

ORIGINAL RESEARCH ARTICLE

Prospective Association of Daily Steps With Cardiovascular Disease: A Harmonized Meta-Analysis

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BACKGROUND: Taking fewer than the widely promoted “10 000 steps per day” has recently been associated with lower risk of all-cause mortality. The relationship of steps and cardiovascular disease (CVD) risk remains poorly described. A meta-analysis examining the dose–response relationship between steps per day and CVD can help inform clinical and public health guidelines.

METHODS: Eight prospective studies (20 152 adults [ie, ≥18 years of age]) were included with device-measured steps and participants followed for CVD events. Studies quantified steps per day and CVD events were defined as fatal and nonfatal coronary heart disease, stroke, and heart failure. Cox proportional hazards regression analyses were completed using study-specific quartiles and hazard ratios (HR) and 95% CI were meta-analyzed with inverse-variance–weighted random effects models.

RESULTS: The mean age of participants was 63.2±12.4 years and 52% were women. The mean follow-up was 6.2 years (123 209 person-years), with a total of 1523 CVD events (12.4 per 1000 participant-years) reported. There was a significant difference in the association of steps per day and CVD between older (ie, ≥60 years of age) and younger adults (ie, <60 years of age). For older adults, the HR for quartile 2 was 0.80 (95% CI, 0.69 to 0.93), 0.62 for quartile 3 (95% CI, 0.52 to 0.74), and 0.51 for quartile 4 (95% CI, 0.41 to 0.63) compared with the lowest quartile. For younger adults, the HR for quartile 2 was 0.79 (95% CI, 0.46 to 1.35), 0.90 for quartile 3 (95% CI, 0.64 to 1.25), and 0.95 for quartile 4 (95% CI, 0.61 to 1.48) compared with the lowest quartile. Restricted cubic splines demonstrated a nonlinear association whereby more steps were associated with decreased risk of CVD among older adults.

CONCLUSIONS: For older adults, taking more daily steps was associated with a progressively decreased risk of CVD. Monitoring and promoting steps per day is a simple metric for clinician–patient communication and population health to reduce the risk of CVD.

Key Words: cardiovascular disease ■ exercise ■ public health ■ risk reduction behavior

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Institutes for Health.

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Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.122.061288>.

For Sources of Funding and Disclosures, see page XXX.

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Clinical Perspective

What Is New?

- In this meta-analysis of 8 studies, taking more daily steps was associated with a progressively lower risk of cardiovascular disease (CVD) among older adults (ie, ≥ 60 years of age).
- Among older adults, taking ≈ 6000 to 9000 steps per day was associated with 40% to 50% lower risk of cardiovascular disease, compared with taking ≈ 2000 steps per day.

What Are the Clinical Implications?

- Monitoring and promoting steps per day can be a simple, easy to interpret metric used for clinician–patient communication and population health to reduce the risk of cardiovascular disease events.
- Findings from the present study suggest that interventions may consider setting attainable step goals for cardiovascular health in older adults that take fewer than 10 000 steps per day.

Nonstandard Abbreviations and Acronyms

CVD cardiovascular disease

Greater amounts of physical activity are associated with decreased risk of cardiovascular disease (CVD), including coronary heart disease, stroke, and heart failure.^{1–3} The 2018 US federal guidelines⁴ and the 2019 ACC/AHA Guideline on the Primary Prevention of CVD⁵ recommend at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity or an equivalent combination of aerobic activity per week. Despite the evidence, many adults do not engage in recommended amounts of physical activity.^{6,7}

Cardiovascular risk reduction interventions using devices, often monitoring steps per day, are effective strategies to increase physical activity.⁸ A standard goal is often 10 000 steps per day, although this goal is not evidence-based, having originated from a marketing campaign in Japan.⁹ A recent meta-analysis on steps and all-cause mortality demonstrated reductions in risk occur at fewer than 10 000 steps per day.¹⁰ A previous meta-analysis of 4 published studies demonstrated a nonlinear association of daily steps and CVD risk.¹¹ However, this meta-analysis included studies with large heterogeneity in CVD definition and analytic approach and was unable to investigate associations by age or sex.

A harmonized meta-analysis of prospective studies examining steps per day would be useful in providing health care professionals with a precise estimate of steps per day needed for CVD benefit, informing provider–patient interactions and population health guidelines.

