Dose-Response Relationships of Step Count Metrics with All-Cause Mortality and Cardiovascular Diseases: A Meta-Analysis

Short title: Step count metrics and health outcomes

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STRUCTURED ABSTRACT

BACKGROUND: The minimal and optimal daily step counts for health improvements remain unclear.

OBJECTIVES: A meta-analysis was performed to quantify dose-response associations of objectively-measured step count metrics in the general population.

METHODS: Electronic databases were searched from inception to October 2022. Primary outcomes included all-cause mortality and incident cardiovascular disease (CVD). Study results were analyzed with generalized least squares and random effects models.

RESULTS: 111,309 individuals from 12 studies were included. Significant risk reductions were observed at 2,517 steps/day for all-cause mortality (adjusted hazard ratio (aHR): 0.92, 95% confidence interval (CI): 0.84, 0.999) and 2,735 steps/day for incident CVD (aHR: 0.89, 95% CI: 0.79, 0.999) compared with 2,000 steps/day (reference). Additional steps resulted in non-linear risk reductions of all-cause mortality and incident CVD with an optimal dose at 8,763 (aHR 0.40, 95% CI: 0.38, 0.43) and 7,126 steps/day (aHR 0.49, 95% CI: 0.45, 0.55), respectively. Increments from a low to an intermediate or high cadence were independently associated with risk reductions of all-cause mortality. Sex did not impact the dose-response associations, but after stratification for assessment device and wear location, pronounced risk reductions were observed for hip-worn accelerometers compared to pedometers and wrist-worn accelerometers.

CONCLUSIONS: As little as ~2,600 and ~2,800 steps/day yields significant mortality and CVD benefits, with progressive risk reductions up to ~8,800 and ~7,200 steps/day respectively. Additional mortality benefits were found at a moderate-to-high *versus* low step cadence. These findings can extent contemporary physical activity prescriptions given the easy-to-understand concept of step count.

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CONDENSED ABSTRACT

Step count-based physical activity goals may represent a promising public health tool. This meta-analysis quantifies dose-response associations of objectively-measured step count metrics in the general population. Our results highlight that as little as ~2,600-2,800 steps/day already yields significant mortality and cardiovascular disease benefits, with progressive risk reductions up to ~7,200-8,800 steps/day. Step count targets were similar when stratified for sex, assessment device and wear location. These findings can extent contemporary physical activity prescriptions given the easy-to-understand concept of step count.

KEYWORDS: Walking, Public Health, Physical Activity, Exercise, Health Outcomes, Population

ABBREVIATION LIST

CI = confidence interval

CVD = cardiovascular disease

aHR = adjusted hazard ratio

IQR = interquartile range

MOOSE = Meta-analysis of Observational Studies in Epidemiology

SD = standard deviation

INTRODUCTION

Regular physical activity reduces the risk of cardiovascular diseases (CVD) and all-cause mortality in the general population(1,2). Walking is an accessible type of physical activity that can be easily and accurately measured via commercially-available smartphones or smartwatches(3), pedometers(4), and accelerometers(5,6). Daily step count represents an easy-to-use metric for the general population, and may therefore have the potential to improve physical activity adherence and subsequent clinical outcomes(7). Indeed, studies found that performing an additional 1,000 daily steps is associated with a 12-15% reduced risk of all-cause mortality (8,9) and lower odds for frailty(10). Despite the potential of walking to improve health, the 2020 World Health Organization Guidelines on Physical Activity and Sedentary Behaviour do not include step count thresholds(11). Several meta-analyses have qualitatively examined the dose-response association of daily step count(8,9,12-15), but objective data extraction to identify minimum and optimum step count doses have not yet been fully established. To enable the integration of evidence-based thresholds in future physical activity guidelines, the role of potential effect modifiers such as walking intensity (i.e., step cadence (16)) should also be delineated as previous studies reported mixed results(17-19). Therefore, this systematic review and meta-analysis examines the dose-response association of objectively-measured step count metrics with all-cause mortality and incident CVD in the general population. In addition, the moderating effects of 1) sex, 2) step cadence and 3) device and wear location of the step count assessment were explored.

METHODS

This systematic review was performed according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist(20) and registered at the PROSPERO database (CRD42021244747).

Information sources and search strategy. A systematic literature search was performed in PubMed and Embase (Ovid), from inception to October 2022, using the search terms daily step count, step intensity, objective step-measuring methods, mortality, and incident CVD alone and in combination (**Supplemental Table 1)**.

Eligibility criteria. Studies were included if they 1) quantified daily step count using objective step-counting methods (i.e., accelerometry, pedometer), 2) examined the associations between step count and all-cause mortality or incident fatal or non-fatal CVD including ischemic/coronary heart disease, stroke, and/or heart failure, 3) had a prospective cohort study design, 4) were peer-reviewed, published in English and accessible online, and 5) included adults aged ≥18 years without CVD at baseline. Studies addressing congenital heart disease were excluded.

Data extraction and quality assessment. Studies were selected by two independent researchers (NS, EB). Potential articles were manually screened using titles and abstracts. Full-text publications were retrieved and reviewed. Both researchers discussed results to reach consensus. Reference lists of relevant studies and systematic reviews were checked to ensure no relevant studies were missing. Extracted descriptive data included the study's primary outcome, cohort name, covariates included in analysis, sample size, age, sex, number of events, body mass index, baseline step count, monitoring period, wear time, assessment

device, wear location, follow-up duration and shape of the dose-response curve. Authors were contacted via email in case insufficient data was reported.

Two researchers (NS, EB) independently scored the risk of bias of included studies using the Newcastle-Ottawa Scale(21). In case of disagreement, consensus was reached by consulting a third researcher (TE). Studies were scored for selection, comparability and outcome on a 0-9 point score, where 1-3, 4-6 and 7-9 points reflect a high, intermediate, or low risk of bias respectively.

Data synthesis and analysis. Categorical and continuous dose-response associations between step count and clinical outcomes were tested. In addition, we explored the moderator effects of sex, step cadence, assessment device, wear location.

Categorical dose-response analysis. Categorical dose-response analyses were performed for step count and cadence. Peak cadence represents the maximal number of steps performed during any specified period of time. Peak 30-minute cadence was included in our analyses, as this parameter was most frequently reported. We used a previously published approach(22,23) to pool study data and generate three categories for step count and cadence each (i.e., low, intermediate, and high; **Supplemental Methods)**. Fully-adjusted hazard ratios (aHRs) were used to control for confounding variables. Transformation of aHRs and 95% confidence intervals (CIs) by the natural logarithm was performed to allow accurate estimation of the 95% CI for the pooled estimate. In essence, we compared the high and intermediate to the low categories using random effects as previously described(24). Additional analyses were performed to examine 1) the moderator effect of device type and wear location (i.e., pedometer, hip-worn and wrist-worn accelerometer) and 2) the interplay

between step cadence and step count. Heterogeneity was assessed using the I^2 and tau^2, with an I^2>50% indicating significant heterogeneity. Publication bias was explored using funnel plots and Egger's tests.

Continuous dose-response analysis. aHRs and 95% CIs per 500 step increment (range 1,500-16,000 steps) were extracted from published dose-response curves using a graphical software program (WebPlotDigitizer version 4.5, Automeris LLC, Pacifica, USA)(25,26). Continuous dose-response associations between daily step count and all-cause mortality or incident CVD were based on a generalized least squares regression model using the maximum likelihood method. Non-linearity was assessed by modelling step count using a restricted cubic spline. We tested three knots (at 5%, 50% and 95% of step count distribution)(27), four knots (at 5%, 35%, 65% and 95%), and five knots (at 5%, 27.5%, 50%, 72.5% and 95%), and subsequently compared the Akaike Information criteria to identify the best fitting model. Linearity was tested using the Wald test. The reference level of the pooled dose-response curves was set at 2,000 steps, which was performed by subtracting the natural log-transformed aHR corresponding to 2,000 steps/day from the natural log-transformed aHRs of the full range of step counts. The dose where minimal risk reductions were observed, was set at the first step count where the lower and upper border of the 95% CI were both lower than 1. The optimal step count dose was defined as the maximal risk reduction at the least effort (steps/day), reflecting the lowest step count at which the lower border of the 95% CI exceeded the upper border of the 95% CI of the lowest aHR (i.e., overlap of confidence intervals). We repeated these analyses with incremental reference categories (+1,000 steps/day) to compose a heatmap of the dose-response association between 2,000 and 16,000 steps/day. Dose-response models were truncated at 16,000 steps/day because of a paucity of data above this value. To explore effect modification, we additionally investigated the role of sex and

accelerometry wear location. To test the robustness of our results, we performed a sensitivity analysis including only high-quality studies (Newcastle-Ottawa Scale ≥ 7).

All analyses were performed in R version 4.02 (R Foundation for Statistical Computing, Vienna, Austria) using *meta* (version 5.1-1)(28) and *rms (*version 6.2-0*)*(29). A two-tailed p-value<0.05 indicated statistical significance. Baseline study characteristics were weighted for sample size to better reflect the characteristics of the overall population. Data is presented as mean ± standard deviation (SD), median with interquartile range [IQR], or frequency and proportion.

RESULTS

Study selection. The systematic search identified 5,414 potential studies: 2,856 from PubMed and 2,558 from Embase (**Figure 1**). A total of 1,078 were duplicates, 4,307 articles were excluded based on title and abstract, leaving 29 articles which were screened for eligibility. Fifteen articles did not meet the inclusion criteria after reading the full-text and two articles(30,31) were excluded because of insufficient data, leaving 12 studies for inclusion. One study(32) shared unpublished data on the association between daily step count and cardiac hospitalizations. In total, eleven studies assessed the association between step count and all-cause mortality (n=111,309)(17-19,32-40); four studies assessed step count and incident CVD (n=85,261)(19,32,40,41) and four assessed step cadence and all-cause mortality (n=102,191)(17-19,40).

Study and population characteristics. The analytical cohort (**Supplemental Table 2**) objectively measured step count data from 111,309 individuals (60.8% women, 62.5±5.3 years old, body mass index 27.0±1.3 kg/m^2). Mean daily step count was 7,069±904 steps/day. Of the twelve included studies, one study included only women(17) and two included only

men(33,41). Step count was quantified using a pedometer (n=3)(35,37,38), or a hip-worn (n=8)(17-19,32-34,36,41) or wrist-worn (n=1)(40) accelerometer. All studies measured step count for 7 days, except for one cohort that measured for two days (38). Most studies corrected for age (n=10), BMI (n=10), sex (n=10), smoking status (n=10), alcohol status (n=9), education level (n=7) and relevant comorbidities (n=8) within their fully-adjusted model. Most studies used national death registries(17-19,32-35,38,40,41) and death certificates(17) to assess endpoints.

Quality assessment and publication bias. All studies had a low risk of bias (Newcastle-Ottawa Scale ≥ 7), except for one(37) which had an intermediate risk of bias (Newcastle-Ottawa Scale = 6; **Supplemental Table 3**). Assessment of publication bias for the association between daily step count and all-cause mortality showed a symmetrical pattern suggesting minimal publication bias (**Supplemental Figure 1**).

