SUPPLEMENTAL MATERIAL

Paluch AE et al., Prospective Association of Daily Steps with Cardiovascular Disease: A Harmonized Meta-Analysis

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Table S1a. Study Level Descriptions of Data Collection and Processing

Study	Case Ascertainment	Device Type (wear location), Settings, Instructions	Stepping Metrics Included	Device Wear Criteria	Summary of Covariates in Final Model
Atherosclerosis Risk in Communities (ARIC) Study	Fatal and nonfatal: physician adjudicated probable myocardial infarction (MI) or definite fatal CHD based on ARIC criteria or coronary revascularization; HF and Stroke by hospitalization record;	ActiGraph wGT3X-bet (waist); 60 second epochs; 7 consecutive days during waking hours	Peak 30 min.	Device worn for 10 hrs/day for ≥ 3 days	Age, sex, race/Ethnicity, education, BMI, device wear time, smoking status, alcohol consumption, hypertension, diabetes, high cholesterol, cancer, self-rated health
British Regional Heart Study (BRHS)	Fatal and nonfatal; physician adjudicated diagnosis MI, HF, or stroke(with symptoms lasting > 24 hours)	ActiGraph GT3X (waist), 60 second epochs; 7 consecutive days during waking hours	None		Age, sex, occupation, BMI, device wear time, smoking status, region of residence, alcohol consumption, duration of night sleep, mobility disability, living alone vs with others
Coronary Artery Risk Development in Young Adults (CARDIA) Study	Fatal and nonfatal: Physician adjudicated diagnosis of HF, CHD (MI, acute coronary syndrome, coronary revascularization) or stroke	ActiGraph 7164 (waist); 60 seconds epochs; 7 consecutive days during waking hours	Peak 30 min. Peak 60 min. Time spent at 40+ steps per min.	Device worn for 10 hrs/day for ≥ 3 days	Age, sex, race/Ethnicity, education, field center, BMI, device wear time, smoking status, healthy eating index, alcohol consumption, diabetes, hypertension, high cholesterol, self-rated health
Framingham Heart Study (FHS)	Fatal and nonfatal: Physician adjudicated CHD (coronary insufficiency syndrome/myocardial infarction), HF, or stroke	Actical model #198-0200- 00; 30 seconds epochs (waist); During Generation 3- exam 2, participants instructed to wear the device 24 hours a day (removed time from 12- 6am); for Gen 2-based exam 9 instructed to wear for wake time only	Peak 30 min. Peak 60 min. Time spent at 40+ steps per min.	Device worn for 10 hrs/day for ≥ 3 days	Age, sex, cohort group, race/Ethnicity, education, BMI, device wear time, smoking status, hypertension, high cholesterol, cancer , self- rated health
Healthy Ageing Initiative (HAI)	Nonfatal: National Patient Register for MI, HF, or stroke	ActiGraph GT3X (waist), 60 second epochs; 7 consecutive days during waking hours	None	Device worn for 10 hrs/day for ≥ 4 days	Age, sex, education, income, BMI, device wear time, smoking status, marital status, hypertension, high cholesterol, cancer, antithrombotic agents, physical function
Jackson Heart Study (JHS)	Fatal and nonfatal: Physician adjudicated HF, CHD, or stroke	Yamax SW-200 pedometer (Yamax Corp., Tokyo, (waist). 3-day monitoring sessions that was repeated for a maximum of three separate occasions within a 6 month period (i.e. max 9 days total)	None	Device worn for ≥ 3 consecutive days for at least one of the assessment periods	Age, sex, race, education, BMI, hypertension, high cholesterol, smoking status, alcohol consumption, hypertension, Type 2 diabetes,

Additional studies on next page

BMI = Body Mass Index; HF = Heart Failure; CHD = Coronary Heart Disease; CVD = Cardiovascular Disease; LFE = Low Frequency Extension

Table S1a cont. Study Level Descriptions of Data Collection and Processing

Study	Case Ascertainment	Device Type (wear location), Settings, Instructions	Stepping Metrics Included	Device Wear Criteria	Summary of Covariates in Final Model
Lifestyle Interventions and Independence for elders (LIFE)	Fatal and nonfatal: Physician adjudicated HF, CHD (MI, angina, revascularization), or stroke or transient ischemic attack	ActiGraph GT3X (waist), 7 consecutive days during waking hours	Peak 30 min.	device worn for 7 consecutive days	Age, sex, race, education, BMI, hypertension, high cholesterol, smoking status, hypertension, Type 2 diabetes, high cholesterol, blood pressure, previous history of CVD
Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research trial (NAVIGATOR)	Fatal and nonfatal: Physician adjudicated CHD (MI, angina, revascularization), or stroke or transient ischemic attack	Accusplit AE120 pedometer (waist) ; instructed to wear it during waking hours for 7 consecutive days. Participants were given a log book to write down their daily step count at the end of each day.	None	Steps per day recorded for 7 days	Age, sex, race/Ethnicity, socio- economic status BMI, smoking status, previous history of CVD, diabetes, high cholesterol, cancer, emphysema,

BMI = Body Mass Index; HF = Heart Failure; CHD = Coronary Heart Disease; CVD = Cardiovascular Disease; LFE = Low Frequency Extension

Study	Detailed Description of Covariates in Final Model
ARIC	age, sex, race/Ethnicity, education (< high school, high school grad, > high school), body mass index (kg/m2), device wear time, smoking status (current, non-smoker), alcohol consumption, Systolic blood pressure (mmHg), hypertension medications (yes/no), HDL cholesterol (mg/dL), LDL cholesterol (mg/dL), triglycerides (mg/dL), diabetes (fasting glucose ≥126 mg/dL or non-fasting ≥200 mg/dL, or taking diabetes medication or self reported diagnosis by a physician, self-rated health
BRHS	age, occupation (manual, non-manual labor), body mass index (kg/m2), device wear time, smoking (current, past, never), region of residence, alcohol consumption, hours of night-time sleep, living along vs with others, mobility disability (Mobility disability was present if reported being unable to do any of: (1) walking 200 yards without stopping and without discomfort, (2) climbing a flight of 12 stairs without holding on and taking a rest, or (3) bending down and picking up a shoe from the floor)
CARDIA	age, sex, race/Ethnicity, education (years), body mass index (kg/m2), device wear time, smoking status (current, former, never), alcohol consumption, healthy eating index score, stage 2 hypertension (systolic pressure ≥ 140 mm Hg and/or diastolic pressure is ≥ 90 mm Hg and/or taking medication), High cholesterol (≥200 mg/dL total cholesterol), Diabetes (fasting glucose ≥126 mg/dL or non-fasting ≥200 mg/dL, or taking diabetes medication), self-rated health
FHS	age, sex, race/Ethnicity, education (< high school, high school grad, > high school), body mass index (kg/m2), cohort, smoking status (current, non-smoker), device wear time, alcohol consumption, stage 1 hypertension (systolic pressure ≥ 130 mm Hg and/or diastolic pressure is ≥ 80 mm Hg and/or taking medication), high cholesterol (self-reported taking medication to lower cholesterol), self-rated health
HAI	sex, education (primary, secondary, post-secondary), body mass index (kg/m2), smoking status (current, non-smoker), device wear time, diabetes (self-reported or physician diagnosis), hypertension (≥ 140 mm Hg and/or diastolic pressure is ≥ 90 mm Hg or taking medication), high cholesterol (>240 mg/dL or taking medication), cancer diagnosis, martial status (married, unmarried, divorced, widowed), household income (continuous as Swedish Krona), physical function (timed-up- and-go test)
JHS	age, sex, education (< high school, high school graduate, > high school), body mass index (kg/m2), alcohol consumption, smoking status (current, non-smoker), stage 2 hypertension (Systolic pressure ≥ 140 mm Hg and/or diastolic pressure is ≥ 90 mm Hg and/or taking medication), high LDL cholesterol (≥ 160 mg/dL)
LIFE	Age, sex, race, education (high school, college, post-graduate, others), intervention arm, device wear time, marital status (currently married, unmarried), live alone, body mass index (kg/m2), smoking status (current, former, never), diabetes (physician diagnosis), systolic blood pressure (mmHg), intake of anti-hypertensive medications, lipid lowering medication, previous history of CVD, self-rated health
NAVIGATOR	Age, sex, body-mass index (kg/m2), region (North America, Europe, Asia, Latin America, other), randomized medication treatment group, smoking status (current, non), diabetes, LDL cholesterol, antihypertensive medication use, previous history of CVD.

	AF	RIC	BRHS	CAI	RDIA	FHS		
	Men	Women	Men	Men	Women	Men	Women	
N	266	186	1172	891	1194	1901	2322	
Age (y), mean (SD)	78.0 (4.5)	79.1 (4.8)	78.28 (4.5)	45.2 (3.5)	45.2 (3.7)	54.1 (14.0)	54.5 (13.8)	
BMI (kg/m2), mean (SD)	27.7 (5.3)	28.5 (4.4)	27.1 (3.8)	28.8 (6.4)	29.2 (7.3)	28.76 (4.7)	27.28 (5.7)	
BMI Categories, n (%)								
BMI < 25.0 kg/m ²	82 (31)	43 (23)	342 (29)	216 (24)	411 (34)	386 (20)	950 (41)	
BMI: 25.0 - < 30.0 kg/m ²	106 (40)	82 (44)	611 (52)	402 (45)	329 (28)	895 (47)	768 (33)	
BMI ≥30.0 kg/m ²	78 (29)	61 (33)	291 (19)	273 (31)	454 (38)	620 (33)	604 (26)	
race/Ethnicity, n (%)								
Non-Hispanic White	202 (76)	159 (85)	>99%	562 (63)	646 (54)	1722 (91)	2082 (90)	
Non-Hispanic Black	64 (24)	27 (15)	-	329 (37)	548 (46)	-	-	
Asian	-	-	-	-	-	-	-	
Hispanic	-	-	-	-	-	-	-	
Other Race	-	-	-	-	-	-	-	
Hypertension (Stage 2), n (%)	197 (74)	143 (77)	1004 (86)	156 (18)	240 (20)	1138 (60)	1009 (43)	
High total cholesterol, n (%)	104 (39)	29 (16)	617 (53)	609 (68)	564 (47)	587 (31)	529 (23)	
Diabetes, n (%)	62 (23)	61 (33)	163 (14)	68 (8)	93 (8)	-	-	
History of Cancer, n (%)	0	1 (0.5)	181 (15)	-	-	225 (12)	336 (14)	
Average Steps/day, mean (SD)	3353 (1760)	3580 (1841)	4985 (2758)	9819 (3231)	9186 (2914)	7721 (4072)	6869 (3551)	
No. of days of compliant device wear, mean (SD)	7.1 (2.4)	6.7 (1.9)	-	7.0 (1.41)	6.9 (1.4)	7.4 (1.32)	7.3 (1.4)	
Minutes/day of device wear, mean (SD)	847 (102)	849 (89)	-	871 (86)	855 (83)	915 (94)	910 (93)	

