SUPPLEMENTAL MATERIAL

Table S1: Description of indicators of SB bout accumulation patterns

SB accumulation measures	Estimation method *	Description with pros (✓) and cons (✗)
Arithmetic mean SB bout duration	$$\frac{\sum \text{time in SB bouts}}{n \text{ SB bouts}}$$	● Summary statistic for normal distributions ● <u>Higher</u> values indicate a more prolonged pattern of SB bout accumulation ✓ Well known statistic, easy to calculate ✗ Higher than the midpoint of midpoint of the distribution of bout duration (log-normal or power-law) ✗ Not a robust statistic for presence of very long bouts
Geometric mean SB bout duration	$$e^{\frac{\sum ln(time \; in \; SB \; bouts)}{n \; SB \; bouts}}$$	● Summary statistic for lognormal distribution † ● Midpoint that is between the median and arithmetic mean ● <u>Higher</u> values indicate a more prolonged pattern of SB bout accumulation durations: could be power-law or lognormal). ✓ Somewhat simple to calculate as mean of log-transformed variable, exponentiated ✓ Robust statistic for presence of very long bouts
Median SB bout duration	For odd number of SB bouts $$X^{\frac{n}{2}}$$ For even number of SB bouts $$\frac{(X^{[\frac{n-1}{2}]} + X^{[\frac{n+1}{2}]})}{2}$$ X = SB bouts ordered by duration n = n SB bouts	● Summary statistic for the midpoint (50%) of the SB bout duration distribution ● Half of all **SB bouts** are longer and half are shorter than the median ● <u>Higher</u> values indicate a more prolonged pattern of SB bout accumulation ✓ Well known statistic, simple to calculate ✓ No distribution assumed ✗ Order statistic, ignores information from the durations of the long bouts that contribute most per bout to total SB time
Fragmentation index	$$\frac{n \; breaks}{\sum time \; in \; SB \; bouts}$$ *or alternatively* $$\frac{n \; SB \; bouts}{\sum time \; in \; SB \; bouts}$$	● Intended to indicate how often SB is interrupted relative to the amount of SB ● Almost or exactly the inverse of arithmetic mean SB bout duration ● <u>Lower</u> values indicate a more prolonged pattern of SB bout accumulation ✓ Simple to calculate ✓ One of the first and most commonly reported SB pattern measures x Can be confused with crude n breaks
% of SB hours in bouts ≥30 min	$$100 \; x \; \frac{\sum \text{time in SB bouts} \geq 30 \text{ min}}{\sum \text{time in SB bouts}}$$	● Intended to indicate the extent to which total SB is comprised of the prolonged type, defined commonly as for 30 min or longer at a time ● <u>Higher</u> values indicate a more prolonged pattern of SB bout accumulation ✓ Simple to calculate ✗ Specific to the threshold selected (here, ≥30 min)
Alpha, $\hat{\alpha}$	Estimated by maximum likelihood methods as: $$\hat{\alpha} = 1 + n \left[\sum_{i=1}^{n} ln \frac{t_i}{t_{min}} \right]^{-1}$$ n = number of SB bouts t = bout duration (min) and t_{min} = shortest bout recorded / recordable by the monitor	● Summary statistic for power-law distribution [b] ● <u>Lower</u> values indicate a more prolonged pattern of SB bout accumulation (higher a more broken up or fragmented pattern) ✓ Robust statistic for the presence of very long bouts ('outliers') – these are expected in power-law distribution / its summary statistics ✗ Unfamiliar statistic / calculation ✗ Only sometimes interpretable in relation to the midpoint

| Usual SB bout duration (also referred to as *w50* or *x50*) | Calculated (in this study) by non-linear regression estimating the following sigmoidal curve function:

$$y = \frac{t^n}{t^n + x50^n}$$

where t = SB bout duration (min), n = a free parameter, x50 = usual SB bout duration (min), and y = the proportion of SB time accumulated in bouts ≤ t | ● Summary statistic for the midpoint (50%) of the cumulative distribution of SB bout duration.
● Half of all SB **time** is accumulated in bouts of this duration or longer
● Effect of each SB bout on the statistic is proportional to how much it contributes to total SB time
● <u>Higher</u> values indicate a more prolonged pattern of SB bout accumulation
✕ Unfamiliar calculation with some computational effort required
✕ Not a robust statistic for the presence of very long bouts |

SB = sedentary behavior.

* In this study, SB accumulation statistics were calculated over all SB bouts on all adherent days rather than calculated per day and averaged. This maximizes the sample of bouts to calculate each statistic and avoids any issues for days with no or too few SB bouts to calculate valid statistics.
† The distribution of SB bout duration is highly skewed (with numerous very short bouts and fewer long bouts) and is arguably approximated by a lognormal or power-law distribution.

Table S2: Spearman's rank order correlation coefficients (r_s) between indicators of SB bout accumulation patterns in middle aged to older adults (n=7563, EPIC-Norfolk).

	Alpha †	Usual SB bout duration	Arithmetic mean	Geometric mean	Median	Fragmentation Index †	% of SB in bouts ≥30 min
Alpha †	**1.00**						
Usual SB bout duration, min	0.74	**1.00**					
Arithmetic mean SB bout duration, min	0.91*	0.95*	**1.00**				
Geometric mean SB bout duration, min	1.00*‡	0.74	0.91*	**1.00**			
Median SB bout duration, min	0.84*	0.47	0.67	0.84*	**1.00**		
Fragmentation index (n SB bouts/SB hours) †	0.91*	0.95*	1.00*§	0.91*	0.67	**1.00**	
% of SB hours in bouts ≥30 min	0.63	0.97*	0.87*	0.63	0.37	0.87*	**1.00**

SB = sedentary behavior.