Therefore, the primary objective of the present analysis is to test whether steps per day is associated with CVD risk. Because of the known age and sex differences in the risk of CVD,^{2,12,13} all associations were tested among female and male patients, and among younger and older adults. It was hypothesized that there would be a dose–response association of steps per day and stepping rate with CVD.

METHODS

The data, methods used in the analyses, and materials that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

The Steps for Health Collaborative is a consortium formed to investigate the associations of device-measured step volume and rate with prospective health outcomes among adults. The Collaborative identified studies through a 2019 systematic review,¹⁴ of which 3 of 4 studies agreed to participate, but there were too few for a meta-analysis. An additional 5 studies were identified through awareness of studies measuring steps and CVD, culminating in 8 studies meeting inclusion criteria of device-measured steps and prospective follow-up for CVD events in adult populations (ie, ≥ 18 years of age).

The Newcastle-Ottawa quality assessment scale was used to assess the methodologic quality of each study.¹⁵ Assessments were performed independently by 2 reviewers (A.P., S.B.), and disagreements were resolved by consensus.

Individual Study Data Processing and Analyses

Investigators from each study processed their participant-level data using a standardized protocol to limit heterogeneity in analyses across studies developed by the Steps for Health Collaborative. Studies quantified step volume as steps per day, averaged for the 3 to 7 days where step data were collected. Baseline was designated as the time point when steps data were collected. A participant's first subsequent fatal or nonfatal CVD event was considered the primary outcome. Each study defined CVD as adjudicated stroke, coronary heart disease, or heart failure (Table S1). All studies were approved by an institutional review committee and participants gave informed consent.

Study-Level Analyses

All studies followed a standardized analytic plan developed by the Collaborative. Studies categorized steps per day into study-specific quartiles and examined associations with CVD events (reference: lowest quartile) using Cox proportional hazards regression (satisfying proportional hazards assumptions) producing hazard ratios (HRs) and 95% CIs. Models were completed for each study's overall sample, by age group and by sex, where applicable. Age was grouped at < 60 years or ≥ 60 years based on the World Health Organization's definition of "older persons" from the 2020 Decade of Healthy Ageing Baseline Report.^{16,17} Model 1 adjusted for age and sex (when studies had both sexes). Model 2 adjusted for age,

sex, race/ethnicity, education or income, body mass index, device wear time, lifestyle factors (eg smoking, alcohol use), and study-specific variables representing diabetes, hypertension, high cholesterol, other chronic conditions, and self-rated health or functional status (Table S1). For the 4 studies with step rate, the same analytic approach was followed; an additional model (model 3) adjusted for steps per day using the residual method where step rate was regressed on steps per day and the resulting step rate residuals and steps per day were independent variables in the model.^{18,19}

Meta-Level Analysis

The total number of participants, CVD events, and person-years of follow-up were summed across all studies. For the total sample, median steps per day by quartile were calculated from the medians of the individual studies. Pooled HRs and 95% CIs were computed using inverse-variance weighted random effects models. The final adjusted model (model 2) was the primary model. Because of the known associations of age and sex with CVD,¹³ a priori stratified analyses were conducted by age and sex for the associations of CVD with steps per day. Heterogeneity across studies was determined by I² statistics,²⁰ representing the proportion of total variation attributable to systematic differences between studies rather than chance. I² values were considered low (<25%), moderate (25%-75%), or high (>75%).²⁰ Funnel plots were used to assess study bias by comparing study HRs against SEs; an Egger test was used for funnel plot symmetry.²¹

Restricted cubic spline models were used to generate log-transformed hazard ratios from model 2 with knots at 10th, 50th, and 90th percentiles of steps per day for the total sample, by age and sex.²² References were set at the median of the study-level medians in the lowest quartile group. Multiplicative interaction terms were used to test for differences by age and sex. The Wald test was used to evaluate nonlinearity.^{23,24}

To evaluate the robustness of findings, the following series of sensitivity analyses was conducted: (1) participants with CVD at baseline were excluded to investigate incident CVD; (2) findings were stratified by publication status to test for publication bias (3 published, 5 unpublished); (3) a "leave-one-out analysis" to exclude 1 study at a time to determine the influence of any single study with an extreme result; (4) stratification by device type (ie, pedometer vs accelerometer); and (5) analysis of stepping rate using several different thresholds—peak 30-minute stepping rate; peak 60-minute stepping rate; minutes per day at a stepping rate >40 steps per minute (intentional walking); and minutes per day at a stepping rate ≥100 steps per minute (moderate intensity walking pace).²⁵ Peak 30- and 60-minute stepping rates were calculated by selecting the 30- or 60-minute time periods (not necessarily consecutive) throughout each day with the most number of steps per minute. Stepping rate variables were calculated per day and averaged across all days.²⁵ Meta-analyses were performed using Rv4.1 and SAS v9.4 (Cary, NC).