Categorical dose-response association between daily step count and clinical outcomes. Among 111,309 individuals, 4,854 died (4.4%) during a median follow-up of 77.8 months [71.6–82.9]. Intermediate step counts (6,000 [5,392-6,775] steps/day) were associated with a significantly lower mortality risk (aHR 0.64, 95% CI: 0.56-0.72; **Figure 2**) compared to the lower tertile (3,166 [2,375-4,191] steps/day). The risk reduction for the association with all-cause mortality was largest (aHR 0.50, 95% CI: 0.42-0.60; **Figure 2**) in individuals in the highest tertile (10,000 [8,843-11,082] steps/day).

A total of 1,224 individuals (1.4%) developed a CVD event during 72.9 [66.4-80.4] months of follow-up. The intermediate (5,737 [5,449-6,000] steps/day) and high step count (11,000 [9,923-12,024] steps/day) categories were associated with a lower risk of CVD (aHR

0.58, 95% CI: 0.46-0.73 and aHR 0.42, 95% CI: 0.33-0.53, respectively) compared to the low step count category (2,022 [1,468-2,885] steps/day; **Figure 3**).

Continuous dose-response association between daily step count and clinical outcomes. The continuous dose-response analyses revealed non-linear trends (p-values for non-linearity <0.001) for the associations between step count versus all-cause mortality and incident CVD (**Central Illustration** and **Supplemental Figure 2**). Risk reductions became statistically significant for the associations with all-cause mortality and CVD at 2,517 steps/day (aHR: 0.92, 95% CI: 0.84-0.999) and 2,735 steps/day (aHR: 0.89, 95% CI: 0.79-0.999), respectively. The minimal effective step count for all-cause mortality and CVD was 479 [399, 644] and 735 [632, 1081] steps/day above the reference category for other cut-offs points (**Supplemental Table 4**). Further increases in step count were associated with a decreased mortality and CVD risk until 8,763 steps/day (aHR: 0.40, 95% CI: 0.38-0.43) and 7,126 (aHR: 0.49, 95% CI: 0.45-0.55) after which additional reductions in mortality and incident CVD risk were not statistically significant (16,000 vs 2,000 steps: aHR 0.35 [95% CI: 0.30-0.40], and aHR 0.42 [95% CI: 0.33-0.53], respectively; **Central Illustration**). Changes in risk estimates following increases or decreases of 1,000 steps/day were strongly dependent on baseline step count (**Figure 4**).

Comparable results were observed when only high-quality studies were examined (**Supplemental Figure 3**). Likewise, no important differences in risk reductions were observed between men and women (**Supplemental Figures 4, 5** and **6**). Studies using hip-worn accelerometry were associated with more pronounced mortality risk reductions than studies using wrist-worn accelerometers (**Supplemental Figures 7, 8** and **9**) and pedometers (**Supplemental Figure 9**).

Step cadence and mortality. Intermediate (63 [63-63] steps/min) and high (88 [88-88] steps/min) cadences were associated with a lower mortality risk (aHR 0.67, 95% CI: 0.56-0.80; and aHR 0.62, 95% CI: 0.40-0.97) than a low cadence (29 [28-30] steps/min, **Supplemental Figure 10**). Additional adjustment for step count attenuated these associations (intermediate cadence: aHR 0.78, 95% CI: 0.65-0.93; and high cadence: aHR 0.79, 95% CI: 0.67-0.94; **Figure 5**).

DISCUSSION

Our meta-analyses quantified the dose-response association of objectively-measured daily step count metrics with all-cause mortality and incident CVD in the general population. A minimal dose of 2,517 and 2,735 steps/day was associated with an 8% reduction in all-cause mortality and a 11% reduction in CVD risk, respectively, compared to individuals accumulating 2,000 steps/day. The optimal doses were found at 8,763 steps/day for all-cause mortality (i.e., 60% risk reduction) and 7,126 steps/day for incident CVD (i.e., 51% risk reduction). Increasing from low to intermediate and high cadence were also associated with a decreased all-cause mortality risk (33% and 38% risk reduction, respectively), even after adjustment for daily step count (22% and 21% risk reduction, respectively). Risk reductions were greater for hip-worn accelerometers than for pedometers and wrist-worn accelerometers. There were no important differences in risk reductions with step count between men and women. Findings from this meta-analysis may optimize physical activity prescription in daily practice given the easy-to-understand concept of step count from a public health perspective.

Minimal dose. We found that the minimal step count dose needed to elicit significant health benefits was ~2,600 steps/day for all-cause mortality and ~2,800 steps/day for incident CVD

in comparison to individuals who accumulated 2,000 steps/day. These findings highlight that behavior changes from physical inactivity to a lifestyle with some physical activity may already produce risk reductions for all-cause mortality and incident CVD. It is important to highlight that such activity levels are feasible for the majority of the general population, including older adults and individuals with chronic diseases(42). Increases of 1,000 steps/day were associated with additional health benefits (**Figure 4**), especially among those with a low number of baseline steps (**Supplemental Table 4)**, highlighting that every step counts.

Optimal dose. The optimal step count dose was observed at ~8,800 and ~7,200 steps for all-cause mortality and incident CVD, respectively. Step counts beyond our optimal dose minimally improved health outcomes. This plateau suggests that most benefits were achieved at step counts less then 10,000 per day, which aligns with observations from recent other meta-analyses(12,14). Although higher step volumes beyond this level were not associated with additional health benefits, there is no reason to discourage individuals from such behavior as a highly physically-active lifestyle may provide other benefits, such as joy, improved quality of life, sleep and mental health(43,44).

Stepping cadence. We found that an intermediate and high cadence was associated with a reduced risk of mortality and CVD morbidity, even after additional adjustment for daily steps. These findings underline that both volume (steps/day) and intensity (cadence, steps/min) are independently associated with health and that their risk reductions are additive. Cadence can be considered a proxy for fitness, since a higher cadence requires a greater oxygen consumption(45,46) and higher fitness is associated with better event-free survival(47,48). Similarly, a greater proportion of vigorous physical activity, relative to the total amount of physical activity, is associated with a reduced mortality risk(49-51). Hence,

accruing step volumes at a higher step cadence may provide additional benefits compared to low cadence.

Device type and wear location. Reductions in mortality and CVD risks were larger for hip-worn accelerometers than pedometers and wrist-worn accelerometers. Hip-mounted devices are potentially more likely to accurately measure steps given their close proximity to locomotion acceleration. Alternatively, this observation may also relate to differences in cohort characteristics (i.e., age, follow-up time, event rate), as we included only one study using a wrist-worn device. The lower risk estimate for pedometers may be due to underestimation of step count compared to accelerometers(52), especially at slower cadences(53). Nevertheless, the impact of these findings may be limited for future guidelines, since the minimal and optimal dose were not affected by the device type or wear location. Therefore, a uniform step count prescription may be adopted using different devices.

Practical implications. This study revealed non-linear dose-response curves between daily steps and health outcomes, with progressive risk reductions for mortality and CVD at a higher number of daily steps, independent of sex. The optimal dose of ~8,800 steps/day for mortality and ~7,200 for CVD may be used in future physical activity guidelines. Step count based targets may enhance adherence to physical activity recommendations since measurement devices are commercially available and provide reliable measurement of walking activity(54). Physicians may stimulate individuals, even those who are moderately active, to increase their physical activity with at least 1,000 steps/day, as this target is feasible and can be achieved during ~10 minutes of walking activity(55). Since walking is accessible to the majority of the population, including those with chronic disease or with a lower social

economic status, and can be adjusted to a pace that matches the individual level of fitness, step count based physical activity goals may become a promising public health tool.

Strengths and limitations. The strengths include the large sample size (n=111,309) and the ability to model continuous dose-response associations, while the risk of bias was low with minimal evidence of publication bias. Nonetheless, several limitations should be considered. First, daily step counts were only investigated at baseline, but physical activity behavior may change over time and is influenced by various factors (e.g., age, sex, socio-economic status, and disease state)(56,57). Repeated measures of daily step count could further strengthen the evidence. Second, we were not able to quantify the effects of reverse causation and other relevant factors that influence daily step count, due to restrictions in available and published dose-response curves. Nonetheless, ten out of 12 studies concluded that their results were not likely to be affected by reverse causation when removing the first(17,33,35,41), second(18,32,34,38,40) or third(37) follow-up year(s). Third, only four studies investigated the additive effects of step cadence to total step count. Future studies are warranted to confirm our results. Fourth, observations from this study may not directly be extrapolated to chronically diseased, older and low-income populations. Whilst the minimal and optimal step count may represent relevant targets for these populations, the magnitude of risk reductions may be different as distinct dose-response relationship between physical activity and health were previously presented for individuals with CVD *versus* healthy controls(58).

CONCLUSIONS

A lower risk for all-cause mortality and incident CVD may already be experienced after ~2,600 and ~2,800 steps/day, respectively. Additional increments of 1,000 steps/day (~10 minutes walking) enhance risk reductions in a non-linear fashion. Optimal health benefits

were achieved at ~8,800 steps/day for all-cause mortality and ~7,200 steps/day for incident CVD. A higher cadence provides additional health benefits beyond the total step volume. As health benefits of daily steps were similar between men and women and step count targets were independent of wear location and device, the integration of uniform daily step targets in future physical activity guidelines may be relevant from a public health perspective as “Every Step Counts”.

CLINICAL PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Using data from 111,309 individuals, minimum (~2,600 and ~2,800 steps/day) and optimum (~8,800 and ~7,200 steps/day) step counts were identified to reduce all-cause mortality and incident cardiovascular disease, respectively. These targets were independent of sex, wear location and device type.

TRANSLATIONAL OUTLOOK: Given the easy-to-understand concept of daily steps from a public health perspective, step count metrics may be used to prescribe the minimal and optimal volume (i.e., steps/day) and intensity (i.e., step cadence) of physical activity for health improvement.

DATA AVAILABILITY

The data underlying this article will be shared upon reasonable request to the corresponding author.