* r >0.8
† Sign of correlations are reversed as required to reflect correlations across increasingly prolonged SB accumulation pattern by both metrics.
‡ alpha and geometric mean SB bout duration are perfect non-linear transforms of each other.
§ fragmentation index and arithmetic mean SB bout duration are perfect inverse of each other.

Table S3: Isometric log-ratio (ilr) parameterization of the 4-part composition of 24-hour time use (non-wear/in-bed, SB, LPA, MVPA).

Parameter	Calculation	Parameter interpretation
z1	$\sqrt{\dfrac{3}{4}} \ \ln \dfrac{Other}{\sqrt[3]{SB \ \times LPA \ \times MVPA}}$	- Extent of waking wear time ↓ - More in-bed & non-wear time, less waking wear time (SB + LPA + MVPA)
z2	$\sqrt{\dfrac{2}{3}} \ \ln \dfrac{SB}{\sqrt[2]{LPA \ \times MVPA}}$	- Sedentariness of waking wear time ↑ - More SB, less physical activity (MVPA + LPA)
z3	$\sqrt{\dfrac{1}{2}} \ \ln \dfrac{LPA}{MVPA}$	- Intensity of physical activity ↓ - More LPA, less MVPA

SB = sedentary behavior; LPA = light intensity physical activity; MVPA = moderate-to-vigorous physical activity

Table S4: Overview of statistical models with relevant adjustments and exclusions for each outcome

Model	Outcomes	Covariate adjustments *	Exclusions †,‡,§
1	ACM, CVD, Cancer	*Gender*	
2a	ACM, CVD, Cancer	*ACM: Gender;* device type; *education level; social class; smoking status; alcohol intake; baseline history of diabetes mellitus or taking diabetes mellitus medications; taking medication for hypertension, taking medication for dyslipidemia, taking medication for depression; family history of CVD (stroke/myocardial infarction), diabetes mellitus, or cancer; and baseline history of stroke/myocardial infarction or cancer.* *CVD: Gender;* device type; *education level; social class; smoking status; alcohol intake; baseline history of diabetes mellitus or taking diabetes mellitus medications; taking medication for hypertension, taking medication for dyslipidemia, taking medication for depression; family history of CVD (stroke/myocardial infarction) or diabetes mellitus.* *Cancer: Gender;* device type; *education level; social class; smoking status; alcohol intake; baseline history of diabetes mellitus or taking diabetes mellitus medications; taking medication for depression; family history of cancer.*	
2b	ACM, CVD, Cancer	Model 2a covariates + additional adjustment for *BMI*	
2c	ACM, CVD, Cancer	Model 2a covariates + additional adjustment for *diet quality*	Missing diet quality data ACM, n=659 CVD, n=374 Cancer, n=540
2d	ACM, CVD, Cancer	Model 2a covariates + additional adjustment for *physical function*	Missing physical function data ACM, n=811 CVD, n=353 Cancer, n=621
2e	ACM only	Same covariates as model 2a (minus adjustment for history of stroke/myocardial infarction and cancer)	Participants with a history of stroke/myocardial infarction or cancer
3a	ACM, CVD, Cancer	Model 2a covariates + additional adjustment for the *composition of 24-hour time use* (z1 and z2; with z3 dropped due to collinearity)	
3b	ACM, CVD, Cancer	Model 3a covariates + additional adjustment for *BMI*	
3c	ACM, CVD, Cancer	Model 3a covariates + additional adjustment for *diet quality*	Same exclusions as Model 2c
3d	ACM, CVD, Cancer	Model 3a covariates + additional adjustment for *physical function*	Same exclusions as Model 2d
3e	ACM only	Same covariates as model 3a (minus adjustment for history of stroke/myocardial infarction or cancer)	Same exclusions as model 2e

SB = sedentary behavior; CVD = cardiovascular disease; ACM = all-cause mortality.

* age as the underlying time scale in all models
† all participants with a history of stroke/myocardial infarction or cancer were excluded from the incident CVD or cancer analyses, respectively.
‡ all participants with early cases (CVD or cancer) and/or deaths within 2 years of follow-up were excluded for all outcomes.
§ all participants with missing data for diet quality or physical function were excluded from those specific models.

Table S5. Descriptive characteristics of sample at baseline for incident CVD, cancer, and all-cause mortality, stratified by gender.

