

SUPPLEMENTAL MATERIAL

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

Table of Contents

Section 1. Study Level Characteristics [Click to View](#)

Table S1a. Study Level Descriptions of Data Collection and Processing

Table S1b. Study Level Description of Covariates in Final Model

Table S1c. Study Level Descriptive Characteristics of Participants

Section 2. Risk of Bias Assessment [Click to View](#) (page 8)

Table S2. Study Quality Assessment

New Castle Ottawa Quality Assessment Scale description

Section 3. Overall Sample Supplement Results [Click to View](#) (page 10)

Figure S1a. Overall Sample Quartile Comparisons, Forest Plots

Figure S1b. Overall Sample Quartile Comparisons, Funnel Plots

Section 4. Age-Stratified Supplement Results [Click to View](#) (page 12)

Figure S2a. Age Subgroup Quartile Comparisons, Forest Plots

Figure S2b. Median Steps/d for Quartiles by Age Group Among Studies Included in Spline Analysis

Section 5. Sex Stratified Supplement Results [Click to View](#) (page 16)

Figure S3a. Sex Subgroup Quartile Comparisons, Forest Plots

Figure S3b. Median Steps/d for Quartiles by Sex Among Studies Included in Sex Stratified Spline Analysis

Figure S3c. Sex Stratified Restricted Cubic Spline

Section 6. Sensitivity Results [Click to View](#) (page 20)

Figure S4. Stratified Results by Publication Status, Forest Plots

Figure S5. Stratified Results by Device Type, Forest Plots

Table S3. Leave-One-Study Out

Table S4. Fixed vs Random Effect Models - Summary Results

Section 7. Stepping Rate results [Click to View](#) (page 24)

Table S5. Stepping Rate Associations with CVD With and Without Adjusting for Volume

Figure S6a. Peak 30-Minute, Forest Plots

Figure S6b. Study Level Peak 30-Minute Medians by Quartile

Figure S7a. Peak 60-Minute, Forest Plots

Figure S7b. Study Level Peak 60-Minute Medians by Quartile

Figure S8a. Time Spent at ≥ 40 steps/min, Forest Plots

Figure S8b. Study Level Time Spent at ≥ 40 steps/min Medians by Quartile

Figure S9a. Time Spent at ≥ 100 steps/min, Forest Plots

Figure S9b. Study Level Time Spent at ≥ 100 steps/min Medians by Quartile

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	Device worn for 10h/d on ≥4 days	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

Table S1b. Study Level Description of Covariates in Final Model

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/m ²), 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/m ²), device wear time, smoking (current, past, never), region of residence, alcohol consumption, hours of night-time sleep, living alone 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/m ²), 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/m ²), 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/m ²), 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, marital 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/m ²), 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/m ²), 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/m ²), 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.

Table S1c. Study Level Descriptive Characteristics of Participants

	ARIC		BRHS	CARDIA		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/m ²), 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 continued. Study Level Descriptive Characteristics of Participants

	HAI		JHS		LIFE		NAVIGATOR	
	Men	Women	Men	Women	Men	Women	Men	Women
N	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/m ²), 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/m ²	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)	-	-

BMI = Body Mass Index, measured by height and weight during study examinations

Table S2: Study Quality Assessment

Newcastle-Ottawa Quality Assessment of Studies									
Study		Selection			Comparability	Outcome			Overall Score
	Representativeness	Selection	Ascertainment Exposure	Outcome		Assessment	Follow-Up	Adequacy	
ARIC	B*	A*	A*	A*	A* B*	A *	A*	B*	9
BRHS	C	A*	A*	A*	A* B*	A *	A*	B*	8
CARDIA	B*	A*	A*	A*	A* B*	A *	A*	B*	9
FHS	B*	A*	A*	A*	A* B*	A *	A*	B*	9
JHS	B*	A*	C	A*	A* B*	A *	A*	B*	8
HAI	B*	A*	A*	A*	A* B*	B *	A*	B*	9
LIFE	C	A*	A*	A*	A* B*	A *	A*	B*	8
NAVIGATOR	C	A*	C	A*	A* B*	A *	A*	B*	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

Note: 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 ✱
- b) somewhat representative of the average adult in the community ✱
- 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 ✱
- 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) Comparability of cohorts on the basis of the design or analysis

- 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

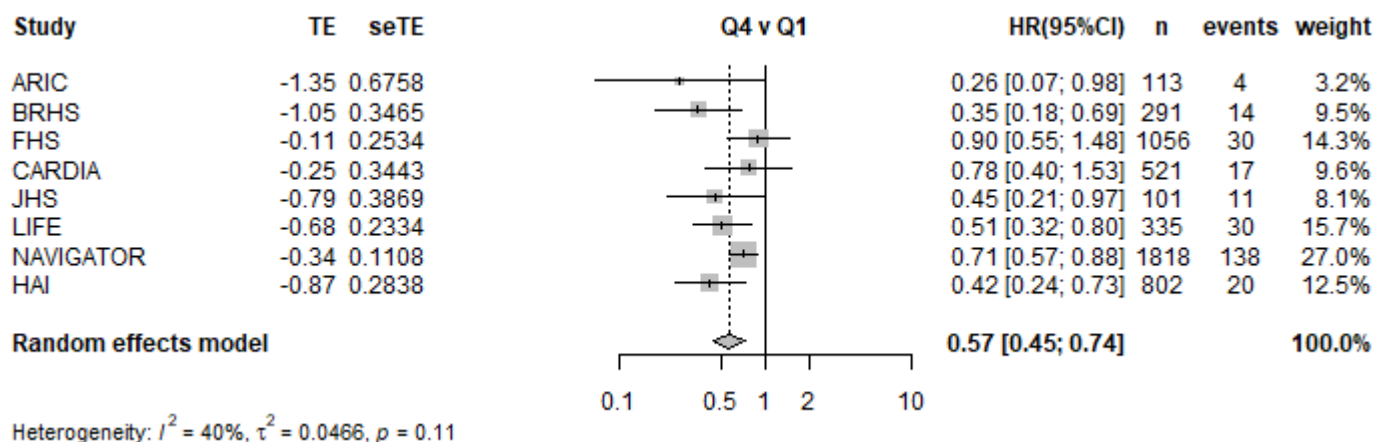
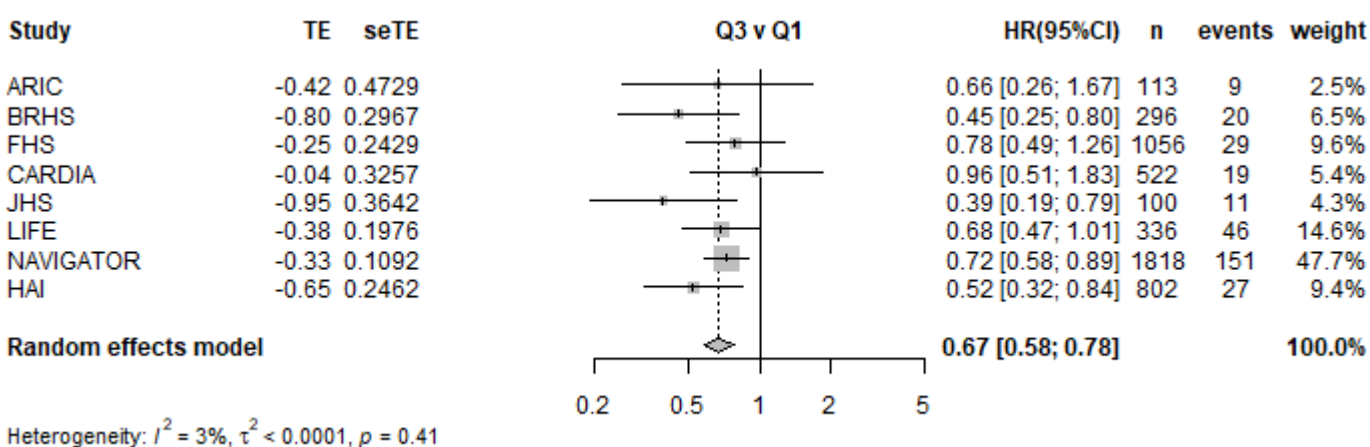
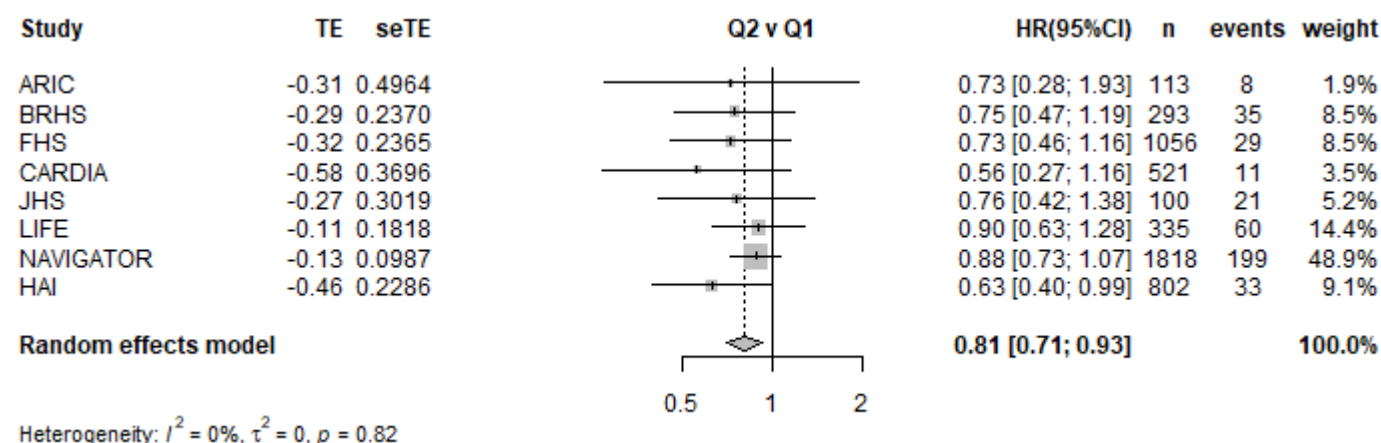
2) Was follow-up long enough for outcomes to occur

- 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

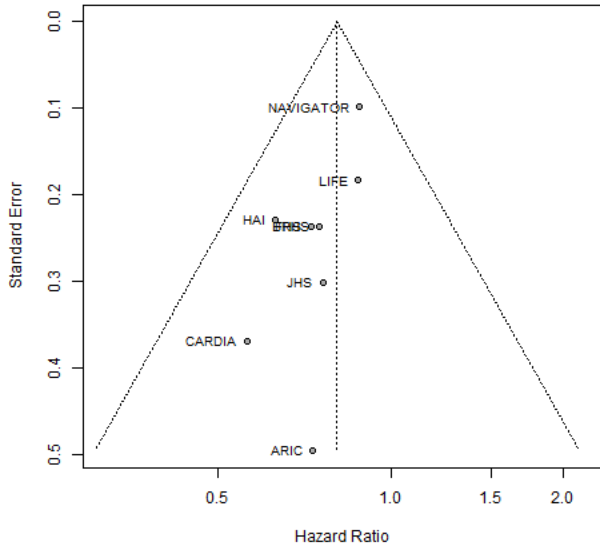
Figure S1a: Overall Sample Quartile Comparisons – Forest Plots



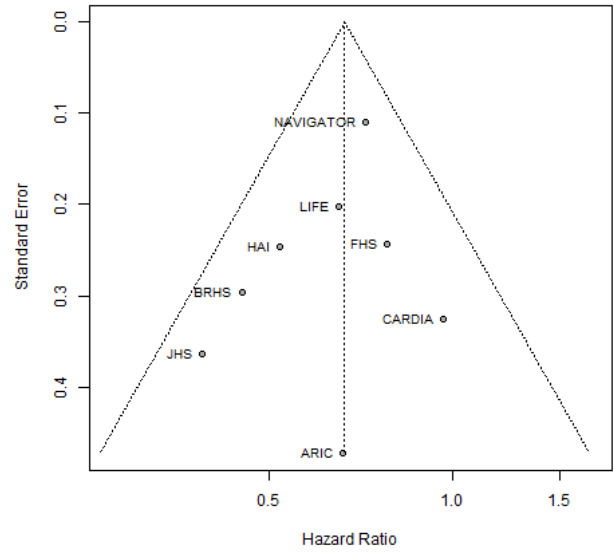
TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.
 Model is adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or income, body mass index, and study-specific 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



