

SUPPLEMENTARY TABLES AND FIGURES

Dose-response associations between accelerometry measured physical activity and sedentary time with all-cause mortality: a systematic review and harmonised meta-analysis

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Supplementary Table 1. Descriptive characteristics of participants. Data are mean (SD) unless otherwise stated.							
	WAT2D		REGARDS		ABC		BRHS
	Men (N=411)	Women (N=243)	Men (N=3580)	Women (N=4282)	Men (N=371)	Women (N=463)	Men (N=1412)
Age (y)	64.4 (7.0)	62.3 (8.8)	69.9 (8.4)	68.2 (8.7)	53.1 (10.5)	52.6 (10.1)	78.4 (4.6)
Height (m)	1.74 (0.07)	1.60 (0.06)	1.78 (0.07)	1.63 (0.07)	1.79 (0.06)	1.66 (0.06)	1.71 (0.07)
Weight (kg)	93.6 (16.2)	87.0 (17.0)	89.6 (16.5)	77.1 (17.8)	83.3 (10.6)	69.8 (11.7)	79.7 (12.6)
BMI	30.8 (4.7)	34.0 (5.8)	28.3 (4.7)	28.9 (6.3)	25.9 (3.0)	25.4 (3.9)	27.1 (3.8)
Normal-weight (%)	7.3	3.7	23.7	29.0	41.4	55.2	29.0
Over-weight (%)	40.4	21.4	47.1	33.9	49.7	32.3	51.2
Obese (%)	52.3	74.9	29.2	37.1	8.8	12.5	19.8
Wear time (min/d)	852 (216)	843 (209)	850 (282)	846 (268)	909 (211)	881 (213)	844 (246)
Mean Counts (counts/min)	318 (147)	258 (116)	103 (78)	84 (64)	358 (89)	341 (211)	186 (80)
Sedentary (min/d)	537 (91)	523 (93)	690 (84)	694 (83)	524 (104)	507 (94)	610 (83)
LPA (min/d)	281.7 (75.9)	294.9 (71.8)	149 (70)	140 (67)	334 (99)	342 (87)	217 (77)
Low LPA (min/d)	202 (47)	215 (50)	123 (53)	122 (55)	245 (63)	254 (62)	175 (55)
High LPA (min/d)	79 (36)	70 (36)	26 (18)	18 (16)	88 (52)	87 (40)	41 (30)
MVPA (min/d)	32.0 (26.6)	19.1 (17.3)	9.8 (14.9)	6.6 (11.6)	35.5 (30.0)	30.5 (30.6)	15.6 (17.6)
MVPA bouts (min/d)	12.8 (18.5)	5.6 (9.8)	5.2 (11.7)	3.9 (9.4)	13.1 (22.2)	12.7 (26.3)	9.0 (15.2)
VPA (min/d)	0.7 (2.6)	0.4 (2.3)	1.2 (5.1)	0.9 (4.3)	2.6 (11.7)	1.8 (13.2)	0.5 (2.8)

Supplementary Table 1 continued. Descriptive characteristics of participants. Data are mean (SD) unless otherwise stated.							
	WHS	FHS		NHANES		NNPAS	
	Women (N=16738)	Men (N=1225)	Women (N=1396)	Men (N=1977)	Women (N=2001)	Men (N=1243)	Women (N=1371)
Age (y)	72.0 (5.7)	64.7 (9.6)	64.6 (9.1)	57.1 (12.5)	58.3 (12.2)	57.2 (10.8)	55.8 (11.0)
Height (m)	1.64 (0.1)	1.75 (0.07)	1.61 (0.06)	1.76 (0.08)	1.62 (0.07)	179.3 (6.5)	166.5 (6.0)
Weight (kg)	70.7 (14.2)	88.7 (15.7)	71.2 (15.8)	88.8 (18.8)	75.4 (18.6)	84.8 (12.4)	69.6 (12.0)
BMI	26.2 (5.0)	29.0 (4.6)	27.6 (5.8)	28.6 (5.5)	28.7 (6.7)	26.3 (3.4)	25.1 (4.2)
Normal-weight (%)	46.3	16.9	35.7	22.3	25.5	28.5	56.4
Over-weight (%)	34.2	47.7	35.9	44.7	31.1	48.9	32.2
Obese (%)	19.5	35.4	28.4	33.0	34.4	12.6	11.4
Wear time (min/d)	900 (260)	884 (288)	875 (290)	864 (232)	850 (231)	910 (247)	905 (239)
Mean Counts (counts/min)	198 (95)	148 (144)	129 (106)	309 (162)	259 (123)	329.5 (150.0)	324.5 (135.5)
Time Sedentary (min/d)	592 (95)	675 (89)	679 (82)	512 (127)	502 (110)	576.8 (87.9)	547.4 (85.0)
LPA (min/d)	285 (79)	180 (72)	171 (64)	319 (102)	326 (91)	275 (80)	303 (77)
Low LPA (min/d)	221 (56)	140 (52)	142 (50)	235 (66)	257 (65)	200 (50)	230 (57)
High LPA (min/d)	63 (36)	39 (26)	28 (19)	84 (48)	69 (40)	77 (40)	74 (37)
MVPA (min/d)	14.8 (16.8)	16.9 (23.3)	13.9 (19.7)	25.6 (24.7)	15.5 (16.6)	36.9 (26.4)	33.5 (23.5)
MVPA bouts (min/d)	7.8 (13.7)	8.7 (19.7)	8.5 (16.9)	6.2 (13.6)	4.8 (10.1)	17.9 (21.6)	18.7 (19.1)
VPA (min/d)	0.3 (2.1)	2.6 (10.9)	2.7 (.8)	1.0 (3.7)	0.5 (2.2)	2.8 (7.7)	2.1 (5.8)

LPA, Light intensity Physical Activity; MVPA, Moderate-and-Vigorous intensity Physical Activity; MVPA bouts, time (min/d) in bouts of 10 minutes; VPA, Vigorous intensity Physical Activity

