

Online-Only Supplement

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eTable 1. Description of cohorts

Study	Participants; cases; year of (accelerometer) baseline assessment; follow-up years (mean)	BMI obtained by; waist circumference obtained by	Definitions used to exclude individuals with prevalent CVD or cancer	Case ascertainment	Accelerometer-device and method	Covariates available in multivariable-adjusted model
REasons for Geographical and Racial differences in Stroke (REGARDS), US	6381; 701; 2003-07; 7.8	BMI and waist circumference measured by trained staff	Self-reported or ECG evidence of myocardial infarction or a self-reported coronary revascularization procedure	Review of death certificates, medical records, and administrative databases. Censoring data was 16-March-2020.	Actical (right hip)	Age, sex, education, race, region of residence, season the accelerometer was worn, current smoking, alcohol use, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate, atrial filtration
Sweden Attitude, Behaviour and Change study (ABC), Sweden	770; 67; 2001-02; 14.5	Self-report; not available	Self-reported history of hypertension, heart disease, cancer, or diabetes	National death register. Censoring data was 31-December-2015.	Actigraph 7164 (lower back)	Age, sex, education, smoking
British Regional Heart Study (BRHS), UK	940; 114; 2010-12; 6.0	BMI and waist circumference measured by trained staff	Self-reported ever receiving a doctor diagnosis of heart attack, heart failure or stroke (with symptoms lasting >24hours) or cancer (not including non-melanoma skin cancers)	National Health Service central registers. Censoring data was 1-June-2016.	Actigraph GT3X (right hip)	Age, season of accelerometer wear, region of residence, lives alone/with others, alcohol, smoking, sleep, locomotor disability, diabetes
Women's Health Study (WHS), US	13,968; 438; 2011-17; 6.3	Self-report; not available	Self-reported MI, stroke, or cancer (not including non-melanoma skin cancers). Confirmed by medical record review.	Medical records, death certificates, or the National Death Index. Censoring data was 31-December-2019.	Actigraph GT3X+ (right hip)	Age, income, smoking, alcohol, intakes of saturated fat, fibre, fruits, and vegetables, hormone therapy, parental history of MI, family history of cancer, general health, and cancer screening

Framingham Heart Study (FHS), US	3009; 56; 2008-11; 7.0	BMI and waist circumference measured by trained staff	Adjudicated by a panel of physicians. Myocardial infarction, angina pectoris, coronary insufficiency, coronary heart disease death, stroke, intermittent claudication, coronary heart failure, or any cancer	Medical records, death certificates. Censoring data was 31-December-2017.	Actical (right hip)	Age, sex, education, BMI, ethnicity, smoking, self-reported health
National Health and Nutrition Examination Study (NHANES), US	2832; 358; 2003-06; 10.5	BMI and waist circumference measured by trained staff	Self-reported congestive heart failure, coronary heart disease, angina pectoris, heart attack, stroke or any cancer	National Death Index, National Center for Health Statistics. Censoring data was 31-December-2016.	Actigraph 7164 (right hip)	Age, sex, education, ethnicity, smoking, alcohol, mobility limitations, diabetes
Norwegian National Physical Activity Survey (NNPAS)	1928; 66; 2008-09; 8.9	Self-report; not available	Self-reported myocardial infarction, angina pectoris, stroke or any cancer	Death certificates, Norwegian death register. Censoring data was 31-December-2017.	Actigraph GT1M (right hip)	Age, sex, education, smoking alcohol, diabetes
The European Prospective Investigation into Cancer and Nutrition (EPIC) Norfolk, UK	4667; 234; 2004-18; 6.7	BMI and waist circumference measured by trained staff	Self-reported and hospital data on myocardial infarction, stroke, or any cancer	Death certificates, Office for National Statistics. Censoring date was 31-March-2018.	Actigraph GT1M and GT3X+ (harmonized, right hip)	Age, sex, education, social class, smoking, alcohol, diabetes, anti-hypertensive drugs, lipid lowering drugs, anti-depression drugs, family history of heart attack, stroke, diabetes or cancer

