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

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Abstract

Background: Steps per day (steps/d) less than the widely-promoted 10,000 steps 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/d with CVD can help inform clinical and public health guidelines.

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

Results: Mean age of participants was 63.2 (12.4) years and 52% women. Mean follow-up was 6.2 years (123,209 person-years), with 1,523 CVD events (12.4 per 1,000 participant-years). There was a significant difference in the association of steps/d and CVD between older (≥60 years) and younger adults (<60 years). For older adults, the HR was 0.80 [quartile 2 (Q2), 95% CI, 0.69, 0.93], 0.62 [Q3, 95% CI, 0.52, 0.74], and 0.51 [Q4, 95% CI, 0.41, 0.63] compared with the lowest quartile. For younger adults, the HR was 0.79 [Q2, 95% CI, 0.46-1.35], 0.90 [Q3, 95% CI, 0.64-1.25], and 0.95 [Q4 95% CI, 0.61-1.48] compared with the lowest quartile.

Restricted cubic splines demonstrated a non-linear association whereby higher steps were associated with lower risk of CVD among older adults.

Conclusion:

For older adults, taking more daily steps was associated with a progressively lower risk of CVD. Monitoring and promoting steps/d is a simple metric for clinician-patient communication and population health to reduce the risk of CVD.

Keywords: Steps per day, Physical activity, Cardiovascular Disease,

Clinical Perspective

What is new?

- In this meta-analysis of eight studies, taking more daily steps was associated with a progressively lower risk of cardiovascular disease (CVD) among older adults ≥60 years of age.
- Among older adults, taking about 6,000 to 9,000 steps/d was associated with 40% to 50% lower risk of CVD, compared to taking about 2,000 steps/d.

What are the clinical implications?

- Monitoring and promoting steps/d can be a simple, easy to interpret metric used for clinician-patient communication and population health to reduce the risk of CVD events.
- Findings from the present study suggest that interventions may consider setting attainable step goals for cardiovascular health in older adults that fall below 10,000 steps/d.

Non-standard Abbreviations and Acronyms

Body Mass Index (BMI)

Diastolic blood pressure (DBP)

Cardiovascular Disease (CVD)

Confidence Interval (CI)

Hazard Ratio (HR)

Steps per day (Steps/d)

Systolic blood pressure (SBP)

Introduction

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 U.S. federal guidelines[4] and the 2019 ACC/AHA Guideline on the Primary Prevention of CVD[5] 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 (steps/d), are effective strategies to increase physical activity.[8] A standard goal is often 10,000 steps/d, 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/d.[10] A previous meta-analysis of four 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/d would be useful for providing health care professionals with a precise estimate of steps/d needed for CVD benefit informing provider-patient interactions and population health guidelines. Thus, the primary objective of the present analysis is to test whether steps/d is associated with risk for CVD. Given the known age and sex differences in risk of CVD,[2, 12, 13] all associations were tested among

females and males, and among younger and older adults. It was hypothesized there would be a dose-response association of steps/d and stepping rate with CVD.

Methods

Data, Methods, and Materials Disclosure Statement

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] Three of four studies from this review agreed to participate but were too few for a meta-analysis. An additional five studies were identified through awareness of studies measuring steps and CVD, culminating in eight studies meeting inclusion criteria of device-measured steps and prospective follow-up for CVD events in adult populations (≥18 years).

The Newcastle Ottawa quality assessment scale was used to assess the methodological quality of each study.[15] Assessments were performed independently by two reviewers (AP and SB), 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/d, averaged over three to seven days where step data were collected. Baseline was designated as the time point when steps data were collected. 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 the subjects gave informed consent.

Study level analyses

All studies followed a standardized analytic plan developed by the collaborative. Studies categorized steps/d 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 [HR] and 95% confidence intervals [95%CI]. Models were completed for each study's overall sample, by age group and by sex, where applicable. Age was grouped at < 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 (BMI), device wear time, lifestyle factors (e.g. smoking, alcohol), and study-specific variables representing diabetes, hypertension, high cholesterol, other chronic conditions, and self-rated health or functional status (Table S1). For the four studies with step rate, the same analytic approach was followed and an additional model (model 3) adjusted for steps/d using the residual method where step rate was regressed on steps/d and the resulting step rate residuals and steps/d 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/d 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/d. Heterogeneity across studies was determined by I^2 statistics,[20] representing the proportion of total variation attributable to systematic differences between studies rather than chance. I^2 values were considered low (<25%), moderate (25%-75%), or high (>75%).[20] Funnel plots were used to assess study bias by comparing study hazard ratios against standard errors and Egger's test 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/d 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 non-linearity.[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 one study at a time to determine the influence of any single study with an extreme result; 4) stratification by device type (i.e., 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≥ 40 steps/min stepping rate (intentional walking) and minutes per day at ≥100 steps/min stepping rate (moderate intensity walking pace).[25] Peak 30- and 60- minute stepping rates were calculated by selecting the 30 or 60 minutes (not necessarily consecutive) throughout each day with the highest

