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SUPPLEMENTARY MATERIALS

Systematic search

We conducted a systematic review following the guidelines for Meta-Analyses and Systematic reviews for Observational Studies (1) and the PRISMA guidelines (2). The review protocol is registered with the PROSPERO database (PROSPERO 2018 CRD42018091808).

Data sources

We performed a systematic search in five databases (PubMed, PsycINFO, Embase, Web of Science, Sport Discus) from database inception until July 31st 2018 and updated the search until March 31st 2020. The following list of search terms was used when searching for eligible articles; (#1"physical activity" OR "physical activities" OR "physically active" OR "physical exercise" OR "exercise" OR "walk" AND #2 "mortality" OR "mortalities" OR " death "OR "fatal" AND #3 "accelerometer" OR "activity monitor"OR "motion sensor" OR "device-based" OR "Actigraph" OR "Actical" or "Sensewear" OR "Actiband" OR "Actiwatch"). We performed forward and backward tracking by examining the reference list of studies potentially eligible for inclusion.

Study selection

Two authors (UE, JSS) independently screened all titles and abstracts. After exclusion of duplicates, one author (JSS) performed a full-text review and the final list of studies was discussed among the writing group. Inclusion criteria were; 1) prospective cohort studies that assessed sedentary time and physical activity by accelerometry; 2) had data on individual level exposure and outcome (all-cause mortality); 3) reported effect estimates as hazard ratios (HR), odds ratios (OR) or relative risk (RR) with 95% confidence intervals (95% CI) for all-cause mortality; 4) were published in English or Scandinavian language. Due to the marked difference in output from accelerometers placed at different body sites (3), which precludes harmonisation of physical activity data, we excluded three studies (4-6) in which physical activity was assessed by monitors placed on the upper arm, wrist and thigh, respectively. One eligible study did not wish to participate in the harmonised meta-analysis (7). We have previously published the results for the separate dose-response associations between different

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intensities of physical activity and sedentary time with all-cause mortality comprising eight of the studies included in this meta-analysis. The updated search identified one additional study eligible for inclusion (8).

Data Extraction

One author (UE) extracted the following information from each eligible study: name of the first author; study location; source and number of participants; age of participants; number of men and women; years of follow-up; number of deaths from all causes; methods of case ascertainment; assessment details for physical activity and sedentary time; and covariates included in final, adjusted models. Data extraction variables were cross-checked by another author (JSS).

Risk of Bias

Using the Newcastle-Ottawa quality assessment scale (9), two authors (UE, JT) independently assessed the studies, and any disagreements were resolved by consensus. This semi-quantitative scale assesses the quality for eight items across three domains (selection, comparability and exposure) using a star system, with a maximum of one star per item for high quality studies except for the comparability domain (two stars). Thus, the total score ranges from zero to nine. Further details of the quality rating are found below (**Supplementary Table 4**).

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Supplementary tables

Supplementary Table 1. Description of studies

Study	Participants; number of cases; year of baseline assessment and follow-up years (median)	Case ascertainment	Accelerometer Device and Method	Covariates adjusted for in final model
Walking Away from Type 2 Diabetes (WAT2D), England (10)	654; 26; 2010-11; 5.7 y	Office for National Statistics	Actigraph GT3X+ (right hip)	Age, sex, BMI, socioeconomic status
Reasons for Geographic and Racial Differences in Stroke (REGARDS); US (11)	7866; 590; 2003-07; 5.3 y	Review of death certificates, medical records, and administrative databases	Actical (right hip)	Age, sex, BMI, education, race, region of residence, season the accelerometer was worn, current smoking, alcohol use, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate, atrial fibrillation, history of coronary heart disease, and history of stroke
Sweden Attitude Behaviour and Change study (ABC), Sweden (12)	834; 79; 2001-02; 14.5 y	National death register	Actigraph 7164 (lower back)	Age, sex, education, BMI, smoking, history of hypertension, heart disease, cancer, and diabetes
British Regional Heart Study (BRHS), UK (13)	1412; 250; 2010-12; 6.0 y	National Health Service central registers	Actigraph GT3X+ (right hip)	Age, BMI, Social class, season of accelerometer wear, region of residence, lives alone / with others, alcohol, smoking, sleep, locomotor disability, previous MI, stroke or heart failure