Quartile 3 v 1



Quartile 4 v 1

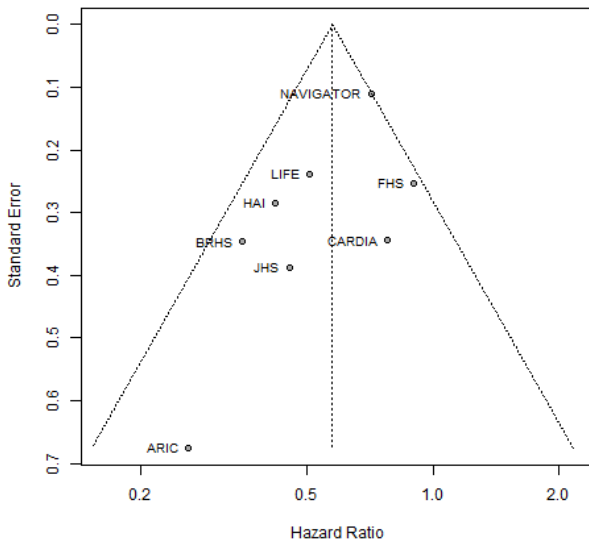
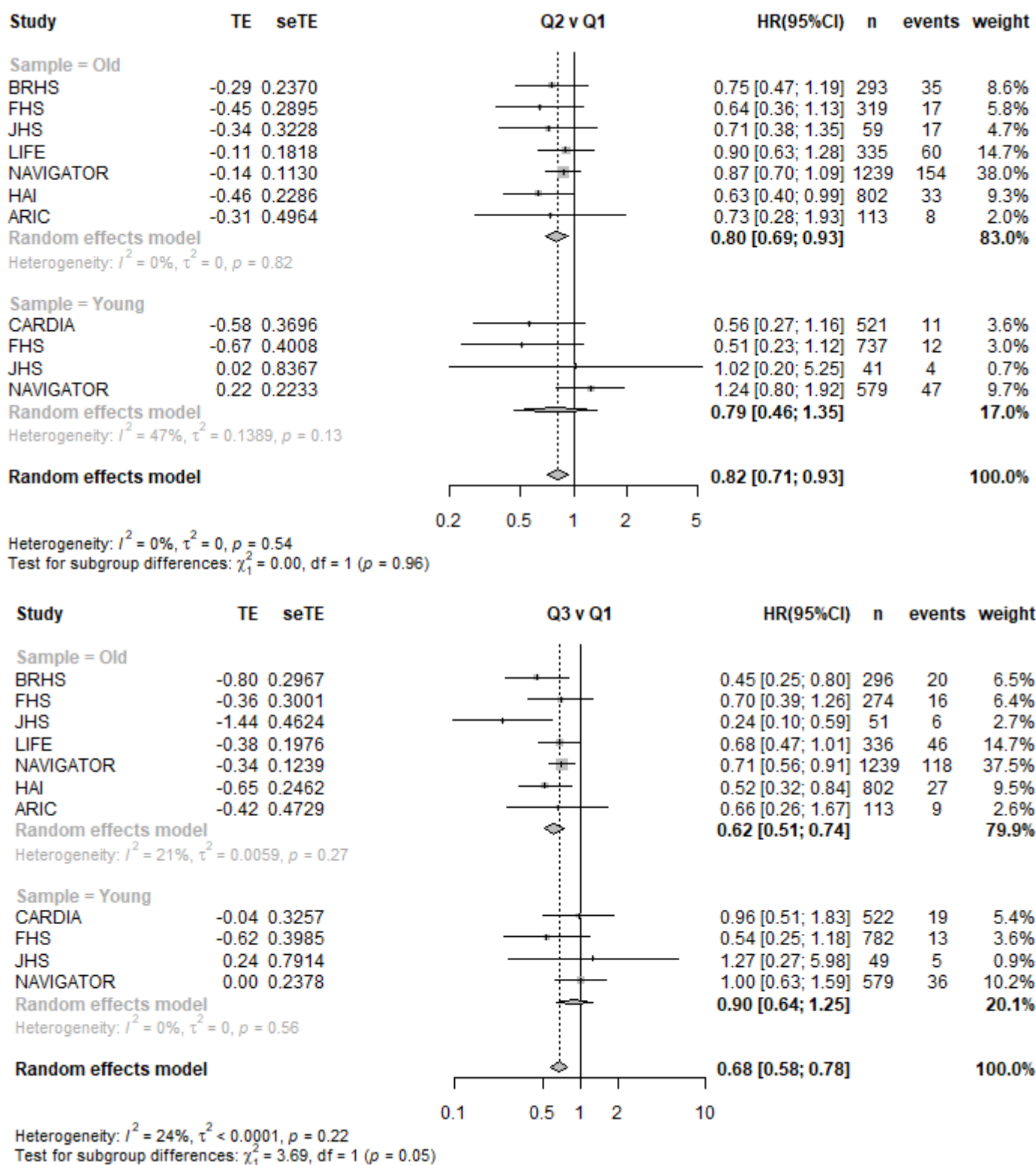


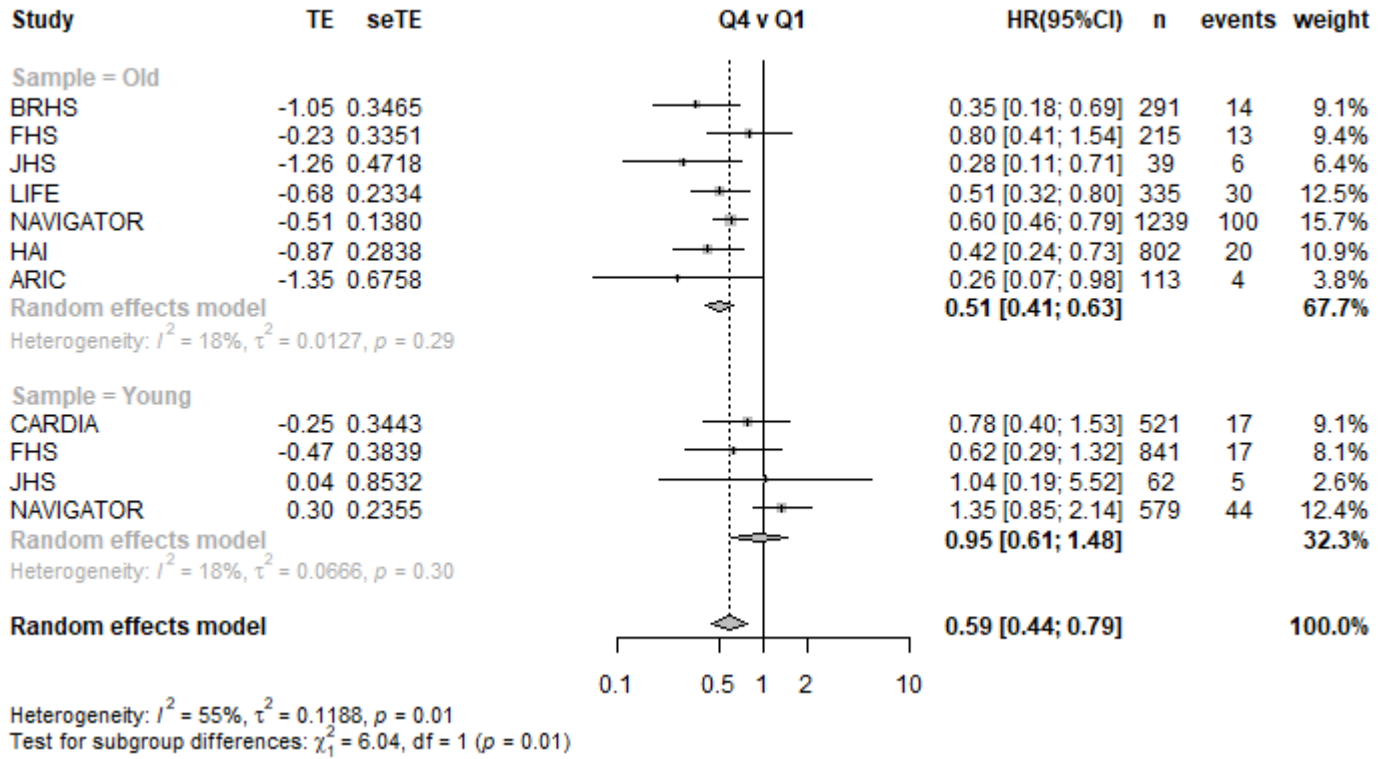
Figure S2a: Association of Steps/Day Quartiles with Cardiovascular Disease Stratified by Younger (<60 years) and Older (≥ 60 years) Adults – Forest Plots – Final Adjusted Model 2



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

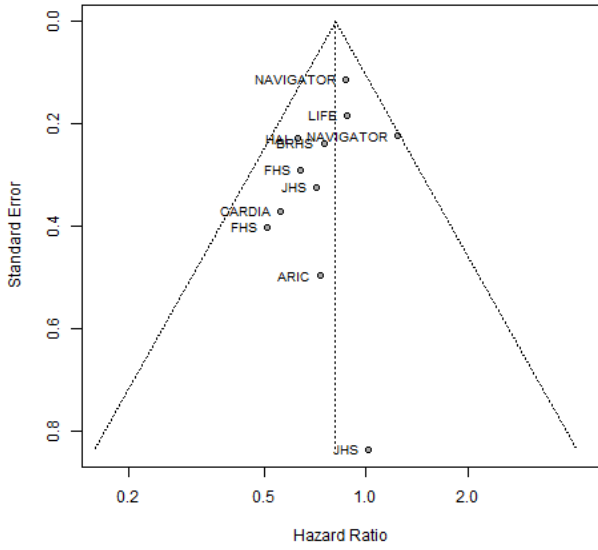


TE = treatment Effect (log hazard ratio); sTE = standard error of treatment estimate; Q = Quartile; HR (95% CI) = Hazard Ratio and 95% Confidence Intervals.

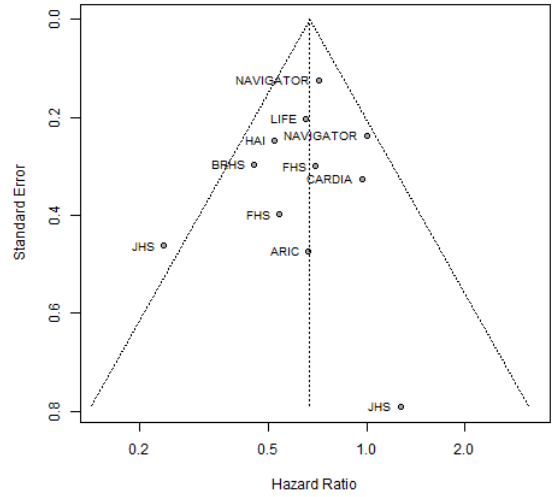
Model is adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or income, body mass index, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement 1b)

Figure S2b: Age Stratified Quartile Comparisons – Funnel Plots

Quartile 2 v 1



Quartile 3 v 1



Quartile 4 v 1

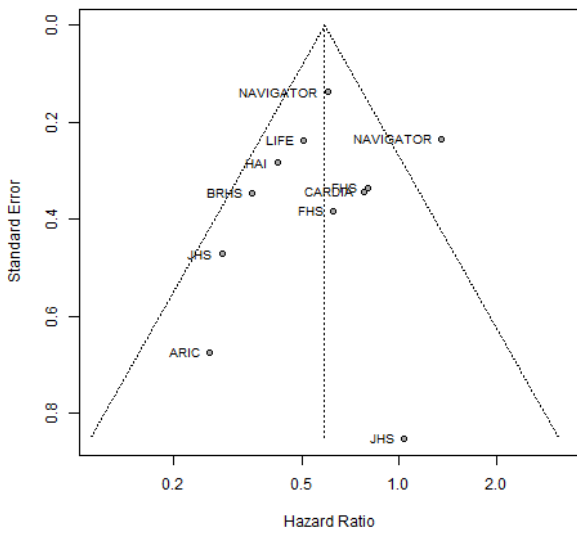


Figure S2c: Median Steps/d for Quartiles by Age Group Among Studies Included in Spline Analysis