RESULTS

The total sample included 20 152 participants (mean age, 63.2±12.4 years; female sex, 52%; race/ethnicity, >70% non-Hispanic White) with a mean study follow-up time of 6.2 years (range, 2.8 to 12.6 years; 123 209 person-

years; Table 1). The overall median of the median steps per day was 4323 [IQR, 2760 to 6924] for older adults and 6911 [IQR, 4783 to 9794] for younger adults. A total of 1523 events were reported (12.4 per 1000 person-years). The Newcastle Ottawa quality scores were high, ranging from 7 to 9 out of a possible 9 points (Table S2).

There were significant subgroup differences by age in the association of steps per day with CVD events in third (P value = 0.048) and fourth quartile comparisons (P value = 0.014) compared to the first quartile (Figure 1). Among 7 studies of older adults (ie, ≥60 years of age), there were 1210 events among 12 741 individuals (19.3 events per 1000 person-years). There was a significant association in age- and sex-adjusted model 1 and results remained significant in the final adjusted model. In the final adjusted model 2, the HR for risk of CVD was 0.80 (0.69 to 0.93) in the second quartile, 0.62 (0.52 to 0.74) in the third quartile, and 0.51 (0.41 to 0.63) in the fourth quartile (Figure 1), compared with the lowest quartile. In the spline model, there was a significant curvilinear association among older adults (ie, ≥60 years of age) P value for nonlinearity <0.0001; Figure 2).

Among 4 studies of younger adults (ie, <60 years of age), there were 313 events among 7411 individuals (5.1 events per 1000 person-years). Compared with the first quartile, there was a significant association in the age- and sex-adjusted model 1's third (0.72 [0.53 to 0.99]) and fourth (0.74 [0.54 to 0.99]) quartiles. Results were no longer significant in the final adjusted model. Compared with the lowest quartile, the HR for risk of CVD was 0.79 (0.46 to 1.35) in the second quartile, 0.90 (0.64 to 1.25) in the third quartile, and 0.95 (0.61 to 1.48) in the fourth quartile in the final adjusted model 2 (Figure 1). There was no significant association of steps per day and CVD events in the spline model for younger adults (Figure 2).

The HR in the final adjusted model in female participants was 0.81 (0.62 to 1.04) in the second quartile, 0.68 (0.48 to 0.97) in the third quartile, and 0.51 (0.35 to 0.76) in the fourth quartile (Figure 1), compared with the lowest quartile. The HR for male participants was 0.76 (0.63 to 0.90) in the second quartile, 0.63 (0.52 to 0.76) in the third quartile, and 0.68 (0.51 to 0.89) in the fourth quartile (Figure 1), compared with the lowest quartile. There were no significant subgroup differences by sex in quartile comparison or spline models. The spline models demonstrated a nonlinear (P value = 0.001 for male participants, P value = 0.012 for female participants for nonlinearity) dose-response association with the leveling of the curve observed at ≈8000 steps per day for male and female patients (Figure S3).

Restricting the analysis to individuals without known CVD at baseline showed similar results. Among 6 studies excluding participants with a history of CVD at baseline, compared with the lowest quartile, the HR for incident CVD events was 0.74 (0.60 to 0.91) in the second quartile, 0.60 (0.47 to 0.77) in the third quartile, and 0.55 (0.40 to 0.76) in the fourth quartile (Table 2).