Women's Health Study (WHS), US (14)	16738; 504; 2011-17; 4.3 y	Medical records, death certificates, or the National Death Index	Actigraph GT3X+ (right hip)	Age, income, BMI, smoking, alcohol, intakes of saturated fat, fibre, fruits, and vegetables, hormone therapy, parental history of myocardial infarction, family history of cancer, general health, history of cardiovascular disease, history of cancer, and cancer screening
Framingham Heart Study (FHS), US (16)	2621; 77; 2008-11; 4.0 y	Medical records, death certificates	Actical (right hip)	Age, sex, education, BMI, ethnicity, smoking, self-reported health
National Health and Nutrition Examination Survey (NHANES), US (18)	4319; 1065; 2003-06; 10.5 y	National Death Index, National Center for Health Statistics	Actigraph 7164 (right hip)	Age, socioeconomic status, BMI, ethnicity, smoking, alcohol, mobility limitations, number of medical conditions (diabetes, congestive heart failure, coronary heart disease, angina pectoris, heart attack, stroke, cancer)
Norwegian National Physical Activity Survey 1 (NNPAS) (17)	2284; 131; 2008-09; 8.9 y	Death certificates, Norwegian death register	Actigraph GT1M (right hip)	Age, sex, education, BMI, smoking, alcohol, number of medical conditions (diabetes, coronary heart disease, angina pectoris, heart attack, stroke, cancer)
The European Prospective Investigation into Cancer and Nutrition (EPIC) Norfolk, UK (9)	7657; 721; 2004-16; 5.4 y	Death certificates, Office for National Statistics	Actigraph GT1M and GT3X+ (harmonised; right hip)	Age, sex, education, BMI, social class, smoking, alcohol, diabetes, antihypertensive drugs, lipid lowering drugs, anti-depression drugs, cardiovascular disease, cancer, family history of disease (heart attack, stroke, diabetes, cancer)

References to original studies within brackets (see reference list in main document)

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Supplementary Table 2. Study specific medians (Interquartile range) of total physical activity, sedentary time and MVPA by tertiles.