Supplementary Table 2. Quality assessment of studies included in the meta-analysis.								
Study	Selection				Comparability	Outcome		
	Representativeness	Selection	Ascertainment Exposure	Outcome		Assessment	Follow Up	Adequacy
WAT2D (Bakrania et al, 2017)	D	A*	A*	A*	A* B	B*	A*	A*
REGARDS (Diaz et al, 2017)	C	A*	A*	A*	A* A*	B*	A*	A*
ABC (Dohrn et al, 2017)	B*	A*	A*	A*	A* B	B*	A*	A*
BRHS (Jefferis et al, 2018)	C	A*	A*	A*	A* A*	B*	A*	A*
WHS (Lee et al, 2018)	C	A*	A*	A*	A* A*	B*	A*	A*
NHANES (Matthews et al, 2016)	A*	A*	A*	A*	A* A*	B*	A*	A*
Framingham (Murabito et al, 2015)	B*	A*	A*	A*	A* A*	B*	A*	A*
NPASS (Hansen et al, 2012))	A*	A*	A*	A*	A* A*	B*	A*	A*

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

Supplementary table 3. Median of exposure variables stratified by quartiles according to Model B.									
	WAT2D	REGARDS	ABC	BRHS	WHS	FHS	NHANES	NNPAS	Median of medians* (range)
Total Physical Activity (CPM)									
Quartile 1	155	30	196	72	99	53	124	180	139.5 (53-196)
Quartile 2	237	58	291	134	156	96	210	274	223.5 (134-291)
Quartile 3	318	94	371	199	212	139	291	351	304.5 (199-371)
Quartile 4	464	165	522	315	304	222	435	479	449.5 (304-522)
Sedentary (min/d)									
Quartile 1	433	597	405	519	484	579	371	463	448 (371-519)
Quartile 2	506	668	483	588	563	651	469	534	520 (469-588)
Quartile 3	565	719	542	639	621	709	545	591	578 (542-639)
Quartile 4	637	786	624	705	696	772	637	663	650 (624-705)
LPA (min/d)									
Quartile 1	197	66	231	132	196	101	210	202	199.5 (132-231)
Quartile 2	252	118	301	191	257	149	290	261	258.5 (191-301)
Quartile 3	298	160	363	237	307	190	352	310	308.5 (237-363)
Quartile 4	363	224	444	305	376	250	437	383	379.5 (305-444)
Low LPA (min/d)									
Quartile 1	153	60	182	113	159	85	173	157	158 (113-182)
Quartile 2	187	103	228	156	202	122	226	197	199.5 (156-228)
Quartile 3	219	137	269	191	236	154	268	228	232 (191-269)
Quartile 4	262	184	323	236	285	199	326	279	282 (236-326)
High LPA (min/d)									
Quartile 1	30	3	43	11	26	10	24	36	28 (11-43)
Quartile 2	57	12	69	27	48	23	53	59	55 (27-69)
Quartile 3	80	23	94	44	69	36	80	81	80 (44-94)
Quartile 4	121	44	132	75	104	59	127	117	119 (75-132)
MVPA (min/d)									
Quartile 1	4	0	10	1	0	1	2	9	1.5 (0-10)
Quartile 2	14	1	22	5	5	5	7	24	6 (1-24)
Quartile 3	26	5	36	15	14	14	17	38	16 (5-38)
Quartile 4	56	20	61	36	33	33	40	63	38 (20-63)

LPA, Light intensity Physical Activity; MVPA, Moderate-and-Vigorous intensity Physical Activity; VPA, Vigorous intensity Physical Activity

*Median of the medians calculated from six studies using the Actigraph accelerometer except for MVPA

Supplementary table 4. Meta-analysis for the associations between bouted moderate and vigorous intensity physical activity (MVPA) and vigorous intensity physical activity (VPA) with all-cause mortality (**Model B** adjusted for sex, age, BMI and socio-economic position; [N=36383, 2149 deaths]; **Model C** additionally adjusted for covariates listed in Table 1, [N=35932, 2047 deaths]). Data are Hazard Ratios and 95% Confidence Intervals by Cox regression.

	Model B				Model C			
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Quartile 1	Quartile 2	Quartile 3	Quartile 4
MVPA bouted (min/d)	1 (Ref) (N=18963; 1585)	0.72 (0.62; 0.83) (N=5712; 222)	0.68 (0.56; 0.83) (N=5863; 182)	0.60 (0.48; 0.77) (N=5845; 160)	1 (Ref) (N=18692; 1499)	0.78 (0.67; 0.91) (N=5684; 212)	0.77 (0.65; 0.90) (N=5809; 179)	0.66 (0.54; 0.82) (N=5783; 157)
VPA (min/d)	1 (Ref) (N=28826; 1921)	1.01 (0.80; 1.27) (N=2487; 109)	0.66 (0.49; 0.89) (N=2556; 67)	0.62 (0.45; 0.84) (N=2514; 52)	1 (Ref) (N=28439; 1824)	1.09 (0.88; 1.35) (N=2461; 106)	0.73 (0.55; 0.96) (N=2534; 66)	0.70 (0.51; 0.97) (N=2498; 51)

MVPA bouted, time (min/d) in bouts of 10 minutes

Supplementary Table 5. Dose-response associations (Hazard Ratios and 95% Confidence Intervals) for total physical activity, time spent in light intensity physical activity, low light intensity physical activity, high light intensity physical activity, moderate and vigorous intensity physical activity and sedentary time with all-cause mortality. Data are adjusted for age, sex, body mass index, socio-economic status and wear time. The exposure reference is set as the median of the medians in the reference group (Supplementary Table 3).