Table S1c. Study Level Descriptive Characteristics of Participants

Table S1c continued. Study Level Descriptive Characteristics of Participants

	Н	AI	١٢	IS	LII	E	NAVIO	GATOR
	Men	Women	Men	Women	Men	Women	Men	Women
Ν	1445	1762	157	244	448	893	3573	3698
Age (y), mean (SD)	70.4 (0.1)	70.4 (0.1)	59.0 (10.5)	61.0 (9.3)	79.3 (5.2)	78.5 (5.3)	63.9 (7.0)	63.6 (7.7)
BMI (kg/m2), mean (SD)	26.5 (3.6)	26.3 (4.6)	29.4 (6.2)	31.9 (7.1)	30.1 (5.5)	30.5 (6.3)	29.6 (4.6)	31.2 (5.9)
BMI Categories,								
n (%)								
BMI < 25.0 kg/m ²	499 (40)	791 (45)	28 (18)	28 (11)	71 (16)	172 (19)	452 (12)	466 (13)
BMI 25.0 -< 30.0 kg/m ²	725 (43)	657 (37)	67 (43)	78 (32)	181 (40)	285 (32)	1671 (47)	1265 (34)
BMI ≥30.0 kg/m²	221 (17)	314 (18)	62 (39)	138 (57)	196 (44)	436 (49)	1450 (41)	1967 (53)
race/Ethnicity, n (%)								
Non-Hispanic White	>99%	>99%	-	-	385 (86)	635 (71)	3006 (84)	2956 (80)
Non-Hispanic Black	-	-	157 (100)	244 (100)	42 (9)	196 (22)	65 (2)	101 (3)
Asian	-	-	-	-	4 (1)	7 (1)	276 (8)	270 (7)
Hispanic	-	-	-	-	10 (2)	40 (4)	-	-
Other Race	-	-	-	-	7 (2)	15 (2)	226 (6)	371 (10)
Hypertension (Stage 2), n (%)	1144 (79)	1378 (78)	90 (57)	166(68)	393 (88)	753 (84)	2677 (75)	2998 (81)
High total cholesterol, n (%)	765 (53)	1123 (64)	22 (14)	40 (16)	318 (71)	591 (66)	1656 (46)	1604 (43)
Diabetes, n (%)	138 (10)	107 (6)	-	-	147 (32)	232 (26)	1191 (33)	1530 (41)
History of Cancer, n (%)	-	-	-	-	-	-	57 (2)	74 (2)
Average Steps/day, mean (SD)	7243 (3036)	7248 (3138)	6386 (4031)	4941 (3693)	2691 (1623)	2657 (1399)	5945 (3961)	6600 (4803)
No. of days of compliant device wear, mean (SD)	7 (0.9)	7(0.8)	_	_	7.9 (3.2)	8.0 (3.3)	6.3 (1.0)	6.6 (1.0)
Minutes/day of device wear, mean (SD)	883 (101)	873 (94)	-	-	834 (104)	838 (114)	-	-

Table S2: Study Quality Assessment

		Ne	wcastle-Ottaw	va Quality	Assessment o	f Studies			-
Stud	ly	Selection							
	Representat iveness	Selection	Ascertainment Exposure	Outcome	Comparability	Assessment	Follow- Up	Adequacy	Overall Score
ARIC	В*	A*	A*	A*	A* B*	A *	A*	В*	9
BRHS	С	A*	A*	A*	A* B*	A *	A*	В*	8
CARDIA	В*	A*	A*	A*	A* B*	A *	A*	В*	9
FHS	В*	A*	A*	A*	A* B*	A *	A*	В*	9
JHS	В*	A*	С	A*	A* B*	A *	A*	В*	8
HAI	В*	A*	A*	A*	A* B*	B *	A*	В*	9
LIFE	С	A*	A*	A*	A* B*	A *	A*	В*	8
NAVIGATOR	С	A*	С	A*	A* B*	A *	A*	В*	7

A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability. Overall score sums the number of stars.

See the following page for detailed scoring descriptions (e.g. A, B, C)

COHORT STUDIES

<u>Note</u>: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

- 1) Representativeness of the exposed cohort
 - a) truly representative of the average adult in the community ${f lpha}$
 - b) somewhat representative of the average adult in the community lpha

c) selected group of users e.g. nurses, volunteers, only those with a precondition/morbidity, only men or only women

- d) no description of the derivation of the cohort
- 2) Selection of the non exposed cohort
 - a) drawn from the same community as the exposed cohort lpha
 - b) drawn from a different source
 - c) no description of the derivation of the non exposed cohort
- 3) Ascertainment of exposure
 - a) secure record (eg surgical records) *
 - b) structured interview *
 - c) written self report (if participants reported their steps per day on a log)
 - d) no description
- 4) Demonstration that outcome of interest was not present at start of study
 - a) yes 🟶

b) no

Comparability

- 1) <u>Comparability of cohorts on the basis of the design or analysis</u>
 - a) study controls for AGE (select the most important factor) *
- b) study controls for any additional factors (gender, SES, and CVD risk factors (e.g. diabetes, hypertension, high cholesterol, BMI) *

Outcome

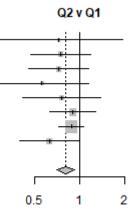
- 1) Assessment of outcome
 - a) independent blind assessment *
 - b) record linkage 🟶
 - c) self report
 - d) no description
- 2) Was follow-up long enough for outcomes to occur
 - a) yes (at least 2 years) *
 - b) no
- 3) Adequacy of follow up of cohorts
 - a) complete follow up all subjects accounted for *****
 - b) subjects lost to follow up unlikely to introduce bias *
 - c) follow up rate low and no description of those lost
 - d) no statement

Figure S1a: Overall Sample Quartile Comparisons – Forest Plots

Study	TE	seTE
ARIC	-0.31	0.4964
BRHS	-0.29	0.2370
FHS	-0.32	0.2365
CARDIA	-0.58	0.3696
JHS	-0.27	0.3019
LIFE	-0.11	0.1818
NAVIGATOR	-0.13	0.0987
HAI	-0.46	0.2286

Random effects model

Heterogeneity: $l^2 = 0\%$, $\tau^2 = 0$, p = 0.82



HR(95%CI)	n	events	weight
0.73 [0.28; 1.93]	113	8	1.9%
0.75 [0.47; 1.19]	293	35	8.5%
0.73 [0.46; 1.16]	1056	29	8.5%
0.56 [0.27; 1.16]	521	11	3.5%
0.76 [0.42; 1.38]	100	21	5.2%
0.90 [0.63; 1.28]	335	60	14.4%
0.88 [0.73; 1.07]	1818	199	48.9%
0.63 [0.40; 0.99]	802	33	9.1%
0.81 [0.71; 0.93]			100.0%

events weight

2.5%

6.5%

9.6%

5.4%

4.3%

14.6%

47.7%

100.0%

9.4%

9

20

29

19

11

46

151

27

Study	TE seTE	Q3 v Q1	HR(95%Cl) n
ARIC	-0.42 0.4729		0.66 [0.26; 1.67] 113
BRHS	-0.80 0.2967		0.45 [0.25; 0.80] 296
FHS	-0.25 0.2429		0.78 [0.49; 1.26] 1056
CARDIA	-0.04 0.3257	- <u>i</u> -+	0.96 [0.51; 1.83] 522
JHS	-0.95 0.3642		0.39 [0.19; 0.79] 100
LIFE	-0.38 0.1976		0.68 [0.47; 1.01] 336
NAVIGATOR	-0.33 0.1092		0.72 [0.58; 0.89] 1818
HAI	-0.65 0.2462		0.52 [0.32; 0.84] 802
Random effects n	nodel	,, ↓	0.67 [0.58; 0.78]

0.2

0.5

1

Q4 v Q1

2

5

Heterogeneity: $I^2 = 3\%$, $\tau^2 < 0.0001$, p = 0.41

Study	TE	seTE
ARIC BRHS FHS CARDIA	-1.05 -0.11	0.6758 0.3465 0.2534 0.3443
JHS LIFE NAVIGATOR HAI	-0.68 -0.34	0.3869 0.2334 0.1108 0.2838
Random effects model		

٦ 0.1 0.5 1 2 10

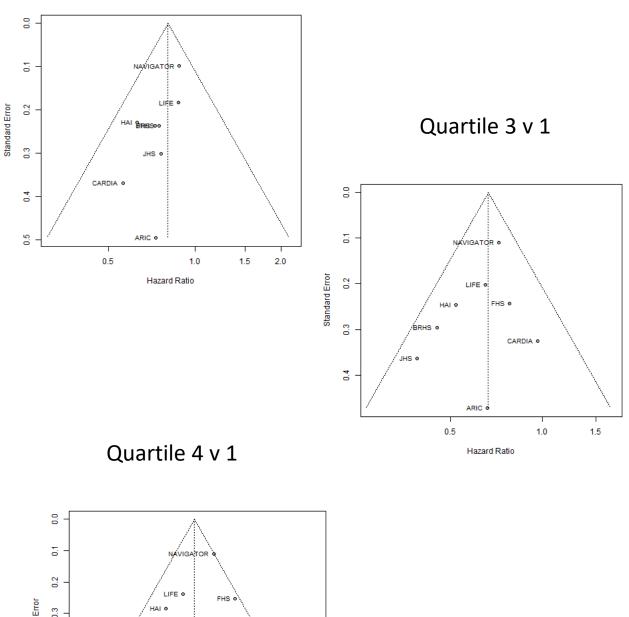
HR(95%CI)	n	events	weight
0.26 [0.07; 0.98] 0.35 [0.18; 0.69] 0.90 [0.55; 1.48] 0.78 [0.40; 1.53] 0.45 [0.21; 0.97] 0.51 [0.32; 0.80] 0.71 [0.57; 0.88] 0.42 [0.24; 0.73]	291 1056 521 101 335 1818	4 14 30 17 11 30 138 20	3.2% 9.5% 14.3% 9.6% 8.1% 15.7% 27.0% 12.5%
0.57 [0.45; 0.74]			100.0%

Heterogeneity: $I^2 = 40\%$, $\tau^2 = 0.0466$, p = 0.11

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.

Model 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 (see supplement 1b)

Figure S1b: Overall Sample Quartile Comparisons – Funnel Plots



Quartile 2 v 1

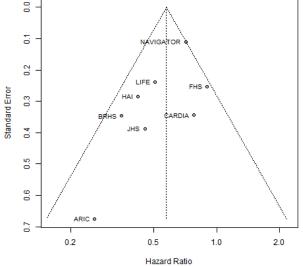


Figure S2a: Association of Steps/Day Quartiles with Cardiovascular Disease Stratified by Younger (<60 years) and Older (≥ 60 years) Adults – Forest Plots – Final Adjusted Model 2