Table 1. Selected Characteristics of Studies

	Country	Study entry	Step device	No. of participants	Age, mean±SD, y	Female sex (%)	Steps per day, median [interquartile range]	Follow-up, mean, y	No. of cardiovascular events*
Published studies									
British Regional Heart Study ⁴¹	United Kingdom	2010–2012	ActiGraph GT3X	1172	78.4±4.6	0%	4572 [2848–6296]	4.6	122
Lifestyle Interventions and Independence for Elders ⁴²	United States	2010–2013	ActiGraph GT3X	1341	78.7±5.2	67%	2415 [1627–3353]	3.1	202
Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research ⁴³	40 Countries	2002–2004	Accusplit AE120	7271	63.7±6.9	51%	5662 [3435–8563]	6.3	730
Unpublished studies									
Atherosclerosis Risk in Communities Study	United States	2016–2017	ActiGraph GT3X	452	78.4±4.7	59%	3065 [2083–4454]	2.8	34
Coronary Artery Risk Development in Young Adults	United States	2005–2006	ActiGraph 7164	2085	45.2±3.6	57%	9164 [7324–11163]	10.7	71
Framingham Heart Study	United States	2008–2014	Actical	4223	55.3±13.9	54%	6906 [4809–9419]	7.0	151
Healthy Ageing Initiative	Sweden	2012–2018	ActiGraph GT3X	3207	70.4±0.1	51%	6967 [5032–8991]	3.2	139
Jackson Heart Study	United States	2000	Yamax SW200	401	60.2±9.8	61%	4748 [2847–7284]	12.6	74
Summary†		Range, 2000–2018	5 devices (all waist-worn)	20 152	63.2±12.4	52%	5459 [3353–8029]	6.2	1523

*Cardiovascular events are defined as fatal or nonfatal and include coronary heart disease, stroke, and heart failure.

†Summary age, percentage female, and years of follow-up are calculated as means at the individual-level; summary steps per day is calculated as the median at the study-level.

In sensitivity analyses, there were no subgroup differences by publication status (3 published vs 5 unpublished; [Figure S4](#)) or by device type (6 accelerometer vs 2 pedometer; [Figure S5](#)). There was no significant effect modification by device type influencing the studies' effect sizes when including device type as a covariate in the meta-regression model (P values for test of interaction > 0.05). The magnitude or direction of association between steps per day and CVD did not change when excluding any one study ([Table S3](#)). We reanalyzed data using fixed effects inverse-variance method, and the main findings were unchanged ([Table S4](#)). Heterogeneity (I^2) was low to moderate, ranging from 0 to 54% across quartiles ([Figure 1](#)). Funnel plots had minor asymmetry among lower weighted studies with visual inspection ([Figure S2B](#)). Egger's test for symmetry suggested no evidence of study selection bias. There was no association between any threshold of stepping rate (30-minute, 60-minute, or time spent at ≥ 40 or ≥ 100 steps per minute) and CVD events before or after adjusting for steps per day ([Table S5](#), [Figures S5 to S9](#)).

DISCUSSION

In this meta-analysis of 8 prospective studies, taking more steps per day was associated with lower CVD in older adults (ie, ≥ 60 years of age). Taking 6000 to 9000 steps per day was associated with a 40% to 50% lower

risk of CVD, compared with taking 2000 steps per day. Findings from this meta-analysis can be used to generate evidence-based guidelines for cardiovascular benefit.

The curvilinear pattern observed in the steps and CVD dose-response curves are similar to a recent meta-analysis on steps and all-cause mortality in which there was an incrementally lower risk of mortality until leveling occurred at ≈ 6000 to 8000 in older adults.¹⁰ These recent results on steps and mortality included 15 studies, 7 of which are included in the present meta-analysis on CVD. The steep early slope suggests that taking more steps is better, particularly for less active individuals taking fewer steps per day. In addition, although the slope is not as steep after 6000 steps per day, larger step counts appear to be associated with a continuing reduced risk of CVD in older adults. This curvilinear relationship is consistent with meta-analyses on self-reported physical activity and coronary heart disease and stroke.^{1,26} Conversely, a meta-analysis on heart failure risk reported a linear dose-response relationship with self-reported physical activity.²⁷ The present study was unable to examine associations of steps with subtypes of CVD (eg, heart failure, stroke) representing an area for future investigation.

Older adults who achieve higher thresholds of steps per day demonstrate a 40% to 50% lower risk for CVD, a magnitude that is similar to previous studies using accelerometer-measured total minutes per day of physical activity.^{28,29} This magnitude of association is stronger