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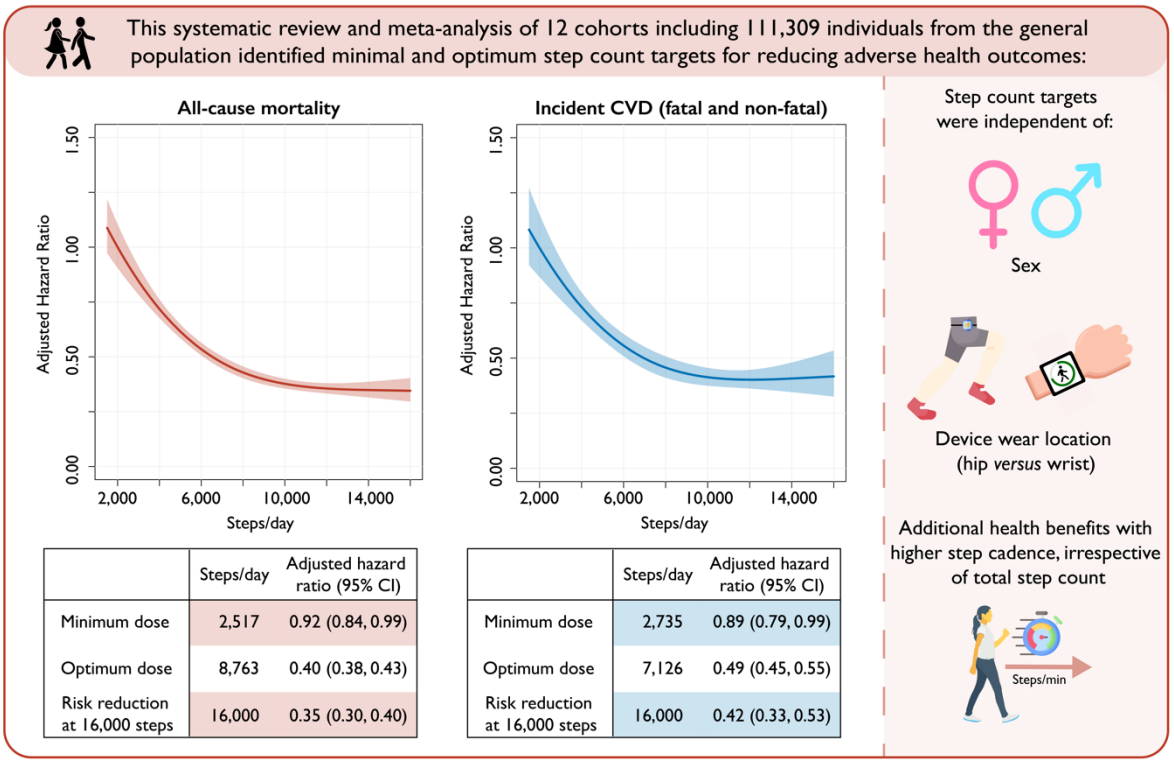
FIGURE LEGENDS



	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,517	0.92 (0.84, 0.99)
Optimum dose	8,763	0.40 (0.38, 0.43)
Risk reduction at 16,000 steps	16,000	0.35 (0.30, 0.40)

	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,735	0.89 (0.79, 0.99)
Optimum dose	7,126	0.49 (0.45, 0.55)
Risk reduction at 16,000 steps	16,000	0.42 (0.33, 0.53)

Central Illustration. Dose-response associations of daily step count with clinical outcomes.

Dose-response curves for the association between daily step count versus all-cause mortality (left panel) and incidence of cardiovascular diseases (CVD; middle panel). Adjusted hazard ratios from published dose-response curves were extracted and pooled using restricted cubic spline models. Compared to the reference level of 2,000 steps/day, the minimum dose to significantly reduce the risk for adverse outcomes was 2,517 steps/day for all-cause mortality and 2,735 steps/day for incident CVD. The optimum dose, defined as the maximal risk reduction at the least effort, was established at 8,763 steps/day for all-cause mortality and 7,126 steps/day for incident CVD. Shaded areas indicate the corresponding 95% confidence interval. aHR adjusted hazard ratio, CVD cardiovascular disease.

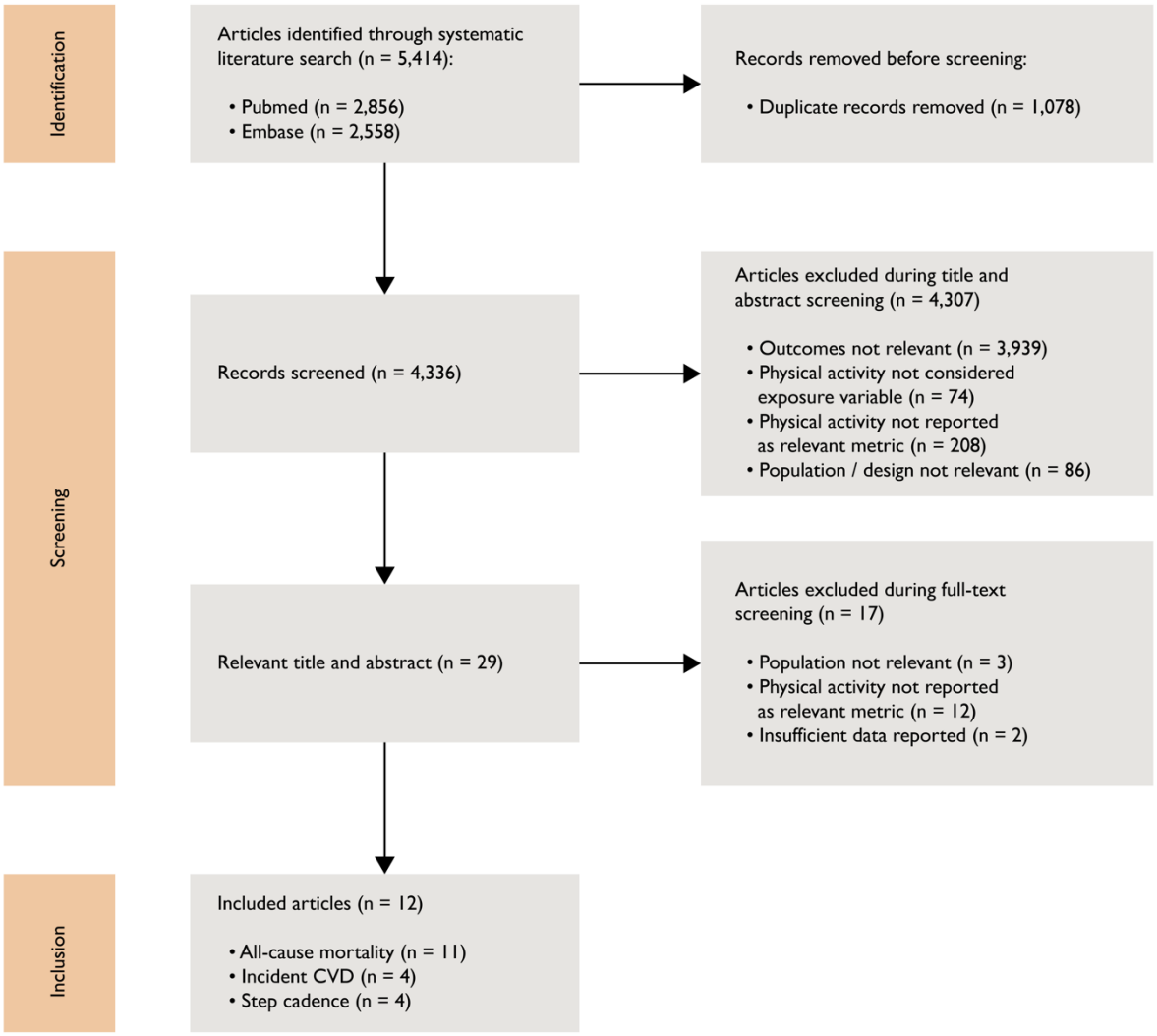


Figure 1. PRISMA flowchart of the review process of potential articles.

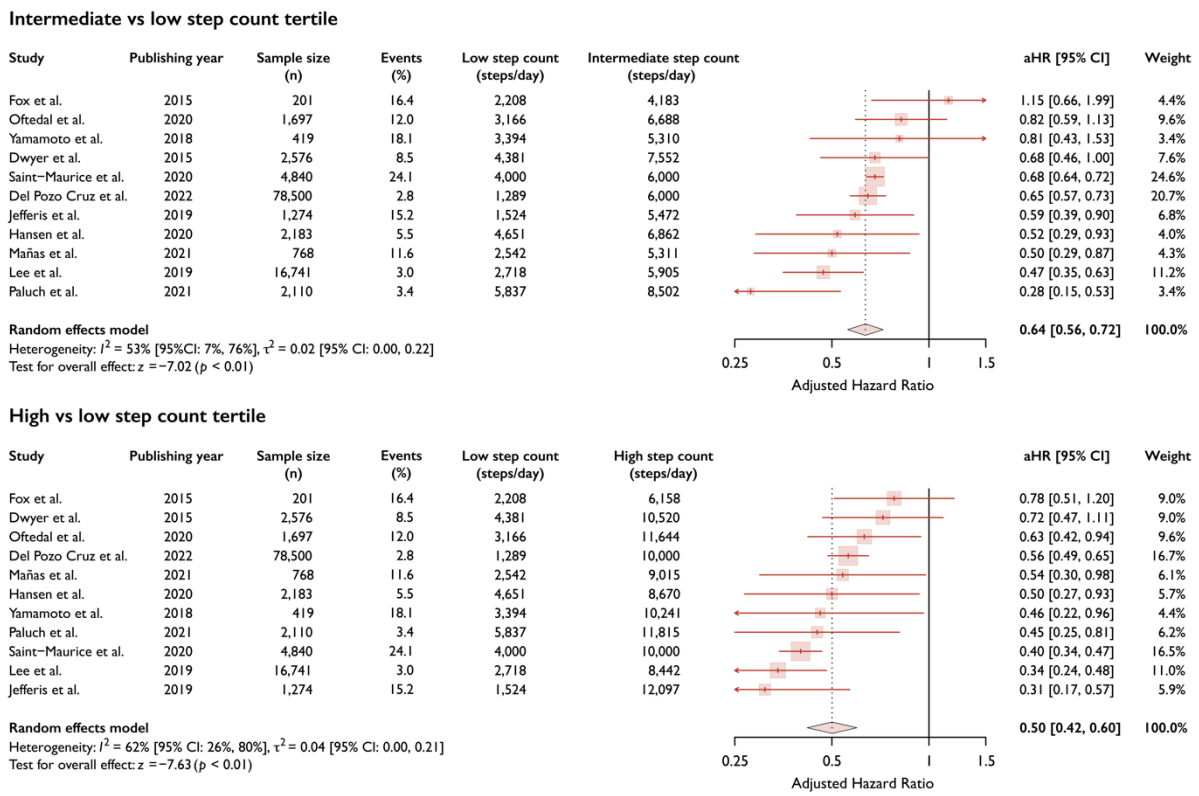


Figure 2. Association between daily step count tertiles and all-cause mortality.

Individuals in the intermediate (6,000 [5,392-6,775] steps/day) and high step count tertile (10,000 [8,843-11,082] steps/day) had a significantly lower mortality risk (36 and 50%, respectively) compared to the low step count tertile (3,166 [2,375-4,191] steps/day). For each study, red vertical and horizontal lines represent the effect estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and were presented as red squares and percentages. The red diamond represents the pooled estimate and its 95% confidence interval. The low, intermediate and high step counts reflect the average step count of the subjects in the respective group. CI = confidence interval, aHR = adjusted hazard ratio, IQR = interquartile range.