Study	TE	seTE	Q2 v Q1	HR(95%CI)	n	events	weight
Sample = Old			11				
BRHS	-0.29	0.2370		0.75 [0.47; 1.19]		35	8.6%
FHS		0.2895		0.64 [0.36; 1.13]		17	5.8%
JHS		0.3228		0.71 [0.38; 1.35]		17	4.7%
LIFE		0.1818		0.90 [0.63; 1.28]		60	14.7%
NAVIGATOR		0.1130		0.87 [0.70; 1.09]			38.0%
HAI		0.2286		0.63 [0.40; 0.99]		33	9.3%
ARIC Dandom offects model		0.4964		0.73 [0.28; 1.93]	113	8	2.0%
Random effects model			Ť.	0.80 [0.69; 0.93]			83.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.82					
Sample = Young							
CARDIA		0.3696		0.56 [0.27; 1.16]		11	3.6%
FHS		0.4008		0.51 [0.23; 1.12]		12	3.0%
JHS		0.8367		- 1.02 [0.20; 5.25]		4	0.7%
NAVIGATOR		0.2233		1.24 [0.80; 1.92]	579	47	9.7%
Random effects model				0.79 [0.46; 1.35]			17.0%
Heterogeneity: $I^2 = 47\%$, τ	= 0.13	89, p = 0.13					
Random effects model	I		♦	0.82 [0.71; 0.93]			100.0%
				-			
Heterogeneity: $I^2 = 0\%$, τ^2 Test for subgroup differen	= 0, p = ices: χ ₁ ²	0.54 = 0.00, df = 1		5			
Study	TE		Q3 v Q1	HR(95%CI)	n	events	weight
Study				HR(95%CI)	n	events	e weight
Study Sample = Old	TE	seTE					_
Study	-0.80			HR(95%Cl) 0.45 [0.25; 0.80] 0.70 [0.39; 1.26]	296	20	6.5% 6.4%
Study Sample = Old BRHS	-0.80 -0.36	seTE		0.45 [0.25; 0.80]	296 274	20	6.5%
Study Sample = Old BRHS FHS	-0.80 -0.36 -1.44	seTE 0.2967 0.3001		0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01]	296 274 51 336	20 16 6 46	6.5% 6.4% 2.7% 14.7%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR	-0.80 -0.36 -1.44 -0.38	seTE 0.2967 0.3001 0.4624		0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91]	296 274 51 336 1239	20 16 6 46 118	6.5% 6.4% 2.7% 14.7% 37.5%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462		0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84]	296 274 51 336 1239 802	20 16 6 46 118 27	6.5% 6.4% 2.7% 14.7% 37.5% 9.5%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42	seTE 0.2967 0.3001 0.4624 0.1976 0.1239		0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67]	296 274 51 336 1239 802 113	20 16 6 46 118 27	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84]	296 274 51 336 1239 802 113	20 16 6 46 118 27	6.5% 6.4% 2.7% 14.7% 37.5% 9.5%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: 1 ² = 21%,	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67]	296 274 51 336 1239 802 113	20 16 6 46 118 27	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: 1 ² = 21%, Sample = Young	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 Η τ ² = 0.00	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, <i>p</i> = 0.27	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 0.74]	296 274 51 336 1239 802 113	20 16 6 16 118 27 9	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: 1 ² = 21%, Sample = Young CARDIA	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 Η τ ² = 0.00	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, p = 0.27	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 0.74]	296 274 51 336 1239 802 113	20 16 6 118 27 9	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: / ² = 21%, Sample = Young CARDIA FHS	-0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 €I τ ² = 0.00 -0.04 -0.62	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 059, p = 0.27 0.3257 0.3985	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 0.74] 0.96 [0.51; 1.83] 0.54 [0.25; 1.18]	296 274 51 336 1239 802 113 522 782	20 16 6 118 27 9 19 13	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9% 5.4% 3.6%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: J ² = 21%, Sample = Young CARDIA FHS JHS	TE -0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 $\tau^2 = 0.00$ -0.04 -0.04 -0.62 0.24	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, p = 0.27 0.3257 0.3985 0.7914	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 0.74] 0.96 [0.51; 1.83] 0.54 [0.25; 1.18] 1.27 [0.27; 5.98]	296 274 51 336 1239 802 113 522 782 49	20 16 6 118 27 9 19 13 5	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9% 5.4% 3.6% 0.9%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: 1 ² = 21%, Sample = Young CARDIA FHS JHS NAVIGATOR	TE -0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 $\tau^2 = 0.00$ $\tau^2 = 0.00$ -0.04 -0.62 0.24 0.00	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 059, p = 0.27 0.3257 0.3985	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 1.83] 0.54 [0.25; 1.18] 1.27 [0.27; 5.98] 1.00 [0.63; 1.59]	296 274 51 336 1239 802 113 522 782 49 579	20 16 6 118 27 9 19 13 5	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9% 5.4% 3.6% 0.9% 10.2%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: J ² = 21%, Sample = Young CARDIA FHS JHS	TE -0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 M $\tau^2 = 0.00$ -0.04 -0.04 0.24 0.00	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, p = 0.27 0.3257 0.3985 0.7914 0.2378	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 0.74] 0.96 [0.51; 1.83] 0.54 [0.25; 1.18] 1.27 [0.27; 5.98]	296 274 51 336 1239 802 113 522 782 49 579	20 16 6 118 27 9 19 13 5	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9% 5.4% 3.6% 0.9%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: J^2 = 21%, Sample = Young CARDIA FHS JHS NAVIGATOR Random effects mode Heterogeneity: J^2 = 0%, τ	TE -0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 $\tau^2 = 0.00$ $\tau^2 = 0.04$ -0.04 -0.0	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, p = 0.27 0.3257 0.3985 0.7914 0.2378		0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 1.83] 0.54 [0.25; 1.18] 1.27 [0.27; 5.98] 1.00 [0.63; 1.59] 0.90 [0.64; 1.25]	296 274 51 336 1239 802 113 522 782 49 579	20 16 6 118 27 9 19 13 5	6.5% 6.4% 2.7% 14.7% 37.5% 2.6% 79.9% 5.4% 3.6% 0.9% 10.2% 20.1%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: J^2 = 21%, Sample = Young CARDIA FHS JHS NAVIGATOR Random effects mode	TE -0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 $\tau^2 = 0.00$ $\tau^2 = 0.04$ -0.04 -0.0	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, p = 0.27 0.3257 0.3985 0.7914 0.2378	Q3 v Q1	0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 1.83] 0.54 [0.25; 1.18] 1.27 [0.27; 5.98] 1.00 [0.63; 1.59]	296 274 51 336 1239 802 113 522 782 49 579	20 16 6 118 27 9 19 13 5	6.5% 6.4% 2.7% 14.7% 37.5% 9.5% 2.6% 79.9% 5.4% 3.6% 0.9% 10.2%
Study Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects mode Heterogeneity: J^2 = 21%, Sample = Young CARDIA FHS JHS NAVIGATOR Random effects mode Heterogeneity: J^2 = 0%, τ	TE -0.80 -0.36 -1.44 -0.38 -0.34 -0.65 -0.42 M $\tau^2 = 0.00$ -0.04 -0.62 0.24 0.00 -0.04 -0.62 0.24 0.00 -0.04 -0.62 0.24 -0.04 -0.62 0.24 -0.04 -0.62 -0.24 -0.64 -0.64 -0.64 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.64 -0.65 -0.42 -0.64 -0.65 -0.44 -0.65 -0.42 -0.64 -0.65 -0.64 -0.65 -0.04 -0.64 -0.64 -0.64 -0.64 -0.64 -0.64 -0.65 -0.42 -0.04 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.42 -0.65 -0.44 -0.62 -0.65 -0.44 -0.62 -0.65 -0.64 -0.65 -0.64 -0.62 -0.64 -0.64 -0.64 -0.64 -0.64 -0.64 -0.64 -0.64 -0.65 -0.64	seTE 0.2967 0.3001 0.4624 0.1976 0.1239 0.2462 0.4729 0.59, p = 0.27 0.3257 0.3985 0.7914 0.2378 = 0.56		0.45 [0.25; 0.80] 0.70 [0.39; 1.26] 0.24 [0.10; 0.59] 0.68 [0.47; 1.01] 0.71 [0.56; 0.91] 0.52 [0.32; 0.84] 0.66 [0.26; 1.67] 0.62 [0.51; 1.83] 0.54 [0.25; 1.18] 1.27 [0.27; 5.98] 1.00 [0.63; 1.59] 0.90 [0.64; 1.25]	296 274 51 336 1239 802 113 522 782 49 579	20 16 6 118 27 9 19 13 5	6.5% 6.4% 2.7% 14.7% 37.5% 2.6% 79.9% 5.4% 3.6% 0.9% 10.2% 20.1%

Test for subgroup differences: $\chi_1^2 = 3.69$, df = 1 (p = 0.05)

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.

Model 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 (see supplement 1b)

Figure S2a cont: Association of Steps/Day Quartiles with Cardiovascular Disease Stratified by Younger (<60 years) and Older (≥ 60 years) Adults – Forest Plots – Final Adjusted Model 2

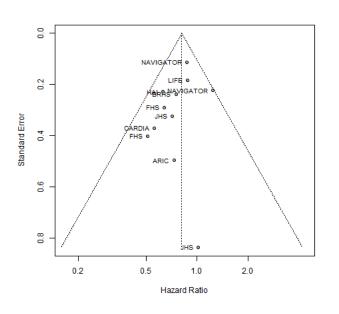
Study	TE seTE	Q4 v Q1	HR(95%CI) n	events weight
Sample = Old BRHS FHS JHS LIFE NAVIGATOR HAI ARIC Random effects m Heterogeneity: / ² = 18	-1.05 0.3465 -0.23 0.3351 -1.26 0.4718 -0.68 0.2334 -0.51 0.1380 -0.87 0.2838 -1.35 0.6758 odel 3%, $\tau^2 = 0.0127, p = 0.29$		0.35 [0.18; 0.69] 291 0.80 [0.41; 1.54] 215 0.28 [0.11; 0.71] 39 0.51 [0.32; 0.80] 335 0.60 [0.46; 0.79] 1239 0.42 [0.24; 0.73] 802 0.26 [0.07; 0.98] 113 0.51 [0.41; 0.63]	
Sample = Young CARDIA FHS JHS NAVIGATOR Random effects m	-0.25 0.3443 -0.47 0.3839 0.04 0.8532 0.30 0.2355		0.78 [0.40; 1.53] 521 0.62 [0.29; 1.32] 841 1.04 [0.19; 5.52] 62 1.35 [0.85; 2.14] 579 0.95 [0.61; 1.48]	17 9.1% 17 8.1% 5 2.6% 44 12.4% 32.3%
Random effects m	odel	0.1 0.5 1 2 10	0.59 [0.44; 0.79]	100.0%
Heterogeneity: $I^2 = 55$	5%, τ ² = 0.1 <u>1</u> 88, <i>p</i> = 0.01		-	

Test for subgroup differences: $\chi_1^2 = 6.04$, df = 1 (p = 0.01)

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.