Characteristics	Incident CVD		Incident Cancer		All-Cause Mortality	
	Men (n=2021)	Women (n=2996)	Men (n=2845)	Women (n=3389)	Men (n=3374)	Women (n=4189)
Follow-up time (years), mean±SD	5.9 ± 2.7	6.2 ± 2.7	6.2 ± 2.7	6.4 ± 2.8	6.3 ± 2.7	6.5 ± 2.8
Age (years), mean±SD	69.0 ± 7.0	68.2 ± 7.0	70.4 ± 7.4	69.3 ± 7.5	70.9 ± 7.5	69.7 ± 7.5
Education level, n (%)						
None	377 (18.7)	770 (25.7)	588 (20.7)	961 (28.4)	678 (20.1)	1,184 (28.3)
General Certificate of Education (GCE) Ordinary Level	211 (10.4)	437 (14.6)	272 (9.6)	500 (14.8)	319 (9.5)	588 (14.0)
GCE Advanced Level	980 (48.5)	1,281 (42.8)	1,375 (48.3)	1,402 (41.4)	1,653 (49.0)	1,749 (41.8)
Bachelor's degree, and above	453 (22.4)	508 (17.0)	610 (21.4)	526 (15.5)	724 (21.5)	668 (15.9)
Social class, n (%)						
Unemployed	15 (0.7)	31 (1.0)	23 (0.8)	36 (1.1)	24 (0.7)	44 (1.1)
Professional	208 (10.3)	249 (8.3)	262 (9.2)	268 (7.9)	327 (9.7)	335 (8.0)
Managerial/Technical	838 (41.5)	1,198 (40.0)	1,196 (42.0)	1,307 (38.6)	1,409 (41.8)	1,651 (39.4)
Skilled non-manual	236 (11.7)	553 (18.5)	319 (11.2)	650 (19.2)	387 (11.5)	781 (18.6)
Skilled manual	457 (22.6)	580 (19.4)	654 (23.0)	666 (19.7)	773 (22.9)	816 (19.5)
Semi-skilled	228 (11.3)	325 (10.8)	337 (11.8)	384 (11.3)	389 (11.5)	464 (11.1)
Non-skilled	39 (1.9)	60 (2.0)	54 (1.9)	78 (2.3)	65 (1.9)	98 (2.3)
Smoking status, n (%)						
Current	97 (4.8)	166 (5.5)	138 (4.9)	181 (5.3)	158 (4.7)	233 (5.6)
Former	1,027 (50.8)	1,052 (35.1)	1,538 (54.1)	1,224 (36.1)	1,841 (54.6)	1,500 (35.8)
Never	897 (44.4)	1,778 (59.3)	1,169 (41.1)	1,984 (58.5)	1,375 (40.8)	2,456 (58.6)
Alcohol intake (units/week), median (IQR)	6.0 (2.0-13.0)	3.0 (0.0-7.0)	6.0 (2.0-13.0)	2.5 (0.0-7.0)	6.0 (2.0-13.0)	2.5 (0.0-7.0)
Baseline history of diabetes or taking diabetes medications, n (%)	71 (3.5)	55 (1.8)	152 (5.3)	103 (3.0)	184 (5.5)	132 (3.2)
Anti-hypertensive medication, n (%)	329 (16.3)	468 (15.6)	883 (31.0)	910 (26.9)	1,081 (32.0)	1,150 (27.5)
Lipid-lowering medication, n (%)	256 (12.7)	285 (9.5)	633 (22.2)	485 (14.3)	768 (22.8)	626 (14.9)
Anti-depressant medication, n (%)	72 (3.6)	234 (7.8)	121 (4.3)	291 (8.6)	144 (4.3)	364 (8.7)
Family history of CVD (stroke, myocardial infarction), n (%)	874 (43.2)	1,431 (47.8)	1,337 (47.0)	1,717 (50.7)	1,589 (47.1)	2,127 (50.8)

Family history of cancer, n (%)	780 (38.6)	1,201 (40.1)	1,098 (38.6)	1,329 (39.2)	1,327 (39.3)	1,688 (40.3)
Family history of diabetes, n (%)	228 (11.3)	407 (13.6)	381 (13.4)	478 (14.1)	438 (13.0)	595 (14.2)
Body mass index (kg/m^2), mean±SD	99.4 ± 9.8	88.6 ± 11.2	100.9 ± 10.2	90.0 ± 11.9	100.8 ± 10.2	90.1 ± 11.9
Maximum handgrip (kg), mean±SD	40.1 ± 8.0	24.5 ± 5.5	39.0 ± 8.3	23.9 ± 5.8	38.8 ± 8.2	23.8 ± 5.8
Usual walking speed (m/s), mean±SD	1.2 ± 0.2	1.2 ± 0.2	1.1 ± 0.2	1.1 ± 0.3	1.1 ± 0.2	1.1 ± 0.3
Chair stand speed (stands/min), mean±SD	28.6 ± 8.2	27.2 ± 8.0	27.9 ± 8.0	26.7 ± 8.0	27.7 ± 8.1	26.5 ± 8.0
Physical function (z-score), mean±SD *	0.2 ± 0.7	0.2 ± 0.7	0.1 ± 0.7	0.1 ± 0.7	0.1 ± 0.7	0.1 ± 0.7
Accelerometer results						
Valid wear days, mean±SD	6.7 ± 0.6	6.7 ± 0.6	6.7 ± 0.6	6.6 ± 0.6	6.7 ± 0.6	6.6 ± 0.6
Valid wear-time, min/day, mean±SD	877.8 ± 59.1	860.0 ± 56.0	872.7 ± 60.3	856.7 ± 58.2	871.1 ± 60.0	856.2 ± 57.8
Moderate-to-vigorous-intensity physical activity (cpm ≥2020), min/day, median (IQR)	22.3 (10.8-38.0)	16.5 (7.3-30.0)	19.6 (8.0-35.3)	14.3 (5.7-27.6)	18.9 (7.4-34.6)	13.5 (5.1-26.6)
Light-intensity physical activity (cpm 100-2019, hr/day, mean±SD	4.5 ± 1.3	4.9 ± 1.2	4.4 ± 1.3	4.8 ± 1.3	4.3 ± 1.3	4.8 ± 1.3
Sedentary behaviour (cpm <100), hr/day, mean±SD	9.6 ± 1.4	9.0 ± 1.3	9.8 ± 1.4	9.2 ± 1.4	9.8 ± 1.4	9.2 ± 1.4
Usual SB bout duration, min, median (IQR)	18.1 (14.1-23.1)	15.1 (11.8-19.3)	19.1 (14.5-24.4)	15.6 (12.2-20.4)	19.3 (14.7-24.8)	15.8 (12.4-20.7)
Alpha, mean±SD	1.8 ± 0.1	1.9 ± 0.1	1.8 ± 0.1	1.9 ± 0.1	1.8 ± 0.1	1.9 ± 0.1

SB = sedentary behavior; CVD = cardiovascular disease; cpm = counts per minute.

* An overall z-score derived from hand grip strength (kg), usual walking speed (m/sec), and a timed chair stand speed (stand/min).