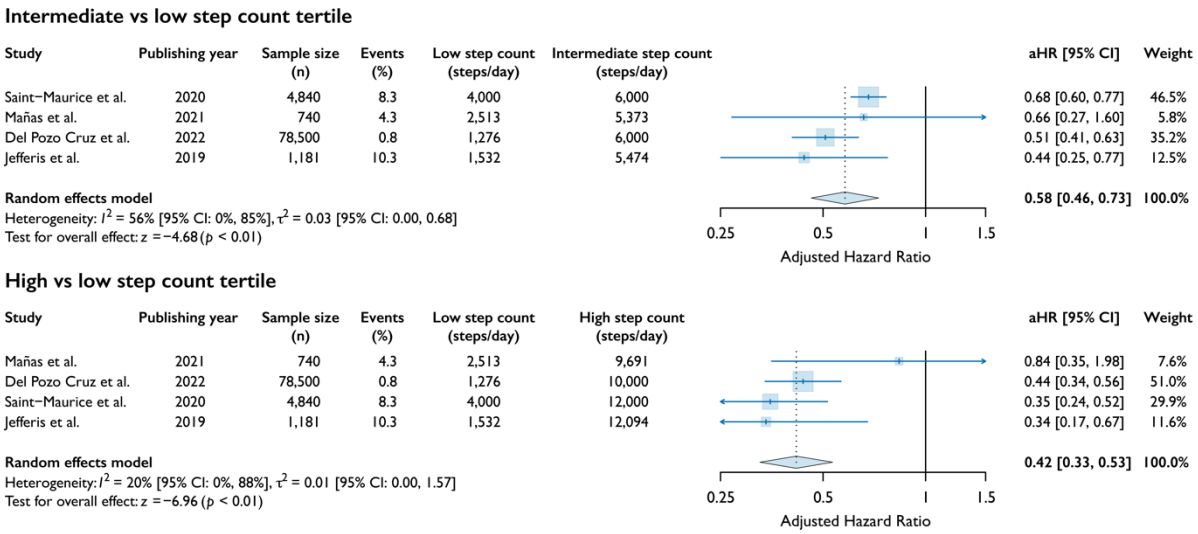


Figure 3. Association between daily step count tertiles and incident CVD.

Individuals in the intermediate (5,737 [5,449-6,000] steps/day) and high step count tertile (11,000 [9,923-12,024] steps/day) had a lower risk for incident CVD (42 and 58%, respectively) compared to the low step count tertile (2,022 [1,468-2,885] steps/day). For each study, blue vertical and horizontal lines represent the effect estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and were presented as blue squares and percentages. The blue diamond represents the pooled estimate and its 95% confidence interval. The low, intermediate and high step counts reflect the average step count of the subjects in the respective group. CI confidence interval, CVD cardiovascular disease, aHR adjusted hazard ratio, IQR interquartile range.

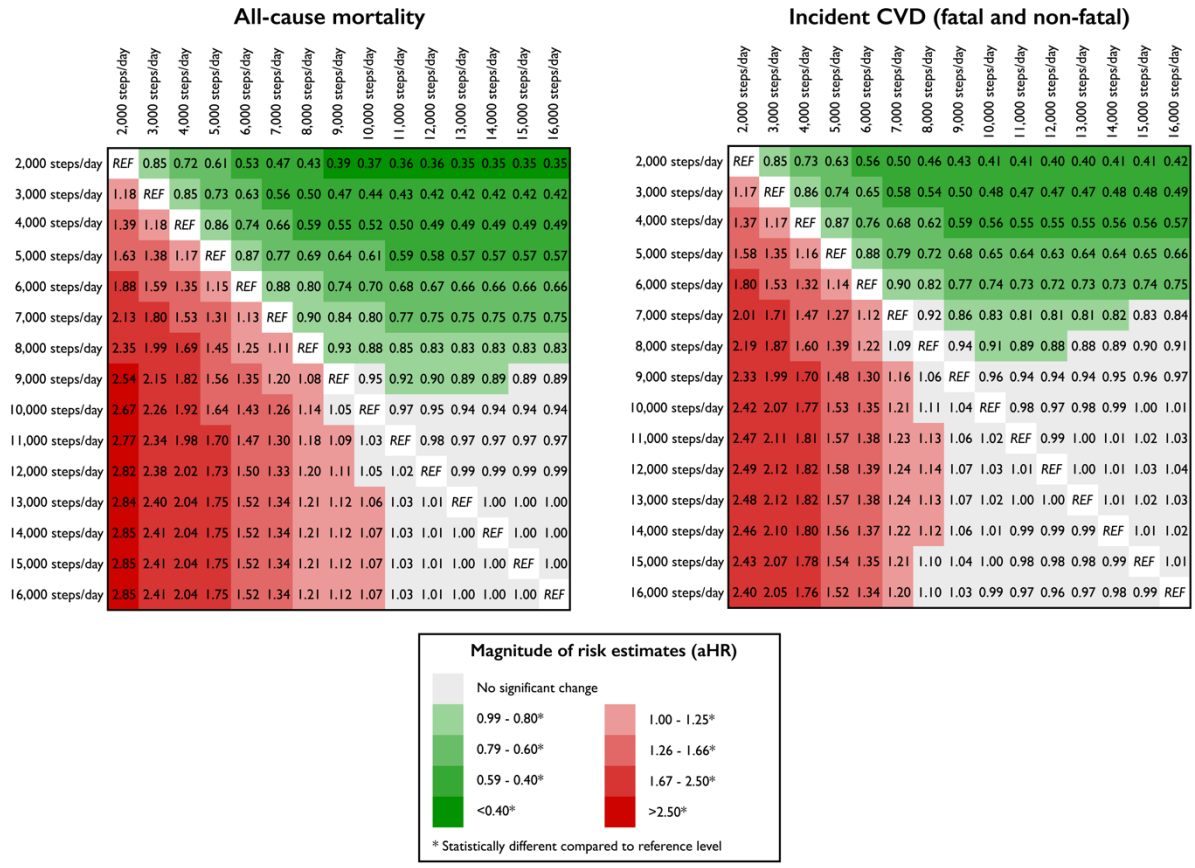


Figure 4. Associations between different step count volumes and clinical outcomes.

Heatmap visualization of the interplay between different step count volumes with all-cause mortality (left heatmap) and incident CVD risk (right heatmap). Heatmaps should be interpreted row-wise. Green and red values indicate significant reductions and increases in risk, respectively, whereas grey cells indicate no significant difference compared to the reference level. aHR adjusted hazard ratio, CVD cardiovascular disease, REF reference level.

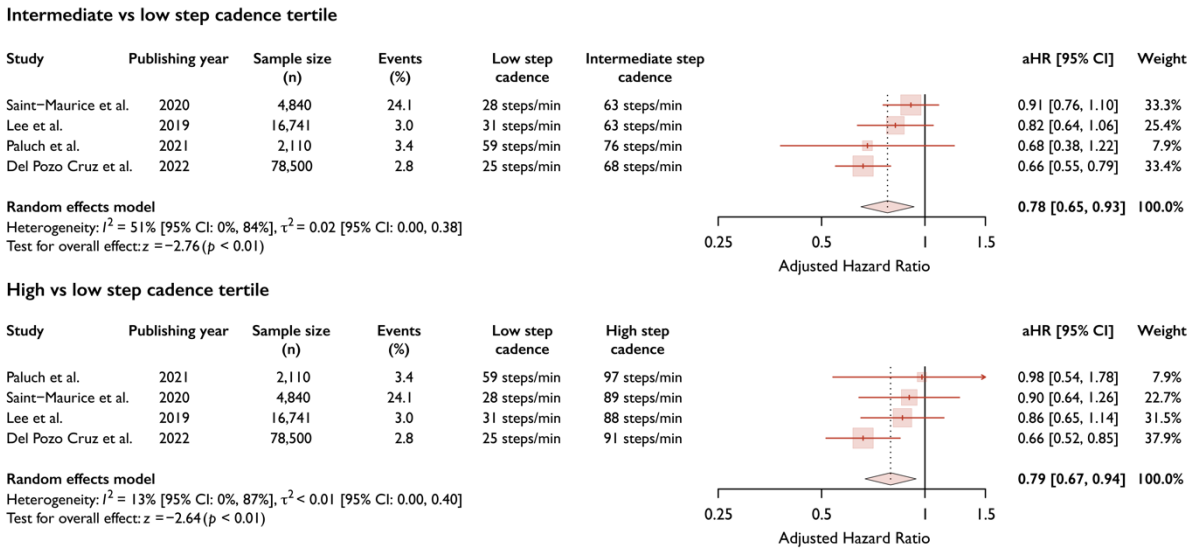


Figure 5. Association between step cadence tertiles and all-cause mortality.

Forest plot highlighting the association between 30-minute peak cadence with all-cause mortality, adjusted for confounders and total step count. Individuals in the intermediate (66 [63-67] steps/min) and high step cadence tertile (90 [89-90] steps/min) had a significantly lower mortality risk (22 and 21% respectively) compared to the low step cadence tertile (25 [25-25] steps/min) after adjustment for total step count. For each study, red vertical and horizontal lines represent the effect estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and are presented as red squares and percentages. The red diamond represents the pooled estimate and its 95% confidence interval. The low, intermediate and high step cadence reflect the average step cadence of the subjects in the respective group. CI confidence interval, aHR adjusted hazard ratio, IQR interquartile range.

Supplemental Appendix

Dose-Response Relationships of Step Count Metrics with All-Cause Mortality and Cardiovascular Diseases: A Meta-Analysis

Supplemental Methods.

Methods for creating daily step count and step cadence tertiles for categorical dose-response analysis.

Three groups were generated (i.e., low, intermediate and high daily step count) to assess the impact of stepping volume on all-cause mortality and incident CVD. For all studies the lowest and highest step count groups corresponded to the low and high step count tertile. For studies with three step count groups, the second group corresponded to the intermediate stepping tertile. For studies with four step count groups, one step count group, which was not the highest or lowest step count group, corresponded to the intermediate step count tertile based on its similarly of the median step count in that group to the intermediate tertile of the meta-analysis.

If the median daily step count was not reported, the mean daily step count was used. If only upper and lower boundaries of the step count range were reported, the midpoint was calculated to approximate the median. If the upper boundary was not presented, the assigned value corresponded to the lower boundary plus half times the spread of the group below it. Likewise, if the lower boundary was not presented, the assigned value corresponded to half times the spread of the group above it. The above-described approach was also used to create step cadence tertiles, based on the peak 30-minute cadence.

Supplemental Table 1. Systematic literature search for PubMed and Embase.