CVD; cardiovascular disease, ECG; electrocardiography, M; myocardial infarction

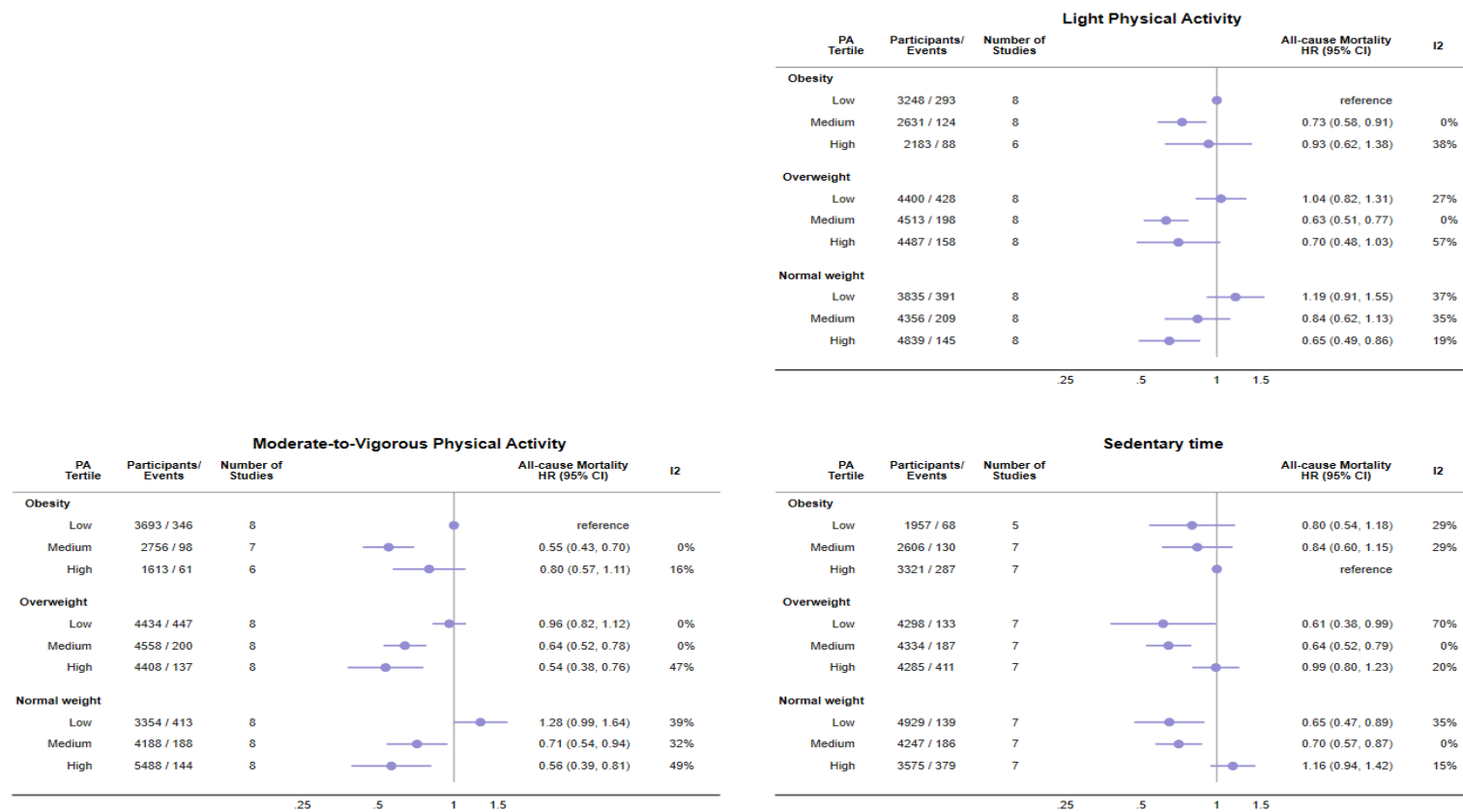
eTable 2. Physical activity (medians (interquartile range)) levels across combinations of physical activity and BMI