Table S6: Linear association of incident CVD and cancer events and all-cause mortality with SB bout accumulation patterns – stratified by gender.

	Incident CVD		Incident Cancer		All-Cause Mortality	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Usual SB bout duration, min						
Men						
Model 2a	1.04 (0.95-1.15)	0.397	1.19 (1.05-1.35)	0.007	1.24 (1.12-1.38)	<0.001
Model 3a	1.02 (0.91-1.14)	0.709	1.14 (0.99-1.32)	0.063	1.12 (0.99-1.27)	0.061
Women						
Model 2a	0.97 (0.89-1.06)	0.529	1.01 (0.86-1.19)	0.922	1.04 (0.92-1.19)	0.510
Model 3a	0.98 (0.89-1.08)	0.727	1.03 (0.85-1.25)	0.741	0.96 (0.83-1.12)	0.625
Alpha						
Men						
Model 2a	0.96 (0.87-1.07)	0.488	0.84 (0.73-0.97)	0.016	0.72 (0.63-0.83)	<0.001
Model 3a	0.98 (0.87-1.11)	0.749	0.85 (0.72-1.00)	0.057	0.77 (0.65-0.90)	0.002
Women						
Model 2a	1.00 (0.92-1.10)	0.963	0.95 (0.81-1.12)	0.528	0.92 (0.80-1.07)	0.280
Model 3a	0.98 (0.87-1.10)	0.717	0.90 (0.74-1.11)	0.321	1.02 (0.85-1.23)	0.820

Hazard Ratios and 95% confidence intervals (CIs) depicting the association (per 1 standard deviation change) between mean SB bout duration and incident CVD, incident cancer and all-cause mortality. SB = sedentary behavior; CVD = cardiovascular disease.

Model 2a (age as the underlying time scale) is adjusted for device type; education level; social class; smoking status; alcohol intake; baseline history of diabetes mellitus or taking diabetes mellitus medications (not for cancer); taking medication for hypertension/dyslipidemia (not for cancer outcome), or depression; and family history of CVD (stroke/myocardial infarction), diabetes mellitus, or cancer (not CVD or diabetes for cancer outcome). Model 3a includes the same covariates as Model 2a and further adjusts for the composition of 24-hour time use (z1 and z2; with z3 dropped due to collinearity). Further details on specific covariate adjustments per outcome are detailed in Table S4.

Participants with a history of stroke/myocardial infarction or cancer were excluded for all incident CVD or cancer outcome models, respectively. For all-cause mortality, history of stroke/myocardial infarction or cancer was statistically adjusted for.

- Incident CVD: Men (n=2,021, events=488, person years=11,876); Women (n=2,996, events=593, person years=18,549).
- Incident Cancer: Men (n=2,845, events=265, person years=17,560); Women (n=3,389, events=175, person years=21,674).
- **All-Cause Mortality:** Men (n=3,374, events=354, person years=21,144); Women (n=4,189, events=258, person years=27,160).

Table S7: Linear association of incident CVD and cancer events and all-cause mortality with SB bout accumulation patterns – sensitivity analyses with additional adjustment for BMI, diet quality, or physical function, and exclusion of prevalent disease for all-cause mortality models.

	Incident CVD		Incident Cancer		All-Cause Mortality			Incident CVD		Incident Cancer		All-Cause Mortality	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*		HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Usual SB bout duration, min							**Alpha**						
Model 2b	0.97 (0.91-1.03)	0.328	1.10 (0.99-1.21)	0.074	1.16 (1.07-1.27)	<0.001	*Model 2b*	1.03 (0.96-1.10)	0.407	0.90 (0.81-1.01)	0.065	0.81 (0.73-0.90)	<0.001
Model 2c	1.00 (0.93-1.07)	0.951	1.09 (0.98-1.21)	0.097	1.15 (1.05-1.25)	0.002	*Model 2c*	0.99 (0.92-1.06)	0.787	0.91 (0.82-1.02)	0.106	0.84 (0.75-0.93)	0.001
Model 2d	1.00 (0.93-1.07)	0.980	1.17 (1.06-1.30)	0.002	1.09 (0.99-1.20)	0.090	*Model 2d*	1.01 (0.94-1.09)	0.715	0.84 (0.75-0.95)	0.004	0.84 (0.75-0.95)	0.006
Model 2e					1.16 (1.03-1.31)	0.017	*Model 2e*					0.80 (0.67-0.95)	0.010
Model 3b	0.98 (0.91-1.05)	0.501	1.09 (0.97-1.22)	0.152	1.08 (0.98-1.18)	0.127	*Model 3b*	1.02 (0.94-1.11)	0.626	0.88 (0.77-1.00)	0.057	0.87 (0.77-0.99)	0.030
Model 3c	0.99 (0.92-1.07)	0.776	1.10 (0.98-1.24)	0.121	1.06 (0.96-1.17)	0.279	*Model 3c*	1.00 (0.91-1.09)	0.950	0.88 (0.76-1.00)	0.058	0.91 (0.79-1.04)	0.150
Model 3d	1.00 (0.92-1.07)	0.909	1.16 (1.03-1.30)	0.015	1.02 (0.92-1.14)	0.682	*Model 3d*	1.02 (0.94-1.11)	0.628	0.85 (0.74-0.98)	0.021	0.88 (0.76-1.01)	0.077
Model 3e					1.07 (0.93-1.24)	0.343	*Model 3e*					0.88 (0.72-1.08)	0.235

Hazard Ratios and 95% confidence intervals (CIs) depicting the linear association (per 1 standard deviation change) between usual SB bout duration and alpha with incident CVD, incident cancer and all-cause mortality. SB = sedentary behavior; CVD = cardiovascular disease.