number of steps/min. Stepping rate variable 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, 52% women, >70% non-Hispanic White race) 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/d was 4323 [IQR 2760-6924] for older adults and 6911 [IQR 4783-9794] for younger adults. A total of 1,523 events were reported (12.4 per 1,000 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/d 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 seven studies of older adults ≥60 years there were 1210 events among 12,741 individuals (19.3 events per 1,000 person-years). There was a significant association in the age and sex adjusted model 1 and the results remained significant in the final adjusted model. In the final adjusted (model 2), compared to the lowest quartile, HR for risk of CVD were 0.80 [0.69-0.93] in the second quartile, 0.62 [0.52-0.74] in the third quartile, and 0.51 [0.41-0.63] in the fourth quartile (Figure 1). In the spline model, there was a significant curvilinear association among older adults ≥60 years (p-value for nonlinearity <0.0001, Figure 2).

Among four studies of younger adults <60 years there were 313 events among 7411 individuals (5.1 events per 1,000 person years). Compared to the first quartile, there was a significant association in the age and sex adjusted model 1 in the third (0.72 [0.53-0.99]) and

fourth (0.74 [0.54-0.99]) quartiles. Results were no longer significant in the final adjusted model. Compared to the lowest quartile, HRs for risk of CVD were 0.79 [0.46-1.35] in the second quartile, 0.90 [0.64-1.25] in the third quartile, and 0.95 [0.61-1.48] in the fourth quartile in the final adjusted model 2 (Figure 1). There was no significant association of steps/d and CVD events in the spline model for younger adults (Figure 2).

The HR in the final adjusted model in females was 0.81 [0.62-1.04] in the second quartile, 0.68 [0.48-0.97] in the third quartile, and 0.51 [0.35-0.76] in the fourth quartile (Figure 1), compared to the lowest quartile. The HR for males was 0.76 [0.63-0.90] in the second quartile, 0.63 [0.52-0.76] in the third quartile, and 0.68 [0.51-0.89] in the fourth quartile (Figure 1), compared to the lowest quartile. There were no significant subgroup differences by sex in quartile comparison or spline models. The spline models demonstrated a non-linear (p-value=0.001 for males and p-value =0.012 for females for non-linearity) dose response association with the leveling of the curve observed at approximately 8,000 steps/d for males and females (Figure S3).

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

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/d and CVD did not change when excluding any one study (Table S3). We re-analyzed 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 steps/min or ≥100 steps per min) and CVD events before or after adjusting for steps/d (Table S5, Figures S5-S9).

Discussion

In the present meta-analysis of eight prospective studies, taking more steps/d was associated with lower CVD in older adults ≥60 years. Taking 6,000 to 9,000 steps/day was associated with 40% to 50% lower risk of CVD, compared to taking 2,000 steps/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 incremental lower risk of mortality until leveling around 6,000-8,000 in older adults.[10] These recent results on steps and mortality included 15 studies, seven of which are included in the present meta-analysis on CVD. The steep early slope suggests taking more steps is better, particularly among individuals at lower steps/d. Additionally, although the slope is not as steep above 6,000, higher step counts appear to be associated with a continuing lower 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 (e.g. heart failure, stroke) representing an area for future investigation.

Older adults who achieve higher thresholds of steps/d demonstrate a 40-50% 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 compared with studies using self-reported physical activity, which report a 20-30% lower risk of CVD.[1, 26, 27] For example, adults reporting high levels of physical activity of at least 300 minutes per week of moderate-intensity had a 20% (0.74 to 0.88) lower risk of coronary heart disease compared to adults reporting no leisure-time physical activity.[1] The stronger associations may be due to the improved precision and lower bias seen with device-measured activity compared to self-reported questionnaires.[30]

In a prior meta-analysis, including only four studies demonstrated a non-linear 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 analytical approaches were uniform and events were similarly defined and adjudicated. The present study was additionally 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