	WAT2D	REGARDS*	ABC	BRHS	WHS	FHS*	NHANES	NNPAS	EPIC-NORFOLK	Median of medians**
Total Physical Activity (CPM)										
Low PA	169 (131-200)	35 (15-50)	201 (167-246)	85 (61-106)	126 (99-147)	60 (28-92)	138 (102-171)	200 (153-232)	131 (99-157)	138
Medium PA	272 (248- 304)	74 (50-98)	316 (296- 346)	166 (142-188)	205 (185- 226)	115 (86-144)	251 (223-277)	309 (286-338)	225 (204-248)	251
High PA	439 (373- 503)	147 (77-217)	465 (413- 546)	287 (244-356)	313 (277- 371)	200 (111-289)	396 (347 - 478)	444 (401-523)	345 (307-410)	396
Sedentary (hours/d)										
Low sedentary	7.6 (6.8-8.1)	10.6 (9.0-12.1)	7.1 (6.4-7.6)	9.1 (8.4-9.6)	8.7 (8.1-6.9)	10.4 (9.4-11.4)	6.5 (5.7-7.3)	8.5 (7.6-9.4)	8.2 (7.5-8.6)	8.5
Medium sedentary	8.9 (8.4-9.5)	11.8 (10.2-13.2)	8.6 (8.1- 9.2)	10.3 (9.8-10.9)	9.9 (9.6-10.2)	11.6 (11.0-12.9)	8.6 (7.9-9.2)	9.3 (8.6-10.1)	9.4 (9.1-9.7)	9.4
High sedentary	10.2 (9.4- 10.8)	12.4 (10.8-14.0)	10.0 (9.3- 10.8)	11.3 (10.6-12.0)	11.2 (10.8-11.8)	12.9 (12.2-13.5)	10.2 (9.3-11.2)	10.3 (9.4-11.1)	10.7 (10.3-11.2)	10.7
Sedentary (% time)										
Low sedentary	54 (50-57)	75 (64-86)	48 (43-51)	64 (60-68)	58 (54-64)	71 (64-78)	47 (42-51)	57 (51-62)	58 (54-61)	58
Medium sedentary	63 (61-65)	83 (73-94)	58 (54-62)	73 (70-77)	66 (64-68)	79 (75-82)	60 (58-63)	63 (58-67)	67 (65-69)	66
High sedentary	72 (69-75)	88 (76-99)	67 (63-73)	81 (76-85)	75 (72-79)	88 (83-92)	72 (68-77)	70 (67-75)	76 (73-79)	75
MVPA (min/d)										
Low PA	6.4 (3.1-10.1)	0 (0-0.3)	10.6 (5.3- 14.8)	1.1 (0.4-2.3)	1.8 (0.1-2.7)	0.9 (0-3.5)	2.3 (1.1-3.7)	12.4 (6.1-20.6)	7.7 (4-12)	2.3
Medium PA	20.8 (16.4-24.6)	2.2 (0-4.7)	27.0 (22.4-32.6)	9.3 (6.7-13.0)	9.0 (0.6-11.7)	9.7 (4.4-14.1)	11.2 (8.3-15.3)	31.0 (23.4-39.1)	24.8 (20.0-29.7)	11.2
High PA	48.1 (37.3-64.1)	16.4 (0-33)	52.2 (43.2-65.6)	30.6 (22.9-43.0)	28.8 (19.8-39.6)	28.1 (8.8-38.7)	34.3 (26.1-48.4)	56.3 (43.4-71.9)	51.6 (42.1-67.0)	34.3
MVPA (% time)										

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Low PA	0.8 (0.4-1.2)	0.0 (0-0.003)	1.2 (0.6-1.6)	0.1 (0.0-0.27)	0.2 (0.1-0.3)	0.1 (0-0.4)	0.3 (0.1-0.4)	1.5 (0.7-2.3)	0.9 (0.5-1.4)	0.3
Medium PA	2.4 (2.0-2.90)	0.3 (0-0.6)	3.0 (2.5-3.6)	1.1 (0.8-1.5)	1.0 (0.7-1.3)	1.1 (0.5-1.6)	1.3 (1.0 - 1.8)	3.5 (2.7-4.4)	2.9 (2.4-3.5)	1.3
High PA	5.8 (4.5-7.4)	1.9 (0-3.9)	5.8 (4.8-7.3)	3.6 (2.7-5.1)	3.2 (2.2, 4.4)	3.2 (1.0-4.4)	4.0 (3.0 - 5.7)	6.2 (4.9-7.9)	5.9 (4.9-7.7)	4.0

*Data based on Actical accelerometer; **median of medians based on Actigraph accelerometer (excluding REGARDS and FHS)

Supplementary Table 3. E-values (upper or lower 95% CI within brackets) for different combinations of time spent in MVPA and sedentary time with all-cause mortality. Data are from the multivariate adjusted model (Figure 2d) (N=42303, 2508 deaths)			
	Low sedentary	**Medium Sedentary**	**High Sedentary**
High MVPA	REF	1.62 (1.51)	2.10 (1.68)
Medium MVPA	1.27 (1.80)	1.91 (1.01)	2.67 (1.61)
Low MVPA	2.62 (1.75)	2.60 (1.72)	4.63 (3.20)