	NNPAS	ABC	EPIC-NORFOLK	BRHS	FHS	REGARDS	NHANES	WHS	Median of medians*
Total Physical Activity (CPM)									
Normal weight – low total activity	217 (86)	219 (73)	158 (62)	95 (46)	80 (29)	36 (23)	180 (66)	124 (49)	169
Normal weight – medium total activity	321 (47)	318 (49)	247 (46)	179 (49)	135 (27)	78 (25)	272 (54)	210 (41)	260
Normal weight – high total activity	457 (130)	493 (135)	367 (114)	322 (134)	239 (115)	157 (83)	442 (155)	345 (101)	405
Overweight – low total activity	214 (70)	220 (78)	156 (56)	94 (46)	79 (37)	38 (20)	173 (61)	126 (47)	165
Overweight – medium total activity	310 (49)	314 (51)	243 (43)	175 (42)	134 (30)	78 (24)	274 (47)	209 (40)	259
Overweight – high total activity	445 (111)	438 (129)	361 (103)	290 (101)	222 (87)	152 (68)	430 (134)	338 (92)	396
Obese – low total activity	198 (80)	185 (78)	145 (60)	90 (46)	77 (35)	37 (20)	174 (60)	123 (48)	160
Obese – medium total activity	317 (62)	312 (34)	241 (43)	177 (46)	135 (29)	76 (24)	271 (49)	209 (43)	256
Obese – high total activity	435 (105)	431 (85)	350 (99)	258 (61)	211 (66)	141 (60)	394 (100)	321 (73)	372
Light Physical Activity (%/day)									
Normal weight – low LPA	25.5 (5.0)	29.0 (5.6)	24.0 (4.9)	18.0 (3.7)	15.1 (3.7)	9.8 (5.2)	30.1 (6.2)	23.4 (5.3)	24.8
Normal weight – medium LPA	32.2 (3.3)	38.0 (4.7)	30.6 (3.2)	26.0 (3.4)	20.6 (3.0)	16.6 (3.1)	40.2 (5.4)	31.9 (3.4)	32.0
Normal weight – high LPA	41.6 (6.0)	47.8 (6.8)	38.5 (5.8)	34.0 (6.7)	27.8 (5.9)	24.8 (6.4)	49.8 (8.0)	41.6 (6.4)	41.6
Overweight – low LPA	24.9 (5.5)	29.9 (6.4)	23.7 (5.0)	19.0 (4.2)	14.8 (4.0)	9.9 (4.5)	29.2 (7.1)	23.4 (5.4)	24.3
Overweight – medium LPA	32.5 (3.5)	37.9 (4.9)	30.6 (3.1)	25.9 (3.4)	20.7 (3.0)	16.9 (3.3)	39.5 (4.8)	31.8 (3.6)	32.2
Overweight – high LPA	41.6 (6.3)	48.0 (5.6)	38.1 (5.8)	34.0 (5.8)	28.2 (6.4)	24.6 (6.0)	50.5 (7.2)	41.5 (6.2)	41.6
Obese – low LPA	24.6 (7.0)	28.9 (8.3)	22.4 (5.8)	18.6 (5.4)	14.6 (4.1)	9.9 (4.9)	29.7 (7.1)	22.6 (6.2)	23.6
Obese – medium LPA	32.3 (3.2)	38.7 (3.0)	30.5 (2.9)	25.4 (3.3)	20.8 (2.7)	16.5 (3.0)	39.7 (4.3)	31.8 (3.4)	32.1
Obese – high LPA	40.7 (5.7)	46.9 (4.7)	38.4 (6.1)	32.7 (5.1)	28.3 (5.6)	24.6 (6.1)	50.0 (7.9)	41.0 (5.4)	40.9
Moderate-to-Vigorous Physical Activity (%/day)									
Normal weight – low MVPA	1.54 (1.32)	1.49 (1.06)	1.41 (1.08)	0.22 (0.27)	0.4 (0.4)	0.01 (0.04)	0.44 (0.44)	0.23 (0.24)	0.42
Normal weight – medium MVPA	3.56 (1.02)	2.98 (1.14)	3.41 (1.13)	1.38 (0.71)	1.5 (0.8)	0.34 (0.35)	1.75 (0.98)	1.12 (0.65)	1.63
Normal weight – high MVPA	6.67 (2.56)	6.17 (2.87)	6.59 (2.79)	4.32 (2.55)	3.7 (2.3)	2.12 (2.13)	4.72 (2.99)	3.89 (2.17)	4.52
Overweight – low MVPA	1.74 (1.17)	1.18 (1.09)	1.35 (1.05)	0.20 (0.27)	0.3 (0.5)	0.00 (0.04)	0.41 (0.41)	0.23 (0.23)	0.41
Overweight – medium MVPA	3.56 (0.90)	3.04 (1.01)	3.37 (1.11)	1.27 (0.76)	1.4 (0.7)	0.31 (0.33)	1.76 (0.87)	1.09 (0.62)	1.58
Overweight – high MVPA	6.34 (2.47)	5.75 (2.31)	6.38 (2.78)	3.67 (2.31)	3.5 (2.0)	2.00 (1.92)	4.55 (2.99)	3.64 (1.92)	4.11
Obese – low MVPA	1.18 (1.32)	0.71 (1.05)	1.14 (1.10)	0.13 (0.29)	0.4 (0.5)	0.00 (0.03)	0.49 (0.46)	0.24 (0.22)	0.49
Obese – medium MVPA	3.31 (1.09)	2.66 (0.83)	3.20 (1.14)	1.39 (0.82)	1.4 (0.7)	0.27 (0.31)	1.75 (0.97)	1.02 (0.61)	1.58
Obese – high MVPA	5.49 (2.45)	5.64 (2.11)	6.07 (2.58)	3.47 (1.43)	3.3 (1.5)	1.71 (1.61)	4.03 (1.87)	3.34 (1.59)	3.75
Sedentary time (%/day)									
Normal weight – low sedentary	53.7 (6.4)	47.9 (7.1)	56.7 (6.7)	62.5 (6.3)	69.1 (6.9)	73.5 (7.2)	45.5 (8.9)	55.9 (7.2)	54.8