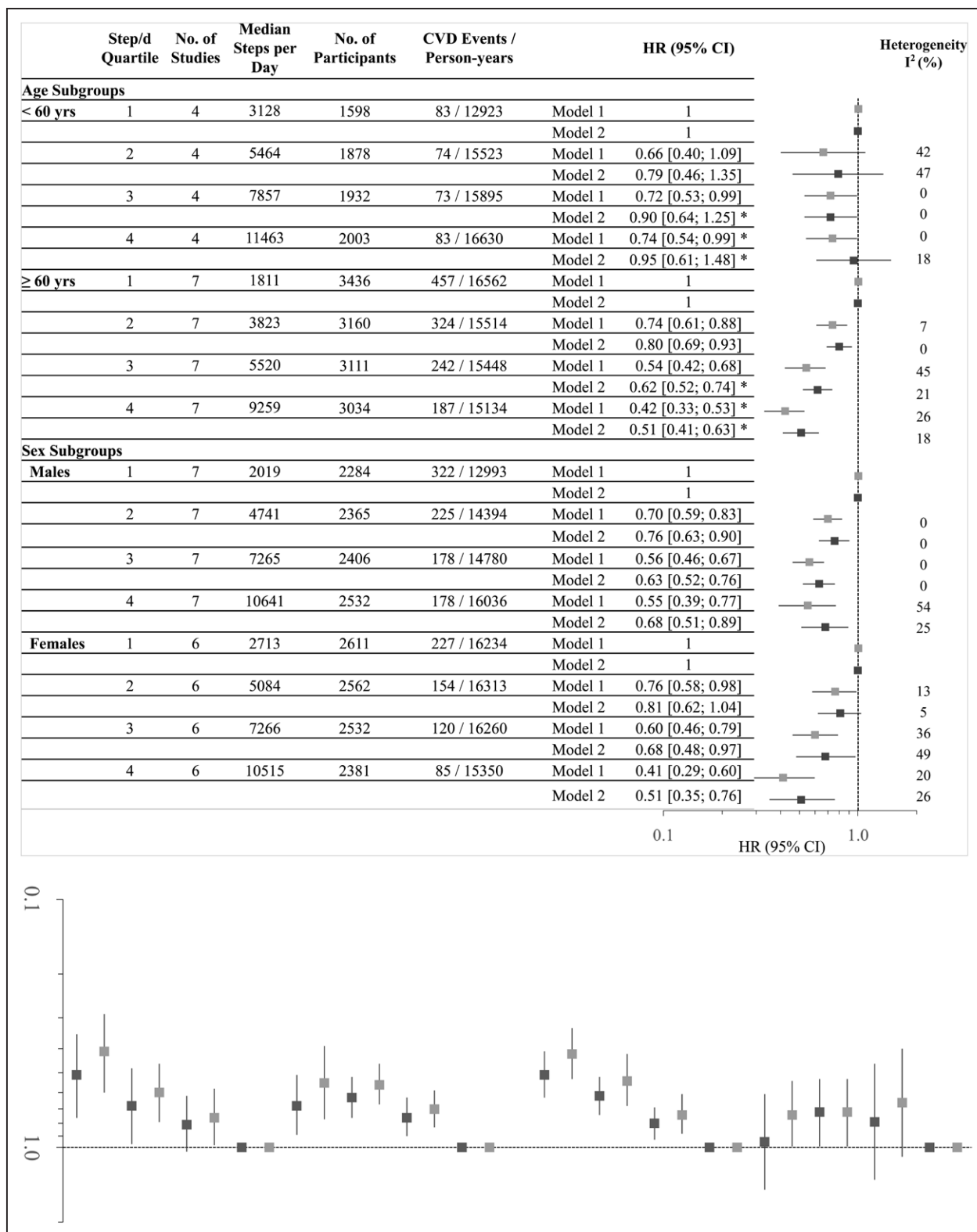


Figure 1. Association of steps per day and CVD events stratified by age and sex. Model 1: age- and sex-adjusted (if applicable). Model 2: Model 1 + device wear time, race/ethnicity (if applicable), education or income, and body mass index, plus study-specific variables for lifestyle factors (eg, smoking, alcohol), hypertension, diabetes, dyslipidemia, chronic conditions, and general health status. I² values were considered low (<25%), moderate (25–75%), or high (>75%). The x-axis is a log scale. *P<0.05 for subgroup difference. CVD indicates cardiovascular disease; and HR, hazard ratio.