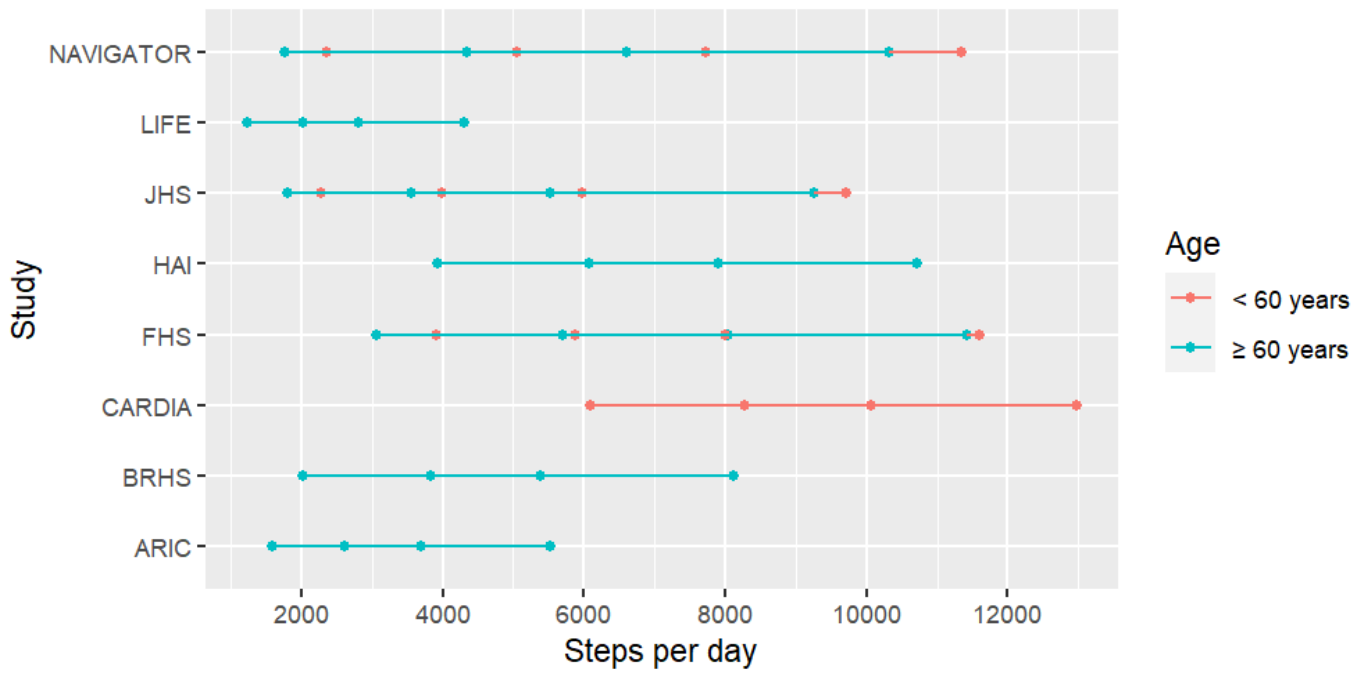
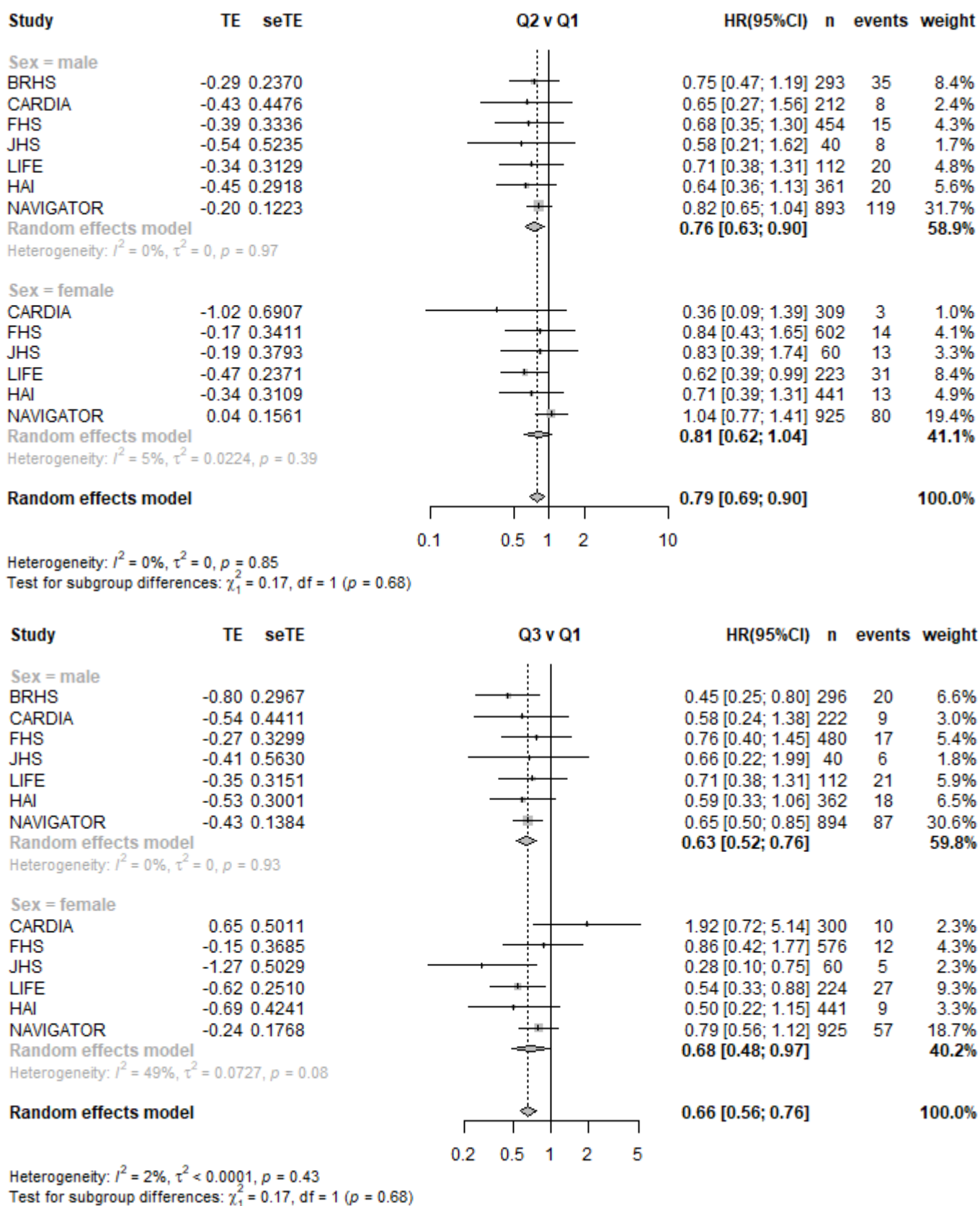


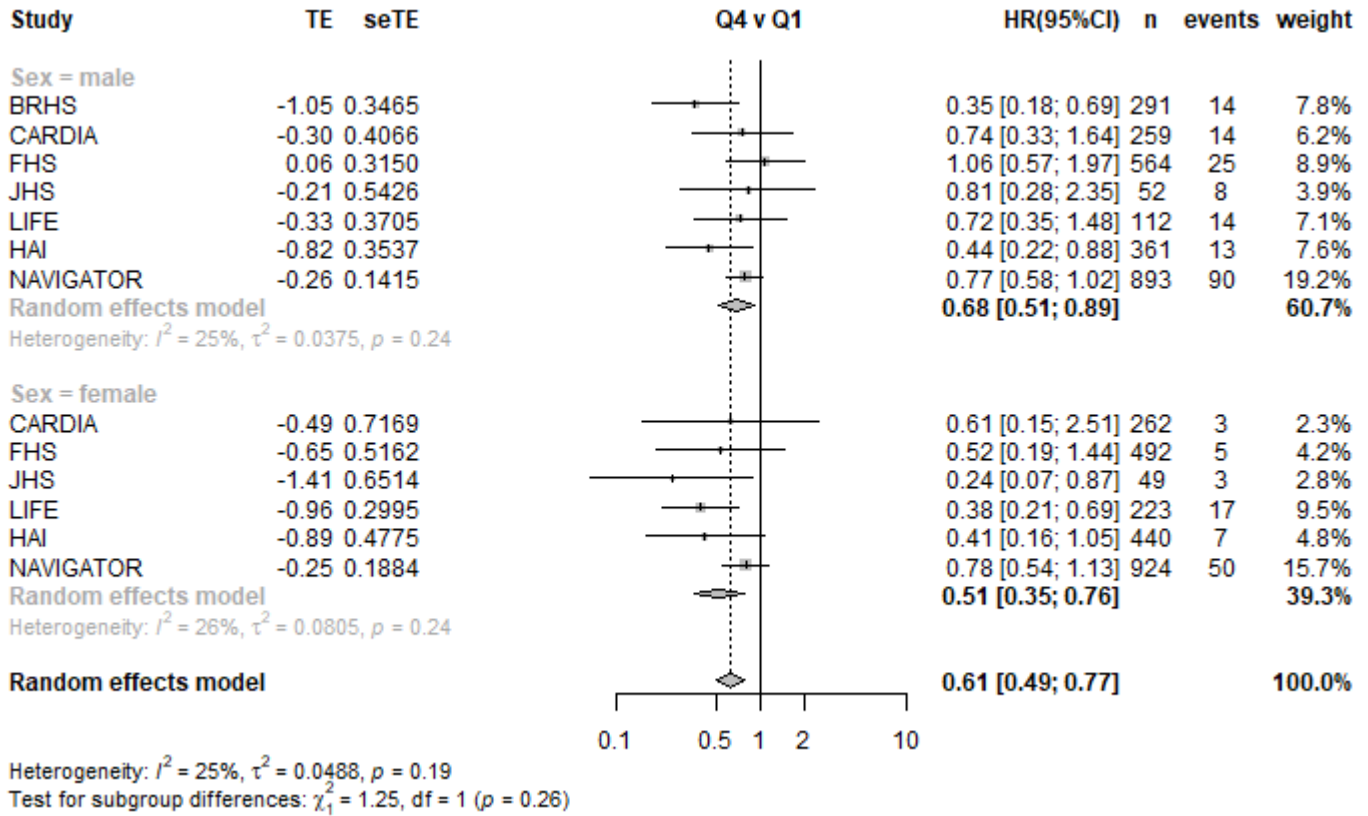
Figure S3a: Association of Steps/Day Quartiles with CVD Stratified by Sex – Forest Plots – Final Adjusted Model 2



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)

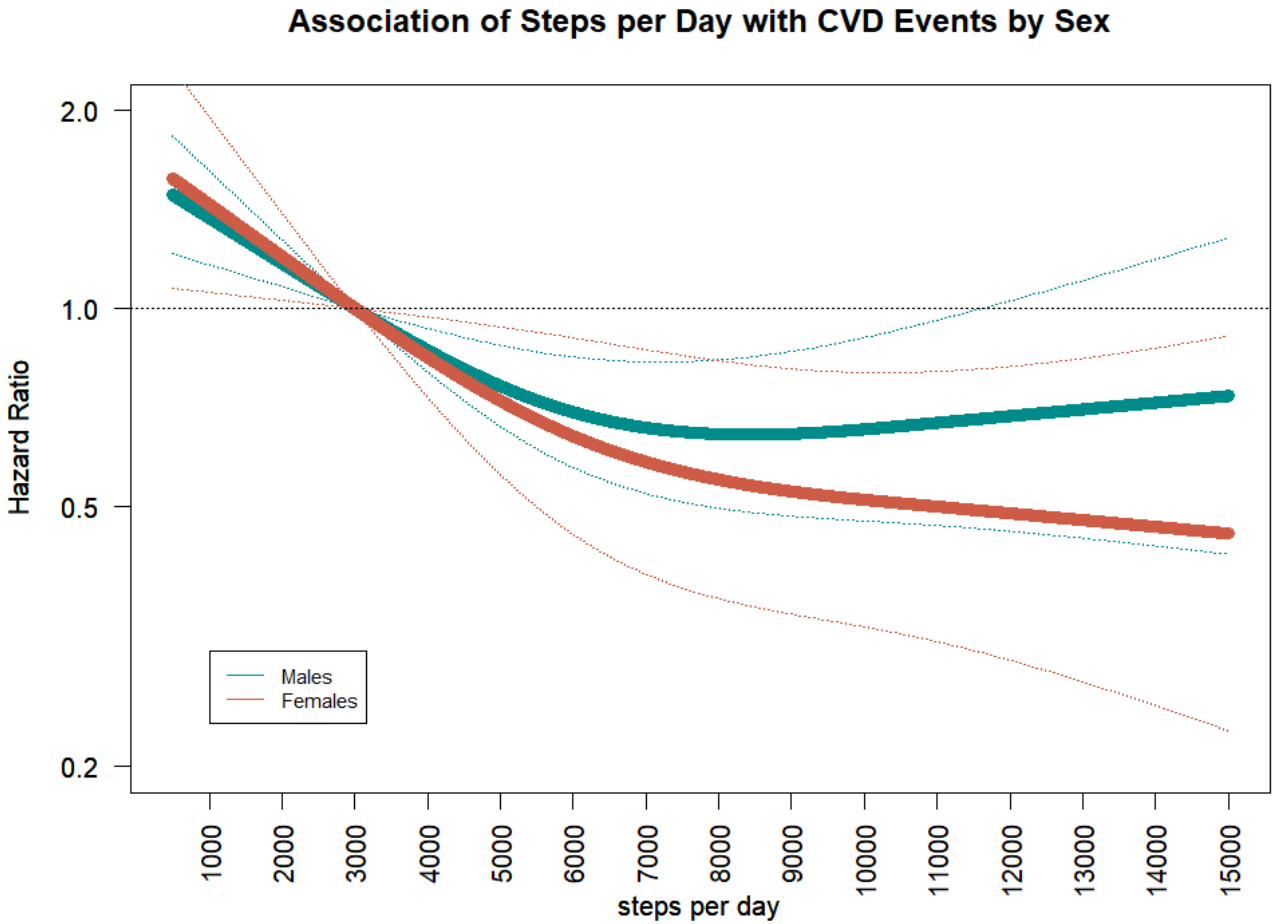
Figure S3a cont: Association of Steps/Day Quartiles with CVD Stratified by Sex – Forest Plots – Final Adjusted Model 2