PubMed <1963 to 2022 October 12>

1	step count[Title/Abstract] OR stepping count[Title/Abstract] OR step counts[Title/Abstract] OR step volume[Title/Abstract] OR stepping volume[Title/Abstract] OR incidental step[Title/Abstract] OR incidental steps[Title/Abstract] OR incidental stepping[Title/Abstract] OR sporadic step[Title/Abstract] OR sporadic steps[Title/Abstract] OR sporadic stepping[Title/Abstract] OR purposeful step[Title/Abstract] OR purposeful steps[Title/Abstract] OR purposeful stepping[Title/Abstract] OR aerobic step[Title/Abstract] OR aerobic steps[Title/Abstract] OR aerobic stepping[Title/Abstract] OR daily step[Title/Abstract] OR daily steps[Title/Abstract] OR daily stepping[Title/Abstract]	8,300
2	accelerometer[Title/Abstract] OR accelerometry[Title/Abstract] OR actigraph[Title/Abstract] OR actigraphs[Title/Abstract] OR pedometer[Title/Abstract] OR pedometers[Title/Abstract] OR pedometry[Title/Abstract]	22,051
3	cadence[Title/Abstract] OR step rate[Title/Abstract] OR stepping rate[Title/Abstract] OR step intensity[Title/Abstract] OR stepping intensity[Title/Abstract] OR gait speed[Title/Abstract] OR walking speed[Title/Abstract] OR walk speed[Title/Abstract]	17,493
4	#1 OR #2 OR #3	44,875
5	mortality[MeSH Terms] OR mortality[Title/Abstract] OR survival[Title/Abstract] OR cardiovascular disease[Title/Abstract] OR cardiovascular diseases[MeSH Terms] OR coronary heart disease[Title/Abstract] OR coronary disease[MeSH Terms] OR ischemic heart disease[Title/Abstract] OR myocardial ischemia[MeSH Terms] OR coronary artery disease[MeSH Terms] OR coronary artery disease[Title/Abstract] OR coronary artery disease[MeSH Terms] OR stroke[Title/Abstract] OR stroke[MeSH Terms] OR heart failure[Title/Abstract] OR heart failure[MeSH Terms]	4,542,595
6	#4 AND #5	6,534

7	epidemiological studies[MeSH Terms] OR cohort studies[MeSH Terms] OR prospective studies[MeSH Terms] OR longitudinal studies[MeSH Terms] OR follow up studies[MeSH Terms]	3,018,729
8	cohort[Title/Abstract] OR prospective[Title/Abstract] OR longitudinal[Title/Abstract] OR follow-up[Title/Abstract] OR follow-up[Title/Abstract]	2,349,508
9	#7 OR #8	4,093,269
10	#6 AND #9	2,985
11	#10 NOT ("heart defects, congenital"[MeSH Terms] OR "congenital heart defect"[Title/Abstract] OR "congenital heart disease"[Title/Abstract])	2,946
12	#11 NOT (review[Publication Type] OR case reports[Publication Type])	**2,856**

Embase <1974 to 2022 October 12>

1	(step* adj3 (volume or count* or incidental or sporadic or purposeful or aerobic or daily)).ti,ab,kf.	7,754
2	exp step count/	1,431
3	exp accelerometer/	16,099
4	exp actimetry/	11,300
5	exp pedometer/	2,734
6	(acceleromet* or pedomet* or actigraph*).ti,ab,kf	41,590
7	exp walking speed/	21,079
8	cadence.ti,ab,kf.	5,515
9	(step* adj3 (rate or intensity)).ti,ab,kf.	23,504
10	(speed adj3 (walk* or gait)).ti,ab,kf.	22,208
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	105,244
12	exp cardiovascular disease/	4,662,868
13	exp ischemic heart disease/	740,655
14	exp cerebrovascular accident/	279,362
15	exp heart failure/	593,873
16	exp heart muscle ischemia/	98,646

17	exp coronary artery disease/	371,044
18	(cardiovascular disease or coronary heart disease or ischemic heart disease or myocardial ischemia or coronary artery disease or stroke or heart failure).ti,ab,kf.	1,198,566
19	12 or 13 or 14 or 15 or 16 or 17 or 18	4,815,556
20	11 and 19	13,247
21	20 not (congenital heart defects/ or congenital heart disease.ti,ab,kf.)	13,125
22	cohort studies/	769,061
23	longitudinal studies/	159,180
24	follow-up studies/	1,444,164
25	prospective studies/	694,736
26	(cohort or longitudinal or prospective).ti,ab,kf.	2,324,757
27	(follow* adj2 up).ti,ab,kf.	1,936,877
28	22 or 23 or 24 or 25 or 26 or 27	4,366,773
29	21 and 28	3,909
30	limit 29 to (conference abstract or conference paper or "conference review" or erratum)	1,311
31	29 not 30	2,598
32	remove duplicates from 31	**2,558**

Supplemental Table 2. Characteristics of the included studies.

Study	Outcome	Cohort	Population	Sample size, % women	Events, No. (%)	Follow-up, years	Age, years	Minimum wear time to be included in analysis	Daily step count, steps/day (± SD)	Fully-adjusted model
Dwyer et al., 2015 (38)	All-cause mortality	TASPED pooled cohort, Australia	Adults from Tasmania	2,576 (52.4)	219 (8.5)	11.1 (mean)	58.8 ± 13.2	Unspecified	8,856 ± 4,510	Age, sex, BMI, total energy intake, current smoking status, alcohol intake, education level, study cohort
Fox et al., 2015 (36)	All-cause mortality	OPAL project, UK	Adults aged ≥ 70 years	201 (48.8)	33 (16.4)	4.2 (mean)	70–74.9 (36.6%) 75–79.9 (26.8%) 80–84.9 (24.9%) 85+ (11.7%)	At least 10 hours for ≥ 5 days	Tertiles (%) <3,196 (31.8%) 3,196-5,170 (33.3%) >5,170 (34.8%)	Age, sex, education level, IMD, weight status, general practitioner management system, number of self-reported illnesses at baseline
Yamamoto et al., 2018 (37)	All-cause mortality	Prospective cohort, Japan	Physically-independent community-dwelling adults aged 71 years	419 (45.6)	76 (18.1)	9.8 (mean)	71 ± 0.0	≥ 3 days (no minimum hours specified)	6,470 ± 2,732	Sex, BMI, smoking status, alcohol intake, medication use

Lee et al., 2019 (17)	All-cause mortality	Women's Health study, USA	Women aged ≥ 45 years	16,741 (100)	504 (3.0)	4.3 (mean)	72.0 ± 5.7	At least 10 hours for ≥ 4 days	5,499 ± SD not reported	Age, wear time, smoking status, alcohol intake, diet, hormone therapy, family history of MI and cancer, history of CVD, cancer, and hypertension, general health, cancer screening, BMI, cholesterol, diabetes
Jefferis et al., 2019 (33)	All-cause mortality	British Regional Heart Study, UK	Men aged 71-92 years	1,274 (0)	194 (15.2)	5.0 (median)	78.4 ± 4.6	At least 10 hours for ≥ 3 days	4,938 ± 2,794	Age, geographic region, season of wear, social class, alcohol intake, smoking, sleep time, living status, BMI, mobility disability, MVPA, LIPA
Jefferis et al., 2019 (41)	CVD mortality and events	British Regional Heart Study, UK	Men aged 71-92 years	1,181 (0)	122 (10.3)	4.9 (median)	78.4 ± 4.6	At least 10 hours for ≥ 3 days	4,938 ± 2,794	Age, geographic region, season of wear, wear time, social class, alcohol intake, smoking status, sleep time, living status, BMI, mobility disability
Hansen et al., 2020 (34)	All-cause mortality	Prospective cohort, Norway	Adults and older people (20-85 years)	2,183 (43.2)	119 (5.5)	9.1 (median)	57.0 ± 10.9	At least 10 hours for ≥ 4 days	8,002 ± 3,113	Sex, wear time, VPA, education level, BMI, smoking status, alcohol intake, number of medical conditions

Oftedal et al., 2020 (35)	All-cause mortality	Hunter community study, Australia	Community-dwelling adults aged 55-86 years	1,697 (49.3)	204 (12.0)	9.6 (median)	64.4 ± 7.1	At least 9 hours for ≥ 3 days	6,898 ± 2,970	Age, diet quality score, income, smoking status
Saint-Maurice et al., 2020 (19)	All-cause mortality	NHANES, USA	Non-institutionalized individuals, aged ≥ 40 years	4,840 (50.3)	1,165 (24.1)	10.1 (mean)	56.8 ± 21.3	At least 10 hours for ≥ 1 day	9,124 ± 7,388	For both endpoints: Age, diet quality, BMI, education level, alcohol intake, smoking status, diabetes, stroke, coronary heart disease, heart failure, cancer, chronic bronchitis, emphysema, mobility limitations, self-reported general health
	CVD mortality			4,840 (50.3)	406 (8.3)	10.1 (mean)	56.8 ± 21.3		9,124 ± 7,388	
Mañas et al., 2021 (32)	All-cause mortality	Toledo Study for Healthy Aging, Spain	Adults aged ≥ 65 years	768 (53.9)	89 (11.6)	5.7 (mean)	78.8 ± 4.9	At least 8 hours for ≥ 4 days	5,835 ± 3,445	For both endpoints: Wear time, age, sex, BMI, education level, income, marital status, comorbidities
	Cardiac hospitalizations			740 (53.9)	32 (4.3)	4.8 (mean)	76.7 ± 4.9		5,816 ± 3,435	

Paluch et al., 2021 (18)	All-cause mortality	CARDIA, USA	Adults aged 38 – 50 years	2,110 (57.1)	72 (3.4)	10.8 (mean)	45.2 ± 3.6	At least 10 hours for ≥ 3 days	9,146 [7,307, 11,162]	Age, wear time, race, sex, education level, study center, BMI, smoking status, alcohol intake, SBP, hypertension, diabetes, hyperlipidemia, history of CVD, self-rated health
Del Pozo Cruz et al. (2022) (40)	All-cause mortality CVD mortality	UK Biobank, UK	Adults aged 35-85 years	78,500 (55.3)	2,179 (2.8) 664 (0.8)	7.0 (median) 7.0 (median)	61.1 ± 7.9	At least 16 hours for ≥ 3 days	7,198 ± 4,609	For both endpoints: age, sex, race, education, socioeconomic status, smoking status, alcohol, fruit and vegetable consumption, family history of cancer and/or CVD, medication use, accelerometer-measured sleep time, and number of days accelerometer was worn.

Data are presented as mean ± SD, median [IQR], or number (%), as appropriate. BMI body mass index, CVD cardiovascular disease, GP general practitioner, IMD index of multiple deprivation, IQR interquartile range, LIPA light physical activity, MI myocardial infarction, MVPA moderate to vigorous physical activity, SBP systolic blood pressure, SD standard deviation, VPA vigorous physical activity

Supplemental Table 3. Quality assessment for the included studies using the Newcastle-Ottawa Scale.

Study	Year	Outcome	S1) Representativeness	S2) Selection non-exposed cohort	S3) Ascertainment exposure	S4) Absence outcome start of	C1) Comparability cohorts	C1) Comparability cohorts	O1) Outcome Assessment	O2) Follow-up duration	O3) Loss to follow-up	Selection score	Comparability score	Outcome score	Total score
Del Pozo Cruz et al. (40)	2022	Mortality CVD	* *	* *	* *	* *	* *	* *	* *	* *	* *	4	2	3	9
Dwyer et al. (38)	2015	Mortality	*	*	*	*	*	*	*	*	*	4	2	3	9
Fox et al. (36)	2015	Mortality		*	*	*	*	*	*	*	*	3	2	3	8
Hansen et al. (34)	2020	Mortality	*	*	*	*		*	*	*	*	4	1	3	8
Jefferis et al. (33)	2019	Mortality	*	*	*	*	*	*	*	*		4	2	2	8
Jefferis et al. (41)	2019	CVD	*	*	*		*	*	*	*		3	2	2	7

Lee et al. (17)	2019	Mortality	*	*	*	*	*	*	*	*	*	4	2	3	9
Mañas et al. (32)	2021	Mortality CVD	* *	* *	* *		* *	* *	* *	* *	* *	3 3	2 2	3 3	8 8
Oftedal et al. (35)	2020	Mortality	*	*	*	*	*	*	*	*		4	2	2	8
Paluch et al. (18)	2021	Mortality	*	*	*		*	*	*	*	*	3	2	3	8
Saint-Maurice et al. (19)	2020	Mortality CVD	* *	* *	* *	*	* *	* *	* *	* *	* *	4 3	2 2	3 3	9 8
Yamamoto et al. (37)	2018	Mortality		*	*	*		*		*	*	3	1	2	6