Total PA (CPM)	HR (95% CI)	LPA (min/d)	HR (95% CI)	Low LPA (min/d)	HR (95% CI)	High LPA (min/d)	HR (95% CI)	MVPA (min/d)	HR (95% CI)	Sedentary (h/d)	HR (95% CI)
75	1.88 (1.68, 2.12)	150	1.48 (1.34, 1.63)	100	1.76 (1.41, 2.20)	10	1.62 (1.45, 1.80)	0	Reference	6	0.89 (0.74, 1.07)
100	1.48 (1.37, 1.59)	175	1.22 (1.16, 1.28)	125	1.38 (1.22, 1.56)	20	1.24 (1.18, 1.30)	2	0.89 (0.85, 0.92)	6.5	0.93 (0.82, 1.05)
125	1.16 (1.13, 1.19)	200	Reference	150	1.08 (1.05, 1.11)	28	Reference	4	0.79 (0.73, 0.85)	7	0.96 (0.91, 1.02)
140	Reference	225	0.82 (0.78, 0.86)	158	Reference	30	0.95 (0.94, 0.96)	6	0.70 (0.62, 0.79)	7.5	Reference
175	0.71 (0.67, 0.76)	250	0.68 (0.62, 0.75)	175	0.85 (0.79, 0.90)	40	0.73 (0.68, 0.78)	8	0.62 (0.53, 0.73)	8	1.04 (0.98, 1.10)
200	0.56 (0.50, 0.62)	275	0.58 (0.51, 0.66)	200	0.67 (0.57, 0.78)	50	0.56 (0.49, 0.64)	10	0.56 (0.45, 0.68)	8.5	1.08 (0.96, 1.22)
225	0.46 (0.39, 0.53)	300	0.52 (0.45, 0.59)	225	0.56 (0.46, 0.68)	60	0.46 (0.38, 0.55)	12	0.50 (0.40, 0.64)	9	1.15 (0.98, 1.36)
250	0.39 (0.33, 0.53)	325	0.49 (0.43, 0.57)	250	0.51 (0.43, 0.62)	70	0.41 (0.33, 0.51)	14	0.46 (0.35, 0.61)	9.5	1.28 (1.06, 1.54)
275	0.36 (0.29, 0.43)	350	0.49 (0.40, 0.59)	275	0.49 (0.41, 0.59)	80	0.40 (0.31, 0.52)	16	0.43 (0.32, 0.59)	10	1.48 (1.22, 1.79)
300	0.34 (0.27, 0.43)	375	0.48 (0.38, 0.63)	300	0.47 (0.38, 0.59)	90	0.41 (0.30, 0.56)	18	0.41 (0.30, 0.58)	10.5	1.75 (1.44, 2.13)
325	0.35 (0.26, 0.45)	400	0.48 (0.34, 0.68)	325	0.45 (0.34, 0.60)	100	0.42 (0.29, 0.61)	20	0.40 (0.28, 0.58)	11	2.07 (1.68, 2.56)
350	0.35 (0.26, 0.48)	425	0.48 (0.31, 0.74)			110	0.43 (0.27, 0.68)	22	0.40 (0.27, 0.58)	11.5	2.46 (1.94, 3.12)
375	0.35 (0.24, 0.51)	450	0.48 (0.29, 0.80)			120	0.45 (0.24, 0.83)	24	0.39 (0.26, 0.59)	12	2.92 (2.24, 3.82)

Supplementary Table 6. Sensitivity analyses excluding deaths (N=544) within the first two years of follow-up for the associations between overall physical activity, sedentary time and different intensities of physical activity stratified by quartiles with all-cause mortality (N=35729, 1605 deaths). Data (Hazard Ratios, 95% Confidence Intervals) from Cox regression models are adjusted for sex, age, BMI, socio-economic position and wear time and sedentary time and moderate-and-vigorous intensity physical activity are mutually adjusted. Data are derived from 7 studies due to only one death in the ABC study.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Total PA (CPM)	1 (Ref) (N=8792; 883)	0.47 (0.40; 0.54) (N=8949; 342)	0.33 (0.26; 0.41) (N=8948, 219)	0.29 (0.23; 0.35) (N=9010; 161)
LPA (min/d)	1 (Ref) (N=8758; 791)	0.60 (0.53; 0.68) (N=8954; 390)	0.45 (0.38; 0.52) (N=8985; 249)	0.38 (0.28; 0.51) (N=9032; 175)
MVPA (min/d)	1 (Ref) (N=8741; 842)	0.66 (0.54; 0.80) (N=9020; 354)	0.51 (0.43; 0.66) (N=8976; 266)	0.53 (0.43; 0.66) (N=8987; 183)
Sedentary (min/d)	1 (Ref) (N=8962; 248)	1.19 (0.92; 1.54) (N=8969; 320)	1.57 (1.13; 2.20) (N=8934; 425)	2.32 (1.59; 3.38) (N=8845; 612)

CPM, Counts Per Minute; LPA, Light intensity Physical Activity; MVPA, Moderate-and-Vigorous intensity Physical Activity;

Supplementary Table 7. Sensitivity analyses excluding two studies (FHS and REGARDS) in which physical activity was assessed by a different monitor (N=25900; 1482 deaths) and excluding two studies (FHS and NNPAS) in which data on mortality have not been previously published (N=31487; 1941) for the associations between total physical activity (CPM) stratified by quartiles with all-cause mortality. Data (Hazard Ratios, 95% Confidence Intervals) from Cox regression models are adjusted for sex, age, BMI, and socio-economic position.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Total PA (CPM) ¹	1 (Ref) (N=6476; 809)	0.48 (0.41; 0.55) (N=6484; 326)	0.38 (0.26; 0.55) (N=6474; 188)	0.31 (0.25; 0.38) (N=6466; 159)
Total PA (CPM) ²	1 (Ref) (N=7870; 1056)	0.49 (0.44; 0.55) (N=7879; 448)	0.36 (0.25; 0.50) (N=7869; 241)	0.28 (0.23; 0.34) (N=7860; 196)