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)¹⁷

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



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

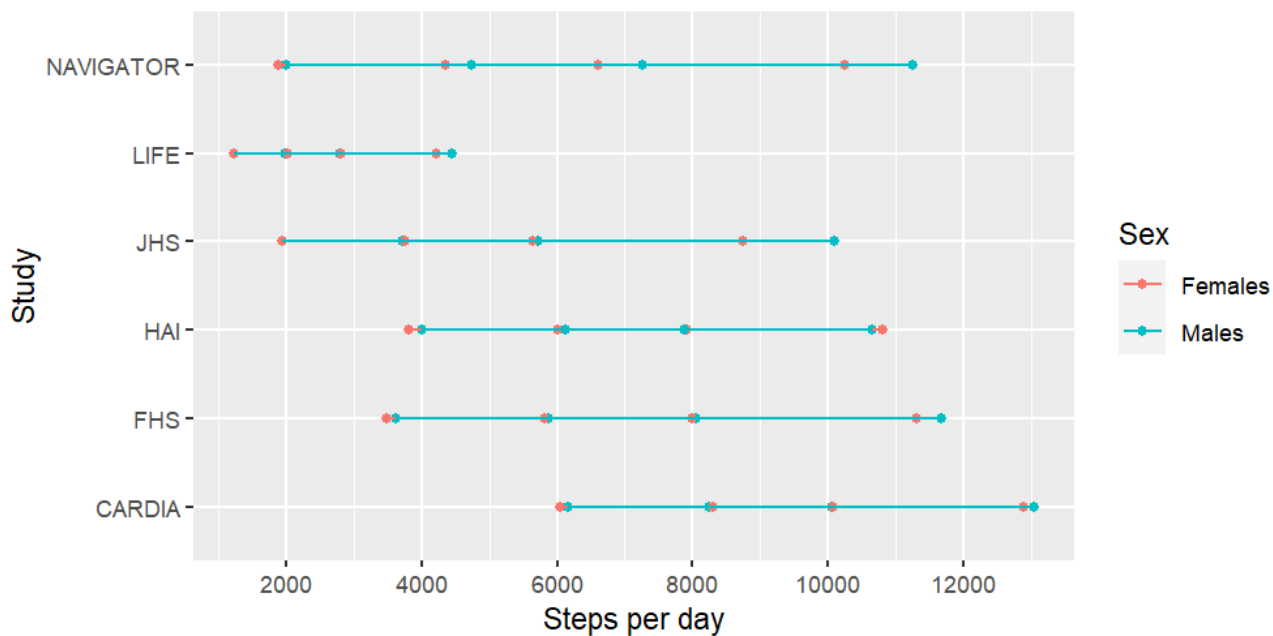
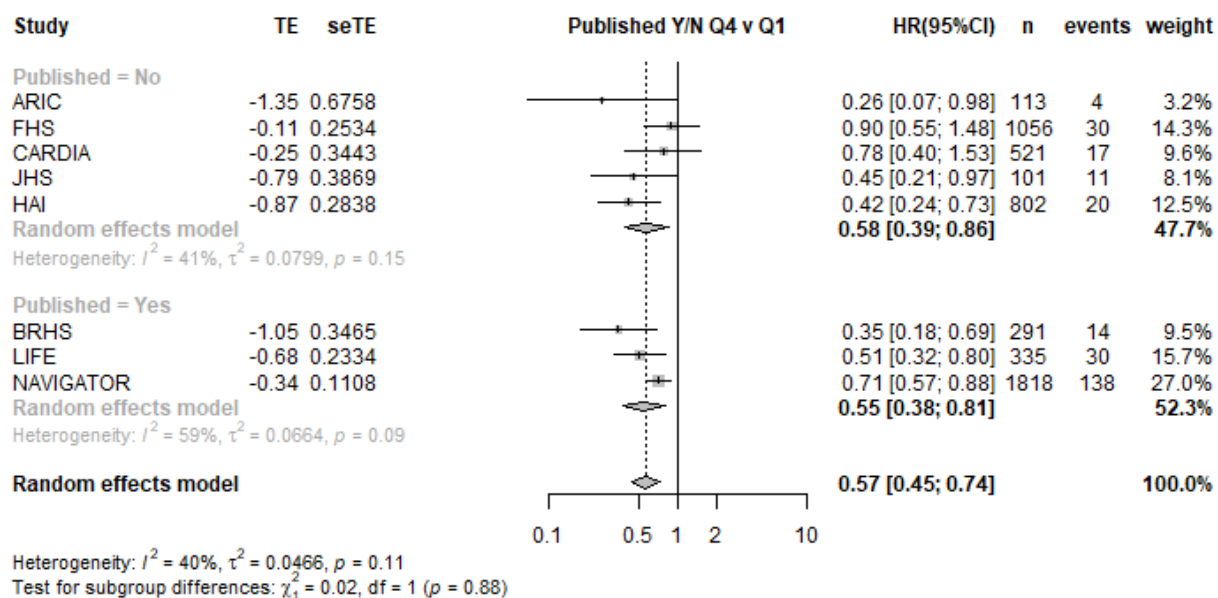
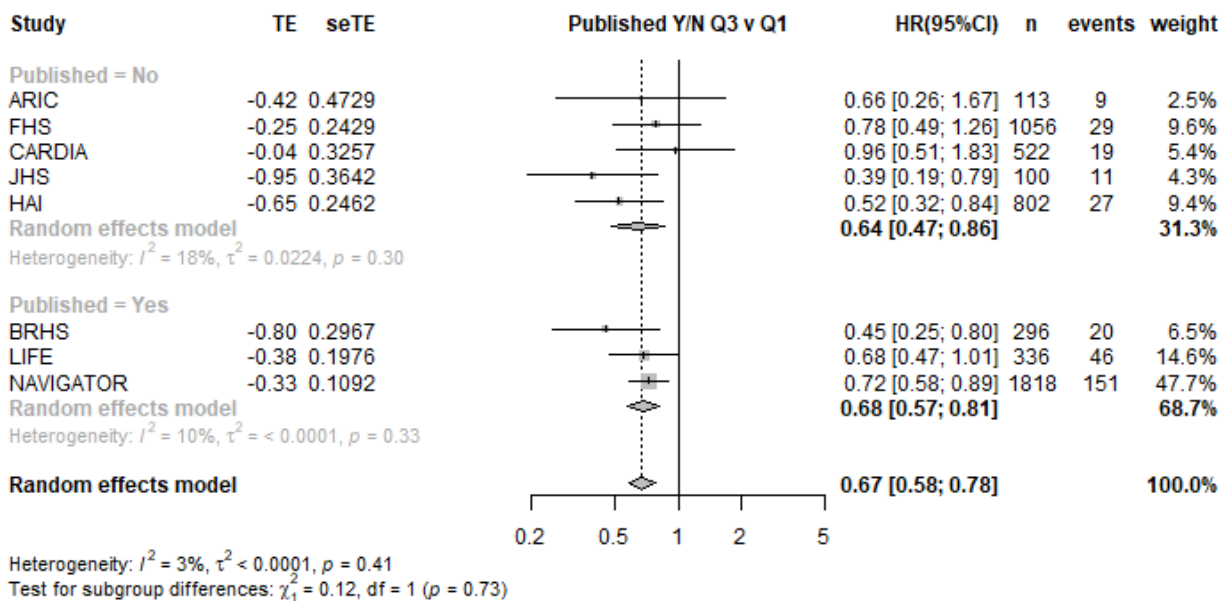
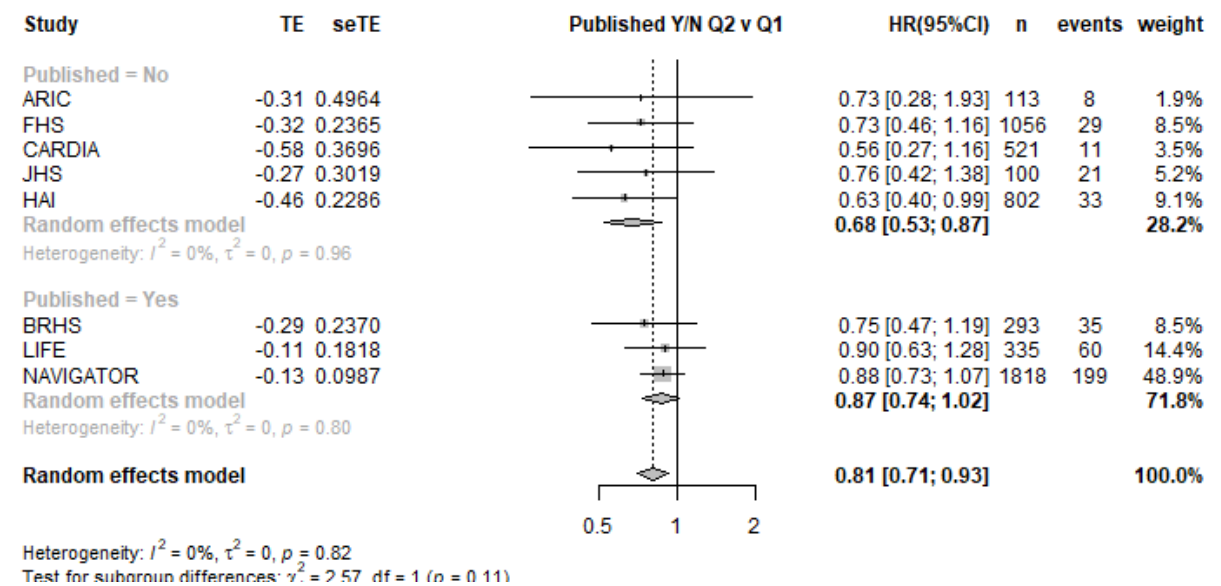
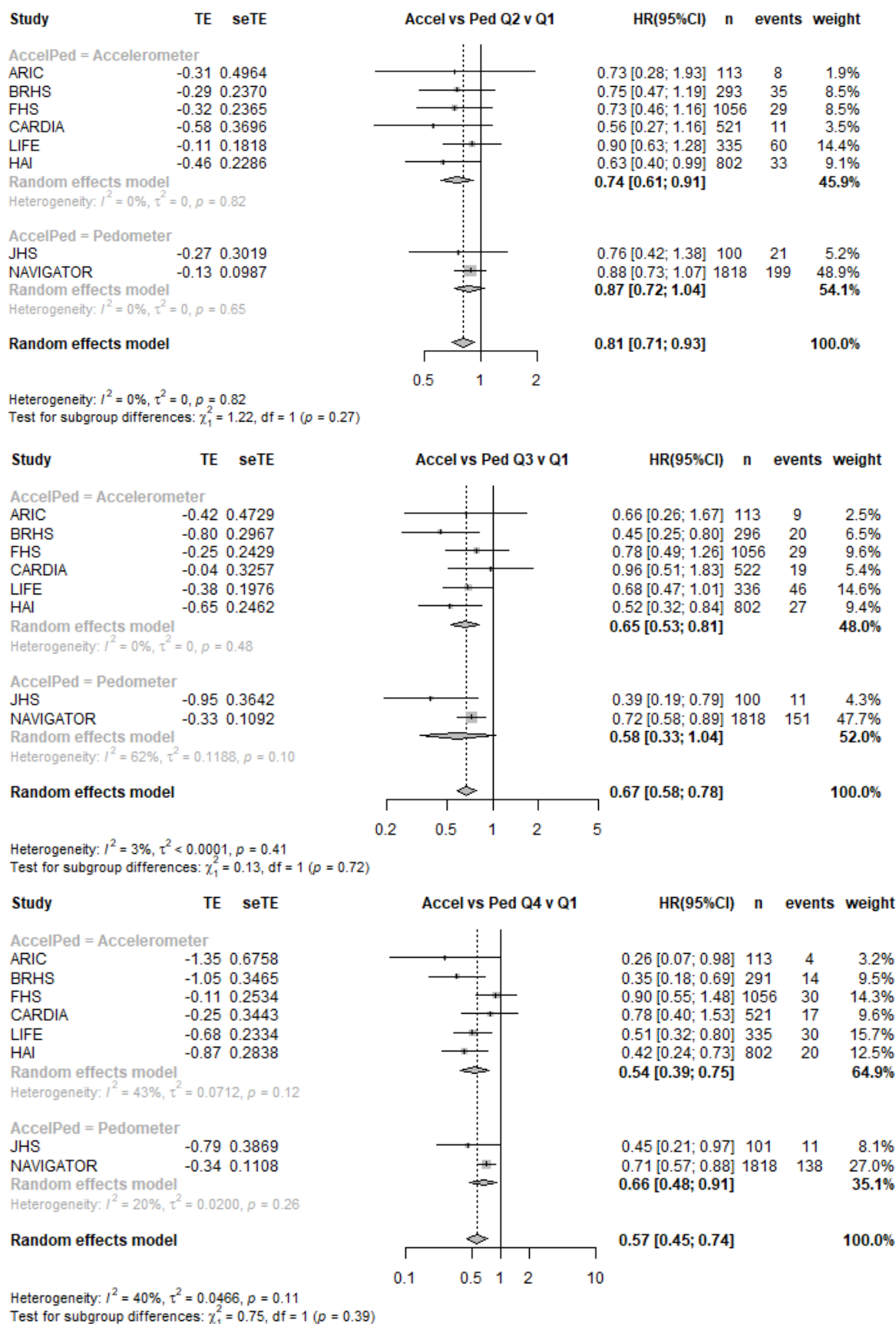