For reference, Model 1 was adjusted for gender and device type (with age as the underlying time scale). Model 2a was adjusted as for model 1 plus education level; social class; smoking status; alcohol intake; baseline history of diabetes mellitus or taking diabetes mellitus medications (not for cancer); taking medication for hypertension/dyslipidemia (not for cancer outcome), or depression; and family history of CVD (stroke/myocardial infarction), diabetes mellitus, or cancer (not CVD or diabetes for cancer outcome). Model 3a includes the same covariates as Model 2a and further adjusts for the composition of 24-hour time use (z1 and z2; with z3 dropped due to collinearity).

Models 2b, 2c and 2d include the same covariates as Model 2a and further adjust for BMI, diet quality or physical function, respectively. Models 3b, 3c and 3d include the same covariates as Model 3a and further adjust for BMI, diet quality or physical function, respectively. Further details on specific covariate adjustments per outcome are detailed in Table S4.

Participants with a history of stroke/myocardial infarction or cancer were excluded all for incident CVD or cancer outcome models, respectively. For all-cause mortality, history of stroke/myocardial infarction or cancer was statistically adjusted for in models 2 and 3 (a-d). Models 2e and 3e include the same covariates as Models 2a and 3a, but exclude participants with a history of stroke/myocardial infarction or cancer.

- Incident CVD: Model 2b & 3b (n=5016, events=1081); Models 2c & 3c (n=4643, events=1010); Models 2d & 3d (n=4664, events=962).
- Incident Cancer: Model 2b & 3b (n=6231, events=440); Models 2c & 3c (n=5694, events=402); Models 2d & 3d (n=5613, events=381).
- **All-Cause Mortality:** Model 2b & 3b (n=7557, events=610); Models 2c & 3c (n=6904, events=547); Models 2d & 3d (n=6752, events=455); Models 2e & 3e (n=4709, events=238).

Table S8: Association of incident CVD and cancer events and all-cause mortality with (arithmetic) mean SB bout duration across percentiles of the population.

Percentile	Incident CVD (n=5,017; no. of events=1,081; person years=30,425)				Incident Cancer (n=6,234; no. of events=440; person years=39,234)				All-Cause Mortality (n=7,563; no. of events=612; person years=48,303)			
	p10	p30	p60	p90	p10	p30	p60	p90	p10	p30	p60	p90
Mean SB duration, min												
	5	6	8	10	5	6	8	10	5	6	8	10
Model 1	1	1.01 (0.91-1.12)	1.00 (0.84-1.20)	1.08 (0.90-1.29)	1	0.98 (0.82-1.18)	1.22 (0.90-1.63)	1.41 (1.06-1.88)	1	0.96 (0.80-1.17)	1.11 (0.84-1.47)	1.29 (0.99-1.67)
Model 2a	1	0.98 (0.88-1.10)	0.95 (0.79-1.14)	0.99 (0.82-1.20)	1	1.02 (0.85-1.23)	1.27 (0.94-1.72)	1.48 (1.11-1.99)	1	1.02 (0.83-1.25)	1.19 (0.88-1.61)	1.42 (1.06-1.90)
Model 3a	1	0.98 (0.87-1.10)	0.94 (0.77-1.15)	0.97 (0.77-1.23)	1	1.03 (0.85-1.26)	1.31 (0.93-1.83)	1.57 (1.10-2.25)	1	1.00 (0.81-1.24)	1.09 (0.78-1.51)	1.17 (0.84-1.65)

Data are Hazard Ratios and 95% confidence intervals (CIs) and were fitted with the use of restricted cubic splines (3 evenly spaced knots). Results presented approximate the 10th (reference), 30th, 60th and 90th percentiles across all three outcomes for mean SB bout duration= 5, 6, 8, 10 (min). Covariates that violated the proportional hazard assumptions (education level; social class, family history of diabetes mellitus and CVD) were included as baseline strata. SB = sedentary behavior; CVD = cardiovascular disease.

Model 1 is adjusted for gender and device type (with age as the underlying time scale). Model 2a is adjusted as for model 1 plus education level; social class; smoking status; alcohol intake; baseline history of diabetes mellitus or taking diabetes mellitus medications (not for cancer); taking medication for hypertension/dyslipidemia (not for cancer outcome), or depression; and family history of CVD (stroke/myocardial infarction), diabetes mellitus, or cancer (not CVD or diabetes for cancer outcome). Model 3a includes the same covariates as Model 2a and further adjusts for the composition of 24-hour time use (z1 and z2; with z3 dropped due to collinearity). Further details on specific covariate adjustments per outcome are detailed in Table S4.

Participants with a history of stroke/myocardial infarction or cancer were excluded for all incident CVD or cancer outcome models, respectively. For all-cause mortality, history of stroke/myocardial infarction or cancer was statistically adjusted for in models 2a and 3a.