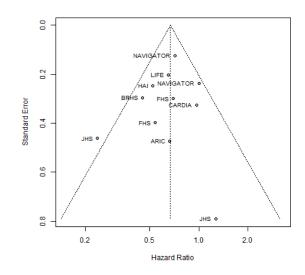
Model is adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or income, body mass index, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b) 13

Figure S2b: Age Stratified Quartile Comparisons – Funnel Plots

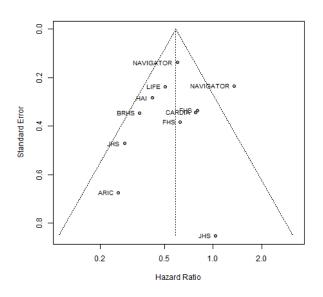


Quartile 2 v 1





Quartile 4 v 1



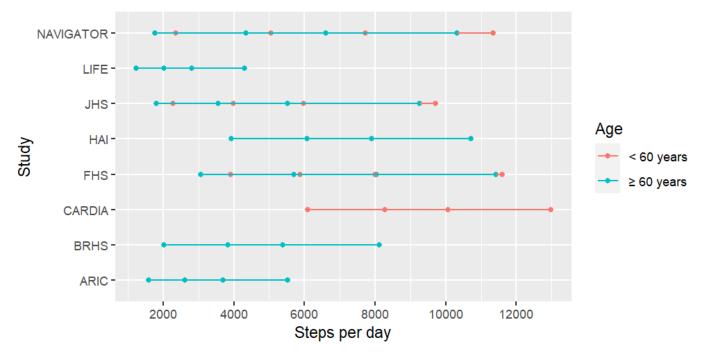


Figure S2c: Median Steps/d for Quartiles by Age Group Among Studies Included in Spline Analysis

Figure S3a: Association of Steps/Day Quartiles with CVD Stratified by Sex – Forest Plots – Final Adjusted Model 2

Study	TE	seTE		Q2 v Q1	ŀ	IR(95%CI)	n	events	weight
Sex = male									
BRHS	-0.29	0.2370			0.75 [0	0.47; 1.19]	293	35	8.4%
CARDIA	-0.43	0.4476	-		0.65 0	0.27; 1.56]	212	8	2.4%
FHS	-0.39	0.3336				0.35; 1.30]			4.3%
JHS	-0.54	0.5235			0.58 (0	0.21; 1.62]	40	8	1.7%
LIFE	-0.34	0.3129			0.71[0	0.38; 1.31]	112	20	4.8%
HAI	-0.45	0.2918			0.64 [0	0.36; 1.13]	361	20	5.6%
NAVIGATOR	-0.20	0.1223		- 	0.82 [0	0.65; 1.04]	893	119	31.7%
Random effects mode	I			*	0.76 [0).63; 0.90]			58.9%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.97							
Sex = female									
CARDIA	-1.02	0.6907		<u>→</u>	0.36 [0	0.09; 1.39]	309	3	1.0%
FHS	-0.17	0.3411		} 	0.84 [0	0.43; 1.65]	602	14	4.1%
JHS	-0.19	0.3793			0.83 [0).39; 1.74]	60	13	3.3%
LIFE	-0.47	0.2371			0.62 [0	0.39; 0.99]	223	31	8.4%
HAI	-0.34	0.3109			0.71[0).39; 1.31]	441	13	4.9%
NAVIGATOR	0.04	0.1561		<u>+</u>	1.04 [0	0.77; 1.41]	925	80	19.4%
Random effects mode					0.81 [0).62; 1.04]			41.1%
Heterogeneity: $I^2 = 5\%$, τ^2	= 0.0224	l, p = 0.39							
Random effects mode	I				0.79 [0).69; 0.90]			100.0%
11-1			0.1	0.5 1 2	10				
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.85							

Test for subgroup differences: $\chi_1^2 = 0.05$ Test for subgroup differences: $\chi_1^2 = 0.17$, df = 1 (p = 0.68)

Study	TE	seTE	Q3 v Q1	HR(95%CI)	n	events	weight
Sex = male BRHS CARDIA FHS JHS LIFE HAI NAVIGATOR Random effects mode Heterogeneity: / ² = 0%, τ ²	-0.54 -0.27 -0.41 -0.35 -0.53 -0.43	0.2967 0.4411 0.3299 0.5630 0.3151 0.3001 0.1384 0.93		0.45 [0.25; 0.80] 0.58 [0.24; 1.38] 0.76 [0.40; 1.45] 0.66 [0.22; 1.99] 0.71 [0.38; 1.31] 0.59 [0.33; 1.06] 0.65 [0.50; 0.85] 0.63 [0.52; 0.76]	222 480 40 112 362	9 17 6 21 18	6.6% 3.0% 5.4% 1.8% 5.9% 6.5% 30.6% 59.8%
Sex = female CARDIA FHS JHS LIFE HAI NAVIGATOR Random effects mode Heterogeneity: / ² = 49%, o	-0.15 -1.27 -0.62 -0.69 -0.24	0.5011 0.3685 0.5029 0.2510 0.4241 0.1768 7, p = 0.08		1.92 [0.72; 5.14] 0.86 [0.42; 1.77] 0.28 [0.10; 0.75] 0.54 [0.33; 0.88] 0.50 [0.22; 1.15] 0.79 [0.56; 1.12] 0.68 [0.48; 0.97]	576 60 224 441	12 5 27 9	2.3% 4.3% 2.3% 9.3% 3.3% 18.7% 40.2%
Random effects mode	4			0.66 [0.56; 0.76]			100.0%

Heterogeneity: $l^2 = 2\%$, $\tau^2 < 0.0001$, p = 0.43Test for subgroup differences: $\chi^2_1 = 0.17$, df = 1 (p = 0.68)

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.

0.2 0.5 1 2

5

Model is adjusted for age, device wear time, race/Ethnicity (if applicable), education or income, body mass index, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b)

Figure S3a cont: Association of Steps/Day Quartiles with CVD Stratified by Sex – Forest Plots – Final Adjusted Model 2

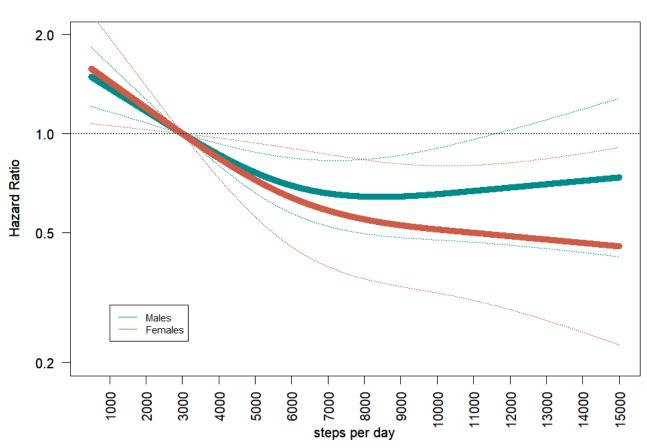
Study	TE seTE	Q4 v Q1	HR(95%CI) n	events	weight
Sex = male BRHS CARDIA FHS JHS LIFE HAI NAVIGATOR Random effects mode Heterogeneity: / ² = 25%, 1			0.35 [0.18; 0.69] 291 0.74 [0.33; 1.64] 259 1.06 [0.57; 1.97] 564 0.81 [0.28; 2.35] 52 0.72 [0.35; 1.48] 112 0.44 [0.22; 0.88] 361 0.77 [0.58; 1.02] 893 0.68 [0.51; 0.89]	14 14 25 8 14 13 90	7.8% 6.2% 8.9% 3.9% 7.1% 7.6% 19.2% 60.7%
Sex = female CARDIA FHS JHS LIFE HAI NAVIGATOR Random effects mode Heterogeneity: / ² = 26%, 1	-0.49 0.7169 -0.65 0.5162 -1.41 0.6514 -0.96 0.2995 -0.89 0.4775 -0.25 0.1884		0.61 [0.15; 2.51] 262 0.52 [0.19; 1.44] 492 0.24 [0.07; 0.87] 49 0.38 [0.21; 0.69] 223 0.41 [0.16; 1.05] 440 0.78 [0.54; 1.13] 924 0.51 [0.35; 0.76]	3 5 3 17 7 50	2.3% 4.2% 2.8% 9.5% 4.8% 15.7% 39.3%
Random effects mode Heterogeneity: $l^2 = 25\%$, 1	-	0.1 0.5 1 2 10	0.61 [0.49; 0.77]		100.0%

Heterogeneity: $l^{2} = 25\%$, $\tau^{2} = 0.0488$, p = 0.19Test for subgroup differences: $\chi_{1}^{2} = 1.25$, df = 1 (p = 0.26)

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.

Model is adjusted for age, device wear time, race/Ethnicity (if applicable), education or income, body mass index, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement $1b^{7}$

Figure S3b: Sex Stratified Restricted Cubic Spline – Final adjusted Model



Association of Steps per Day with CVD Events by Sex

Restricted cubic splines of hazard ratios of steps per day with CVD events. Knots at 10th, 50th, and 90th, percentile of steps/d. Reference at 3000 steps/day (median of lowest quartile). Model is adjusted for age, device wear time, race/Ethnicity (if applicable), education or income, body mass index, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b)

The y-axis is a log scale.

Wald test p-value=0.0008 for males and p-value =0.013 for females for non-linearity

Figure S3c: Median Steps/d for Quartiles by Sex among Studies Included in Sex Stratified Spline analysis

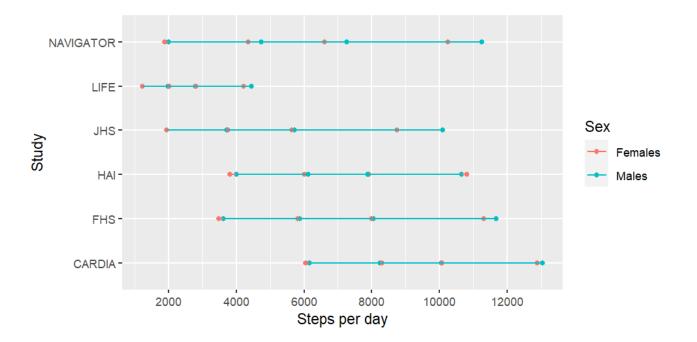


Figure S4. Forest Plots Stratified by Publication Status (Yes/No)

Study	TE		seTE	
Published = No				
ARIC		_	.4964	
FHS		-	.2365	
CARDIA			.3696	
JHS		_	.3019	
HAI Dandom offecto model		0	.2286	
Random effects model				
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p :	= 0.	.96	
Published = Yes				
BRHS	-0.20	0	.2370	
LIFE			.1818	
NAVIGATOR		_	.0987	
Random effects model			.0507	
Heterogeneity: $I^2 = 0\%$, τ^2		= 0	80	
	0,10			
Random effects model				
Heterogeneity: $I^2 = 0\%$, τ^2 Test for subgroup differen	= 0, p	= 0	.82	
Test for subbroup differen	CES 7.	=	2.57 df = 1 (b = 0.11)	
Study	TE	1	seTE	
Published = No				
ARIC	-0.42	0.	4729	
FHS	-0.25	0.	2429	
CARDIA	-0.04	0.	3257	
JHS	-0.95	0.	3642	
	-0.65	0.	2462	
Random effects model				

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0.5	1	1	2

Published Y/N Q2 v Q1 . .

HR(95%)	CI) n	events	weight
0.73 [0.28; 1.9 0.73 [0.46; 1.1 0.56 [0.27; 1.1 0.76 [0.42; 1.3 0.63 [0.40; 0.9 0.68 [0.53; 0.8	16] 1056 16] 521 38] 100 99] 802	8 29 11 21 33	1.9% 8.5% 3.5% 5.2% 9.1% 28.2%
0.75 [0.47; 1.1 0.90 [0.63; 1.2 0.88 [0.73; 1.0 0.87 [0.74; 1. 0	28] 335)7] 1818	35 60 199	8.5% 14.4% 48.9% 71.8%
0.81 [0.71; 0.9	3]		100.0%

Study	TE	seTE	Published Y/N Q3 v Q1	HR(95%CI)	n	events	weight
Published = No ARIC FHS CARDIA JHS HAI Random effects model Heterogeneity: 1 ² = 18%, t	-0.25 -0.04 -0.95 -0.65	0.4729 0.2429 0.3257 0.3642 0.2462 24, <i>p</i> = 0.30		0.66 [0.26; 1.67] 0.78 [0.49; 1.26] 1 0.96 [0.51; 1.83] { 0.39 [0.19; 0.79] 0.52 [0.32; 0.84] { 0.64 [0.47; 0.86]	1056 522 100	9 29 19 11 27	2.5% 9.6% 5.4% 4.3% 9.4% 31.3%
Published = Yes BRHS LIFE NAVIGATOR Random effects mode Heterogeneity: / ² = 10%, or Random effects mode	-0.38 -0.33 ² = < 0.0	0.2967 0.1976 0.1092 001, p = 0.3	,,	0.45 [0.25; 0.80] 2 0.68 [0.47; 1.01] 3 0.72 [0.58; 0.89] 1 0.68 [0.57; 0.81] 0.67 [0.58; 0.78]	336	20 46 151	6.5% 14.6% 47.7% 68.7% 100.0%
			0.2 0.5 1 2 5	5			