Figure S4. Forest Plots Stratified by Publication Status (Yes/No)



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)

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



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)

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

Study Left Out	HR	95 %CI	
ARIC	0.5923	0.4118	0.852
BRHS	0.5988	0.4126	0.8692
FHS	0.5319	0.3638	0.7777
CARDIA	0.5509	0.3795	0.7997
JHS	0.5813	0.4013	0.8421
LIFE	0.5796	0.3957	0.8491
NAVIGATOR	0.5188	0.3401	0.7915
HAI	0.5922	0.4062	0.8633

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)

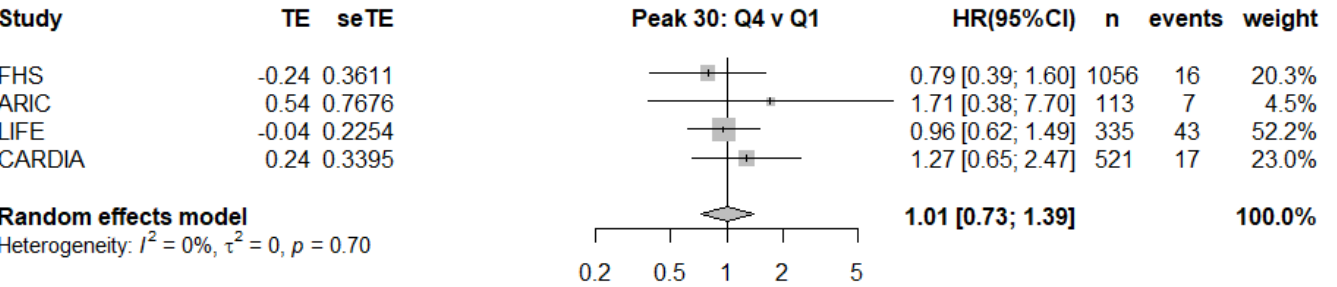
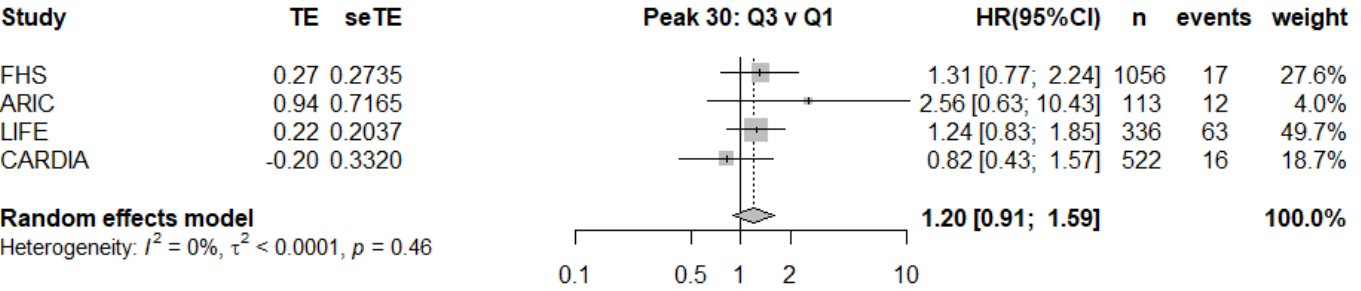
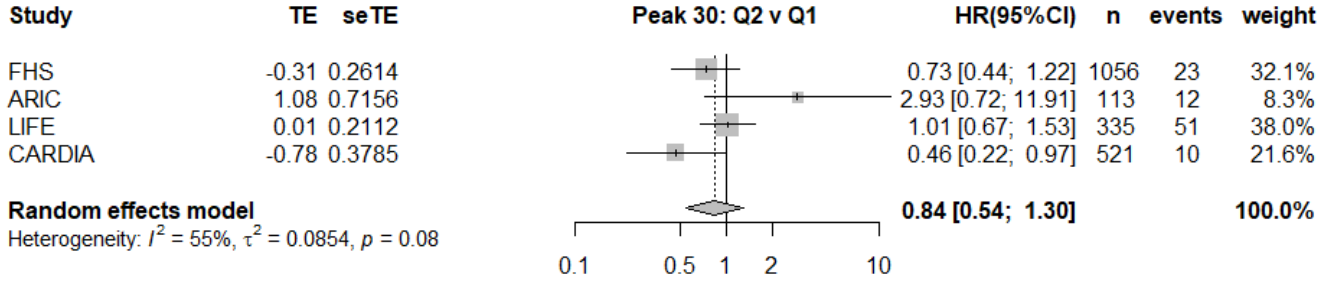
Hazard Ratio and 95% Confidence Intervals [HR (95% CI)] adjusted for age, device wear time, race/Ethnicity (if applicable), sex (if applicable), education or occupation, BMI, and study-specific variables for lifestyle, chronic conditions or risk factors, and general health status (see supplement table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

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

	Step/d Quartile	No. of Studies	No. of Participants	CVD Events	HR (95% CI)
Peak 30					
Model 2: Full Adjusted Model (not including step volume)					
	Q1	4	2024	160	1
	Q2	4	2025	107	0.81 [0.62; 1.05]
	Q3	4	2027	113	0.91 [0.66; 1.26]
	Q4	4	2025	78	0.72 [0.46; 1.13]
Model 3: Full Adjusted Model PLUS Step Volume					
	Q1	4	2024	135	1
	Q2	4	2025	96	0.84 [0.54; 1.30]
	Q3	4	2027	108	1.20 [0.91; 1.59]
	Q4	4	2025	83	1.01 [0.73; 1.39]
Peak 60					
Model 2: Full Adjusted Model (not including step volume)					
	Q1	3	1989	96	1
	Q2	3	1690	52	0.75 [0.45; 1.23]
	Q3	3	1691	61	0.94 [0.66; 1.34]
	Q4	3	1690	47	0.82 [0.55; 1.21]
Model 3: Full Adjusted Model PLUS Step Volume					
	Q1	3	1689	89	1
	Q2	3	1690	47	0.62 [0.41; 0.93]
	Q3	3	1691	40	1.02 [0.67; 1.54]
	Q4	3	1690	44	1.00 [0.62; 1.60]
Time (in min) spent at ≥40 spm					
Model 2: Full Adjusted Model (not including step volume)					
	Q1	3	1686	96	1
	Q2	3	1693	59	0.86 [0.59; 1.25]
	Q3	3	1690	47	0.69 [0.47; 1.01]
	Q4	3	1691	54	0.82 [0.57; 1.20]
Model 3: Full Adjusted Model PLUS Step Volume					
	Q1	3	1688	84	1
	Q2	3	1690	44	1.01 [0.65; 1.55]
	Q3	3	1692	43	1.06 [0.67; 1.68]
	Q4	3	1690	50	1.24 [0.74; 2.07]
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; 0.95]
	Q3	2	1572	54	1.10 [0.60; 2.00]
	Q4	2	1580	38	0.76 [0.50; 1.15]
Model 3: Full Adjusted Model PLUS Step Volume					
	Q1	2	1577	78	1
	Q2	2	1576	36	0.77 [0.52; 1.13]
	Q3	2	1576	43	1.11 [0.53; 2.30]
	Q4	2	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



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.

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 4b. Quartiles of Peak 30 Intensity by Study (Median Steps per Minute)

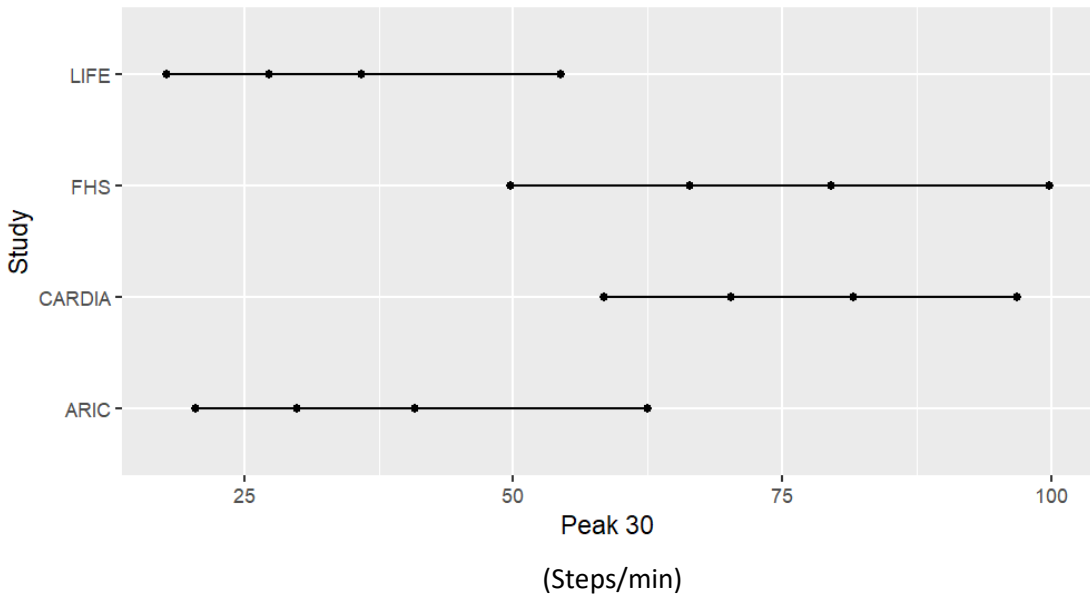
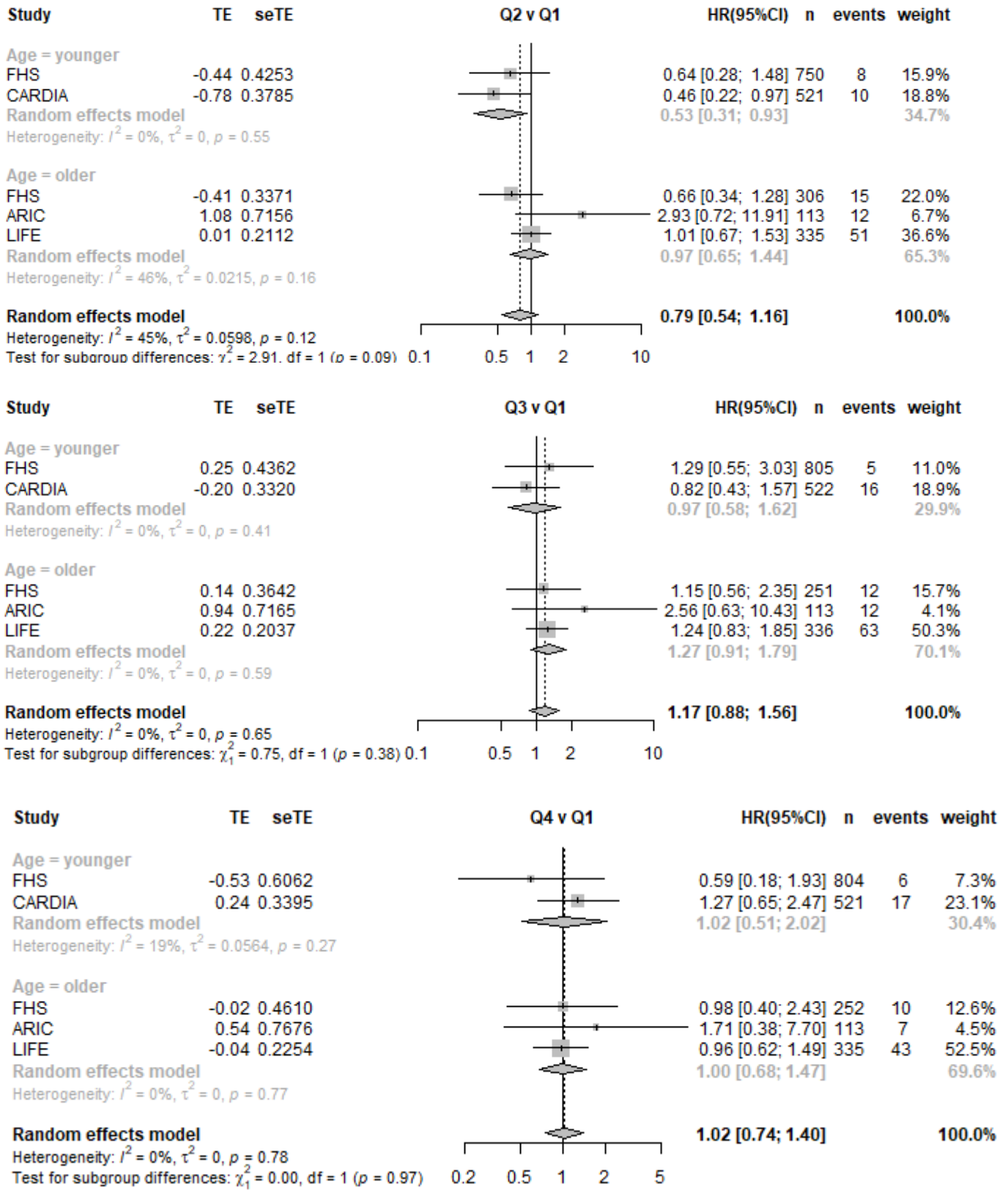