Normal weight – medium sedentary	63.5 (3.3)	58.5 (4.4)	65.2 (3.6)	72.0 (3.9)	77.2 (2.9)	82.3 (3.6)	58.1 (5.4)	66.4 (3.7)	64.4
Normal weight – high sedentary	70.7 (5.6)	67.9 (5.5)	72.8 (5.6)	80.5 (5.2)	83.2 (4.1)	90 (5.4)	68.1 (6.2)	75.6 (5.8)	71.8
Overweight – low sedentary	53.9 (6.8)	48.3 (6.5)	56.8 (6.8)	63.1 (6.5)	69.3 (6.7)	74.1 (6.4)	46.0 (8.1)	56.1 (6.6)	55.0
Overweight – medium sedentary	63.4 (3.6)	58.7 (4.4)	65.6 (3.6)	72.1 (4.1)	77.3 (3.0)	82.3 (3.3)	58.3 (4.8)	66.4 (3.9)	64.5
Overweight – high sedentary	71.3 (6.0)	66.7 (7.6)	73.5 (5.7)	80.8 (4.3)	83.7 (4.5)	89.8 (4.8)	68.8 (7.7)	75.6 (5.9)	72.4
Obese – low sedentary	55.1 (6.2)	48.9 (6.3)	57.0 (6.4)	64.9 (4.2)	69.5 (5.7)	73.9 (6.3)	46.6 (9.4)	57.1 (5.4)	56.1
Obese – medium sedentary	62.7 (4.2)	57.7 (4.0)	65.6 (3.5)	74.0 (3.9)	77.4 (3.0)	82.6 (3.5)	58.6 (5.1)	66.7 (3.6)	64.2
Obese – high sedentary	72.2 (87.1)	69.5 (10.9)	74.7 (6.7)	80.3 (5.7)	84.5 (4.8)	89.9 (5.1)	68.5 (7.4)	76.5 (6.4)	73.5

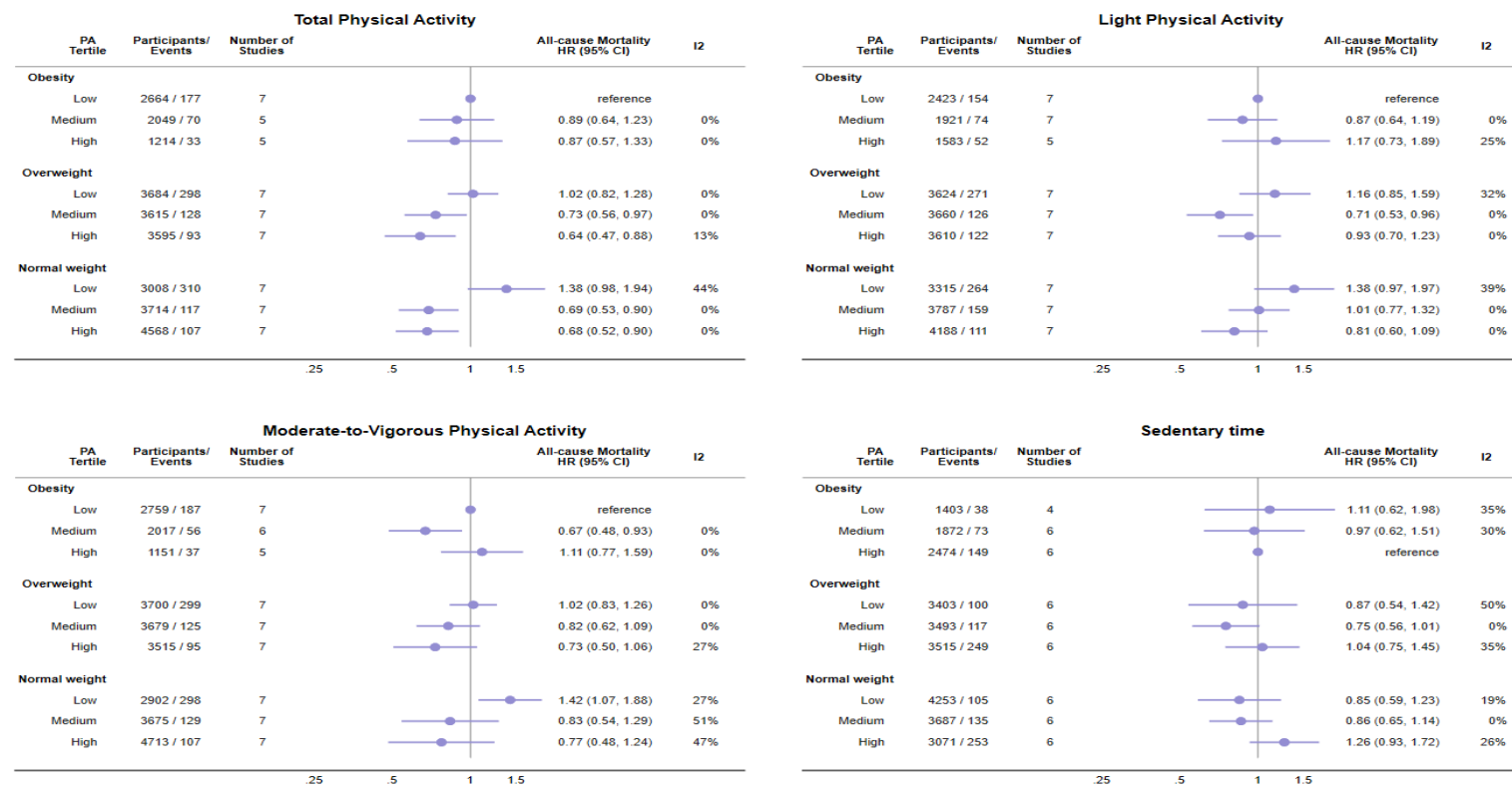
Participants without cardiovascular disease and cancer at baseline (in REGARDS, participants are only free from cardiovascular disease). REGARDS; REasons for Geographical and Racial differences in Stroke, ABC; Sweden Attitude, Behaviour and Change study, BRHS; British Regional Heart Study, WHS; Women's Health Study, FHS; Framingham Heart Study, NHANES; National Health and Nutrition Examination Study, NNPAS; Norwegian National Physical Activity Survey, EPIC-Norfolk; The European Prospective Investigation into Cancer and Nutrition – Norfolk. *CPM, light physical activity, and sedentary time not including cohorts with Actical monitors as absolute levels are not comparable.