Heterogeneity: $I^2 = 3\%$, $\tau^2 < 0.0001$, p = 0.41Test for subgroup differences: $\chi_1^2 = 0.12$, df = 1 (p = 0.73)

Study	TE seTE	Published Y/N Q4 v Q1	HR(95%Cl) n	events weight
Published = No ARIC FHS CARDIA JHS HAI Random effects mo Heterogeneity: 1 ² = 410	-1.35 0.6758 -0.11 0.2534 -0.25 0.3443 -0.79 0.3869 -0.87 0.2838 del $\%, \tau^2 = 0.0799, p = 0.15$		0.26 [0.07; 0.98] 113 0.90 [0.55; 1.48] 1056 0.78 [0.40; 1.53] 521 0.45 [0.21; 0.97] 101 0.42 [0.24; 0.73] 802 0.58 [0.39; 0.86]	4 3.2% 30 14.3% 17 9.6% 11 8.1% 20 12.5% 47.7%
Published = Yes BRHS LIFE NAVIGATOR Random effects mo Heterogeneity: / ² = 59 ⁶	-1.05 0.3465 -0.68 0.2334 -0.34 0.1108 del %, $\tau^2 = 0.0664$, $p = 0.09$	*	0.35 [0.18; 0.69] 291 0.51 [0.32; 0.80] 335 0.71 [0.57; 0.88] 1818 0.55 [0.38; 0.81]	14 9.5% 30 15.7% 138 27.0% 52.3%
Random effects mo	del		0.57 [0.45; 0.74]	100.0%
Heterogeneity: / ² = 40 ^o	%, τ ² = 0.0466, ρ = 0.11	0.1 0.5 1 2 10		

Heterogeneity: $l^2 = 40\%$, $\tau^2 = 0.0466$, p = 0.11Test for subgroup differences: $\chi_1^2 = 0.02$, df = 1 (p = 0.88)

Figure S5. Forest Plots Stratified by Device type (Accelerometer vs Pedometer)

Accel vs Ped Q2 v Q1

HR(95%CI) n

0.73 [0.28; 1.93] 113

0.75 [0.47; 1.19] 293

0.73 [0.46; 1.16] 1056

0.56 [0.27; 1.16] 521

0.90 [0.63; 1.28] 335

0.63 [0.40; 0.99] 802

0.76 [0.42; 1.38] 100

0.88 [0.73; 1.07] 1818

0.74 [0.61; 0.91]

0.87 [0.72; 1.04]

0.81 [0.71; 0.93]

2

events weight

1.9%

8.5%

8.5%

3.5%

14.4%

9.1%

45.9%

5.2%

48.9%

54.1%

100.0%

8

35

29

11

60

33

21

199

Study	TE	seTE
AccelPed = Accelerom	neter	
ARIC	-0.31	0.4964
BRHS	-0.29	0.2370
FHS	-0.32	0.2365
CARDIA	-0.58	0.3696
LIFE	-0.11	0.1818
HAI	-0.46	0.2286
Random effects model	1	
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.82

AccelPed = Pedometer		
JHS	-0.27	0.3019
NAVIGATOR	-0.13	0.0987
Random effects model		
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0\%$	= 0, p =	0.65

Random effects model

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, p = 0.82Test for subgroup differences: $\chi_1^2 = 1.22$, df = 1 (p = 0.27)

Study	TE	seTE		Accel vs	S Ped	Q3 v Q1		HR(95%CI)	n	events	weight
AccelPed = Accelere	ometer										
ARIC	-0.42	0.4729	-			_	0.	.66 [0.26; 1.67]	113	9	2.5%
BRHS	-0.80	0.2967	-		-		0.	45 [0.25; 0.80]	296	20	6.5%
FHS	-0.25	0.2429			-		0.	78 [0.49; 1.26]	1056	29	9.6%
CARDIA	-0.04	0.3257		\rightarrow	-		0.	.96 [0.51; 1.83]	522	19	5.4%
LIFE	-0.38	0.1976		<u> </u>	_		0.	.68 [0.47; 1.01]	336	46	14.6%
HAI	-0.65	0.2462			-		0.	.52 [0.32; 0.84]	802	27	9.4%
Random effects mo				\rightarrow	-		0.	65 [0.53; 0.81]			48.0%
Heterogeneity: $I^2 = 0\%$,	$\tau^2 = 0, p =$	0.48									
AccelPed = Pedome											
JHS		0.3642						.39 [0.19; 0.79]		11	4.3%
NAVIGATOR		0.1092			-1			72 [0.58; 0.89]		151	47.7%
Random effects mod Heterogeneity: $I^2 = 62\%$		38 p = 0.10			-		0.	58 [0.33; 1.04]			52.0%
	-,										
Random effects mo	del				>		0.	67 [0.58; 0.78]			100.0%
			I	I	1	I	1				
2	2		0.2	0.5	1	2	5				
Heterogeneity: / ² = 3%, Test for subgroup diffe			0.72)								

0.5

1

Study	TE	seTE	Accel vs Ped Q4 v Q1	HR(95%CI)	n	events	weight
AccelPed = Accele	rometer		÷ 1				
ARIC	-1.35	0.6758		0.26 [0.07; 0.98]	113	4	3.2%
BRHS	-1.05	0.3465	+	0.35 [0.18; 0.69]	291	14	9.5%
FHS	-0.11	0.2534		0.90 [0.55; 1.48]	1056	30	14.3%
CARDIA	-0.25	0.3443		0.78 [0.40; 1.53]	521	17	9.6%
LIFE	-0.68	0.2334		0.51 [0.32; 0.80]	335	30	15.7%
HAI	-0.87	0.2838		0.42 [0.24; 0.73]	802	20	12.5%
Random effects m	odel		<u></u>	0.54 [0.39; 0.75]			64.9%
Heterogeneity: I ² = 43	3%, τ ² = 0.071	12, p = 0.12					
AccelPed = Pedom	neter						
JHS	-0.79	0.3869		0.45 [0.21; 0.97]	101	11	8.1%
NAVIGATOR	-0.34	0.1108	-	0.71 [0.57; 0.88]	1818	138	27.0%
Random effects m		0.00	+	0.66 [0.48; 0.91]			35.1%
Heterogeneity: / ² = 20)%,τ = 0.020	JU, p = 0.26					
Random effects m	odel		· · · · · · · · · · · · · · · · · · ·	0.57 [0.45; 0.74]			100.0%
			04 05 4 0 4	<u>,</u>			
	2		0.1 0.5 1 2 10	0			
Heterogeneity: 1 ² = 40)%, τ [−] = 0.046	ю́, p = 0.11					

Test for subgroup differences: $\chi_1^2 = 0.75$, df = 1 (p = 0.39)

Table S3. Leave-One-Study Out Sensitivity Analyses – Comparing Quartile 4 (most steps) vs 1 (ref: least steps)

HR	95 9	%CI
0.5923	0.4118	0.852
0.5988	0.4126	0.8692
0.5319	0.3638	0.7777
0.5509	0.3795	0.7997
0.5813	0.4013	0.8421
0.5796	0.3957	0.8491
0.5188	0.3401	0.7915
0.5922	0.4062	0.8633
	0.5923 0.5988 0.5319 0.5509 0.5813 0.5796 0.5188	0.5923 0.4118 0.5988 0.4126 0.5319 0.3638 0.5509 0.3795 0.5813 0.4013 0.5796 0.3957 0.5188 0.3401

Hazard Ratio and 95% Confidence Intervals [HR (95% CI)] adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or occupation, BMI, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement table 1b).

Table S4. Fixed vs Random Effects Models

Primary Results Fixed vs. Random	Effects	
	HR	95% CI
Quartile 2 vs Quartile 1 (ref)		
Fixed	0.81	(0.70; 0.92)
Random	0.81	(0.70; 0.92)
Quartile 3 vs Quartile 1 (ref)		
Fixed	0.66	(0.57; 0.77)
Random	0.66	(0.57; 0.77)
Quartile 4 vs Quartile 1 (ref)		
Fixed	0.63	(0.53; 0.73)
Random	0.57	(0.45; 0.74)

Hazard Ratio and 95% Confidence Intervals [HR (95% CI)] adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or occupation, BMI, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement table 1b).

Table S5: Association of Stepping Rate Variables with CVD with and without Adjusting for Step Volume