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Supplementary Table 4. Quality assessment of studies included in the meta-analysis.								
Study	**Selection**				**Comparability**	**Outcome**		
	Representativeness	**Selection**	**Ascertainment Exposure**	**Outcome**		**Assessment**	**Follow Up**	**Adequacy**
WAT2D (10)	D	A*	A*	A*	A* B	B*	A*	A*
REGARDS (11)	C	A*	A*	A*	A* A*	B*	A*	A*
ABC (12)	B*	A*	A*	A*	A* B	B*	A*	A*
BRHS (13)	C	A*	A*	A*	A* A*	B*	A*	A*
WHS (14)	C	A*	A*	A*	A* A*	B*	A*	A*
NHANES (16)	A*	A*	A*	A*	A* A*	B*	A*	A*
Framingham (17)	B*	A*	A*	A*	A* A*	B*	A*	A*
NPASS (18)	A*	A*	A*	A*	A* A*	B*	A*	A*
EPIC-Norfolk (9)	B	A*	A*	A*	A* B*	B*	A*	A*

For full details of the coding system (A to D) see
http://www.ohri.ca/programs/clinical_epidemiology/nos_manual.pdf

References to original studies within brackets (see reference list in main document)

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Supplementary Figures

Exposure	Participants	Deaths	I^2	HR (95% CI)
High CPM				
Low %SED	10889	348		1.00
Med %SED	3509	128	0%	1.13 (0.91, 1.41)
High %SED	429	19	27%	1.59 (0.88, 2.85)
Medium CPM				
Low %SED	3810	186	24%	1.39 (1.12, 1.75)
Med %SED	8413	457	41%	1.35 (1.09, 1.68)
High %SED	2589	145	43%	1.45 (1.08, 1.95)
Low CPM				
Low %SED	122	10	5%	2.46 (1.31, 4.62)
Med %SED	2890	252	13%	1.66 (1.37, 2.01)
High %SED	11719	1906	70%	2.98 (2.29, 3.88)

All-cause mortality HR

Supplementary figure 1. The joint association between between total physical activity and sedentary time and all-cause mortality. Analyses are adjusted for age and sex (n=44,370; 3451 deaths).

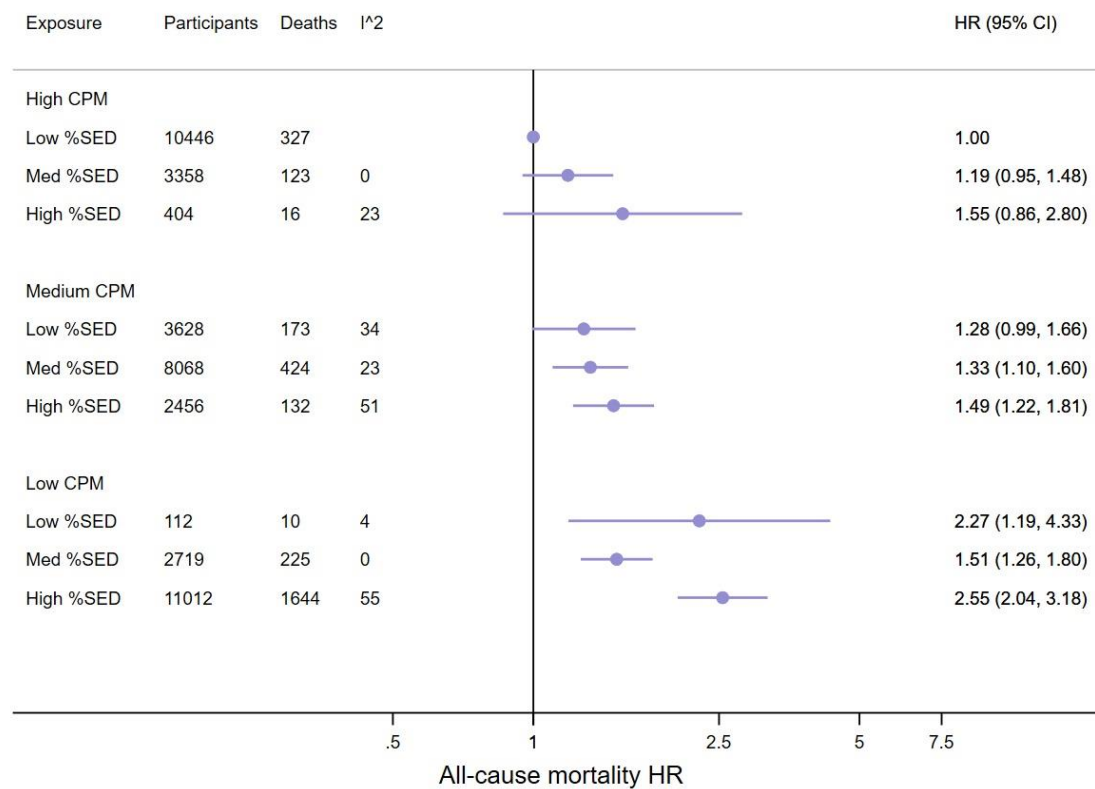| Exposure	Participants	Deaths	I^2		HR (95% CI)
High CPM					
Low %SED	10484	329			1.00
Med %SED	3368	125	0		1.22 (0.98, 1.52)
High %SED	404	16	28		1.66 (0.94, 2.90)
Medium CPM					
Low %SED	3645	175	41		1.42 (1.09, 1.86)
Med %SED	8100	430	26		1.42 (1.17, 1.71)
High %SED	2466	132	39		1.53 (1.14, 2.04)
Low CPM					
Low %SED	113	10	25		2.55 (1.19, 5.45)
Med %SED	2738	231	30		1.74 (1.38, 2.19)
High %SED	11102	1689	67		3.12 (2.40, 4.06)