CPM, Counts Per Minute

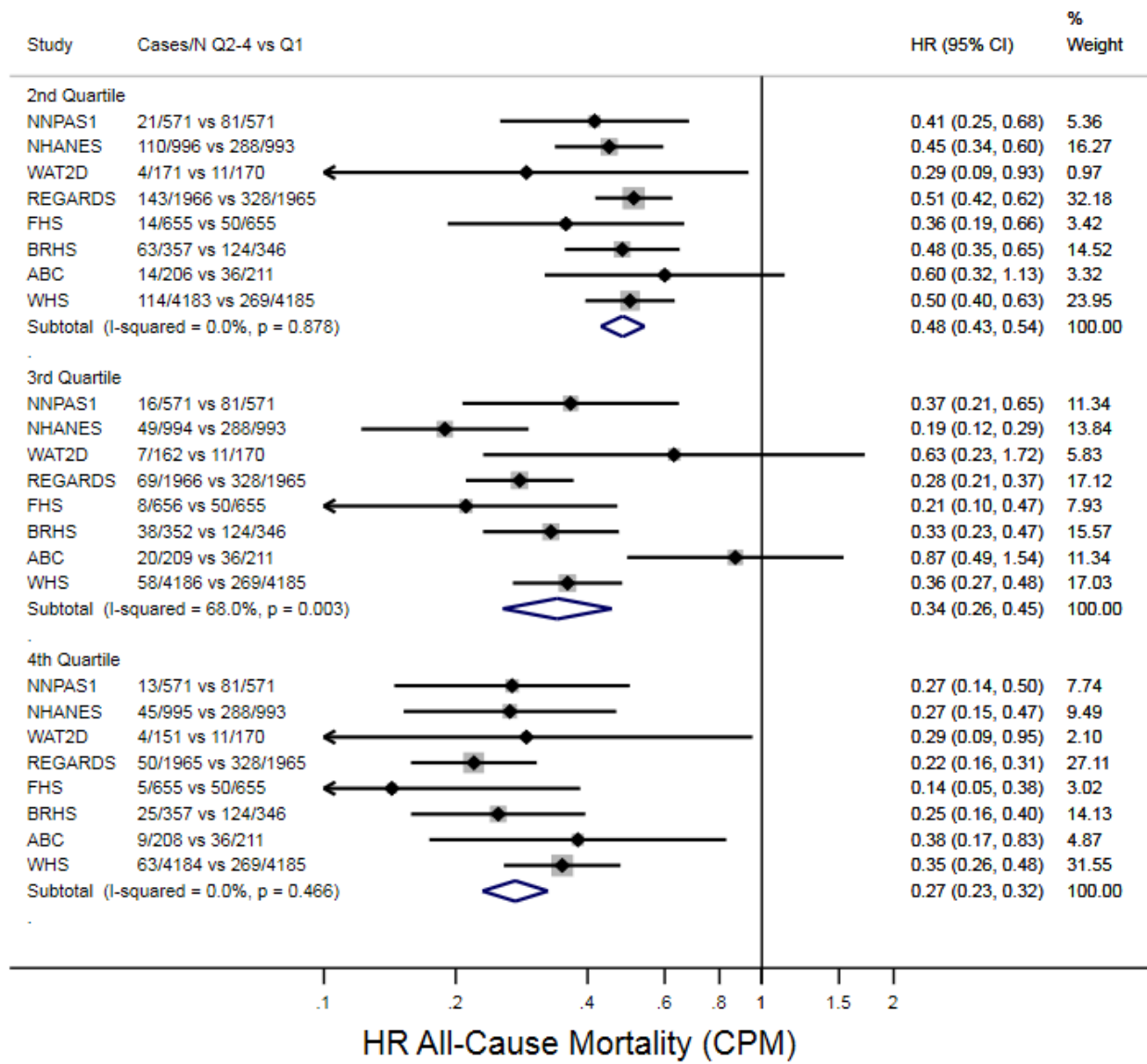
¹excluding FHS and REGARDS

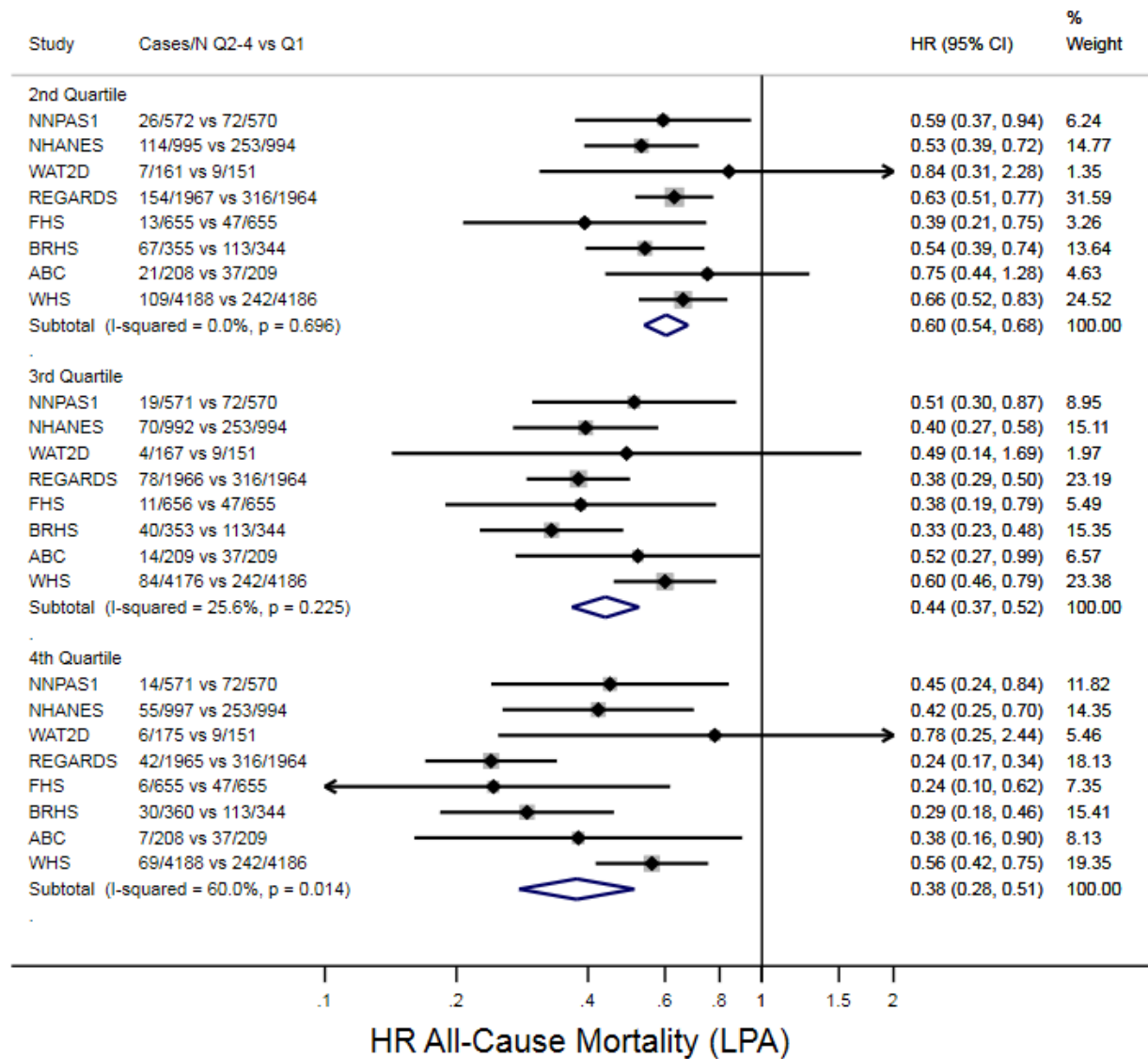
²excluding FHS and NNPAS

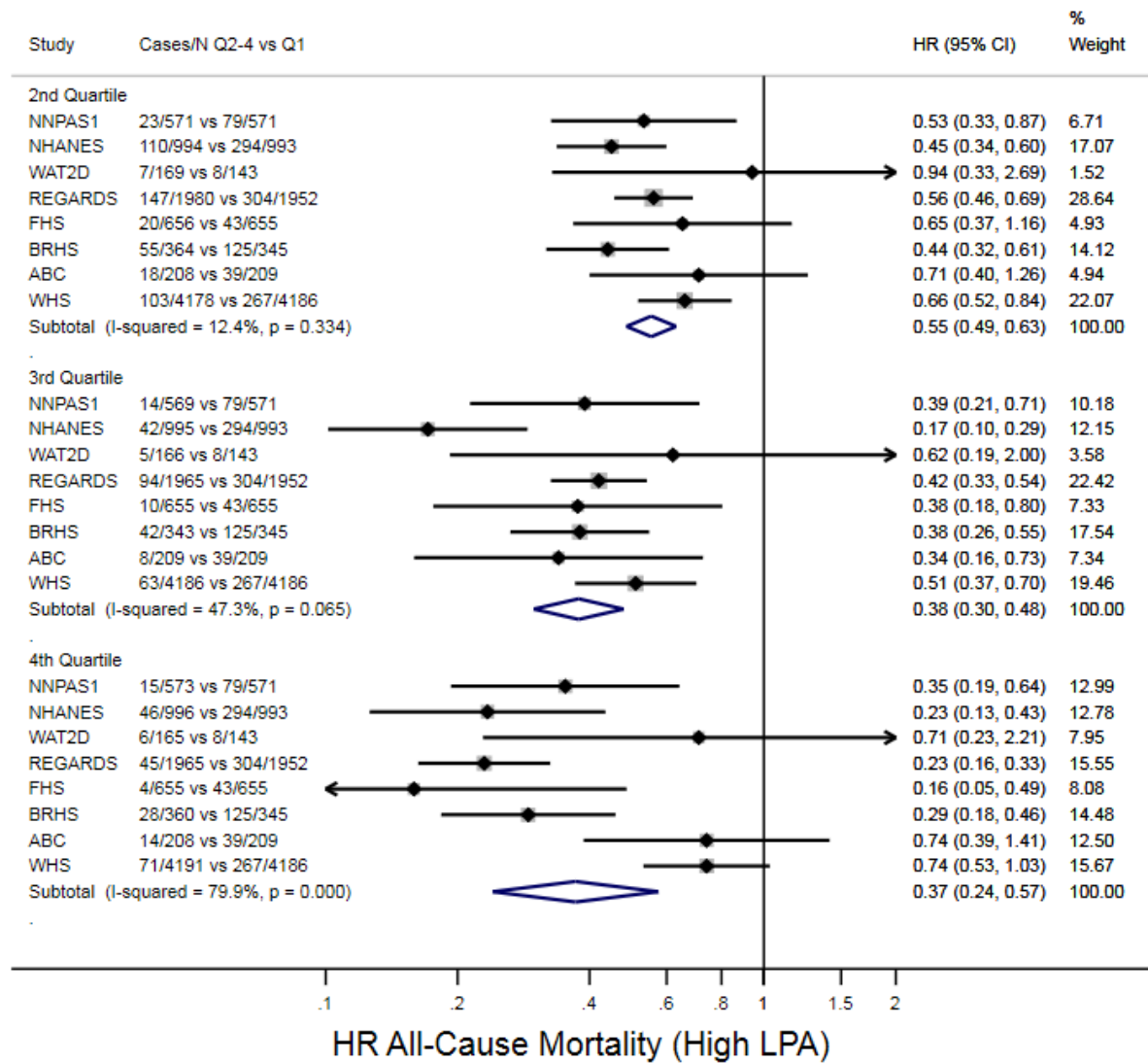
Supplementary Table 8. Knot locations for the 25th, 50th, and 75th percentiles for the dose-response associations between physical activity and sedentary time presented in **Figure 2 a-f**.