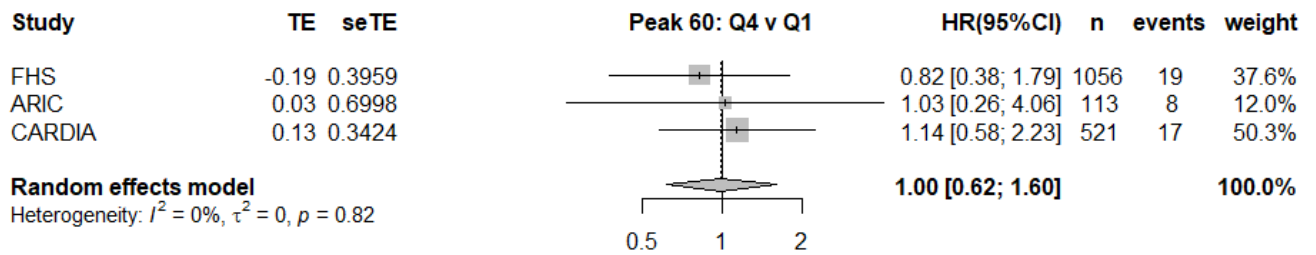
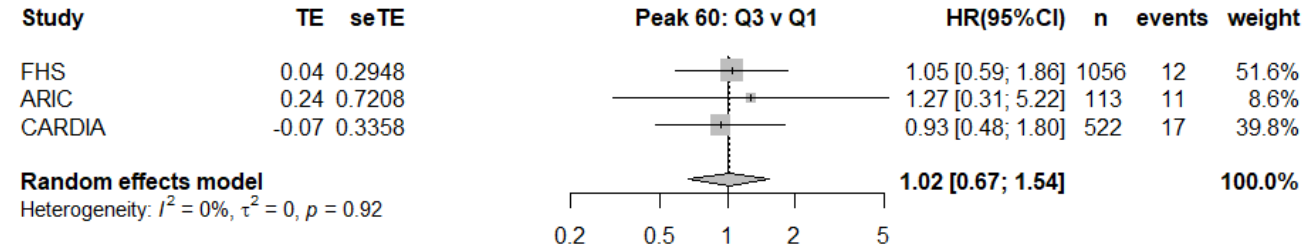
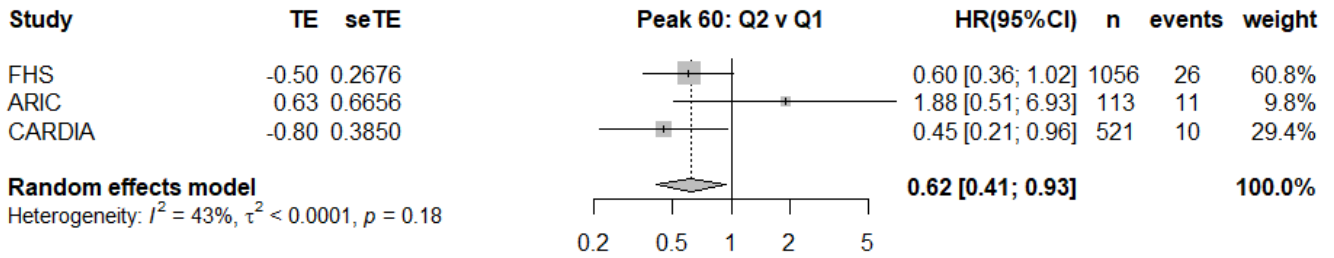
Figure S6b. Peak 30 Minute Intensity – Forest Plots Final Model Adjusting for Steps/Day – Age Stratified



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.

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



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.

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 5b. Peak 60 Minute Intensity Medians by Quartile

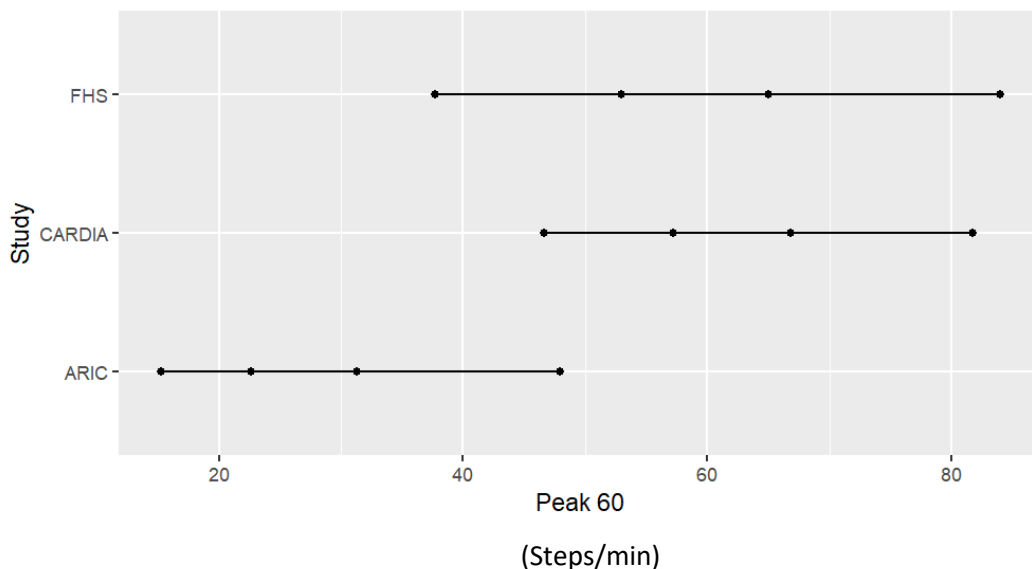
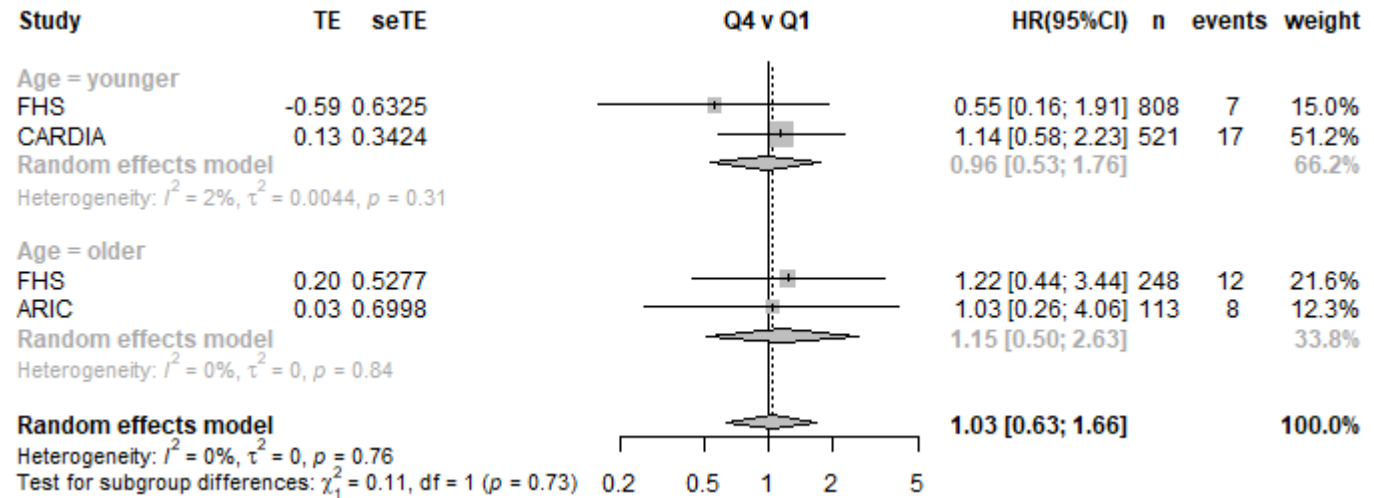
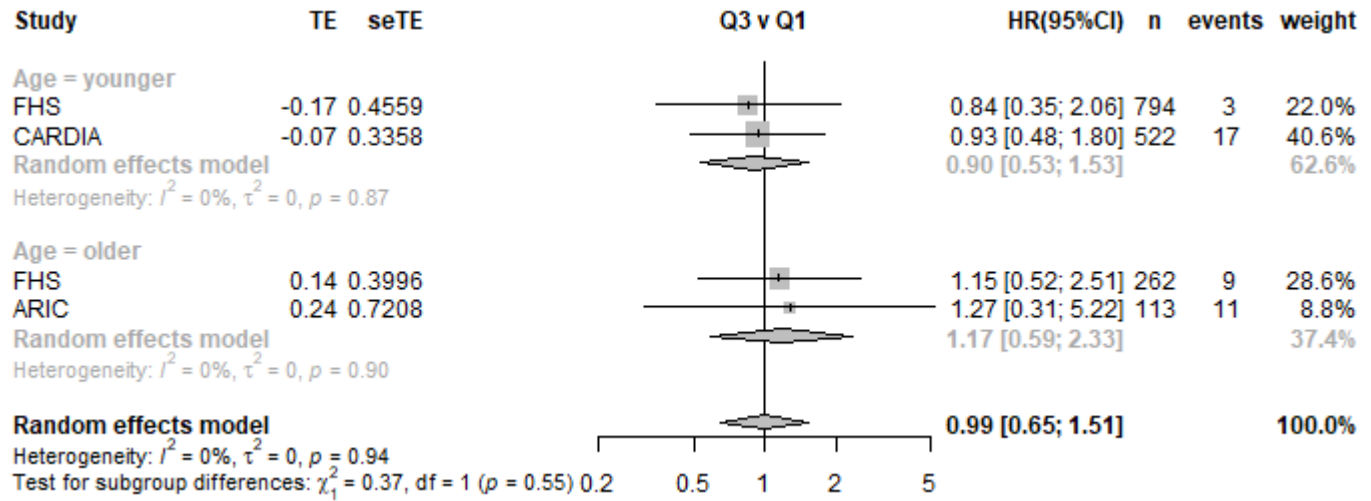
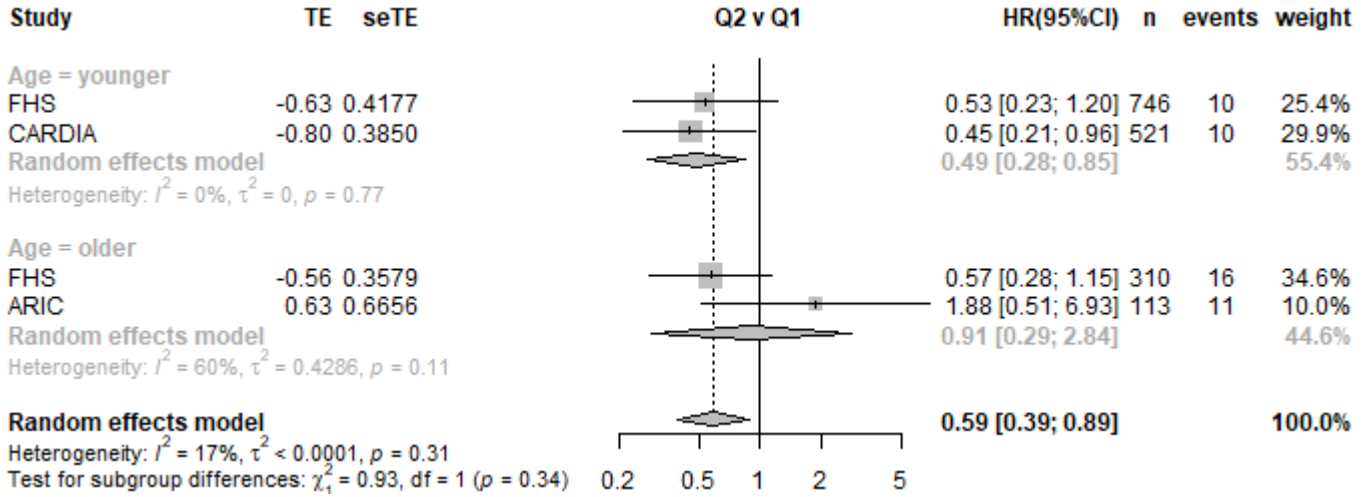