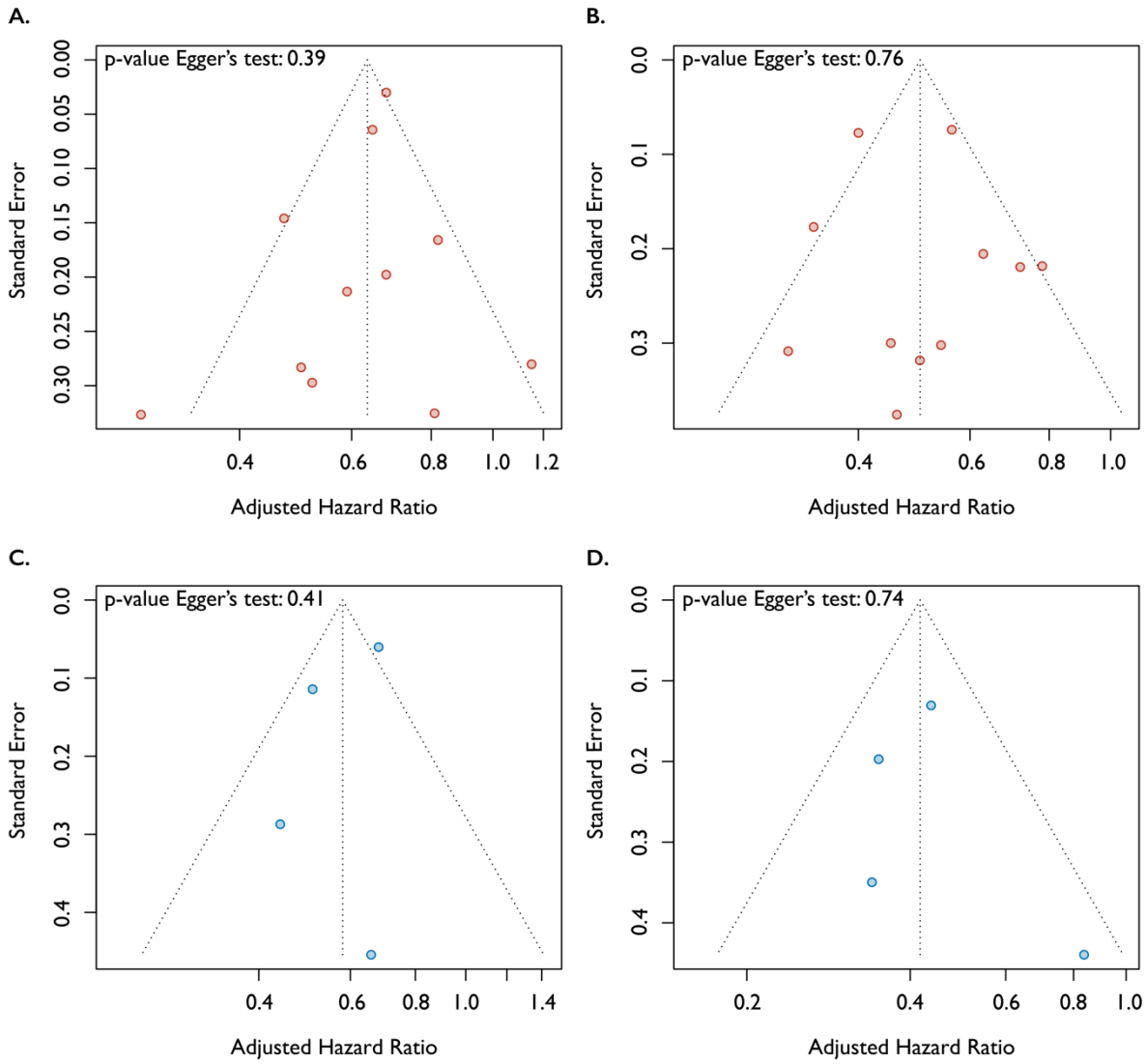
Studies were scored for each criterion of the Newcastle-Ottawa scale, where a total score of 1-3, 4-6 and 7-9 points reflect a high, intermediate, or low risk of bias respectively.

Supplemental Table 4. Minimal dose for health improvement for various baseline step counts.

	All-cause mortality		Incident CVD	
Reference level (steps/day)	Minimal dose for health improvement (steps/day)	Risk reduction compared to reference (aHR [95% CI])	Minimal dose for health improvement (steps/day)	Risk reduction compared to reference (aHR [95% CI])
2,000	2,517	0.92 [0.84, 0.999]	2,735	0.89 [0.79, 0.999]
3,000	3,413	0.93 [0.87, 0.999]	3,605	0.91 [0.83, 0.999]
4,000	4,351	0.95 [0.90, 0.999]	4,564	0.92 [0.85, 0.999]
5,000	5,356	0.95 [0.90, 0.999]	5,659	0.92 [0.84, 0.999]
6,000	6,440	0.95 [0.89, 0.999]	6,894	0.91 [0.82, 0.999]
7,000	7,589	0.94 [0.88, 0.999]	8,268	0.90 [0.81, 0.999]
8,000	8,808	0.94 [0.88, 0.999]	9,932	0.91 [0.82, 0.999]
9,000	10,133	0.94 [0.89, 0.999]	Not identified	Not identified
10,000	Not identified	Not identified	Not identified	Not identified
11,000	Not identified	Not identified	Not identified	Not identified
12,000	Not identified	Not identified	Not identified	Not identified
13,000	Not identified	Not identified	Not identified	Not identified
14,000	Not identified	Not identified	Not identified	Not identified
15,000	Not identified	Not identified	Not identified	Not identified
16,000	Not identified	Not identified	Not identified	Not identified

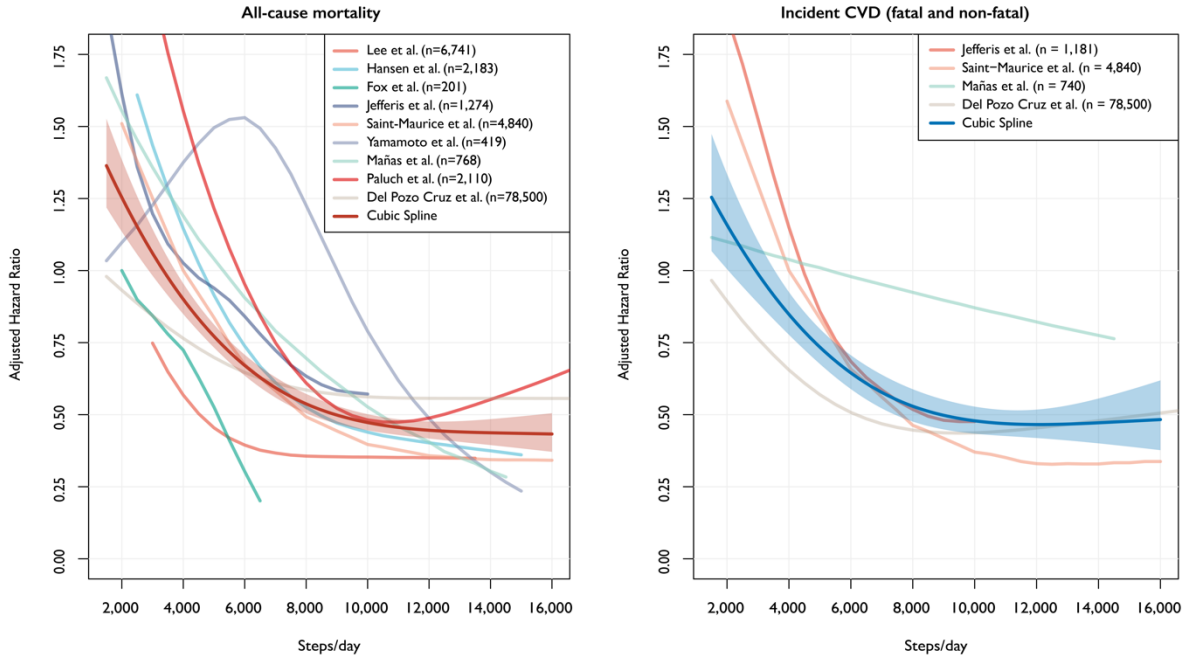
Different step counts and the associated minimal dose to significantly reduce the risk for adverse outcomes are presented for all-cause mortality and incident CVD. The median number of steps to gain significant risk reductions for all-cause mortality and CVD were 479 [IQR: 399, 644] and 735 [IQR: 632, 1081] steps/day above the reference category. aHR = adjusted hazard ratio, CI = confidence interval, IQR = interquartile range.

Supplemental Figure 1. Funnel plots for the association between daily step count categories and health outcomes in the general population.



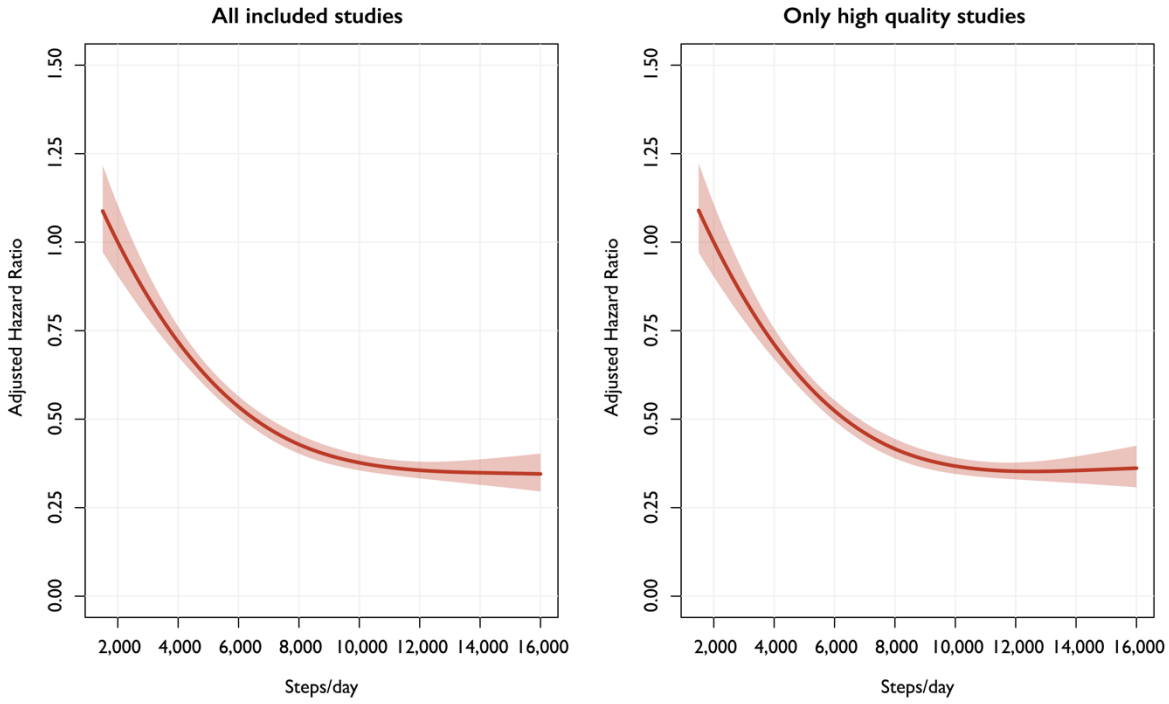
Funnel plots are presented for the association between A) intermediate vs low daily step count and all-cause mortality risk, B) high vs low daily step count and all-cause mortality risk, C) intermediate vs low daily step count and incident CVD risk, and D) high vs low daily step count and incident CVD risk.

