0.01802006	0.60623703	0.00280369
Liu 2020	0.85203617	0.78173717	0.92865692	0.01807302	0.64478027	0.00103372
Shiroma 2014	0.86553923	0.79490942	0.94244469	0.01784052	0.64715758	0.00221814
Shiroma 2014	0.85842139	0.78670329	0.93667752	0.01952738	0.65806533	0.00172781

TE_Estimate=treatment effect estimate, Lower_CI=lower confidence interval, Upper_CI=upper confidence interval, Tau2=between-study variance (Tau-squared), I2=percentage of total variation across studies due to heterogeneity, p-value=probability value for statistical significance



Supplementary Figure 1 Funnel plot and trim and fill plot for all studies included in the meta-analysis