All-cause mortality HR
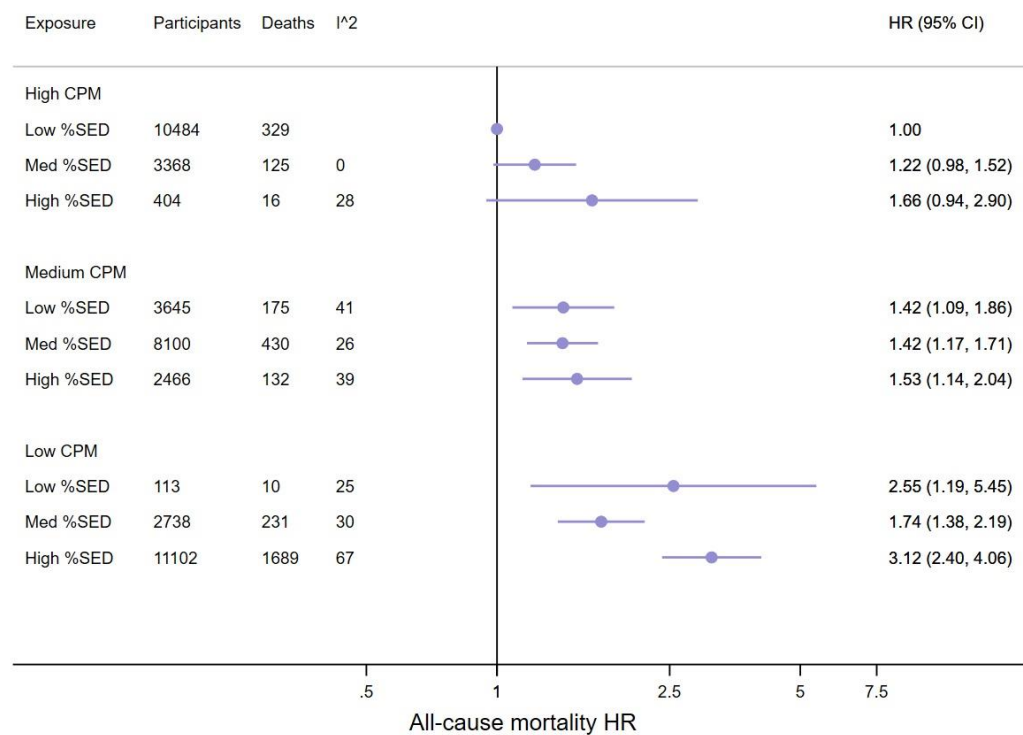
Supplementary figure 2. The joint association between between total physical activity and sedentary time and all-cause mortality. Analyses are adjusted for age, sex, BMI and socio-economic position (n=42,420; 3137 deaths).