Figure S1: Fractional polynomial curves showing relationships of alpha (left) and usual SB bout duration (right) with their highly correlated SB pattern measures ($r_s > 0.8$) in middle aged to older adults (n=7563, EPIC-Norfolk).
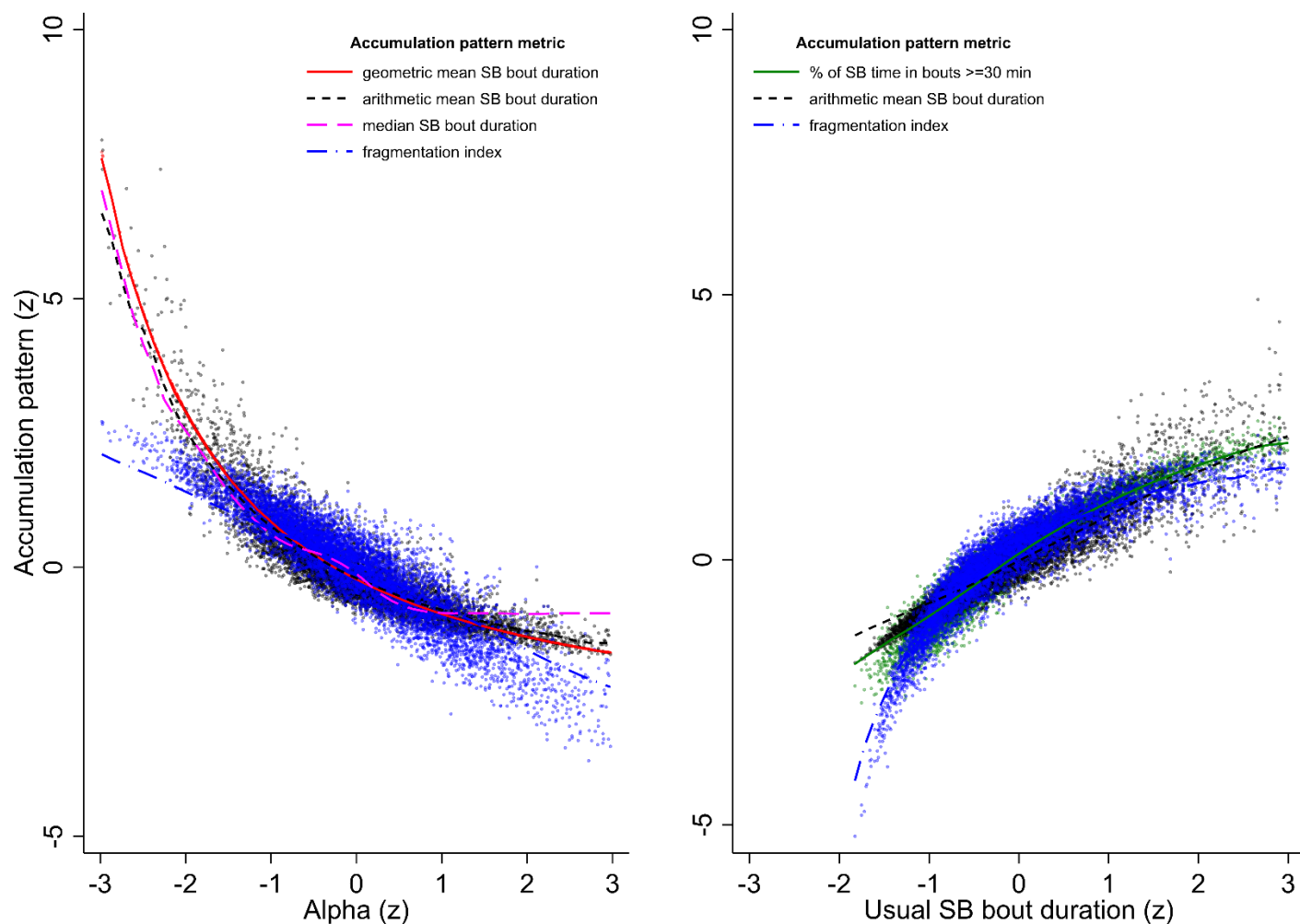

Values are converted to z-scores (by subtracting the population-level mean and dividing by population-level standard deviation, resulting in values that correspond to one standard deviation change; $z = (x-\mu)/\sigma$) to aid interpretation.

Graph displays -3 to +3 z for alpha and usual SB bout duration.

y-axis = -z for fragmentation index. For clarity, only the line is displayed for median SB bout duration.

Figure S2: Directed acyclic graphs (DAG) of causal assumptions and potential confounder / adjusted variables.
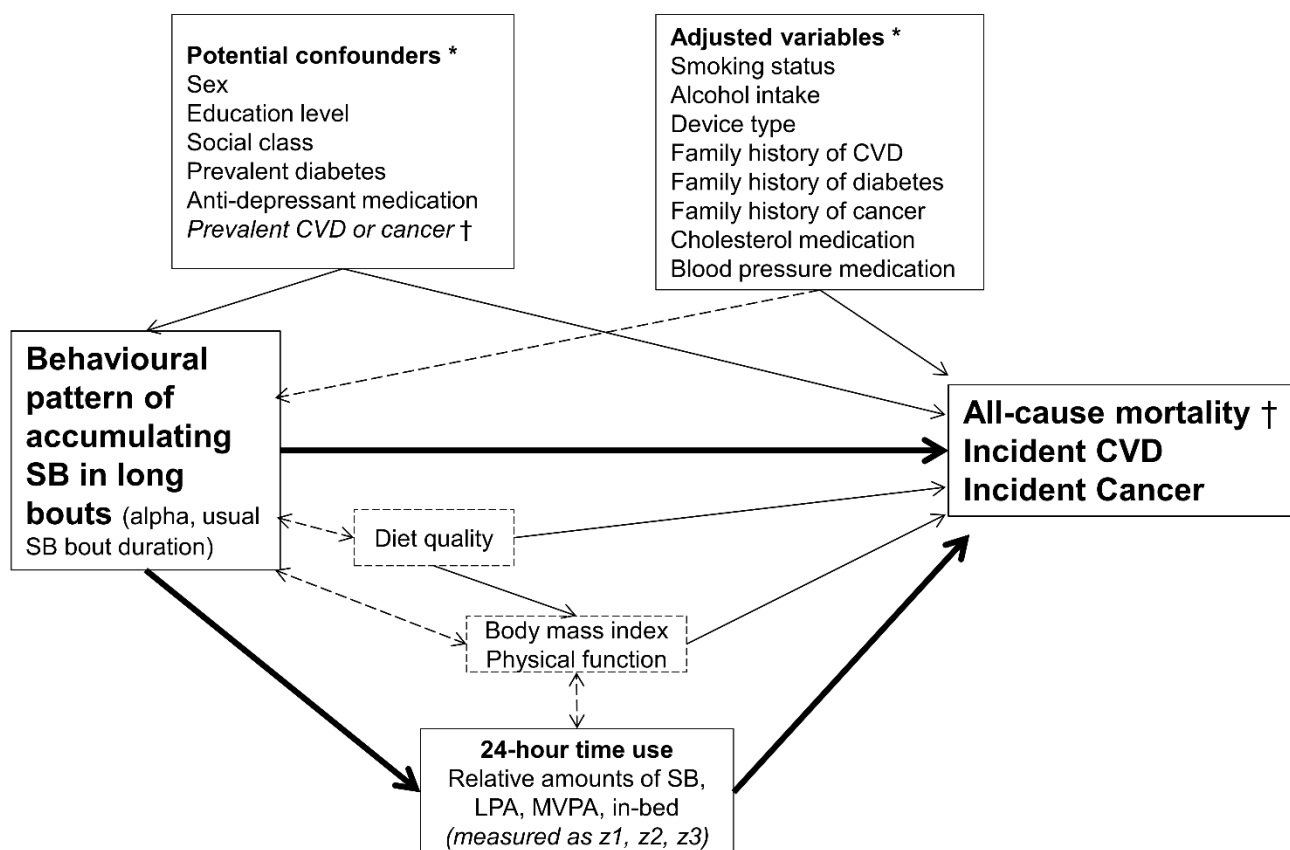
SB = sedentary behavior; CVD = cardiovascular disease.