eFigure 1. Joint associations of physical activity or sedentary time and BMI with risk of all-cause mortality without control for other physical activity intensities



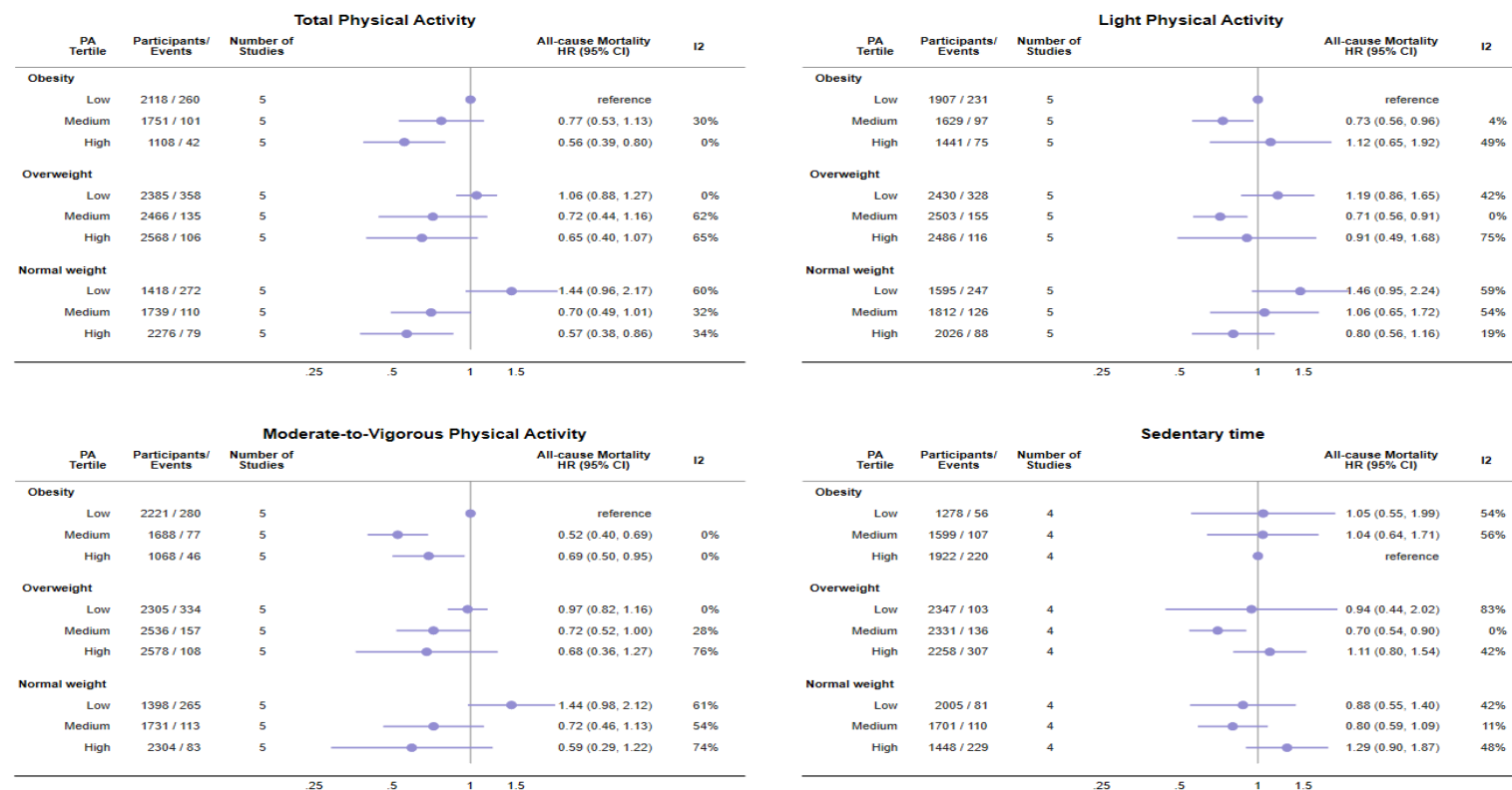
N = 34,492, deaths = 2034. Models are adjusted for age, sex (when applicable), socioeconomic status, smoking, and the covariates included in each study's published final multivariable-adjusted model (see eTable 1 for details).