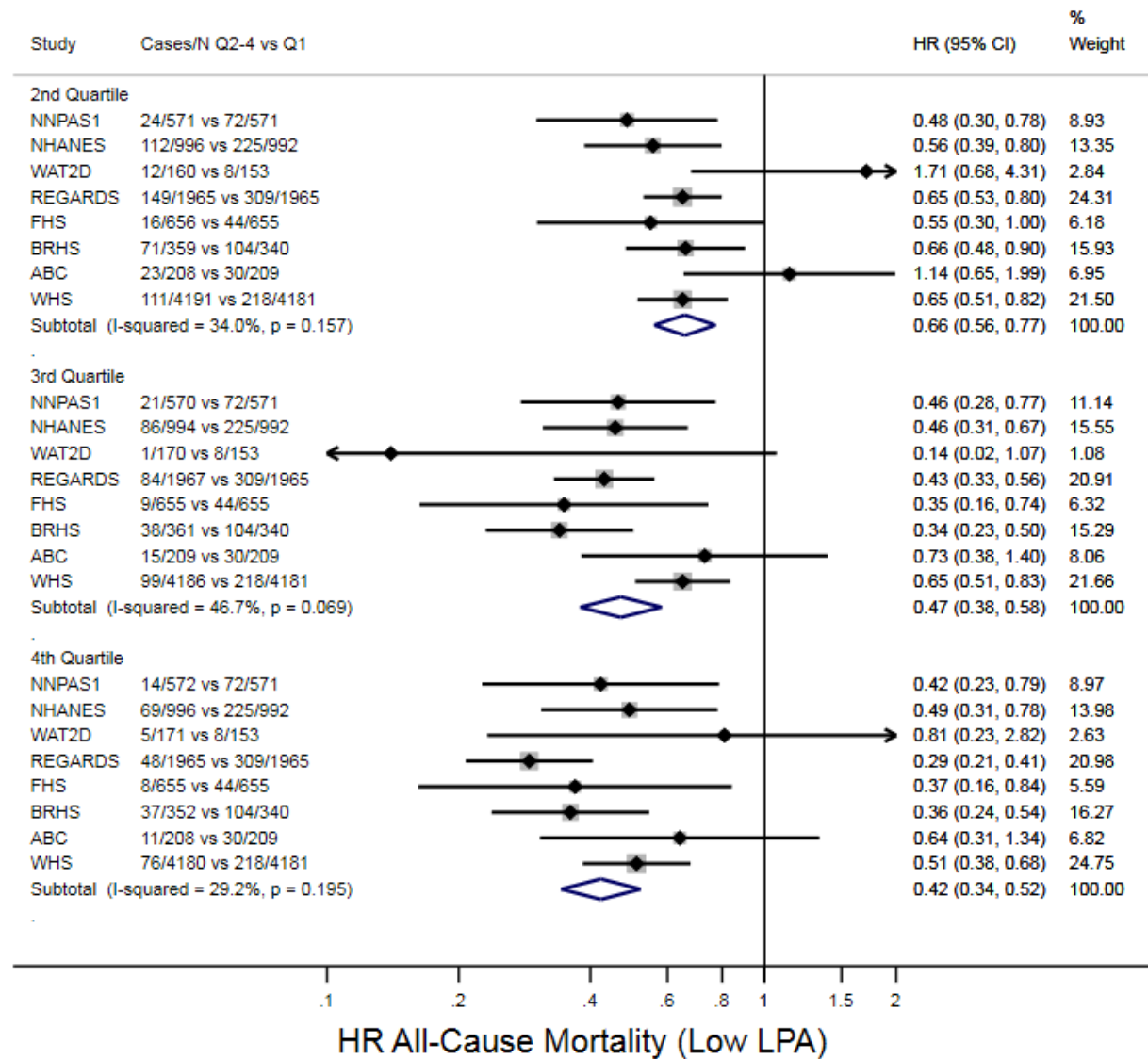
	25 th percentile	50 th percentile	75 th percentile	Goodness of fit (R ²)
Total PA (CPM)	168	256	335	89%
LPA (min/d)	221	294	358	92%
Low LPA (min/d)	178	223	265	84%
High LPA (min/d)	40	64	88	76%
MVPA (min/d)	5	14	33	63%
Sedentary (hrs/d)	8.1	9.2	10.5	86%