Q331690470.69[0.47; 1.0]Q431691540.82[0.57; 1.2]Model 3: Full Adjusted Model PLUS Step VolumeQ131688841Q231690441.01[0.65; 1.5]Q331692431.06[0.67; 1.6]Q431690501.24[0.74; 2.0]Time (in min) spent at ≥100 spmModel 2: Full Adjusted Model (not including step volume)Q121574891Q221582410.65[0.44; 0.5]Q321572541.10[0.60; 2.0]Q421580380.76[0.50; 1.1]Model 3: Full Adjusted Model PLUS Step VolumeQ121577781Q221576360.77[0.52; 1.1]Q321576431.11[0.53; 2.3]	Step, Quart		No. of Participants	CVD Events	HR (95% CI)
Q1 4 2024 160 1 Q2 4 2025 107 0.81 [0.62; 1.1] Q3 4 2027 113 0.91 [0.65; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 78 0.72 [0.46; 1.3] Q2 4 2025 78 0.72 [0.46; 1.3] Q2 4 2025 96 0.84 [0.54; 1.3] Q3 4 2027 108 1.20 [0.31; 1.5] Q3 4 2025 83 1.01 [0.73; 1.5] Q4 4 2025 83 1.01 [0.73; 1.5] Peak 60 Model 2: Full Adjusted Model (not including step volume) Model 3: 1.20 [0.51; 1.7] Model 3: Full Adjusted Model PLUS Step Volume 1690 47 0.82 [0.55; 1.7] Model 3: Full Adjusted Model INC Step Volume 10.02 [0.67; 1.5] Q1 3 1690 47 0.62 [0.41; 0.6] Q2 3 1690 47 0.62 [0.47; 1.0] Q2 3 1690 44 1.00 [0.62; 1.6] Q1 3					
Q2 4 2025 107 0.81 [0.62; 1.0 Q3 4 2027 113 0.91 [0.66; 1.1 Q4 4 2025 78 0.72 [0.46; 1.1 Model 3: Full Adjusted Model PLUS Step Volume 1 1 1 Q2 4 2025 96 0.84 [0.54; 1.2] Q3 4 2027 108 1.20 [0.91; 1.9] Q4 4 2025 83 1.01 [0.73; 1.2] Q4 4 2025 83 1.01 [0.73; 1.2] Peak 60 1 1.02 3 1690 52 0.75 [0.45; 1.2] Q3 3 1690 47 0.82 [0.55; 1.2] 0.43 3 1690 47 0.82 [0.41; 0.5] Model 3: Full Adjusted Model PLUS Step Volume 1 0.22 3 1690 44 1.00 [0.62; 1.6] Q1 3 1690 44 1.00 [0.62; 1.6] 0.2 0.43 1.690 44 1.00 [0.62; 1.6]	· · · · · · · · · · · · · · · · · · ·				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $					
Q4 4 2025 78 0.72 [0.46; 1.1] Model 3: Full Adjusted Model PLUS Step Volume 78 0.72 [0.46; 1.1] Q2 4 2025 96 0.84 [0.54; 1.2] Q3 4 2027 108 1.20 [0.91; 1.5] Q4 4 2025 83 1.01 [0.73; 1.2] Q4 4 2025 83 1.01 [0.73; 1.2] Peak 60 Model 2: Full Adjusted Model [not including step volume) 78 0.75 [0.45; 1.2] Q1 3 1989 96 1 Q2 3 1691 61 0.94 [0.66; 1.2] Q3 3 1690 47 0.82 [0.55; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 89 1 Q2 3 1690 47 0.62 [0.47; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 47 0.62 [0.47; 1.2] <th< td=""><td></td><td></td><td></td><td></td><td></td></th<>					
Model 3: Full Adjusted Model PLUS Step Volume 135 1 Q2 4 2025 96 0.84 [0.54]; 1.5 Q3 4 2027 108 1.20 [0.91]; 1.5 Q4 4 2025 83 1.01 [0.73]; 1.3 Peak 60 Model 2: Full Adjusted Model (not including step volume) Q3 3 1691 61 0.94 [0.66]; 1.3 Q3 3 1690 47 0.82 [0.55]; 1.3 Model 3: Full Adjusted Model PLUS Step Volume Q1 3 1689 89 1 Q2 3 1690 47 0.62 [0.41]; 0.5 Q1 3 1689 89 1 Q2 3 1690 47 0.62 [0.41]; 0.5 <					
Q1 4 2024 135 1 Q2 4 2025 96 0.84 [0.54; 1.3] Q3 4 2027 108 1.20 [0.91; 1.3] Q4 4 2025 83 1.01 [0.73; 1.3] Peak 60 Model 2: Full Adjusted Model (not including step volume) 1 3 1989 96 1 Q2 3 1690 52 0.75 [0.45; 1.4] 0.94 [0.66; 1.3] Q4 3 1690 47 0.82 [0.55; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 20 3 1690 47 0.62 [0.41; 0.6] Q2 3 1690 47 0.62 [0.41; 0.6] 0.63; 1.6] Q3 3 1691 40 1.00 [0.62; 1.6] Q3 3 1691 40 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 47 0.69 [0.47; 1.6] Q4 3 1691				78	0.72 [0.46; 1.13]
Q2 4 2025 96 0.84 [0.54; 1.3] Q3 4 2027 108 1.20 [0.91; 1.5] Q4 4 2025 83 1.01 [0.73; 1.3] Peak 60 Model 2: Full Adjusted Model (not including step volume) Q1 3 1989 96 1 Q2 3 1690 52 0.75 [0.45; 1.2] Q4 3 1690 47 0.82 [0.55; 1.2] Model 3: Full Adjusted Model PLUS Step Volume	•	•		425	
Q3 4 2027 108 1.20 [0.91]; 1.5 Q4 4 2025 83 1.01 [0.73]; 1.5 Peak 60 Model 2: Full Adjusted Model (not including step volume) 96 1 Q2 3 1690 52 0.75 [0.45]; 1.7 Q3 3 1691 61 0.94 [0.66]; 1.3 Q4 3 1690 47 0.82 [0.55]; 1.7 Model 3: Full Adjusted Model PLUS Step Volume 7 0.62 [0.41]; 0.5 Q2 3 1690 47 0.62 [0.41]; 0.5 Q3 3 1691 40 1.02 [0.67]; 1.5 Q3 3 1691 40 1.02 [0.67]; 1.5 Q4 3 1690 47 0.62 [0.47]; 1.0 Q4 3 1690 47 0.62 [0.47]; 1.0 Q4 3 1690 47 0.62 [0.47]; 1.0 Q2 3 1690					
Q4 4 2025 83 1.01 [0.73; 1.3] Peak 60					
Peak 60 Model 2: Full Adjusted Model (not including step volume) Q1 3 1989 96 1 Q2 3 1690 52 0.75 [0.45; 1.2] Q3 3 1691 61 0.94 [0.66; 1.3] Q4 3 1690 47 0.82 [0.55; 1.2] Q4 3 1690 47 0.82 [0.55; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 1 0.2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1691 40 1.02 [0.67; 1.5] 0.2] 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] 1.0] 1.02 [0.67; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] 1.0] 1.03 [0.6] 1.6] Model 2: Full Adjusted Model (not including step volume) 1 1.03 [0.6] 1.6] 1.02 [0.75; 1.2] Q1 3 1681 96 1 1.0] 1.065; 1.5] <td< td=""><td></td><td></td><td></td><td></td><td></td></td<>					
Model 2: Full Adjusted Model (not including step volume) 96 1 Q1 3 1989 96 1 Q2 3 1690 52 0.75 [0.45; 1.2] Q3 3 1691 61 0.94 [0.66; 1.2] Q4 3 1690 47 0.82 [0.55; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 989 1 Q2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1690 47 0.62 [0.41; 0.5] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm 100 1.626 1 Q2 3 1690 47 0.69 [0.47; 1.4] Q1 3 1686 96 1 Q2 3 1690 47 0.69 [0.47; 1.6] Q1 3 1680 84 1 Q2 3 1690 44	Q4	4	2025	83	1.01 [0.73; 1.39]
Q1 3 1989 96 1 Q2 3 1690 52 0.75 [0.45; 1.7] Q3 3 1691 61 0.94 [0.66; 1.3] Q4 3 1690 47 0.82 [0.55; 1.7] Model 3: Full Adjusted Model PLUS Step Volume 99 1 1 Q2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1691 40 1.02 [0.67; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] Q3 3 1691 40 1.02 [0.67; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm Model 2: Full Adjusted Model (not including step volume) Q1 3 1686 96 1 Q2 3 1691 54 0.82 [0.57; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 1 1 1 1 Q2 3 1690 44 1.01 [0.65; 1.5] 1 Q3 3 1690 50 1.24					
Q2 3 1690 52 0.75 [0.45; 1.2] Q3 3 1691 61 0.94 [0.66; 1.3] Q4 3 1690 47 0.82 [0.55; 1.2] Model 3: Full Adjusted Model PLUS Step Volume			• •		
Q3 3 1691 61 0.94 0.66 1.3 Q4 3 1690 47 0.82 0.55 1.2 Model 3: Full Adjusted Model PLUS Step Volume 9 1 Q2 3 1689 89 1 Q2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1690 47 0.62 [0.41; 0.5] Q3 3 1690 47 0.62 [0.41; 0.5] Q3 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm 96 1 1.00 [0.62; 1.6] Q2 3 1693 59 0.86 [0.59; 1.2] Q4 3 1691 54 0.82 [0.57; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 20 3 1690 44 1.01 [0.65; 1.5] Q2 3 <td></td> <td></td> <td></td> <td></td> <td>-</td>					-
Q4 3 1690 47 0.82 [0.55, 1.2] Model 3: Full Adjusted Model PLUS Step Volume 9 1 Q2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1691 40 1.02 [0.67; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm Model 2: Full Adjusted Model (not including step volume) 96 1 Q2 3 1693 59 0.86 [0.59; 1.2] Q3 3 1693 59 0.86 [0.59; 1.2] Q3 3 1691 54 0.82 [0.57; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 90 1 1 Q2 3 1690 44 1.01 [0.65; 1.5] Q3 3 1692 43 1.06 [0.67; 1.6] Q4 3 1690 50					
Model 3: Full Adjusted Model PLUS Step Volume Q1 3 1689 89 1 Q2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1691 40 1.02 [0.67; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm 102 3 1686 96 1 Q1 3 1686 96 1 2 1 3 1686 96 1 2 1 3 1693 59 0.86 [0.59; 1.7] 2 0.63 3 1690 47 0.69 [0.47; 1.0] 0.63 1 2 1					
Q1 3 1689 89 1 Q2 3 1690 47 0.62 [0.41; 0.9] Q3 3 1691 40 1.02 [0.67; 1.9] Q4 3 1690 44 1.00 [0.62; 1.6] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm Model 2: Full Adjusted Model (not including step volume) 01 3 1686 96 1 Q2 3 1693 59 0.86 [0.59; 1.2] 0.43 1.691 54 0.82 [0.57; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 01 3 1688 84 1 1 Q2 3 1690 44 1.01 [0.65; 1.5] 1 0.62 1.4] 1.06 [0.67; 1.6] Q3 3 1690 50 1.24 [0.74; 2.0] 1 2 1.574 89 1 Q4 3 1690 50 1.24 [0.74; 2.0] 1 2 1.577 1				4/	0.82 [0.55; 1.21]
Q2 3 1690 47 0.62 [0.41; 0.5] Q3 3 1691 40 1.02 [0.67; 1.5] Q4 3 1690 44 1.00 [0.62; 1.6] Time (in min) spent at ≥40 spm					
Q3 3 1691 40 1.02 [0.67, 1.5] Q4 3 1690 44 1.00 [0.62, 1.6] Time (in min) spent at ≥40 spm Model 2: Full Adjusted Model (not including step volume) 01 3 1686 96 1 Q2 3 1693 59 0.86 [0.59; 1.2] Q3 3 1690 47 0.69 [0.47; 1.0] Q4 3 1691 54 0.82 [0.57; 1.2] Model 3: Full Adjusted Model PLUS Step Volume 02 3 1690 44 1.01 [0.65; 1.5] Q1 3 1688 84 1 1 0.22 3 1690 50 1.24 [0.74; 2.0] Q1 3 1690 50 1.24 [0.74; 2.0] 0.65 1.64 0.65 1.64 0.65 1.64 0.65 1.64 0.65 1.64 0.65 1.24 [0.74; 2.0] 0.61 1.00 1.06 1.06 1.06 1.24 [0.74; 2.0] 0.22 1.582 41 0.65 <td< td=""><td></td><td></td><td></td><td></td><td></td></td<>					
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Model 3: Full Adjusted Model PLUS Step Volume Q1 3 1688 84 1 Q2 3 1690 44 1.01 [0.65; 1.5] Q3 3 1692 43 1.06 [0.67; 1.6] Q4 3 1690 50 1.24 [0.74; 2.0] Time (in min) spent at ≥100 spm Model 2: Full Adjusted Model (not including step volume) Q1 2 1574 89 1 Q2 2 1582 41 0.65 [0.44; 0.6] 0.6] Q3 2 1572 54 1.10 [0.60; 2.0] Q4 2 1580 38 0.76 [0.50; 1.1] Model 3: Full Adjusted Model PLUS Step Volume 2 1577 78 1 Q1 2 1577 36 0.77 [0.52; 1.1] Q2 2 1576 36 0.77 [0.52; 1.1]	Q3		1690	47	0.69 [0.47; 1.01]
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Q431690501.24 [0.74; 2.0Time (in min) spent at ≥100 spmModel 2: Full Adjusted Model (not including step volume)Q121574891Q221582410.65 [0.44; 0.5Q321572541.10 [0.60; 2.0Q421580380.76 [0.50; 1.1Model 3: Full Adjusted Model PLUS Step VolumeQ121577781Q221576360.77 [0.52; 1.1Q321576431.11 [0.53; 2.3	Q2	3	1690	44	1.01 [0.65; 1.55]
Time (in min) spent at ≥100 spm Model 2: Full Adjusted Model (not including step volume) Q1 2 1574 89 1 Q2 2 1582 41 0.65 [0.44; 0.9] Q3 2 1572 54 1.10 [0.60; 2.0] Q4 2 1580 38 0.76 [0.50; 1.1] Model 3: Full Adjusted Model PLUS Step Volume Volume Volume Q1 2 1577 78 1 Q2 2 1576 36 0.77 [0.52; 1.1] Q3 2 1576 43 1.11 [0.53; 2.3]	Q3	3	1692	43	1.06 [0.67; 1.68]
Model 2: Full Adjusted Model (not including step volume) Q1 2 1574 89 1 Q2 2 1582 41 0.65 [0.44; 0.9 Q3 2 1572 54 1.10 [0.60; 2.0 Q4 2 1580 38 0.76 [0.50; 1.1 Model 3: Full Adjusted Model PLUS Step Volume Volume Volume Volume Q1 2 1576 36 0.77 [0.52; 1.1 Q3 2 1576 43 1.11 [0.53; 2.3	Q4	3	1690	50	1.24 [0.74; 2.07]
Model 2: Full Adjusted Model (not including step volume) Q1 2 1574 89 1 Q2 2 1582 41 0.65 [0.44; 0.9 Q3 2 1572 54 1.10 [0.60; 2.0 Q4 2 1580 38 0.76 [0.50; 1.1 Model 3: Full Adjusted Model PLUS Step Volume Volume Volume Volume Q1 2 1576 36 0.77 [0.52; 1.1 Q3 2 1576 43 1.11 [0.53; 2.3	Time (in min) spent at ≥100 spm				
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Q3 2 1572 54 1.10 [0.60; 2.0] Q4 2 1580 38 0.76 [0.50; 1.1] Model 3: Full Adjusted Model PLUS Step Volume Volume 1 Q1 2 1577 78 1 Q2 2 1576 36 0.77 [0.52; 1.1] Q3 2 1576 43 1.11 [0.53; 2.3]	•	-	•	89	1
Q3 2 1572 54 1.10 [0.60; 2.0] Q4 2 1580 38 0.76 [0.50; 1.1] Model 3: Full Adjusted Model PLUS Step Volume Volume 1 Q1 2 1577 78 1 Q2 2 1576 36 0.77 [0.52; 1.1] Q3 2 1576 43 1.11 [0.53; 2.3]					0.65 [0.44; 0.95]
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Model 3: Full Adjusted Model PLUS Step Volume 1 Q1 2 1577 78 1 Q2 2 1576 36 0.77 [0.52; 1.1] Q3 2 1576 43 1.11 [0.53; 2.3]					0.76 [0.50; 1.15]
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Q3 2 1576 43 1.11 [0.53; 2.3					0.77 [0.52; 1.13]
	Q4		1579	29	0.98 [0.53; 1.80]