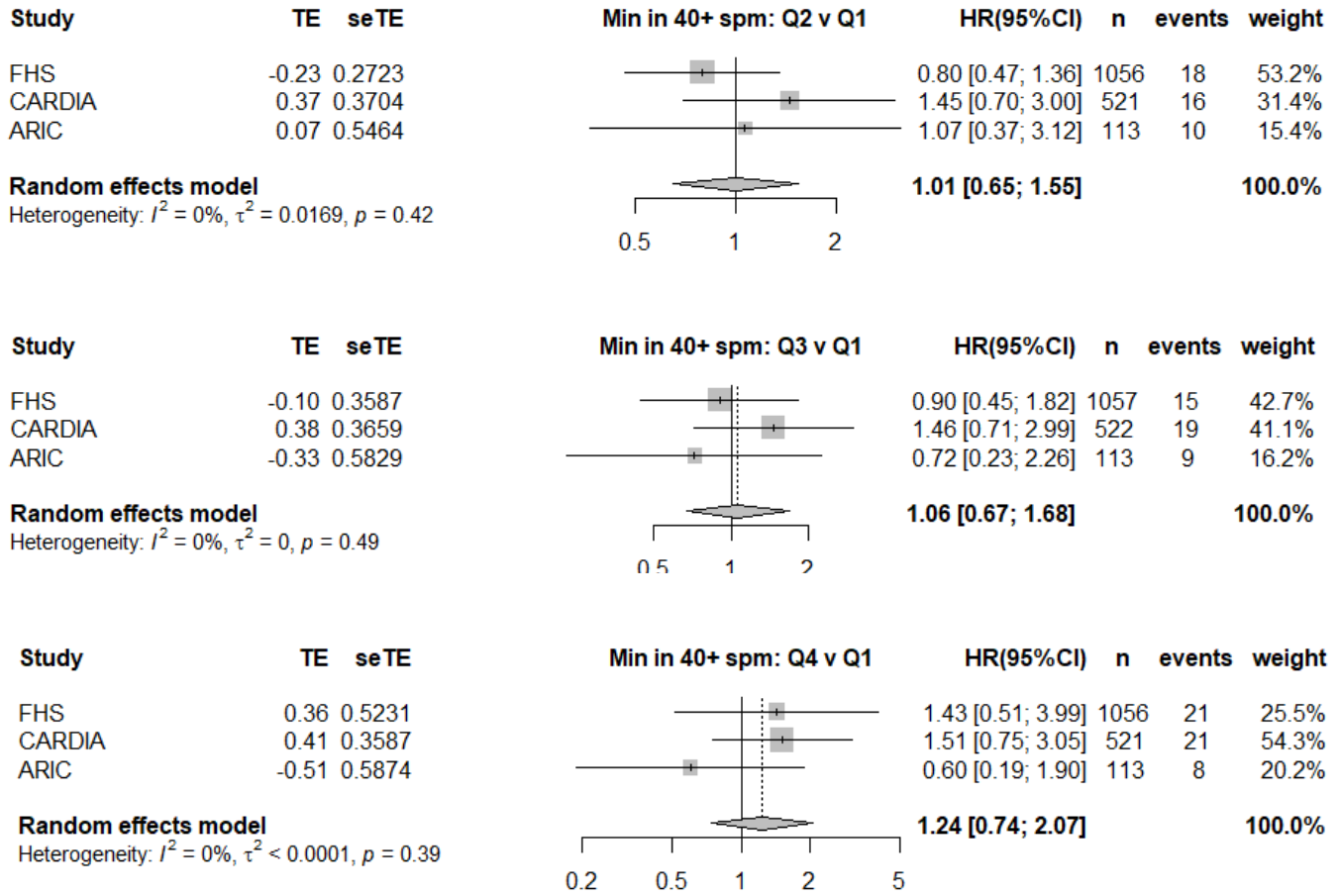
Figure S7b. Peak 60 Minute Intensity – Forest Plots Final Model Adjusting for Steps/Day – Age Stratified



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.

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



Time spent at ≥ 40 steps/min is quantified as the average duration (minutes per day) of steps accumulated at ≥ 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

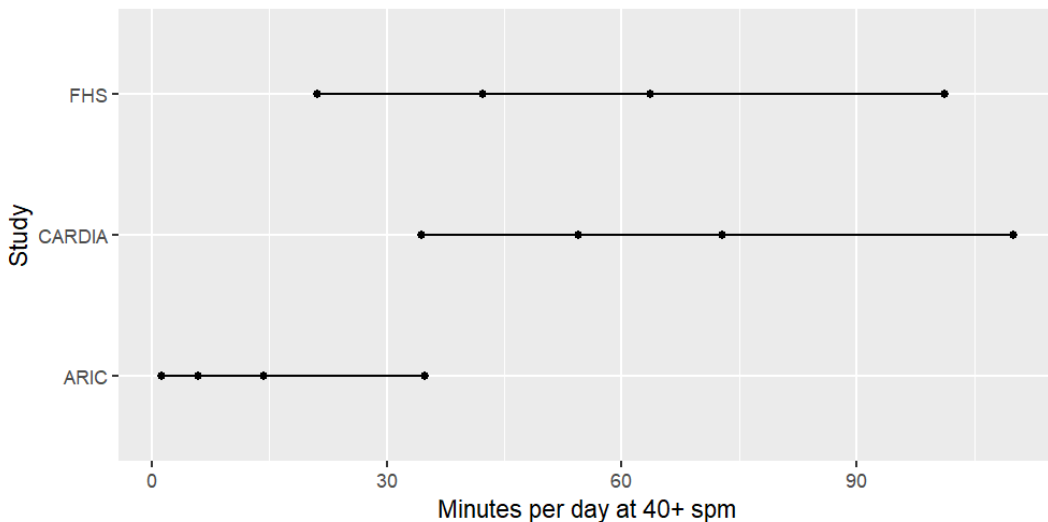
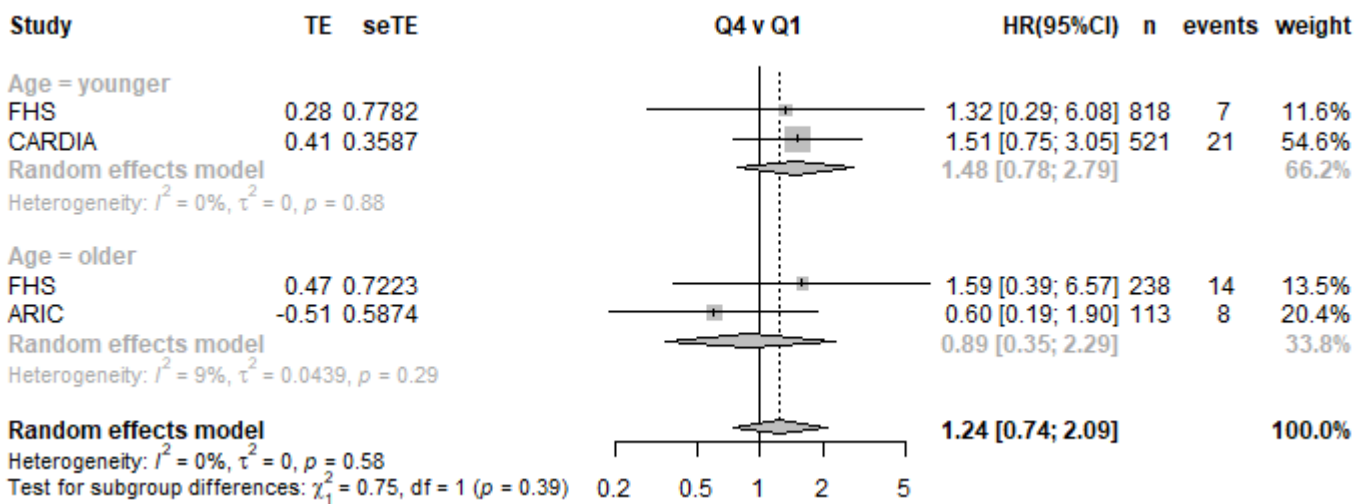
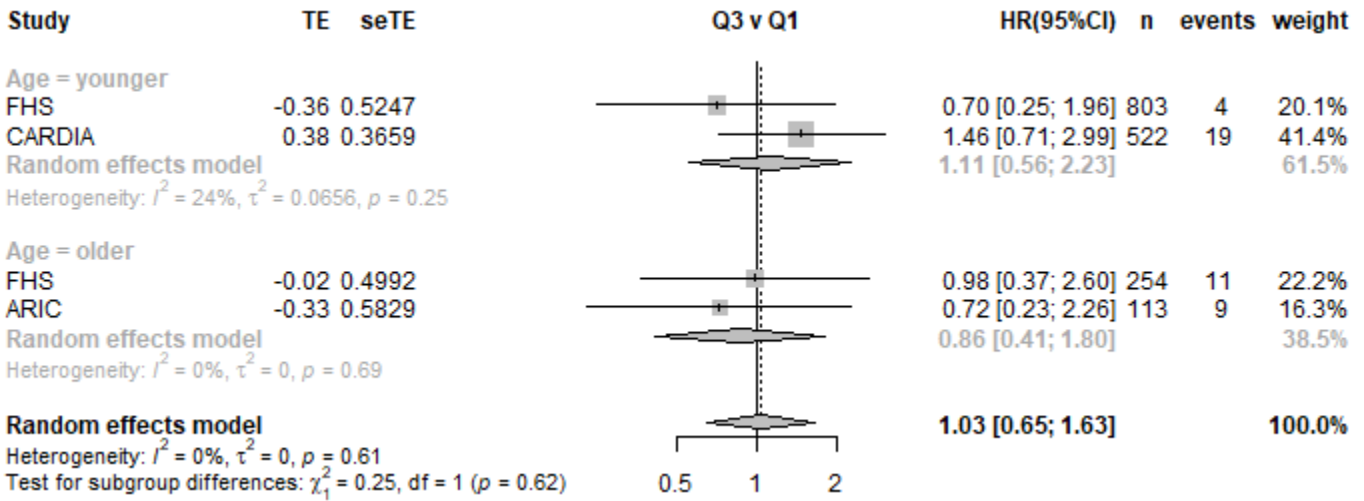
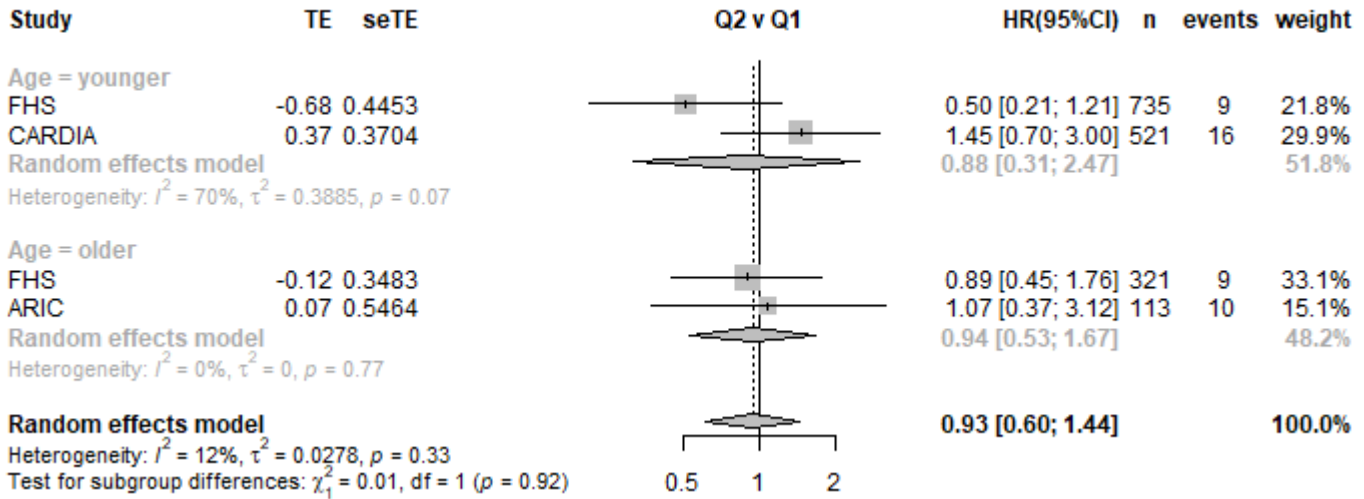