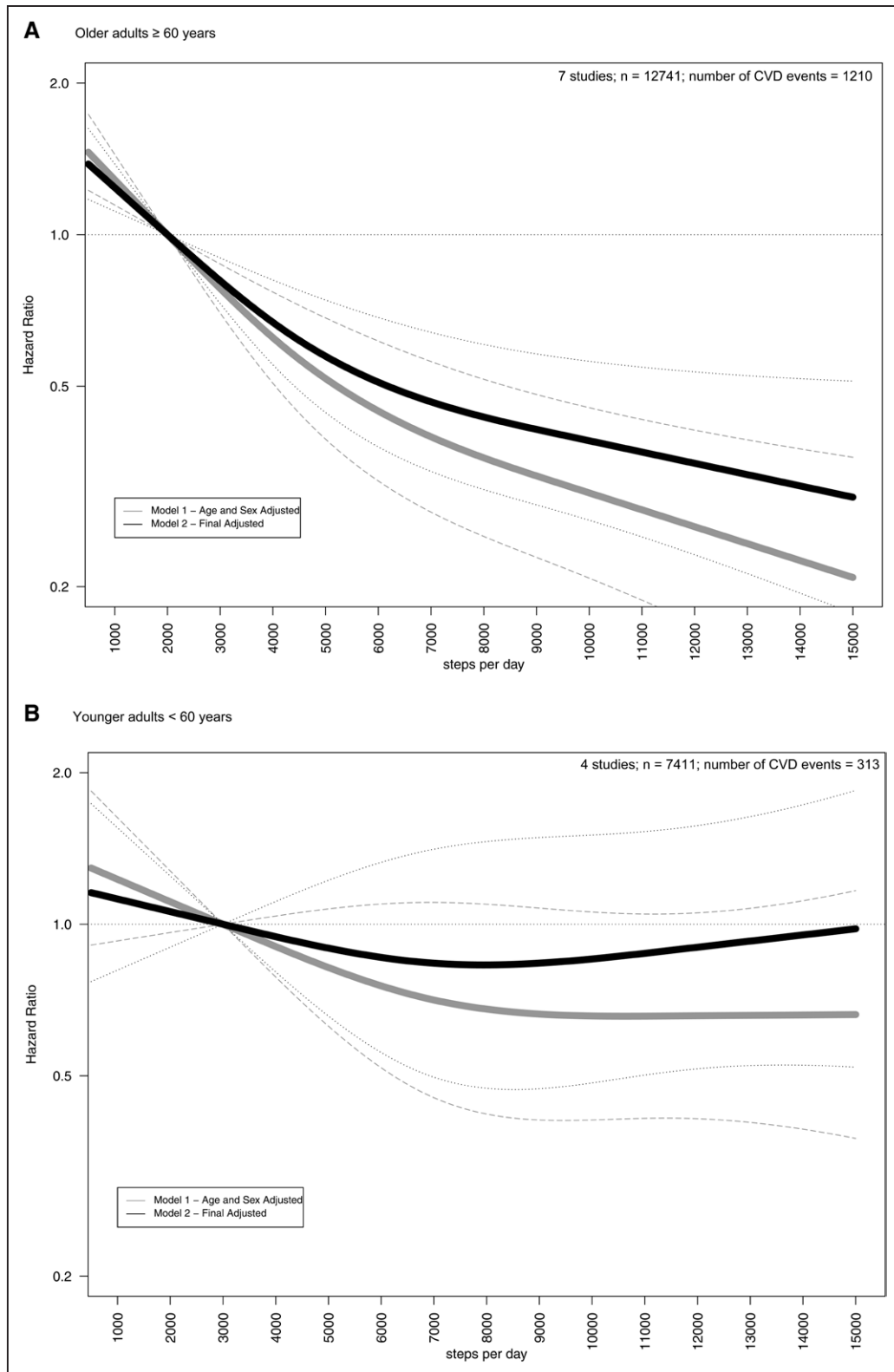


Figure 2. Association of steps per day with CVD events.

A, Older adults ≥ 60 years of age. **B**, Younger adults < 60 years of age. Restricted cubic splines of hazard ratios of steps per day with CVD events. Knots set at 10th, 50th, and 90th percentiles of steps per day. Reference set at median of lowest quartile (2000 for older adults; 3000 for younger adults). Hazard ratios are indicated by solid lines and 95% CIs are indicated by dotted lines. Model 1: age- and sex-adjusted (if applicable). Model 2: Model 1 + device wear time, race/ethnicity (if applicable), education or income, body mass index, lifestyle (smoking, alcohol), hypertension, diabetes, dyslipidemia, and self-rated health. The y-axis is a log scale. CVD indicates cardiovascular disease.