1,000 person years) versus 9.5% of older adults (19.3 per 1,000 person years) in the present study had a subsequent CVD event. These findings are consistent with a nationally-representative sample of U.S. adults, showing the percentage of deaths attributed to inadequate physical activity levels was only significant among older adults.[31] The association of steps/d 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 (i.e., pace or cadence) was not associated with CVD risk beyond that of total steps/d. The absence of an association of stepping rate is consistent with prior research evaluating device measured stepping rate with mortality risk.[10, 32] However, this finding is converse to a previous meta-analysis of self-reported walking which demonstrated walking pace was a stronger independent predictor of CVD risk compared with walking volume.[33] The present findings should be viewed as preliminary, given only four studies reported data on stepping rate.

Implications of the present results for clinical care and public health guidelines reporting are multifold. Steps/d is a simple metric health care professionals can use during patient encounters to help monitor and promote physical activity. Over the past decade, there has been a rapid rise in the adoption of fitness trackers and smartphones monitoring steps and is expected to continue to grow. Steps/d estimates from waist-worn devices used in research studies may not precisely match consumer devices, which are often worn on the wrist. However, steps/d measured by research and consumer devices are highly correlated.[34] Additionally, some step counting devices are less accurate at very slow walking speeds typical of many patient populations.[35] Given 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 that fall below 10,000 steps/d.

Our study has several limitations. Despite adjusting for sociodemographic, lifestyle, and health status characteristics, 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 (e.g. demographics, health status) and design (e.g. 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-sex subgroups was not possible due to sample size limitations within each study. Additionally, 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 are activity are not represented (e.g., $\geq$15,000 steps/d). Participants were primarily among non-Hispanic White adults, which limits generalizability to other race-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, which limits 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/d over time. Other studies, however, have demonstrated three to seven days of device measurement is representative of usual physical

activity.[38, 39] This study represents associations assuming an unchanging level of steps per day with CVD risk. Conclusions on causality require a prospective trial demonstrating increases in steps leads to a reduction in 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. Additionally, unpublished studies were invited to participate to reduce publication bias. Positive findings tend to be published earlier and more often compared to negative or null findings. When only relying on published evidence the pooled effect size can be overestimated.[40] Our meta-analysis demonstrated associations in both published and unpublished providing robust evidence of the association of steps with risk of CVD.

Conclusion

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 6,000 to 9,000 steps/day was associated with 40% to 50% lower risk of CVD. Findings from this meta-analysis can inform step guidelines for promotion of physical activity for cardiovascular health.

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CONFLICT OF INTEREST DISCLOSURES

None.

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Supplemental Material

Tables S1-5

Figures S1-9

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Table 1. Selected Characteristics of Studies

	Country	Study Entry	Step Device	No. of Participants	Mean Age, y (S.D.)	Females (%)	Steps/d, Median [IQR]	Mean Years of follow-up	No. of CVD Events
Published Studies									
British Regional Heart Study (BRHS)[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 (LIFE)[42]	U.S.	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 (NAVIGATOR)[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 (ARIC)	U.S.	2016-2017	ActiGraph GT3X	452	78.4 (4.7)	59%	3065 [2083, 4454]	2.8	34
Coronary Artery Risk Development in Young Adults (CARDIA)	U.S.	2005-2006	ActiGraph 7164	2085	45.2 (3.6)	57%	9164 [7324, 11163]	10.7	71
Framingham Heart Study (FHS)	U.S.	2008-2014	Actical	4223	55.3 (13.9)	54%	6906 [4809, 9419]	7.0	151
Healthy Ageing Initiative (HAI)	Sweden	2012-2018	ActiGraph GT3X	3207	70.4 (0.1)	51%	6967 [5032, 8991]	3.2	139
Jackson Heart Study (JHS)	U.S.	2000	Yamax SW200	401	60.2 (9.8)	61%	4748 [2847, 7284]	12.6	74
SUMMARY		**Range 2000-2018**	**5 devices (all Waist-Worn)**	**20152**	**63.2 (12.4)**	**52%**	**5459 [3353, 8029]**	**6.2**	**1523**

Summary age, % female, and years of follow-up are calculated as means at the individual-level.

Summary steps/d is calculated as the median at the study-level.

CVD events defined as fatal or non-fatal, and including coronary heart disease, stroke, and heart failure.