Supplemental Figure 2. Dose-response associations of daily step count with all-cause mortality and incident CVD, including all individual studies.



Dose-response curves of the different included studies for the association between daily step count versus all-cause mortality (left panel) and incidence of cardiovascular diseases (CVD, right panel) are presented. Adjusted hazard ratios from published dose-response curves were extracted and pooled using restricted cubic spline models. To visualize model fit, the dose-response curves are presented without alteration of the reference level. Shaded areas indicate the corresponding 95% confidence interval. aHR adjusted hazard ratio, CVD cardiovascular disease.

Supplemental Figure 3. Dose-response association between daily step count and all-cause mortality, including only high-quality studies.

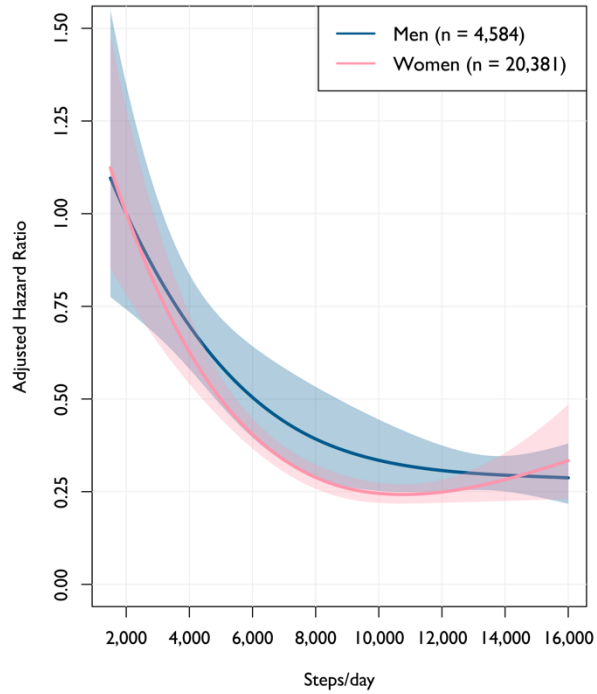


	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,517	0.92 (0.84, 0.99)
Optimum dose	8,763	0.40 (0.38, 0.43)
Risk reduction at 16,000 steps	16,000	0.35 (0.30, 0.40)

	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,522	0.91 (0.84, 0.99)
Optimum dose	8,377	0.40 (0.38, 0.43)
Risk reduction at 16,000 steps	16,000	0.36 (0.31, 0.43)

Dose-response curves for the association between daily step count with all-cause mortality are presented when including all studies (left panel) and only high quality studies (right panel, Newcastle-Ottawa Scale ≥ 7). Adjusted hazard ratios from published dose-response curves were extracted and pooled using restricted cubic spline models. Compared to the reference level of 2,000 steps/day, the minimum dose to significantly reduce the risk of all-cause mortality was 2,517 steps/day (all studies) and 2,522 steps/day (high-quality studies). The optimum dose, defined as the maximal risk reduction at the least effort, was established at 8,763 and 8,377 steps/day when including all studies and only high-quality studies respectively. Shaded areas indicate the corresponding 95% confidence interval. aHR adjusted hazard ratio, CVD cardiovascular disease.

Supplemental Figure 4. Dose-response association between daily step count and all-cause mortality, stratified by sex.

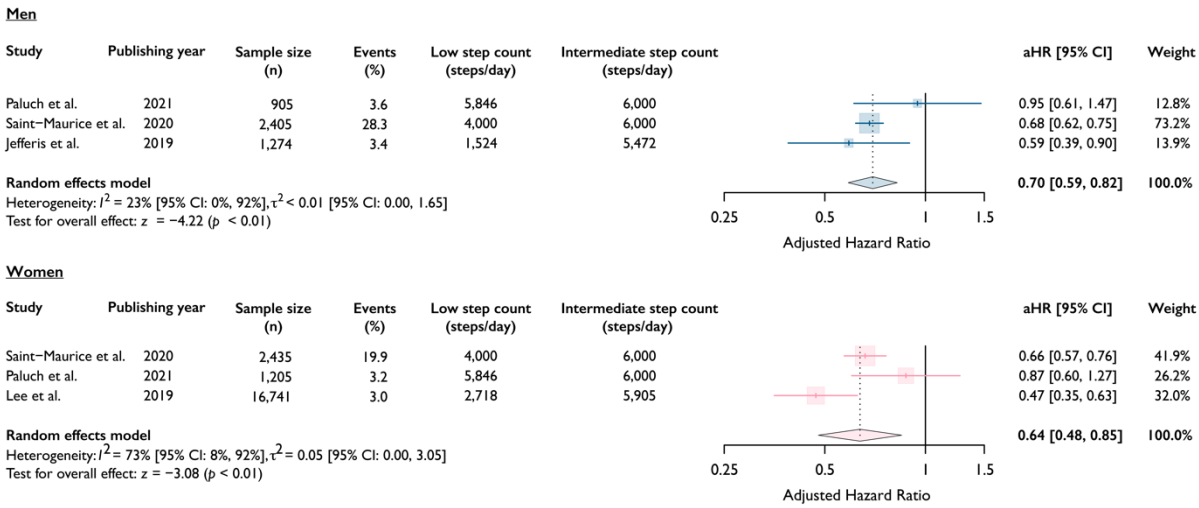


Men	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	3,155	0.81 (0.66, 0.99)
Optimum dose	6,738	0.46 (0.35, 0.60)
Risk reduction at 16,000 steps	16,000	0.29 (0.22, 0.38)

Women	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,864	0.82 (0.67, 0.99)
Optimum dose	7,690	0.30 (0.27, 0.34)
Risk reduction at 16,000 steps	16,000	0.33 (0.23, 0.49)

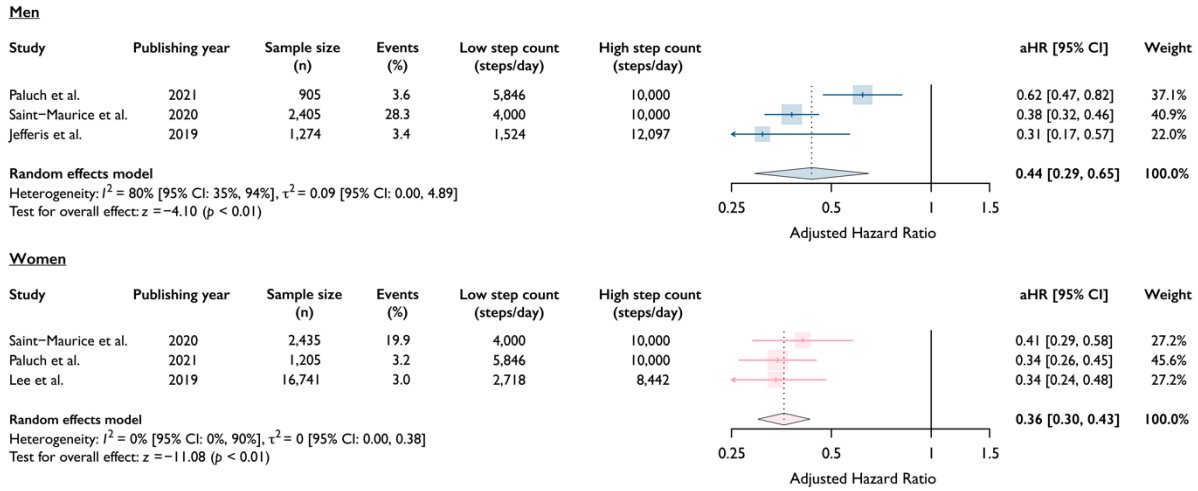
Dose-response curves for the association between daily step count and all-cause mortality are presented for men (blue) and women (pink). Adjusted hazard ratios from published dose-response curves were extracted and pooled using restricted cubic spline models. Compared to the reference level of 2,000 steps/day, the minimum dose to significantly reduce the risk of all-cause mortality was 3,155 steps/day for men and 2,864 steps/day for women. The optimum dose, defined as the maximal risk reduction at the least effort, was established at 6,738 and 7,690 steps/day for men and women respectively. Shaded areas indicate the corresponding 95% confidence interval. aHR adjusted hazard ratio, CVD cardiovascular disease.

Supplemental Figure 5. Forest plot for the association between daily step count and all-cause mortality, stratified for sex – intermediate step count.



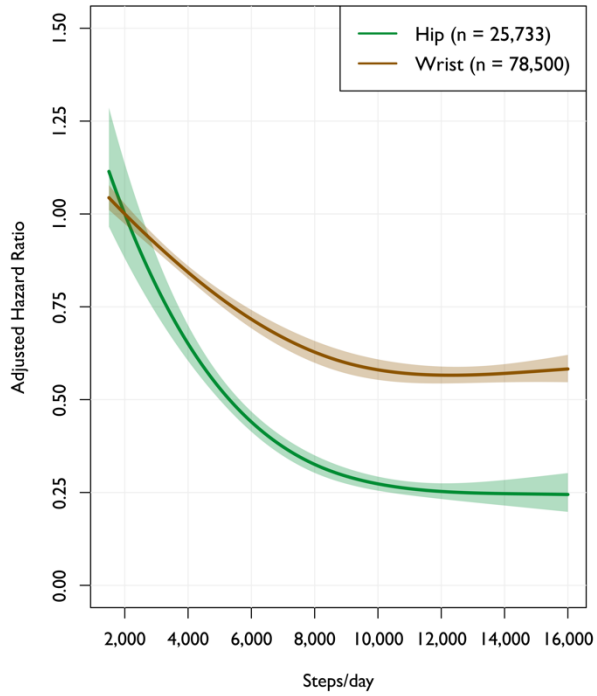
Men (blue, 6,000 [5,763-6,000] steps/day) and women (pink, 6,000 [5,953-6,000]) in the intermediate step count tertile had a significantly lower mortality risk (30 and 36% respectively) compared to men (4,000 [2,762-4923] steps/day) and women (4,000 [3,359-4,923] steps/day) in the low step count tertile. For each study, blue/pink vertical and horizontal lines represent the effect estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and were presented as shaded squares and percentages. The pink/blue diamond represents the pooled estimate and its 95% confidence interval. The low and intermediate step counts reflect the average step count of the subjects in the respective group. CI confidence interval, aHR adjusted hazard ratio, IQR interquartile range.

Supplemental Figure 6. Forest plot for the association between daily step count and all-cause mortality, stratified for sex – high step count.



Men (blue, 10,000 [10,000-11,049] steps/day) and women (pink, 10,000 [9,221-10,000] in the high step count tertile had a significantly lower mortality risk compared to men (4,000 [2,762-4923] steps/day) and women (4,000 [3,359-4,923] steps/day) in the low step count tertile. For each study, blue/pink vertical and horizontal lines represent the effect estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and were presented as shaded squares and percentages. The pink/blue diamond represents the pooled estimate and its 95% confidence interval. The low and high step counts reflect the average step count of the subjects in the respective group. CI confidence interval, aHR adjusted hazard ratio, IQR interquartile range.