Table 2. Associations of Steps per Day With Overall CVD Events and Incidence CVD Events

	No. of studies	Steps per day, median	No. of participants	Events	Hazard ratio (95% CI)
Q1					
Overall CVD events	8	1985	5034	551	1
Incidence CVD events*	6	2778	3005	264	1
Q2					
Overall CVD events	8	4178	5038	396	0.81 (0.71–0.93)
Incidence CVD events*	6	4831	3008	160	0.74 (0.60–0.91)
Q3 vs Q1					
Overall CVD events	8	6327	5043	312	0.67 (0.58–0.78)
Incidence CVD events*	6	6794	3013	127	0.60 (0.47–0.77)
Q4 vs Q1					
Overall CVD events	8	10090	5037	264	0.57 (0.45–0.74)
Incidence CVD events*	6	10 105	3007	107	0.55 (0.40–0.76)

CVD indicates cardiovascular.

*For incidence CVD: NAVIGATOR (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) and ARIC (Atherosclerosis Risk in Communities) removed, and subsample of LIFE (Lifestyle Interventions and Independence for Elders) study participants (sample size reduced from $n=1341$ to 945 participants without previous CVD history at baseline for LIFE study). Hazard ratios (95% CI) are adjusted for age, device wear time, race/ethnicity (if applicable), sex (if applicable), education or income, body mass index, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status.

compared with studies using self-reported physical activity, which report a 20% to 30% lower risk of CVD.^{1,26,27} For example, adults reporting high levels of physical activity (ie, ≥ 300 minutes of moderate-intensity per week) had a 20% (0.74 to 0.88) lower risk of coronary heart disease compared with adults reporting no leisure-time physical activity.¹ The stronger associations may be attributable to the improved precision and lower bias seen with device-measured activity compared to self-reported questionnaires.³⁰

An earlier meta-analysis included only 4 studies demonstrating a nonlinear association with CVD; however, that meta-analysis reported a high degree of heterogeneity ($I^2=80\%$).¹¹ Heterogeneity in the present study was lower because the analytic approaches were uniform and events were similarly defined and adjudicated. The present study was also sufficiently large enough to conduct subgroup analyses by age and sex.

Despite an inverse association of steps with CVD in older adults, there was no association in younger adults. CVD is a disease of aging and often does not present itself as a diagnosed condition until years of progression. Therefore, the follow-up period may not be long enough to capture incidence of CVD for younger adults. Only 4.2% of younger adults (5.1 per 1000 person-years) versus 9.5% of older adults (19.3 per 1000 person-years) in the present study had a subsequent CVD event. These findings are consistent with a nationally representative sample of US adults, showing the percentage of deaths attributed to inadequate physical activity levels was only significant among older adults.³¹ The association of steps per day with intermediate CVD risk factors such as hypertension, high cholesterol,

and diabetes may be the most appropriate outcome in young to middle-aged adults.

Stepping rate (ie, pace or cadence) was not associated with CVD risk beyond that of total steps per day. The absence of an association of stepping rate is consistent with earlier research evaluating device-measured stepping rate and mortality risk.^{10,32} However, this finding is converse to a previous meta-analysis of self-reported walking that demonstrated walking pace was a stronger independent predictor of CVD risk compared with walking volume.³³ The present findings should be viewed as preliminary because only 4 studies reported data on stepping rate.

Implications of the present results for clinical care and public health guidelines reporting are multifold. Steps per day is a simple metric health care professionals can use during patient encounters to help monitor and promote physical activity. During the past decade, there has been a rapid rise in the adoption of step-monitoring fitness trackers and smartphones; this rise is expected to continue. Steps per day estimates from waist-worn devices used in research studies may not precisely match consumer devices, which are often worn on the wrist. However, steps per day measured by research and consumer devices are highly correlated.³⁴ In addition, some step-counting devices are less accurate at very slow walking speeds that are common in many patient populations.³⁵ Because of the low levels of activity in older adults,^{36,37} empirical findings from the present study suggest that interventions may consider setting attainable step goals for cardiovascular health in older adults taking fewer than 10 000 steps per day.