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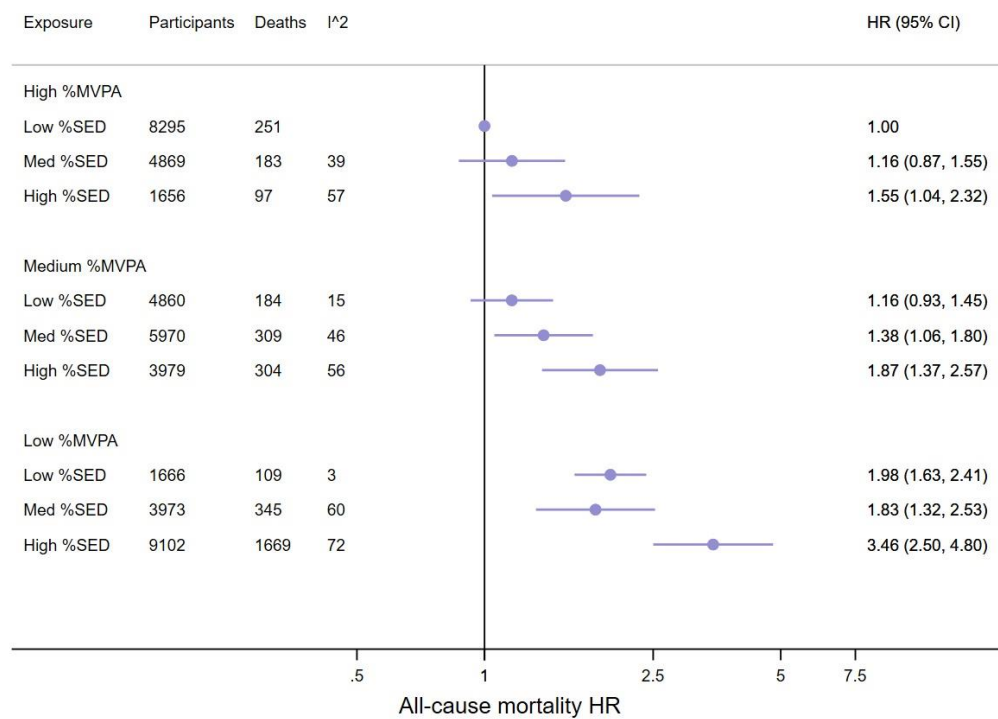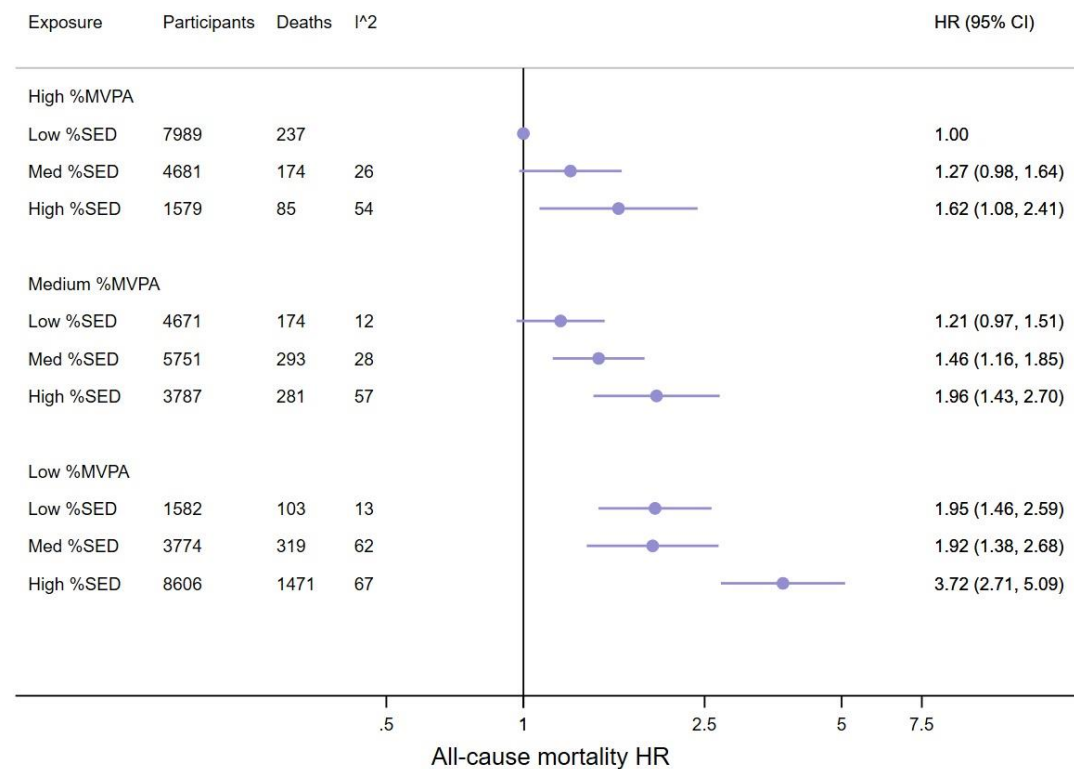| Exposure	Participants	Deaths	I^2		HR (95% CI)
High CPM					
Low %SED	10446	327			1.00
Med %SED	3358	123	0		1.19 (0.95, 1.48)
High %SED	404	16	23		1.55 (0.86, 2.80)
Medium CPM					
Low %SED	3628	173	34		1.28 (0.99, 1.66)
Med %SED	8068	424	23		1.33 (1.10, 1.60)
High %SED	2456	132	51		1.49 (1.22, 1.81)
Low CPM					
Low %SED	112	10	4		2.27 (1.19, 4.33)
Med %SED	2719	225	0		1.51 (1.26, 1.80)
High %SED	11012	1644	55		2.55 (2.04, 3.18)