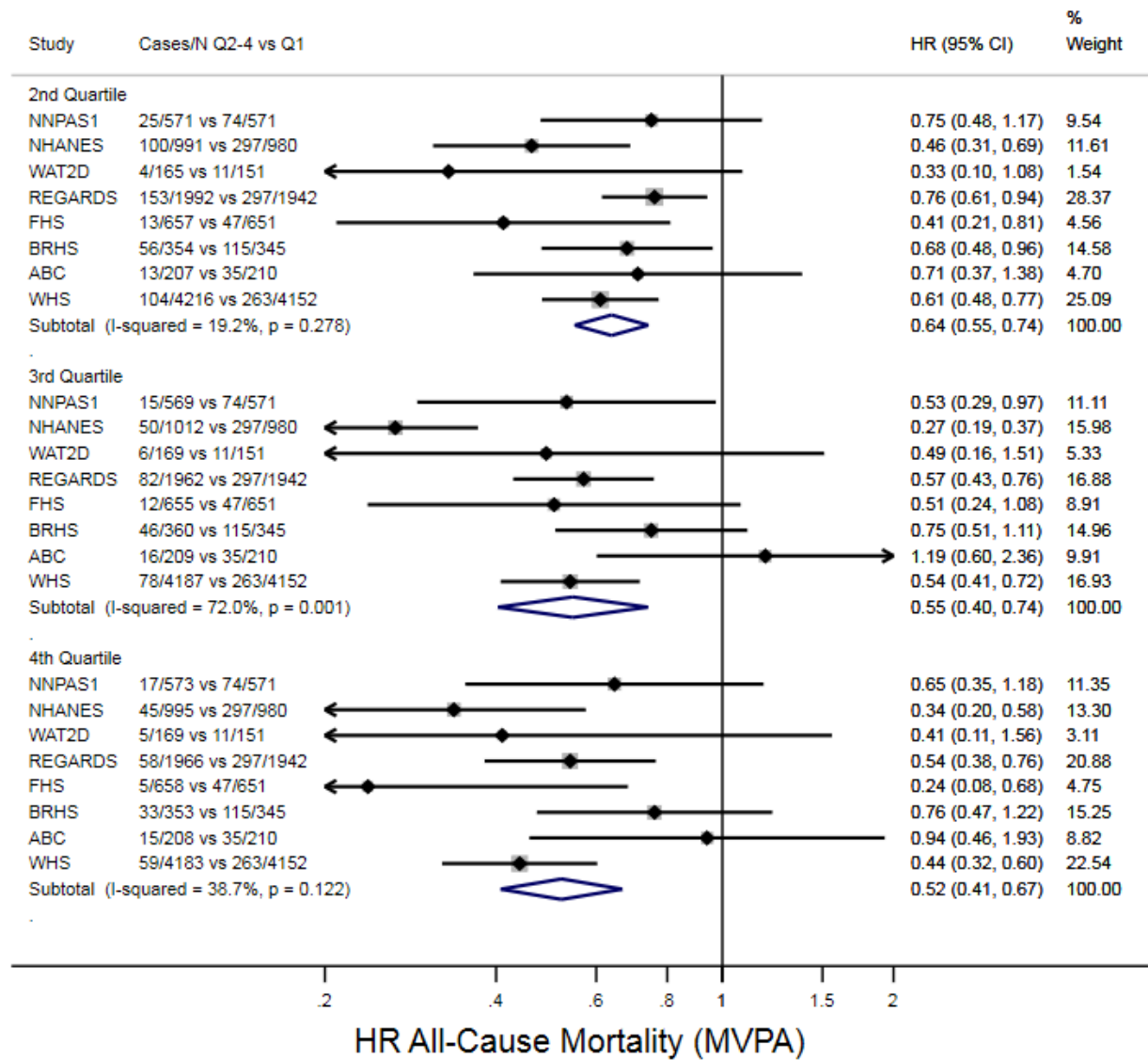
CPM, Counts Per Minute; LPA, Light intensity Physical Activity; MVPA, Moderate-and-Vigorous intensity Physical Activity; VPA, Vigorous intensity Physical Activity