Table 2. Associations of Steps per Day with Overall CVD Events and Incidence CVD Events					
	no of studies	Median Steps/d	n	events	HR (95% CI)
Q1					
Overall CVD Events	8	1985	5034	551	1
Incidence CVD Events[a]	6	2778	3005	264	1
Q2					
Overall CVD Events	8	4178	5038	396	0.81 [0.71; 0.93]
Incidence CVD Events[a]	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[a]	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[a]	6	10105	3007	107	0.55 [0.40; 0.76]

[a] For incidence CVD: NAVIGATOR and ARIC removed, and subsample of LIFE study participants (sample size reduced from n= 1341 to 945 participants without previous CVD history at baseline for LIFE study). Hazard Ratio and 95% Confidence Intervals [HR (95% CI)] is 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.

	Step/d Quartile	No. of Studies	Median Steps per Day	No. of Participants	CVD Events / Person-years		HR (95% CI)	Heterogeneity I^2 (%)
Age Subgroups								
< 60 yrs	1	4	3128	1598	83 / 12923	Model 1	1	
						Model 2	1	
	2	4	5464	1878	74 / 15523	Model 1	0.66 [0.40; 1.09]	42
						Model 2	0.79 [0.46; 1.35]	47
	3	4	7857	1932	73 / 15895	Model 1	0.72 [0.53; 0.99]	0
						Model 2	0.90 [0.64; 1.25] *	0
	4	4	11463	2003	83 / 16630	Model 1	0.74 [0.54; 0.99] *	0
						Model 2	0.95 [0.61; 1.48] *	18
≥ 60 yrs	1	7	1811	3436	457 / 16562	Model 1	1	
						Model 2	1	
	2	7	3823	3160	324 / 15514	Model 1	0.74 [0.61; 0.88]	7
						Model 2	0.80 [0.69; 0.93]	0
	3	7	5520	3111	242 / 15448	Model 1	0.54 [0.42; 0.68]	45
						Model 2	0.62 [0.52; 0.74] *	21
	4	7	9259	3034	187 / 15134	Model 1	0.42 [0.33; 0.53] *	26
						Model 2	0.51 [0.41; 0.63] *	18
Sex Subgroups								
Males	1	7	2019	2284	322 / 12993	Model 1	1	
						Model 2	1	
	2	7	4741	2365	225 / 14394	Model 1	0.70 [0.59; 0.83]	0
						Model 2	0.76 [0.63; 0.90]	0
	3	7	7265	2406	178 / 14780	Model 1	0.56 [0.46; 0.67]	0
						Model 2	0.63 [0.52; 0.76]	0
	4	7	10641	2532	178 / 16036	Model 1	0.55 [0.39; 0.77]	54
						Model 2	0.68 [0.51; 0.89]	25
Females	1	6	2713	2611	227 / 16234	Model 1	1	
						Model 2	1	
	2	6	5084	2562	154 / 16313	Model 1	0.76 [0.58; 0.98]	13
						Model 2	0.81 [0.62; 1.04]	5
	3	6	7266	2532	120 / 16260	Model 1	0.60 [0.46; 0.79]	36
						Model 2	0.68 [0.48; 0.97]	49
	4	6	10515	2381	85 / 15350	Model 1	0.41 [0.29; 0.60]	20
						Model 2	0.51 [0.35; 0.76]	26

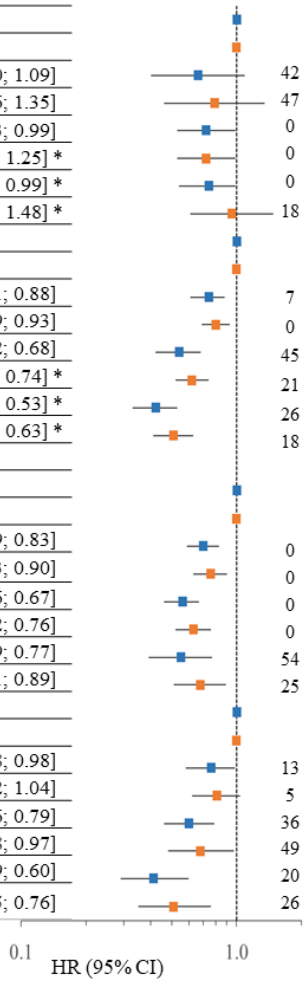

Figure 1. Association of Steps per Day and CVD Events Stratified by Age and Sex. Hazard Ratio and 95% Confidence Intervals [HR (95%CI)]. Model 1 is adjusted for age and sex (if applicable). Model 2: Model 1 + device wear time, race/ethnicity (if applicable), education or income, body mass index, and plus study-specific variables for lifestyle (smoking, alcohol), hypertension, diabetes, dyslipidemia, chronic conditions, and general health status. I^2 values were considered low (<25%), moderate (25%-75%), or high (>75%). The x-axis is a log scale. *p<0.05 for subgroup difference