* For purposes of clarity in this DAG, covariate adjustment variables here are based on the most comprehensively adjusted all-cause mortality models only, but specific covariate adjustments for incident CVD and cancer (i.e. some differences in adjustment for family history of disease and medications) are detailed in Table S4.

† For all-cause mortality only, an additional sensitivity analysis excluded prevalent CVD or cancer (as opposed to only adjusting for them as potential confounders) to examine potential for reverse causality bias (also see Table S4).

Age included as the underlying timescale in all cox models. *Potential confounders* are assumed ancestors of both the exposure and the outcome (or 'true' confounders). *Adjusted variables* are adjusted similarly to potential confounders (i.e., total effects), but labelled as such here given it is debatable whether they are also true ancestors of the exposure (dashed arrows). A separate additional model (model 3a) adjusted for 24-hour time use in terms of the ilr transformed z parameters (see Table S3 and Figure S4) to examine the degree to which effects of SB accumulation pattern are independent of the total amount of SB and physical activity arising from the pattern of behavior (i.e., direct effects).

Body mass index, physical function and *diet quality* have been considered as potential confounders and/or as causal intermediates in previous studies, thus were modelled separately in additional sensitivity analyses. Diet quality was additionally considered separately due to some missing data [n=659 (8.7%) missing] and given its very low correlations with alpha (r_s=0.06) and usual SB bout duration (r_s=0.07).