Our study has several limitations. Despite adjusting for sociodemographic, lifestyle, and health status factors, the potential for residual confounding and reverse causality remains. The study level analyses did not account for competing risk of non-CVD-related death, and therefore may overestimate CVD events and predicted risk. Although the present meta-analysis used study-level data and standardized analyses across studies, the heterogeneity in participants between studies (eg, demographics, health status) and design (eg, step device, covariates) may not be fully accounted for compared to individual-level pooled meta-analysis. Because this study did not have access to individual-level data we were limited to study-specific quartiles and unable to investigate differential effects across individuals or distinct subgroups. For example, further stratification by age and sex subgroups was not possible because of sample size limitations within each study. In addition, this study was unable to investigate associations in patients with CVD at baseline and risk of secondary CVD events. Conclusions in the present study are generalizable only to the range of step counts observed in those samples—thus the very highest levels of activity are not represented (eg, >15 000 steps per day). Participants were primarily non-Hispanic White adults, limiting generalizability to other racial/ethnic groups even though there is no a priori hypothesis to suggest a differential association of activity with CVD by race or ethnicity. The subset of studies included in older versus younger adult comparisons were not identical, limiting the ability to directly compare age groups. As all studies did not have longitudinal measurement of steps, this study only evaluated steps at a single time point and did not investigate the influence of changes in steps per day over time. Other studies, however, have demonstrated that 3 to 7 days of device measurement is representative of usual physical activity.^{38,39} This study represents associations assuming an unchanging level of steps/d with CVD risk. Conclusions on causality require a prospective trial demonstrating that increased step count leads to reduced CVD risk. The majority of the data was obtained from unpublished studies, allowing for a harmonized approach where all studies used a standardized analytic approach to reduce study heterogeneity. In addition, unpublished studies were invited to participate to reduce publication bias. Positive findings tend to be published earlier and more often compared with negative or null findings; relying only on published evidence may result in overestimated pooled effect size.⁴⁰ Our meta-analysis demonstrated associations in both published and unpublished work, providing robust evidence of the association between step count and CVD risk.

Conclusions

Step goals based on empirical evidence are needed to guide technology-based monitoring and promotion of

physical activity. The present meta-analysis is responsive to this gap in the literature since pedometers and accelerometers are more accurate for measuring ambulatory physical activity than self-report methods.³⁰ Among older adults, taking 6000 to 9000 steps per day was associated with 40% to 50% lower risk of CVD. Findings from this meta-analysis can inform step guidelines for the promotion of physical activity for cardiovascular health.

ARTICLE INFORMATION

Received June 15, 2022; accepted October 20, 2022.

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Acknowledgments

The authors acknowledge and express sincere appreciation to all research staff for data collection and participants of all studies for their important contributions.

Sources of Funding

This project was supported by an Intergovernmental Personnel Act Agreement through the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The study-specific funders had no role in the design and conduct of the study; collection, management, analysis, interpretation of the data; preparation, review, approval of or decision to publish the manuscript. The views expressed in this publication are those of the author(s) and not necessarily those of the study-specific funders. The ARIC (Atherosclerosis Risk in Communities) study has been funded in whole or in part with federal funding from the National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), and Department of Health and Human Services (HHSN2682017000011, HHSN2682017000021, HHSN2682017000031, HHSN2682017000041, HHSN2682017000051). Accelerometer data were collected with funding from contract No. R56AG049886. The British Regional Heart Study was supported by grants from the British Heart Foundation (PG/13/86/30546, RG/13/16/30528, RG/19/4/34452). CARDIA (Coronary Artery Risk Development in Young Adults Study) is supported by

NIH, NHLBI, and National Institute on Aging (NIA) HHSN268201800005I, HHSN268201800007I; HHSN268201800003I; HHSN268201800006I; HHSN268201800004I; AG00005). Year 20 accelerometer data was funded by R01 HL078972. The Framingham Heart Study's data collection and analysis was funded by NHLBI (N01-HC25195, HHSN268201500001I, 75N92019D00031); Department of Health and Human Services (N268201500001I, R01-AG047645, R01-HL131029); and the American Heart Association (grant No. 15GPS-GC24800006). Dr Vasani is supported, in part, by the Evans Medical Foundation and the Jay and Louis Coffman Endowment from the Department of Medicine, Boston University School of Medicine. Dr Spartano received funding from Novo Nordisk for an investigator-initiated research grant unrelated to the present work. The Healthy Ageing Initiative's data collection and analysis was funded by the Swedish Research Council (grant 2016-02589 to P. Nordström). The Jackson Heart Study was funded by NIH contracts (N01-HC95170, N01HC95171, N01HC9517) provided by NHLBI and the National Center for Minority Health and Health Disparities. The LIFE (Lifestyle Interventions and Independence for Elders) study was funded by a NIH/NIA Cooperative Agreement (#U01 AG22376) and a supplement from the NHLBI (3U01AG022376-05A2S), and was sponsored, in part, by the Intramural Research Program (NIA, NIH).

Disclosures

None.

Supplemental Material

Tables S1 to S5

Figures S1 to S9

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