Model 2 adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or occupation, BMI, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b),

Model 3 adds steps/d using the residual method.

Figure S6a. Peak 30 Minute Intensity – Forest Plots Final Model Adjusting for Steps/Day

Study	TE seTE	Peak 30: Q2 v Q1	HR(95%Cl) n events weight
FHS ARIC	-0.31 0.2614		0.73 [0.44; 1.22] 1056 23 32.1%
LIFE	1.08 0.7156 0.01 0.2112		
CARDIA	-0.78 0.3785		0.46 [0.22; 0.97] 521 10 21.6%
Random effects mode			0.84 [0.54; 1.30] 100.0%
Heterogeneity: $I^2 = 55\%$,	$\tau^2 = 0.0854, p = 0.08$		
		0.1 0.5 1 2	10
Study	TE seTE	Peak 30: Q3 v Q1	HR(95%Cl) n events weight
FHS	0.27 0.2735		1.31 [0.77; 2.24] 1056 17 27.6%
ARIC	0.94 0.7165	- <u>i</u>	2.56 [0.63; 10.43] 113 12 4.0%
LIFE	0.22 0.2037		1.24 [0.83; 1.85] 336 63 49.7%
CARDIA	-0.20 0.3320		0.82 [0.43; 1.57] 522 16 18.7%
Random effects mode			1.20 [0.91; 1.59] 100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	$^{2} < 0.0001, p = 0.46$		
		0.1 0.5 1 2	10
Study	TE seTE	Peak 30: Q4 v Q1	HR(95%Cl) n events weight
FHS	-0.24 0.3611		0.79 [0.39; 1.60] 1056 16 20.3%
ARIC	0.54 0.7676	<u> </u>	
LIFE	-0.04 0.2254		0.96 [0.62; 1.49] 335 43 52.2%
CARDIA	0.24 0.3395		1.27 [0.65; 2.47] 521 17 23.0%
Random effects model Heterogeneity: $I^2 = 0\%$, τ^2	-	0.2 0.5 1 2	1.01 [0.73; 1.39] 100.0%

Peak 30 minute quantified as the highest steps/min observed in any 30 minutes, not necessarily consecutive, throughout a single day, and averaged across days.



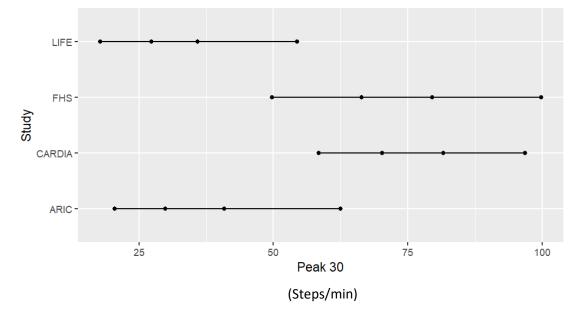


Figure S6b. Peak 30 Minute Intensity – Forest Plots Final Model Adjusting for Steps/Dav – Age Stratified

Study	TE seTE	Q2 v Q1	HR(95%CI) n events we	ight
Age = younger FHS CARDIA Random effects model Heterogeneity: l^2 = 0%, τ^2			0.46 [0.22; 0.97] 521 10 18	.9% .8% I.7%
Age = older FHS ARIC LIFE Random effects model Heterogeneity: / ² = 46%, τ			2.93 [0.72; 11.91] 113 12 6 1.01 [0.67; 1.53] 335 51 36	.0% .7% .6% .3%
Random effects model Heterogeneity: $l^2 = 45\%$, τ Test for subaroup differen	² = 0.0598, p = 0.12 ces: γ ² = 2.91. df = 1 (p = 0.09) 0.1	0.5 1 2 10	- / -).0%
Study	TE seTE	Q3 v Q1	HR(95%CI) n events w	eight
Age = younger FHS CARDIA Random effects model Heterogeneity: I^2 = 0%, τ^2			0.82 [0.43; 1.57] 522 16 1	1.0% 8.9% 29.9%
Age = older FHS ARIC LIFE Random effects model Heterogeneity: $l^2 = 0\%$, τ^2			- 2.56 [0.63; 10.43] 113 12 1.24 [0.83; 1.85] 336 63 5	5.7% 4.1% 0.3% 70.1%
Random effects model Heterogeneity: $I^2 = 0\%$, τ^2 Test for subgroup differen		0.5 1 2	<mark>л 1.17 [0.88; 1.56] 10</mark> 10	0.0%
Study	TE seTE	Q4 v Q1	HR(95%CI) n events	s weight
Age = younger FHS CARDIA Random effects mod Heterogeneity: I ² = 19%,			0.59 [0.18; 1.93] 804 6 1.27 [0.65; 2.47] 521 17 1.02 [0.51; 2.02]	7.3% 23.1% 30.4%

Peak 30 minute quantified as the highest steps/min observed in any 30 minutes, not necessarily consecutive, throughout a single day, and averaged across days.

0.5

2

1

5

0.2

0.98 [0.40; 2.43] 252

1.71 [0.38; 7.70] 113

0.96 [0.62; 1.49] 335

1.00 [0.68; 1.47]

1.02 [0.74; 1.40]

10

7

43

12.6%

52.5%

69.6%

100.0%

4.5%

Age = older FHS

Random effects model

Random effects model

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, p = 0.77

ARIC

LIFE

-0.02 0.4610

0.54 0.7676

-0.04 0.2254

Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78 Test for subgroup differences: χ^2_1 = 0.00, df = 1 (p = 0.97)

Figure S7a. Peak 60 Minute Intensity – Forest Plots Final Model Adjusting for Steps/Day

Study	TE seTE	Peak 60: Q2 v Q1	HR(95%Cl) n events weight	
FHS ARIC CARDIA Random effects mode	-0.50 0.2676 0.63 0.6656 -0.80 0.3850		0.60 [0.36; 1.02] 1056 26 60.8% 1.88 [0.51; 6.93] 113 11 9.8% 0.45 [0.21; 0.96] 521 10 29.4% 0.62 [0.41; 0.93] 100.0%	
Heterogeneity: $I^2 = 43\%$,	$\tau^2 < 0.0001, p = 0.18$	0.2 0.5 1 2 5		
Study	TE seTE	Peak 60: Q3 v Q1	HR(95%Cl) n events weight	
FHS ARIC CARDIA Random effects mod	0.04 0.2948 0.24 0.7208 -0.07 0.3358		1.05 [0.59; 1.86] 1056 12 51.6% 1.27 [0.31; 5.22] 113 11 8.6% 0.93 [0.48; 1.80] 522 17 39.8% 1.02 [0.67: 1.54] 100.0%	
Heterogeneity: $I^2 = 0\%$,		0.2 0.5 1 2 5	1.02 [0.67; 1.54] 100.0%	
Study	TE seTE	Peak 60: Q4 v Q1	HR(95%Cl) n events weight	
FHS ARIC CARDIA	-0.19 0.3959 0.03 0.6998 0.13 0.3424		0.82 [0.38; 1.79]10561937.6%1.03 [0.26; 4.06]113812.0%1.14 [0.58; 2.23]5211750.3%	
Random effects mode Heterogeneity: $I^2 = 0\%$, τ		0.5 1 2	1.00 [0.62; 1.60] 100.0%	

Peak 60 minute quantified as the highest steps/min observed in any 60 minutes, not necessarily consecutive, throughout a single day, and averaged across days.



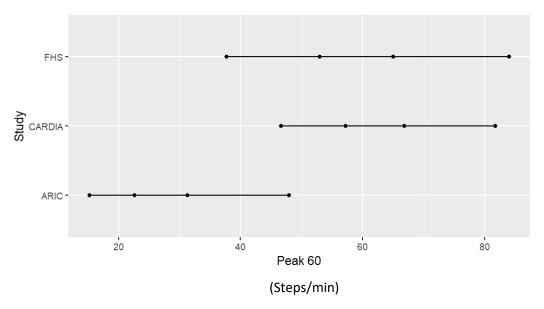


Figure S7b. Peak 60 Minute Intensity – Forest Plots Final Model Adjusting for Steps/Day – Age Stratified