All-cause mortality HR

Supplementary figure 3. The joint association between between total physical activity and sedentary time and all-cause mortality. Analyses are adjusted for age, sex, BMI, socio-economic position, smoking, presence of prevalent diseases or self-reported poor health, other putative confounding factors displayed in **Supplementary Table 1** (n=42,203; 3074 deaths).

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Exposure	Participants	Deaths	I^2		HR (95% CI)
High %MVPA					
Low %SED	8295	251			1.00
Med %SED	4869	183	39		1.16 (0.87, 1.55)
High %SED	1656	97	57		1.55 (1.04, 2.32)
Medium %MVPA					
Low %SED	4860	184	15		1.16 (0.93, 1.45)
Med %SED	5970	309	46		1.38 (1.06, 1.80)
High %SED	3979	304	56		1.87 (1.37, 2.57)
Low %MVPA					
Low %SED	1666	109	3		1.98 (1.63, 2.41)
Med %SED	3973	345	60		1.83 (1.32, 2.53)
High %SED	9102	1669	72		3.46 (2.50, 4.80)

All-cause mortality HR

Supplementary figure 4. The joint association between between moderate-to-vigorous-intensity physical activity and sedentary time and all-cause mortality. Analyses are adjusted for age and sex (n=44,370; 3451 deaths).