Figure S3: Scatterplots of alpha (left) and usual SB bout duration (right) over ilr z coordinates.
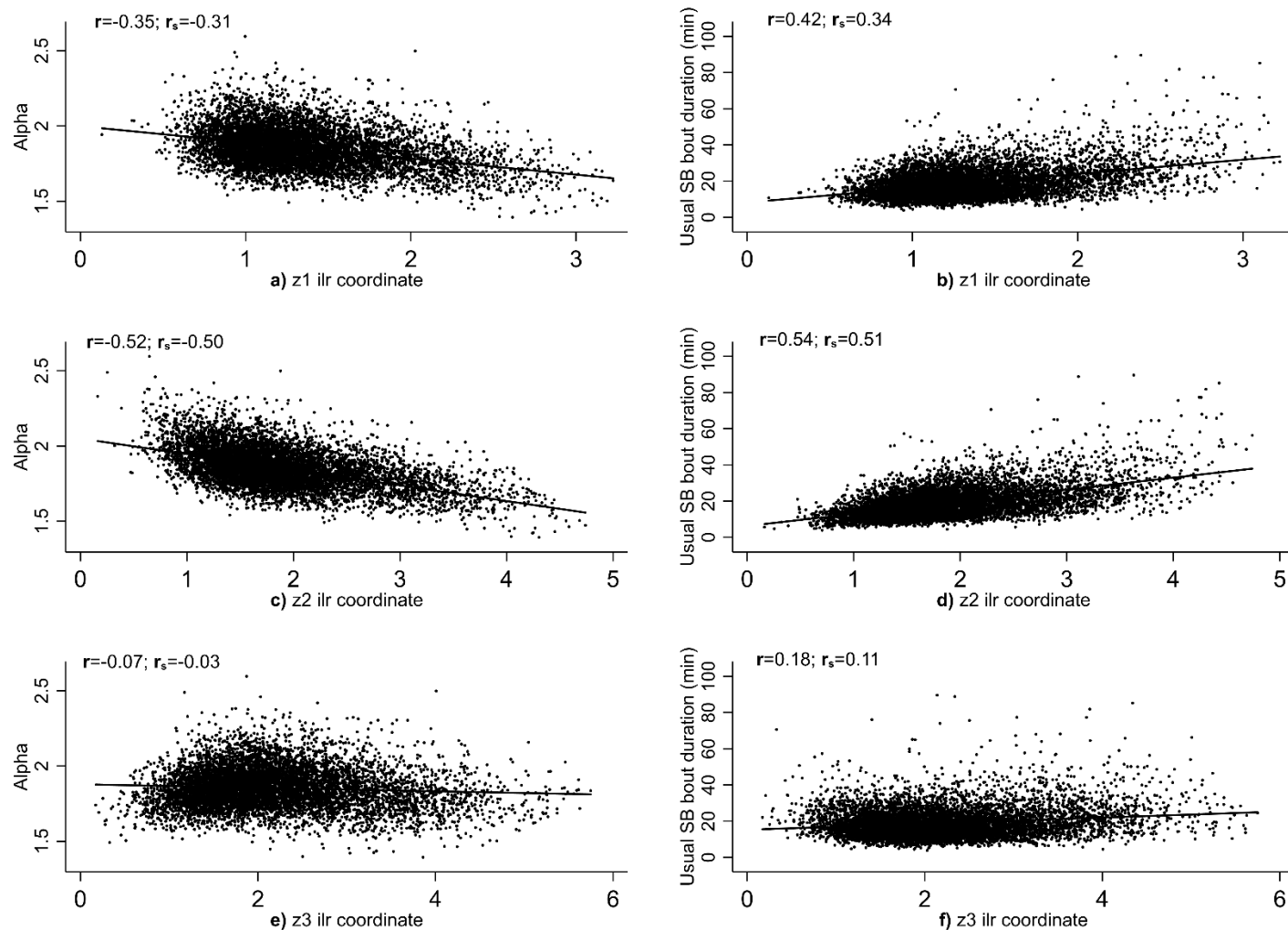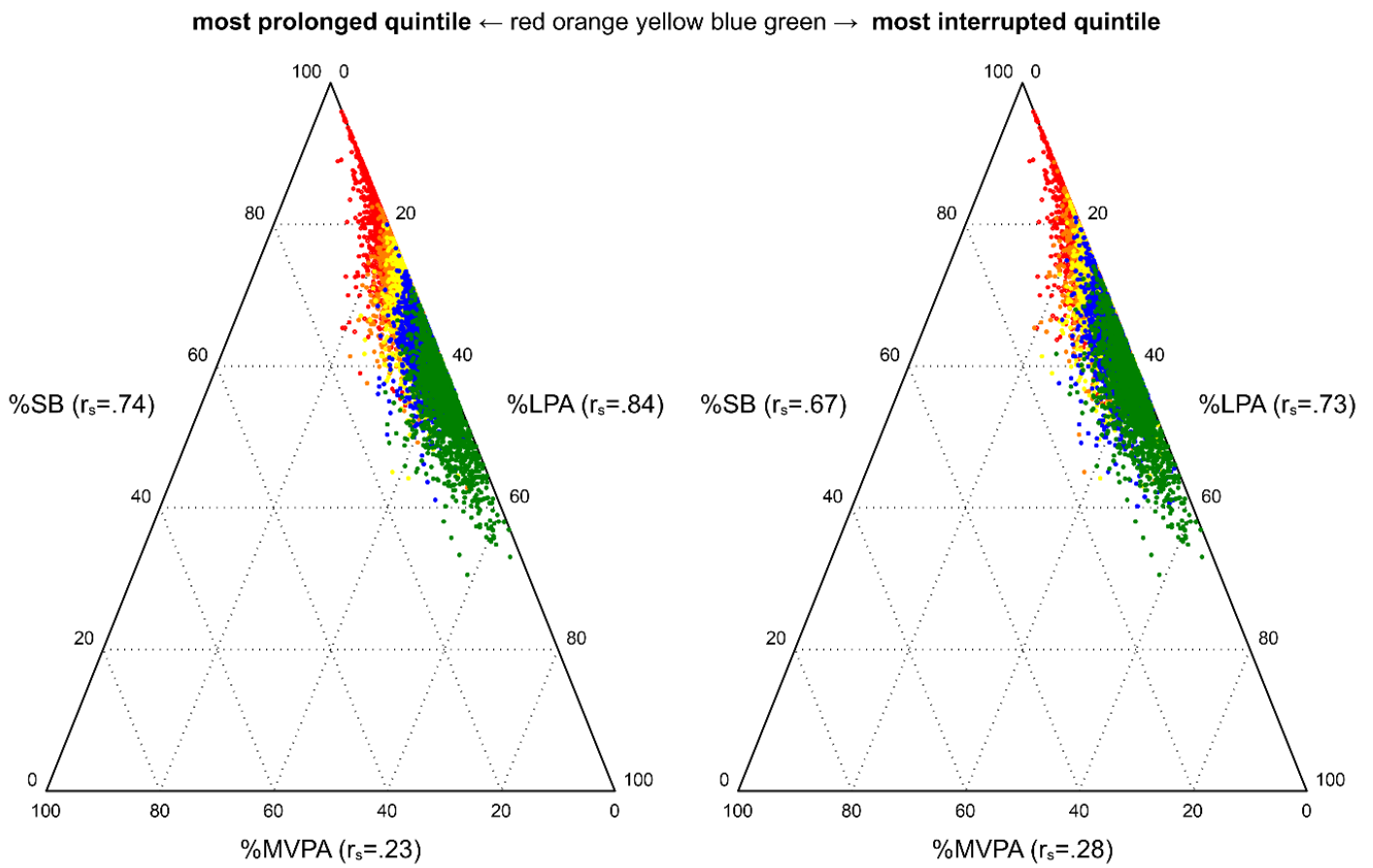

SB = sedentary behavior.

r=pearson; r_s=spearman

z1 (panels a and b) = less waking wear time; z2 (panels c and d) = more SB waking hours; z3 (panels e and f) = less intense physical activity

Figure S4: Tri-plot showing alpha (left) and usual SB bout duration (right) across the composition of 24-hour time use (sub-composition %SB, %LPA, %MVPA displayed)

SB = sedentary behavior; LPA = light intensity physical activity; MVPA = moderate-to-vigorous physical activity

r_s=spearman with alpha (left) and usual bout duration (right).