Supplemental Figure 7. Dose-response association between daily step count and all-cause mortality, stratified by accelerometry wear location.

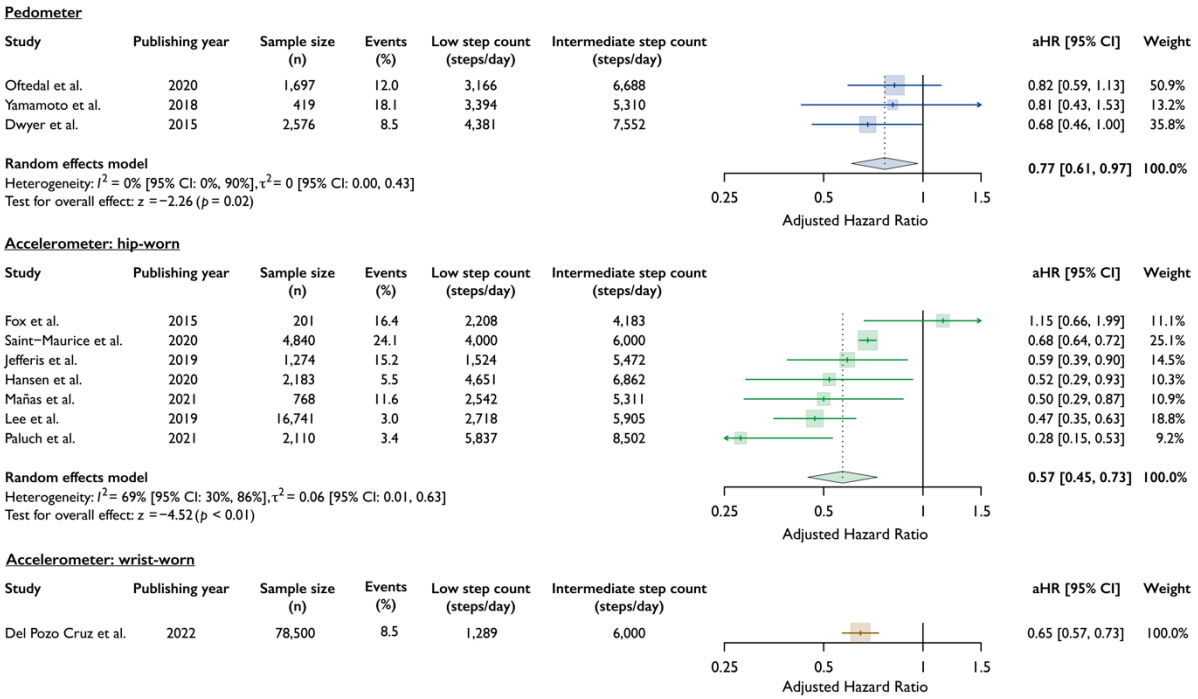


Wrist-worn	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,290	0.98 (0.95, 0.99)
Optimum dose	8,073	0.64 (0.62, 0.67)
Risk reduction at 16,000 steps	16,000	0.63 (0.58, 0.68)

Hip-worn	Steps/day	Adjusted hazard ratio (95% CI)
Minimum dose	2,514	0.90 (0.80, 0.99)
Optimum dose	8,951	0.30 (0.28, 0.32)
Risk reduction at 16,000 steps	16,000	0.25 (0.20, 0.30)

Dose-response curves for the association between daily step count and all-cause mortality are presented for studies using wrist-worn (brown) and hip-worn (green) accelerometers. Adjusted hazard ratios from published dose-response curves were extracted and pooled using restricted cubic spline models. Compared to the reference level of 2,000 steps/day, the minimum dose to significantly reduce the risk of all-cause mortality was 2,290 steps/day and 2,514 steps/day for studies using wrist-worn and hip-worn accelerometers respectively. The optimum dose, defined as the maximal risk reduction at the least effort, was established at 8,073 and 8,951 steps/day for studies using wrist-worn and hip-worn accelerometers respectively. Shaded areas indicate the corresponding 95% confidence interval. aHR adjusted hazard ratio, CVD cardiovascular disease.

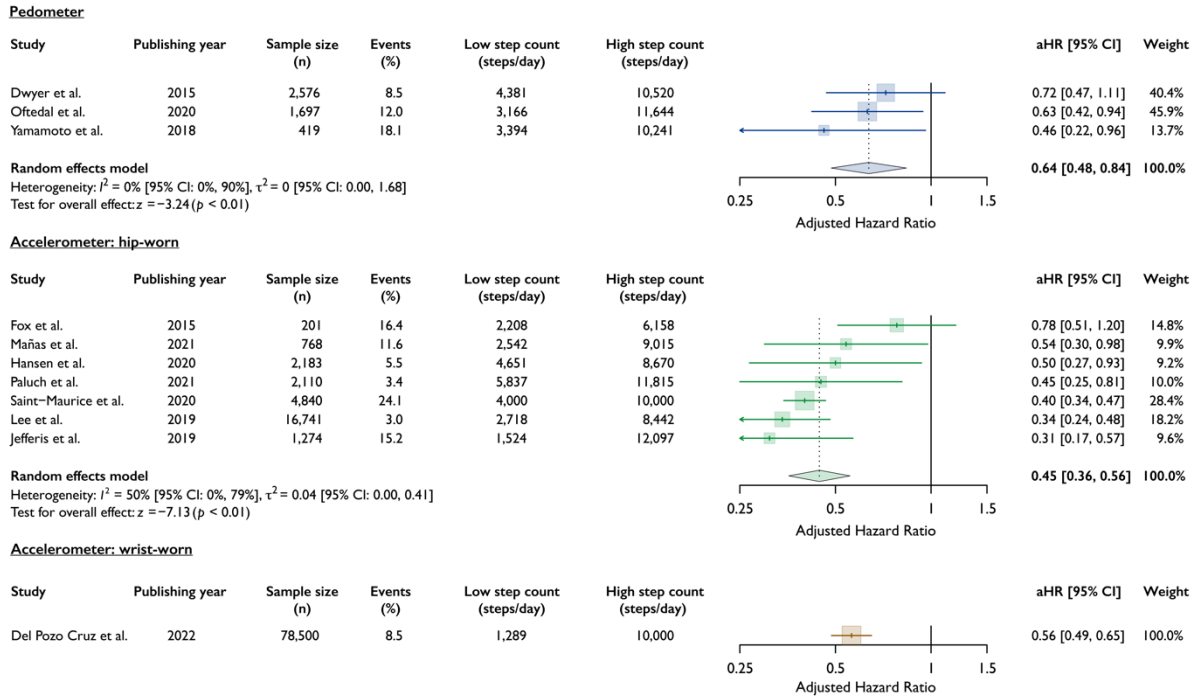
Supplemental Figure 8. Forest plot for the association between step count and mortality, stratified by device type – intermediate step count.



Individuals in the intermediate step count tertile (pedometer: 6,688 [5,999-7,120] steps/day; hip-worn accelerometry: 5,905 [5,392-6,431] steps/day; wrist-worn accelerometry: 6,000 steps/day) had a significantly lower mortality risk compared to those in the low step count tertile (pedometer: 3,394 [3,280-3,888] steps/day; hip-worn accelerometry: 2,718 [2,375-4,326] steps/day; wrist-worn accelerometry: 1,289 steps/day).

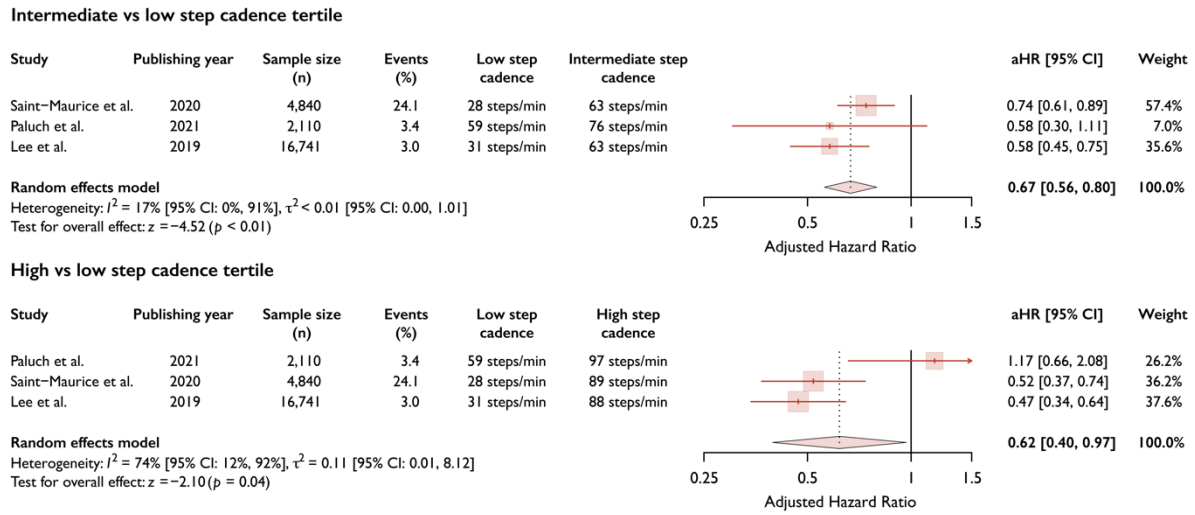
For each study, blue/green/brown vertical and horizontal lines correspond to the point estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and are presented as shaded squares and percentages. The blue/green diamond represents the pooled estimate and its 95% confidence interval. The low and intermediate step counts reflect the average step count of the subjects in the respective group. CI confidence interval, aHR adjusted hazard ratio, IQR interquartile range.

Supplemental Figure 9. Forest plot for the association between step count and mortality, stratified for device type – high step count.



Individuals in the high step count tertile (pedometer: 10,520 [10,381-11,082] steps/day; hip-worn accelerometry: 9,015 [8,556-10,908] steps/day; wrist-worn accelerometry: 10,000 steps/day) had a significantly lower mortality risk (36, 55, and 44% respectively) compared to those in the low step count tertile (pedometer: 3,394 [3,280-3,888] steps/day; hip-worn accelerometry: 2,718 [2,375-4,326] steps/day; wrist-worn accelerometry: 1,289 steps/day). For each study, blue/green/brown vertical and horizontal lines correspond to the point estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and are presented as shaded squares and percentages. The diamonds represent the pooled estimates and their 95% confidence interval. The low and high step counts reflect the average step count of the subjects in the respective group. CI confidence interval, aHR adjusted hazard ratio, IQR interquartile range.

Supplemental Figure 10. Forest plot for the association between stepping cadence and all-cause mortality.



Forest plot highlighting the association between 30-minute peak cadence with all-cause mortality, without additional adjustment for step count. Individuals in the intermediate (63 [63-63] steps/min) and high step cadence tertile (88 [88-88] steps/min) had a significantly lower mortality risk compared to the low step cadence tertile (30 [28-30] steps/min). For each study, red vertical and horizontal lines correspond to the point estimate and 95% confidence intervals. Study weights were obtained via a random-effects analysis and are presented as shaded squares and percentages. The red diamond represents the pooled estimate and its 95% confidence interval. The low, intermediate and high step cadence reflect the average step cadence of the subjects in the respective group. CI confidence interval, aHR adjusted hazard ratio, IQR interquartile range.