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Exposure	Participants	Deaths	I^2		HR (95% CI)
High %MVPA					
Low %SED	7989	237			1.00
Med %SED	4681	174	26		1.27 (0.98, 1.64)
High %SED	1579	85	54		1.62 (1.08, 2.41)
Medium %MVPA					
Low %SED	4671	174	12		1.21 (0.97, 1.51)
Med %SED	5751	293	28		1.46 (1.16, 1.85)
High %SED	3787	281	57		1.96 (1.43, 2.70)
Low %MVPA					
Low %SED	1582	103	13		1.95 (1.46, 2.59)
Med %SED	3774	319	62		1.92 (1.38, 2.68)
High %SED	8606	1471	67		3.72 (2.71, 5.09)

All-cause mortality HR

Supplementary figure 5. The joint association between between moderate-to-vigorous-intensity physical activity and sedentary time and all-cause mortality. Analyses are adjusted for age, sex, BMI and socio-economic position (n=42,420; 3137 deaths).
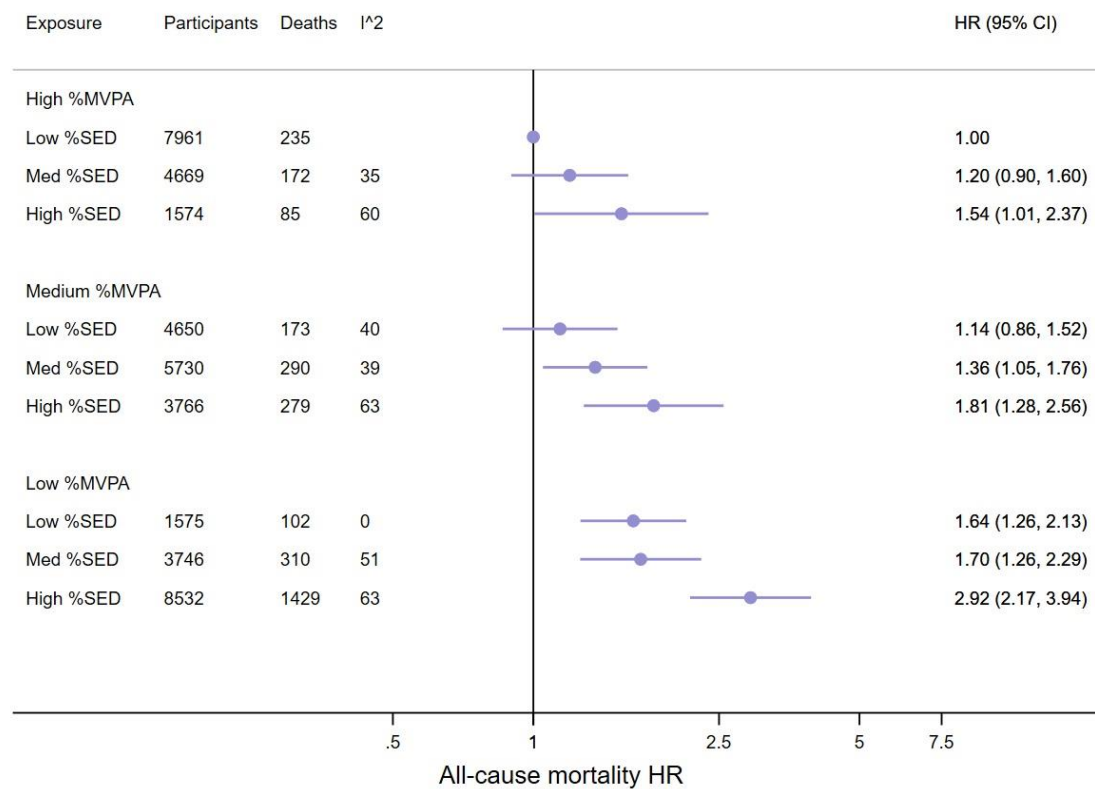
Supplementary figure 6. The joint association between between moderate-to-vigorous-intensity physical activity and sedentary time and all-cause mortality. Analyses are adjusted for age, sex, BMI, socio-economic position, smoking, presence of prevalent diseases or self-reported poor health, other putative confounding factors displayed in **Supplementary Table 1** (n=42,203; 3074 deaths).

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