eFigure 2. Joint associations of physical activity or sedentary time and BMI with risk of all-cause mortality, excluding the REGARDS cohort



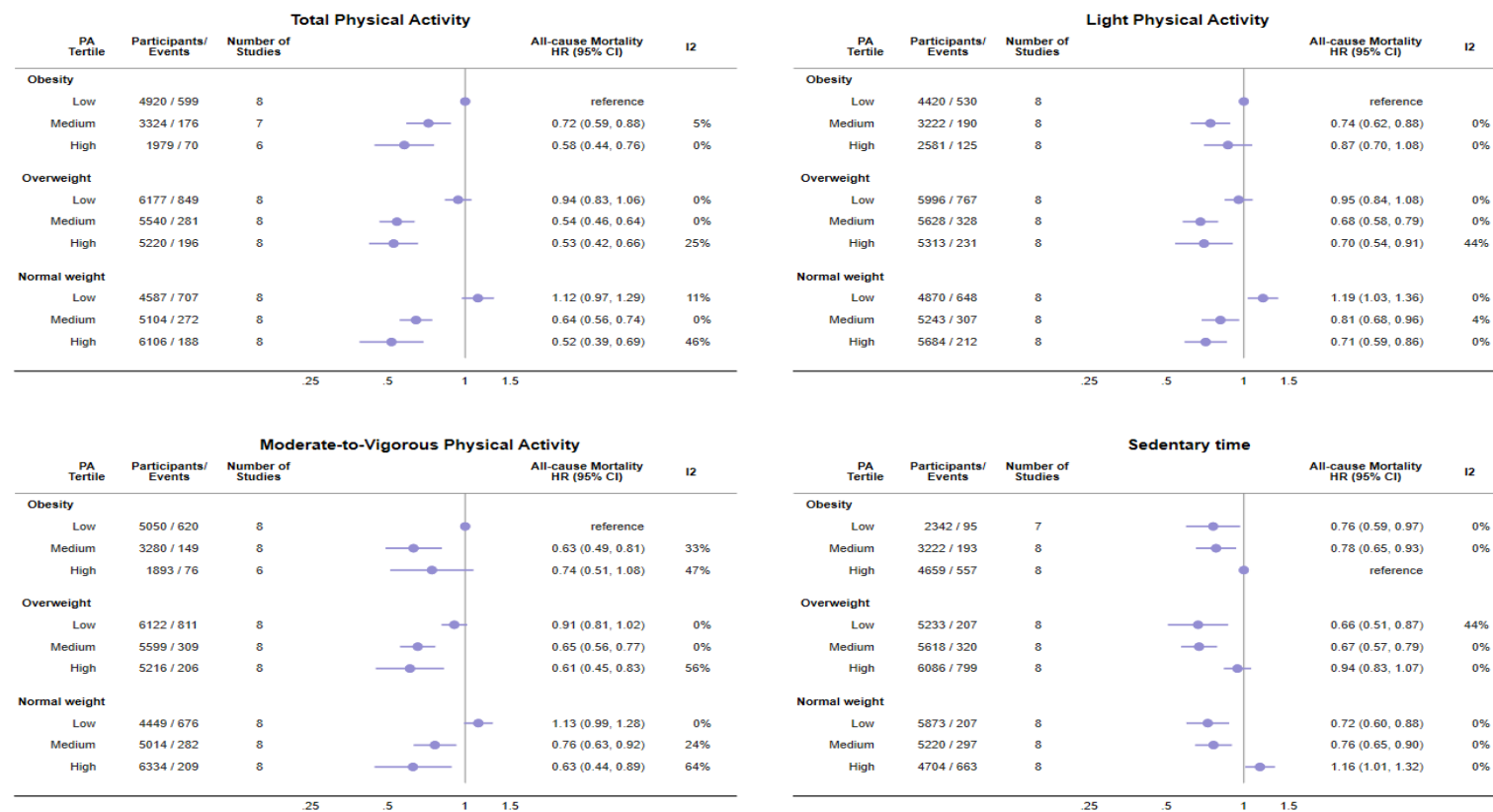
N = 28,111, deaths = 1333. Individuals self-reporting prevalent CVD or cancer are excluded. Analysis of sedentary time includes n = 27,171, 1219 deaths as there were no cases in the reference category in the British Regional Heart Study. Models are adjusted for age, sex (when applicable), socioeconomic status, smoking, and the covariates included in each study's published final multivariable-adjusted model (see eTable 1 for details). Additionally, models using moderate-to-vigorous physical activity were adjusted for sedentary time (continuous form) with sedentary time and light physical activity adjusted for moderate-to-vigorous physical activity (continuous).