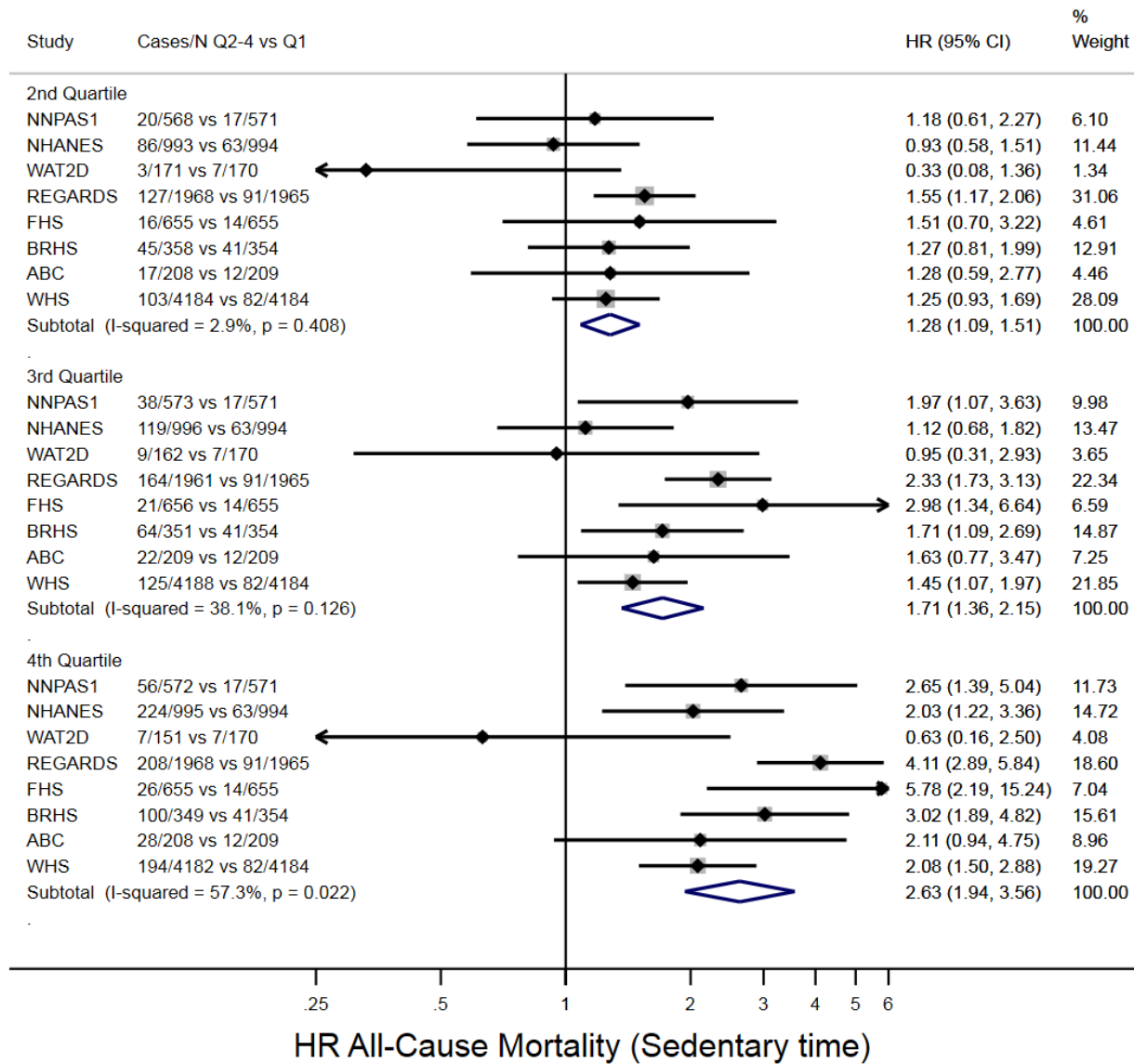




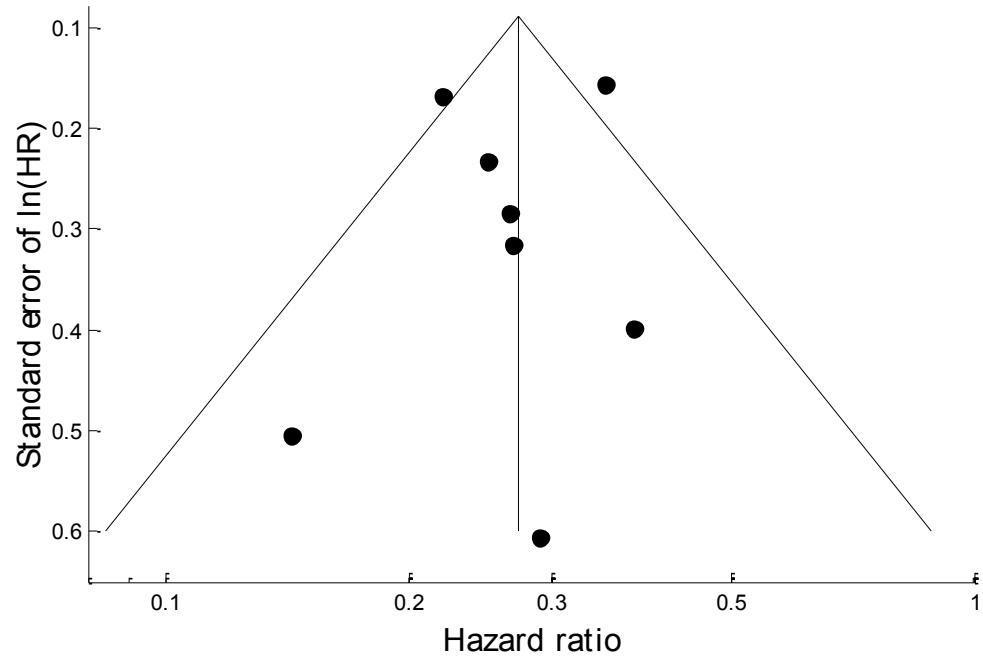




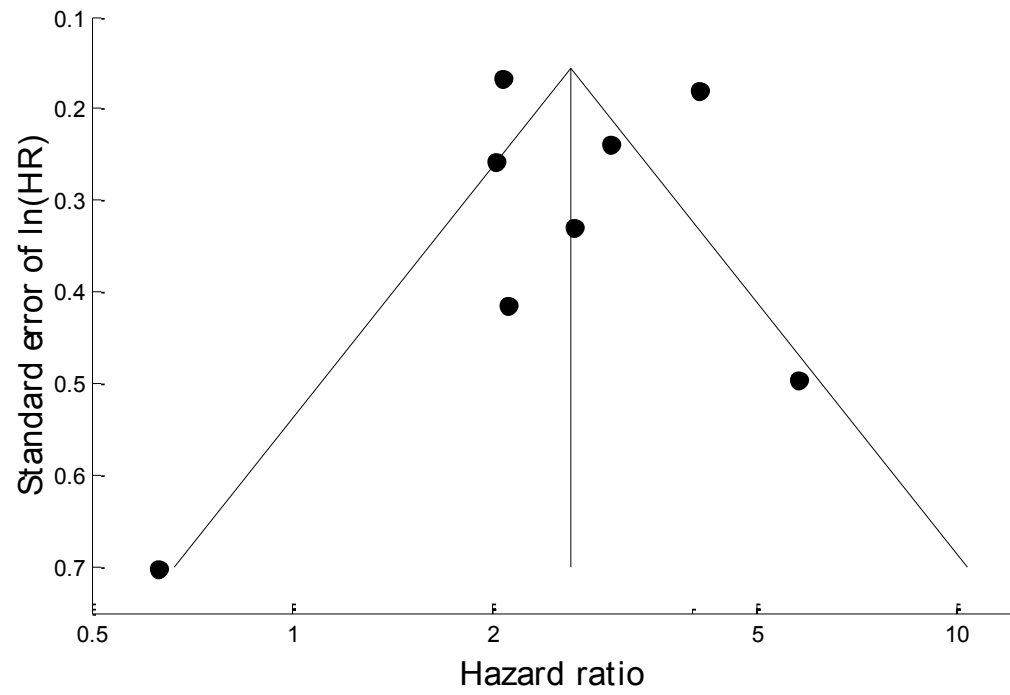




Supplementary Figure 1. Meta-analysis for the association between accelerometer measured total physical activity (CPM, **2a**), Light-intensity physical activity (LPA) (**2b**), low light-intensity physical activity (low LPA) (**2c**), high light-intensity physical activity (high LPA) (**2d**), moderate-to-vigorous intensity physical activity (MVPA) (**2e**) and sedentary time (**2f**) with all-cause mortality stratified by quartiles excluding the reference group (N=36383; 2149 deaths). Data are adjusted for age, sex, body mass index, socio-economic status and wear time. Moderate-to-vigorous intensity physical activity and sedentary time are mutually adjusted. %weight refers to each study's percentage weight to the overall effect size. (NNPAS1, Norwegian National Physical Activity Surveillance 1; NHANES, National Health and Nutrition Examination Survey; WAT2D, Walking Away from Type 2 Diabetes; REGARDS, The REasons for Geographic And Racial Differences in Stroke; FHS, Framingham Heart Study; BRHS, British Regional Heart Study; ABC, Attitude, Behaviour and Change; WHS, Women's Health Study).



Supplementary Figure 2. Funnel plot for total physical activity (CPM) comparing quartile 1 and quartile 4. (Eggers test for funnel plot asymmetry; $P=0.63$)



Supplementary Figure 3. Funnel plot for sedentary time comparing quartile 1 and quartile 4. (Eggers test for funnel plot asymmetry; P=0.59)