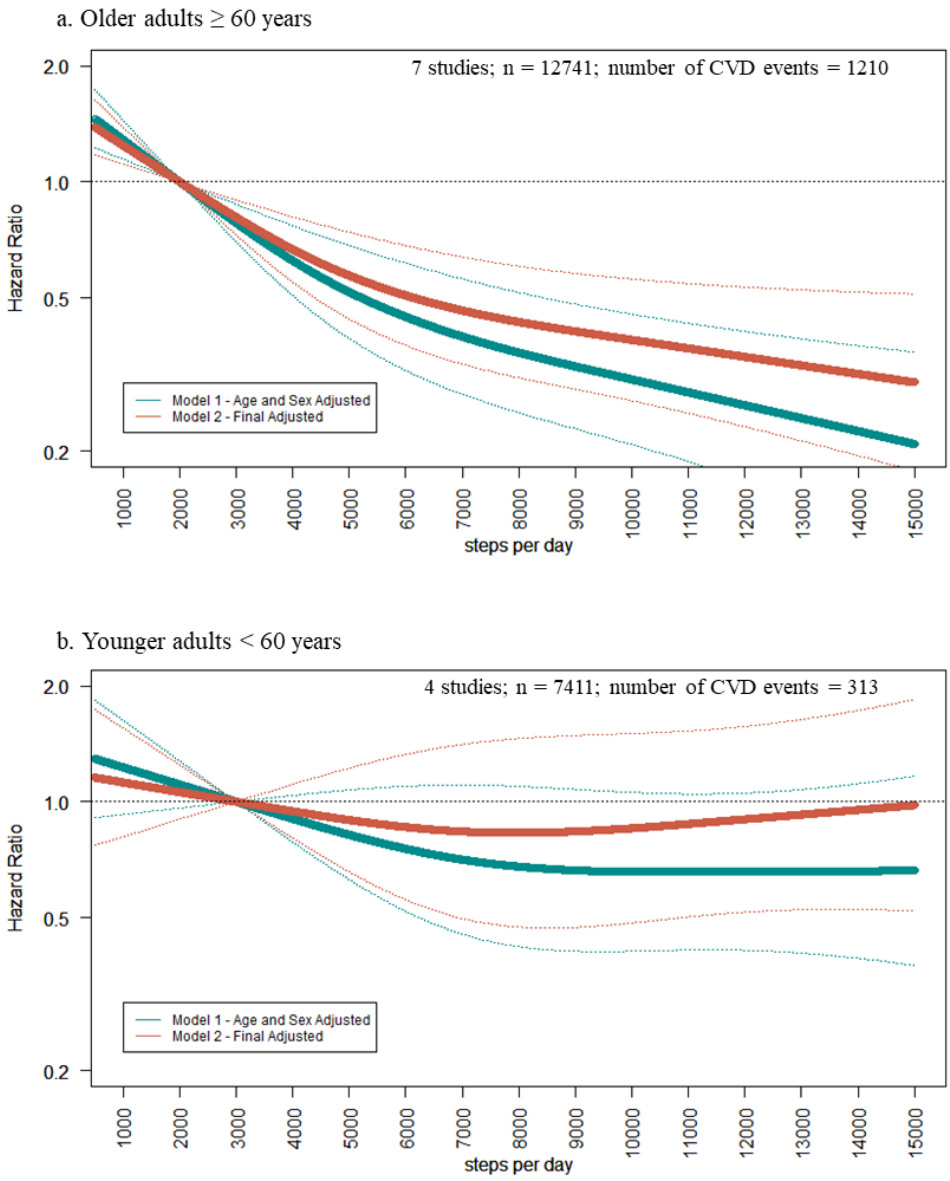

Figure 2. Association of Steps per Day with CVD events for (a) older adults ≥ 60 years and (b) younger adults < 60 year. Restricted cubic splines of hazard ratios of steps/d with CVD events. Knots set at 10th, 50th, and 90th, percentile of steps/d. Reference set at median of lowest quartile (2,000 for older adults, 3,000 for younger adults).Hazard Ratios are indicated by solid lines and 95% Confidence Intervals are indicated by dotted lines. Model 1 adjusted for age and sex (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.