Study	TE	seTE		Q2 v Q1		HR(95%CI)	n	events	weight
Age = younger FHS CARDIA Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 =$	-0.80	0.4177 0.3850 0.77	4		0.4	3 [0.23; 1.20] 5 [0.21; 0.96] 9 [0.28; 0.85]		10 10	25.4% 29.9% 55.4%
Age = older FHS ARIC Random effects model Heterogeneity: I^2 = 60%, τ^2	0.63	0.3579 0.6656 6, <i>p</i> = 0.11	_		- 1.8	7 [0.28; 1.15] 3 [0.51; 6.93] [0.29; 2.84]	113	16 11	34.6% 10.0% 44.6%
Random effects model Heterogeneity: $I^2 = 17\%$, τ^2 Test for subgroup difference	< 0.000 ces: χ^2_1 =	1, p = 0.31 = 0.93, df = 1 (p = 0.34)	0.2	0.5 1 2 5		0 [0.39; 0.89]			100.0%
Study	TE	seTE		Q3 v Q1		HR(95%CI)	n	events	weight
Age = younger FHS CARDIA Random effects model Heterogeneity: $J^2 = 0\%$, τ^2	-0.07	0.4559 0.3358 0.87	_		0.9	4 [0.35; 2.06] 3 [0.48; 1.80] 0 [0.53; 1.53]	522		22.0% 40.6% 62.6%
Age = older FHS ARIC Random effects model Heterogeneity: $J^2 = 0\%$, τ^2	0.24	0.3996 0.7208 0.90			- 1.2	5 [0.52; 2.51] 7 [0.31; 5.22] 7 [0.59; 2.33]	113		28.6% 8.8% 37.4%
Random effects model Heterogeneity: $J^2 = 0\%$, $\tau^2 =$ Test for subgroup differen	= 0. p =	0.94 = 0.37, df = 1 (p = 0.55)	0.2	0.5 1 2	0.9	9 [0.65; 1.51]			100.0%
Study	TE	seTE		Q4 v Q1		HR(95%CI)) n	events	weight
Age = younger FHS CARDIA Random effects model Heterogeneity: $l^2 = 2\%$, τ^2	0.13	0.6325 0.3424 4, <i>p</i> = 0.31			1.1	5 [0.16; 1.91] 4 [0.58; 2.23 6 [0.53; 1.76]	521		15.0% 51.2% 66.2%
Age = older FHS ARIC Random effects model Heterogeneity: l^2 = 0%, τ^2	0.03	0.5277 0.6998 0.84			1.0	2 [0.44; 3.44 3 [0.26; 4.06] 5 [0.50; 2.63]] 113		21.6% 12.3% 33.8%
Random effects model Heterogeneity: $l^2 = 0\%$, τ^2 Test for subgroup differen	= 0, p =	0.76 = 0.11, df = 1 (p = 0.73)	0.2	0.5 1 2	1.0 5	3 [0.63; 1.66]	I		100.0%

Peak 60 minute quantified as the highest steps/min observed in any 60 minutes, not necessarily consecutive, throughout a single day, and averaged across days.

Figure S8a. Time Spent at ≥40 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day

Study	TE seTE	Min in 40+ spm: Q2 v Q1	HR(95%Cl) n	events weight
FHS CARDIA ARIC	-0.23 0.2723 0.37 0.3704 0.07 0.5464		0.80 [0.47; 1.36] 1056 1.45 [0.70; 3.00] 521 1.07 [0.37; 3.12] 113	16 31.4%
Random effects mode Heterogeneity: $I^2 = 0\%$, τ^2	-	0.5 1 2	1.01 [0.65; 1.55]	100.0%
Study	TE seTE	Min in 40+ spm: Q3 v Q1	HR(95%Cl) n	events weight
FHS CARDIA ARIC Random effects model Heterogeneity: $l^2 = 0\%$, τ^2			0.90 [0.45; 1.82] 1057 1.46 [0.71; 2.99] 522 0.72 [0.23; 2.26] 113 1.06 [0.67; 1.68]	15 42.7% 19 41.1% 9 16.2% 100.0%
		0.5 1 2		
Study	TE seTE	Min in 40+ spm: Q4 v Q1	HR(95%Cl) n	events weight
FHS CARDIA ARIC	0.36 0.5231 0.41 0.3587 -0.51 0.5874		1.43 [0.51; 3.99] 105 1.51 [0.75; 3.05] 521 0.60 [0.19; 1.90] 113	21 54.3%
Random effects mode Heterogeneity: $I^2 = 0\%$, τ		0.2 0.5 1 2	1 .24 [0.74; 2.07] 5	100.0%

Time spent at \geq 40 steps/min is quantified as the average duration (minutes per day) of steps accumulated at \geq 40 steps/min, considered intentional walking

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals. Models adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or occupation, BMI, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b), plus steps/d using the residual method.

Figure 6b. Time Spent at ≥40 steps/min Intensity Medians by Quartile

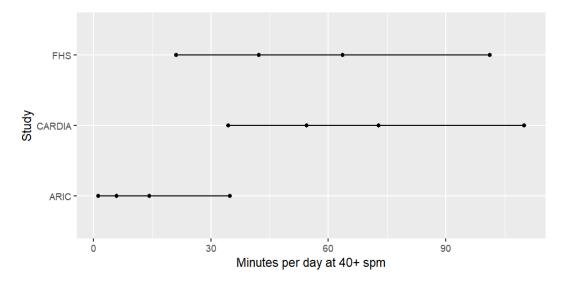


Figure S8b. Time Spent at ≥40 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day – Age Stratified

Study	TE seTE	Q2 v Q1	HR(95%CI) n events weight
Age = younger FHS CARDIA Random effects mode Heterogeneity: I ² = 70%, 1			0.50 [0.21; 1.21] 735921.8%1.45 [0.70; 3.00] 5211629.9%0.88 [0.31; 2.47]51.8%
Age = older FHS ARIC Random effects mode Heterogeneity: I^2 = 0%, τ^2			0.89 [0.45; 1.76] 321 9 33.1% 1.07 [0.37; 3.12] 113 10 15.1% 0.94 [0.53; 1.67] 48.2%
Random effects mode Heterogeneity: / ² = 12%, 1 Test for subgroup differen		0.5 1 2	0.93 [0.60; 1.44] 100.0%
Study	TE seTE	Q3 v Q1	HR(95%CI) n events weight
Study Age = younger FHS CARDIA Random effects mode Heterogeneity: / ² = 24%, m	-0.36 0.5247 0.38 0.3659	Q3 v Q1	HR(95%CI) n events weight 0.70 [0.25; 1.96] 803 4 20.1% 1.46 [0.71; 2.99] 522 19 41.4% 1.11 [0.56; 2.23] 61.5%
Age = younger FHS CARDIA Random effects mode	-0.36 0.5247 0.38 0.3659 1 2 = 0.0656, p = 0.25 -0.02 0.4992 -0.33 0.5829	Q3 v Q1	0.70 [0.25; 1.96] 803 4 20.1% 1.46 [0.71; 2.99] 522 19 41.4%

Study	TE seTE	Q4 v Q1	HR(95%Cl) n e	events weight
Age = younger FHS CARDIA Random effects model Heterogeneity: I^2 = 0%, τ^2			1.32 [0.29; 6.08] 818 1.51 [0.75; 3.05] 521 1.48 [0.78; 2.79]	7 11.6% 21 54.6% 66.2%
Age = older FHS ARIC Random effects mode Heterogeneity: I^2 = 9%, τ^2			- 1.59 [0.39; 6.57] 238 0.60 [0.19; 1.90] 113 0.89 [0.35; 2.29]	14 13.5% 8 20.4% 33.8%
Random effects model Heterogeneity: $l^2 = 0\%$, τ^2 Test for subgroup differen		0.2 0.5 1 2 5	1.24 [0.74; 2.09]	100.0%

Time spent at \geq 40 steps/min is quantified as the average duration (minutes per day) of steps accumulated at \geq 40 steps/min, considered intentional walking

Figure S9a. Time Spent at ≥100 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day

Study	TE seTE	Min in 100+ spm: Q2 v Q1	HR(95%Cl) n events weight
FHS CARDIA	-0.32 0.2288 -0.11 0.3864		0.73 [0.46; 1.14] 1055 22 74.0% 0.90 [0.42; 1.92] 521 14 26.0%
Random effects model Heterogeneity: $I^2 = 0\%$, τ^2		0.5 1 2	0.77 [0.52; 1.13] 100.0%
Study	TE seTE	Min in 100+ spm: Q3 v Q1	HR(95%CI) n events weight
FHS CARDIA	-0.23 0.2436 0.52 0.3627		0.80 [0.49; 1.28] 1054 20 56.4% - 1.69 [0.83; 3.44] 522 23 43.6%
Random effects mode Heterogeneity: $I^2 = 66\%$,		0.5 1 2	1.11 [0.53; 2.30] 100.0%
Study	TE seTE	Min in 100+ spm: Q4 v Q1	HR(95%Cl) n events weight
FHS CARDIA	-0.29 0.2903 0.34 0.3747		0.75 [0.42; 1.32] 1058 14 57.2% - 1.40 [0.67; 2.92] 521 15 42.8%
Random effects mode Heterogeneity: / ² = 43%, 1		0.5 1 2	0.98 [0.53; 1.80] 100.0%

Time spent at \geq 100 steps/min is quantified as the average duration (minutes per day) of steps accumulated at \geq 100 steps/min, considered moderate intensity walking

TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals. Models adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or occupation, BMI, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b), plus steps/d using the residual method.

Figure 7b. Time Spent at ≥100 steps/min Intensity Medians by Quartile

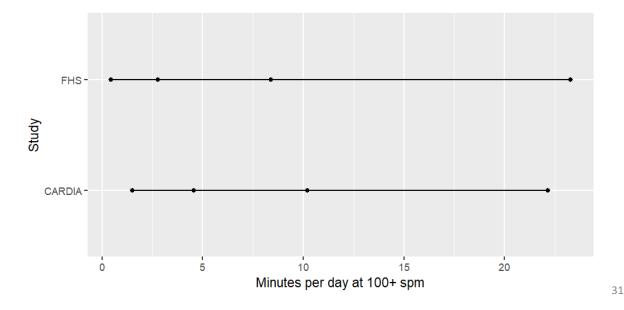


Figure S9b. Time Spent at ≥100 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day – Stratified by Age

Study	TE seTE	Q2 v Q1	HR(95%CI) n	events	weight
Age = younger FHS CARDIA Random effects mode Heterogeneity: $I^2 = 0\%$, τ^2			0.74 [0.36; 1.52] 719 0.90 [0.42; 1.92] 521 0.81 [0.48; 1.37]	7 14	29.4% 26.2% 55.6%
Age = older FHS	-0.49 0.2967		0.61 [0.34; 1.09] 336	15	44.4%
Random effects mode Heterogeneity: $l^2 = 0\%$, τ^2 Test for subgroup differen		0.5 1 2	0.72 [0.49; 1.05]		100.0%

Study	TE seTE	Q3 v Q1	HR(95%CI) n ev	vents weight
Age = younger FHS CARDIA Random effects mode Heterogeneity: 1 ² = 62%,			0.72 [0.34; 1.53] 785 1.69 [0.83; 3.44] 522 1.11 [0.48; 2.57]	7 30.1% 23 32.4% 62.5%
Age = older FHS	-0.29 0.3160		0.74 [0.40; 1.38] 269	13 37.5%
Random effects mode Heterogeneity: $I^2 = 45\%$, Test for subgroup differe		0.5 1 2	0.96 [0.56; 1.65]	100.0%

Study	TE seTE	Q4 v Q1	HR(95%Cl) n e	vents weight
Age = younger FHS CARDIA Random effects mode Heterogeneity: 1 ² = 45%,			0.62 [0.24; 1.58] 795 1.40 [0.67; 2.92] 521 0.98 [0.44; 2.17]	5 23.1% 15 37.9% 61.0%
Age = older FHS	-0.14 0.3697		0.87 [0.42; 1.79] 263	9 39.0%
Random effects mode Heterogeneity: $l^2 = 0\%$, τ^2 Test for subgroup differe	el ² = 0, <i>p</i> = 0.38 nces: χ ₁ = 0.05, df = 1 (<i>p</i> = 0.82)	0.5 1 2	0.96 [0.61; 1.51]	100.0%

Time spent at \geq 100 steps/min is quantified as the average duration (minutes per day) of steps accumulated at \geq 100 steps/min, considered moderate intensity walking