eFigure 3. Joint associations of physical activity or sedentary time and BMI with risk of all-cause mortality, cohorts with measured BMI



N = 17,829, deaths = 1463. Individuals self-reporting prevalent CVD or cancer are excluded. Analysis of sedentary time includes n = 16,889, 1349 deaths as there were no cases in the reference category in the British Regional Heart Study. Models are adjusted for age, sex (when applicable), socioeconomic status, smoking, and the covariates included in each study's published final multivariable-adjusted model (see eTable 1 for details). Additionally, models using moderate-to-vigorous physical activity were adjusted for sedentary time (continuous form) with sedentary time and light physical activity adjusted for moderate-to-vigorous physical activity (continuous).

eFigure 4. Joint associations between physical activity or sedentary time and BMI with risk of all-cause mortality, including individuals with self-reported prevalent CVD or cancer at start of follow-up



N = 42,957, deaths = 3338. Models are adjusted for age, sex (when applicable), socioeconomic status, smoking, CVD, cancer, and the covariates included in each study's published final multivariable-adjusted model (see eTable 1 for details). Additionally, models using moderate-to-vigorous physical activity were adjusted for sedentary time (continuous form) with sedentary time and light physical activity adjusted for moderate-to-vigorous physical activity (continuous).

eTable 3. Descriptive characteristics of cohorts, including participants with self-reported prevalent CVD or cancer

	NNPAS		ABC		EPIC-NORFOLK		BRHS
	Women (n=1167)	Men (n=1048)	Women (n=457)	Men (n=371)	Women (n=4163)	Men (n=3363)	Men (n=1311)
Age, mean (SD), years	55.7 (11.0)	57.1 (10.7)	52.6 (10.2)	53.1 (10.5)	69.7 (7.5)	70.9 (7.5)	78.2 (4.5)
Counts/min, mean (SD)	325 (133)	331 (150)	341 (213)	358 (289)	237 (107)	249 (127)	190 (110)
LPA/day, mean (SD), % of wear-time	34.3 (8.1)	30.9 (8.4)	38.8 (9.4)	37.2 (9.9)	31.5 (8.0)	27.9 (7.7)	25.9 (8.2)
MVPA/day, mean (SD), % of wear-time	3.8 (2.6)	4.2 (2.9)	3.4 (3.0)	4.0 (3.2)	3.2 (2.5)	3.9 (3.1)	1.9 (2.1)
Sedentary time/day, mean (SD), % of wear-time	61.9 (8.8)	65.0 (9.2)	57.8 (10.2)	58.8 (11.2)	65.3 (9.1)	68.2 (9.1)	72.3 (9.1)
BMI, mean (SD), kg/m ²	25.3 (4.2)	26.4 (3.4)	25.4 (3.8)	25.9 (3.0)	26.8 (4.6)	27.2 (3.7)	27.2 (3.8)
Waist circumference, mean (SD), cm	ni	ni	ni	ni	90.3 (11.8)	100.9 (10.2)	100.0 (10.8)
BMI ≥30 kg/m ² , No. (%)	138 (11.8)	138 (13.2)	56 (12.3)	32 (8.6)	832 (20.1)	637 (18.9)	260 (19.8)
Smoking, No. (%)							
Never	534 (45.8)	456 (43.5)	186 (40.8)	160 (43.0)	2455 (59.4)	1402 (41.7)	569 (43.4)
Former	400 (34.3)	430 (41.0)	140 (30.7)	137 (36.8)	1424 (34.4)	1776 (52.8)	695 (53.0)
Current	233 (20.0)	162 (15.5)	130 (28.5)	75 (20.3)	257 (6.2)	185 (5.5)	47 (3.6)
Ethnicity, No. (%)*							
White	ni	ni	ni	ni	4115 (99.8)	3338 (99.5)	1276 (99.5)
Black	ni	ni	ni	ni	1 (0.0)	3 (0.1)	1 (0.1)
Other	ni	ni	ni	ni	6 (0.1)	13 (0.4)	5 (0.4)
Prevalent CVD, No. (%)	54 (4.6)	117 (11.2)	6 (1.3)	22 (6.0)	972 (23.5)	1137 (33.8)	207 (15.8)
Prevalent Cancer, No. (%)	74 (6.3)	67 (6.4)	13 (2.9)	82 (2.2)	729 (17.6)	451 (13.4)	197 (15.0)
	FHS		REGARDS		NHANES		WHS
	Women (n=2046)	Men (n=1765)	Women (n=4061)	Men (n=3339)	Women (n=1878)	Men (n=1840)	Women (n=16175)
Age, mean (SD), years	58.1 (11.9)	58.2 (12.0)	68.2 (8.7)	69.8 (8.4)	57.2 (11.7)	55.8 (11.6)	71.9 (5.6)
Counts/min, mean (SD)	143 (117)	160 (131)	84 (64)	105 (79)	268 (120)	322 (157)	222 (103)
LPA/day, mean (SD), % of wear-time	20.6 (6.8)	21.3 (7.7)	16.6 (7.6)	17.6 (7.7)	39.6 (10.0)	38.3 (11.3)	32.0 (8.4)
MVPA/day, mean (SD), % of wear-time	1.8 (2.2)	2.1 (2.4)	0.8 (1.3)	1.2 (1.7)	1.9 (2.0)	3.1 (2.9)	1.7 (1.8)
Sedentary time/day, mean (SD), % of wear-time	77.7 (7.6)	76.7 (8.5)	82.6 (8.1)	81.3 (8.4)	58.5 (10.8)	58.5 (12.5)	66.3 (9.1)