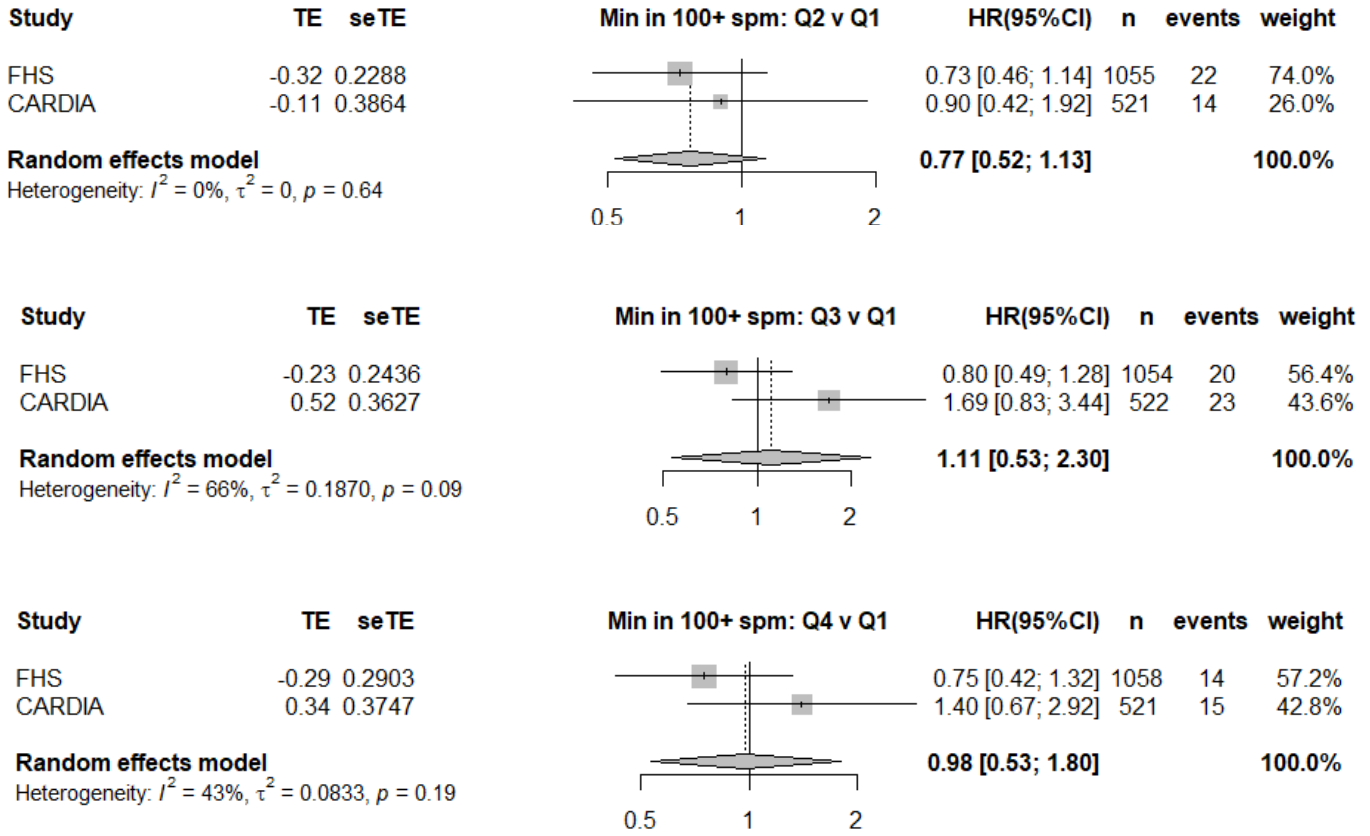
Figure S8b. Time Spent at ≥ 40 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day – Age Stratified



Time spent at ≥ 40 steps/min is quantified as the average duration (minutes per day) of steps accumulated at ≥ 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 S9a. Time Spent at ≥ 100 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day



Time spent at ≥ 100 steps/min is quantified as the average duration (minutes per day) of steps accumulated at ≥ 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

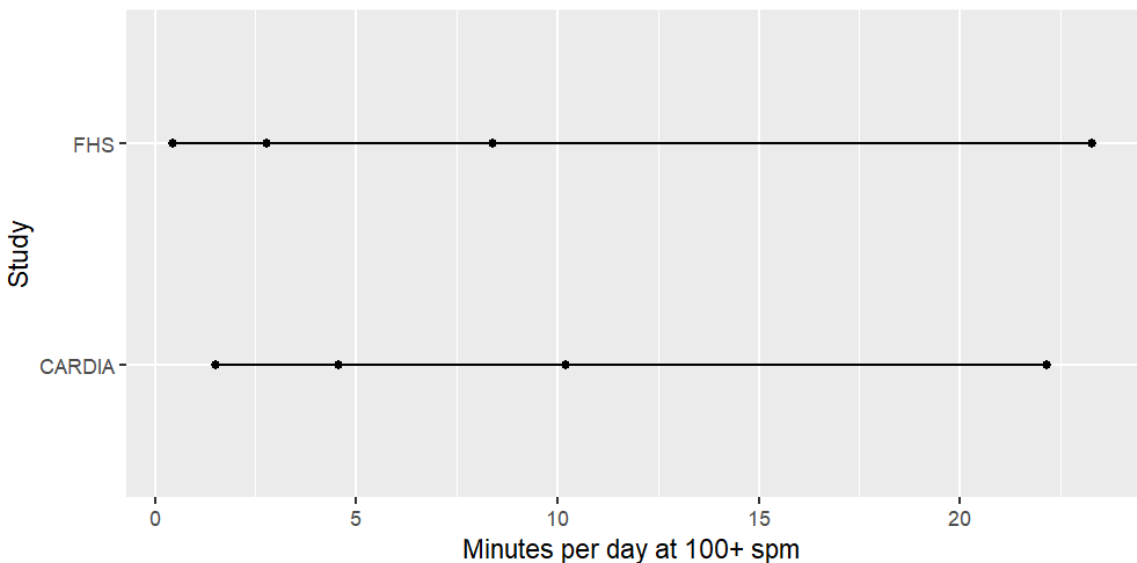
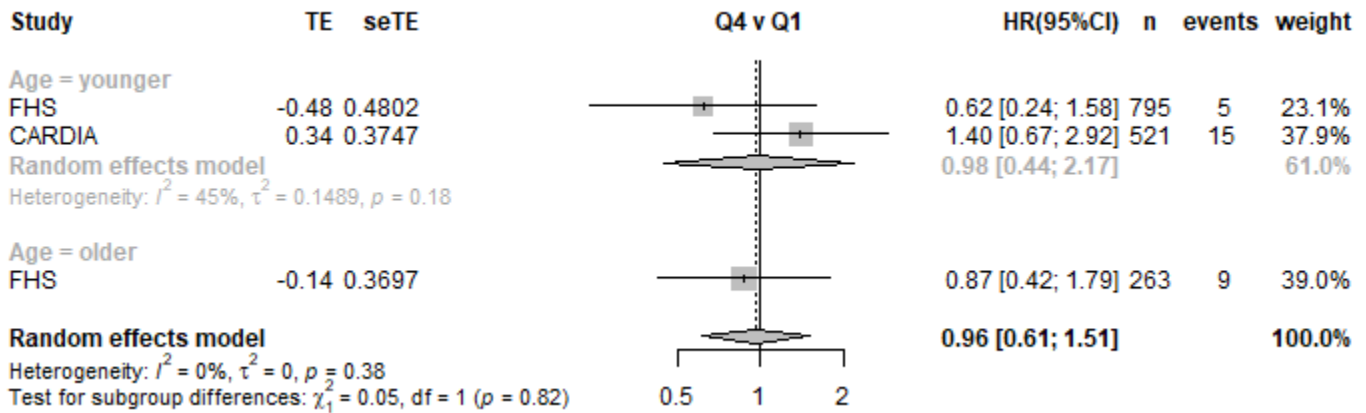
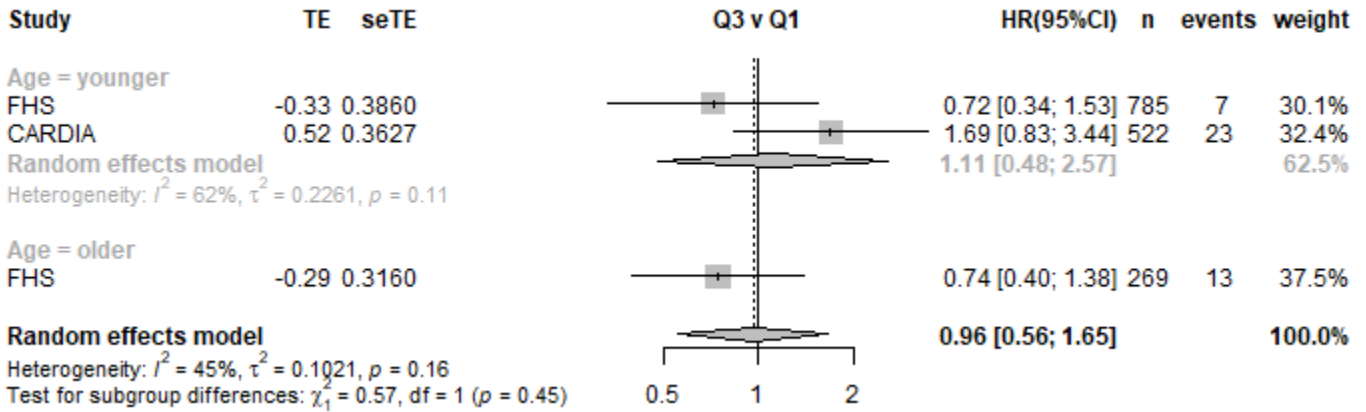
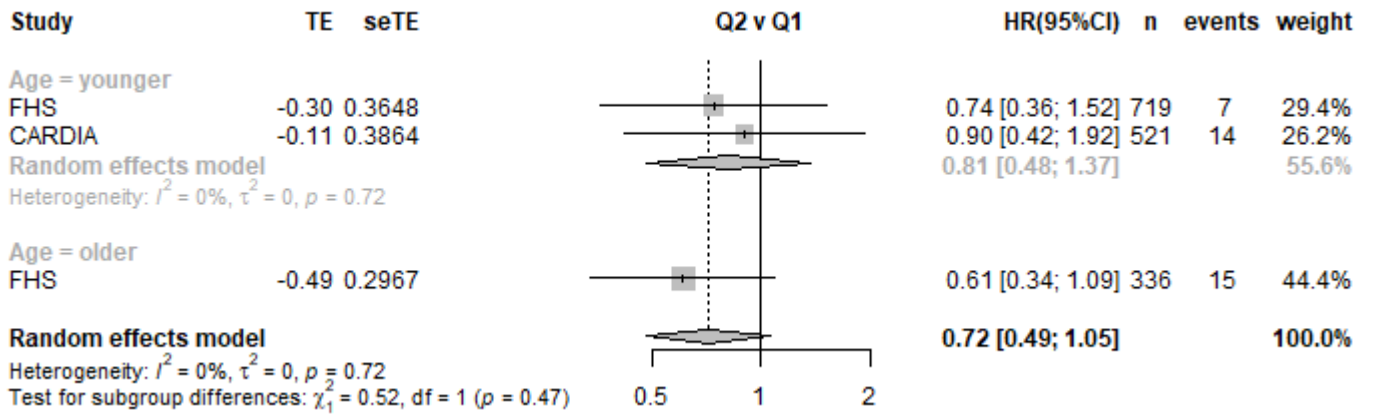


Figure S9b. Time Spent at ≥ 100 steps/min Intensity – Forest Plots Final Model Adjusting for Steps/Day – Stratified by Age



Time spent at ≥ 100 steps/min is quantified as the average duration (minutes per day) of steps accumulated at ≥ 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.