BMI, mean (SD), kg/m ²	27.6 (5.7)	28.9 (4.7)	29.0 (6.2)	28.3 (4.6)	28.9 (6.6)	28.7 (4.9)	26.4 (4.9)
Waist circumference, mean (SD), cm	95.3 (14.5)	103.5 (12.2)	89.5 (14.8)	98.7 (12.0)	95.7 (14.4)	103.6 (12.9)	ni
BMI ≥30 kg/m ² , No. (%)	558 (27.3)	597 (33.8)	1499 (36.9)	982 (29.4)	655 (34.9)	611 (33.2)	3218 (19.9)
Smoking, No. (%)							
Never	1055 (51.6)	944 (53.5)	2331 (57.4)	1356 (40.6)	1070 (57.0)	714 (38.8)	8164 (50.5)
Former	846 (41.3)	713 (40.4)	1316 (32.4)	1646 (49.3)	503 (26.8)	712 (38.7)	7461 (46.1)
Current	145 (7.1)	108 (6.1)	418 (10.3)	341 (10.2)	304 (16.2)	414 (22.5)	550 (3.4)
Ethnicity, No. (%)*							
White	1844 (90.1)	1610 (91.2)	2614 (64.4)	2475 (74.1)	1455 (77.5)	1456 (79.1)	15418 (95.3)
Black	65 (3.2)	40 (2.3)	1447 (35.6)	864 (25.9)	182 (9.7)	160 (8.7)	246 (1.5)
Other	137 (6.7)	115 (6.5)	0 (0.0)	0 (0.0)	241 (12.8)	224 (12.2)	511 (3.2)
Prevalent CVD, No. (%)	133 (5.5)	182 (10.3)	345 (8.5)	564 (16.9)	188 (10.0)	234 (12.7)	379 (2.3)
Prevalent Cancer, No. (%)	332 (16.2)	251 (14.2)	ni	ni	248 (13.2)	184 (10.0)	1886 (11.7)

LPA; light intensity physical activity, MVPA; moderate-to-vigorous physical activity, BMI; body mass index, CVD; cardiovascular disease, Ni: no information, REGARDS; REasons for Geographical and Racial differences in Stroke, ABC; Sweden Attitude, Behaviour and Change study, BRHS; British Regional Heart Study, WHS; Women's Health Study, FHS; Framingham Heart Study, NHANES; National Health and Nutrition Examination Study, NNPAS; Norwegian National Physical Activity Survey, EPIC-Norfolk; The European Prospective Investigation into Cancer and Nutrition – Norfolk. All studies used a version of the Actigraph accelerometers, except REGARDS and FHS which used Actical accelerometers. *Numbers may not sum to total sample due to missing data.