Joint associations of device-measured physical activity and sleep duration with cardiometabolic health in the 1970 British Cohort Study

Abstract

Objectives: Multiple unhealthy lifestyle behaviors could synergistically exaggerate unfavorable health outcomes. The present study aimed to investigate the joint associations of device-measured sleep duration and physical activity with cardiometabolic health markers.

Design: This is a cross-sectional analysis embedded in the 1970 British Cohort Study (BCS70).

Methods: 4,756 participants of the 46-48 years wave of the BCS70, wore an activPAL3 micro accelerometer to measure physical activity and sleep duration. Body mass index (BMI), glycated hemoglobin, triglycerides, c-reactive protein, systolic blood pressure, and total-to-high-density lipoprotein (HDL) cholesterol ratio were continuous outcomes; prevalent hypertension and diabetes were dichotomized outcomes. We examined the joint associations of sleep (<7 hr, short; 7-9 hr, medium; >9 hr, long) and physical activity (median cut of step counts, 9480 steps/d; or moderate-to-vigorous physical activity, MVPA, 085 hr/d) with outcomes.

Results: After adjustment for potential confounders, low physical activity was associated with a higher BMI, regardless of sleep duration. Low physical activity was associated with a higher total-to-HDL cholesterol ratio among participants with long sleep duration (differences from those with moderate sleep and high physical activity: low MVPA: 0.27 [0.08, 0.45], low step counts: 0.31 [0.12, 0.49]). Short sleep duration combined with low step counts showed higher odds for prevalent hypertension and diabetes (1.34 [1.06, 1.69] and 1.98 [1.07, 3.68], respectively). Short sleep duration had two times higher odds (2.04 [1.09, 3.82]) for diabetes, independent of MVPA time.

Conclusions: Low physical activity may exaggerate the detrimental associations between inadequate sleep duration with BMI, blood lipids, hypertension, and diabetes.

Keywords

Diabetes Mellitus, Hypertension, Sleep, Exercise

1. Introduction

Inadequate sleep duration and physical inactivity are behavioral risk factors for cardiometabolic health and mortality[1,2]. Meta-analyses based on longitudinal studies have shown either insufficient (< 5 or < 7 hr) or prolonged (> 8 or > 9 hr) sleep duration could elevate risks of diabetes, hypertension, and all-cause mortality[2–5]. Analyses of the large Australian cohort 45 and Up Study suggested potential synergistic effects of self-reported behavioral risk factors on all-cause mortality and self-rated health[6,7]. Participants with more unhealthy behaviors had higher risks of low self-rated health and high all-cause mortality than those with less unhealthy behaviors. A limited number of studies of the association between lifestyle behaviors and cardiometabolic health outcomes have taken both sleep duration and physical activity into account.[6–8]

To date, the largest study (n= 502,664) extensively investigating the association of different behavior exposures (physical activity, sleep duration, and sitting time) with cardiometabolic diseases was a cross-sectional analysis embedded in the U.K. Biobank cohort[8]. People with type 2 diabetes had 2.14 times higher odds for the behavioral combination of physical inactivity (< 918 MET-min/wk), inadequate sleep duration (< 7 or > 8 hr/d), and high television time (> 3 hr/d) compared to the healthy population. The same study also suggested people with cardiovascular diseases (CVD) and type 2 diabetes tended to engage in multiple unhealthy behaviors simultaneously. The 45 and Up Study has shown people with both poor sleep duration (< 7 or > 9 hr/d) and physical inactivity (< 150 min/wk of moderate-to-vigorous physical activity, MVPA) conferred a higher mortality risk than the sum of risks conferred by only poor sleep duration and only physical inactivity[6]. Based on the same cohort, Ding et al.[7] found people with both a poor lifestyle index (including physical inactivity, alcohol drinking, unhealthy diet, and smoking) and inadequate sleeping (< 7 or > 9 hr/d) had higher risks for the low self-rated quality of life and health, compared to those with only poor lifestyle index.

Despite the potential codependency and synergetic effects physical activity and sleep duration have[9], few studies have examined the joint association of both the behaviors with cardiometabolic health[10,11]. The existing studies used self-report measures of physical activity, which is prone to misclassification and recall

bias and cannot capture the whole spectrum of free-living physical activity (*e.g.*, questionnaires cannot capture light-intensity physical activity)[10-12]. The 2018 U.S. Physical Activity Guidelines Advisory Committee evidence review highlighted that, beyond MVPA, the number of daily steps (incorporating any physical activity intensity) is associated with a lower risk of CVD events and type 2 diabetes risk[13]. Besides physical activity measurements, a recent meta-analysis based on self-reported sleep also recommended device-based methods to quantify sleep duration to reduce measurement error[2].

The aim of this analysis was to investigate the joint associations of device-estimated sleep duration and physical activity (both MVPA and total step counts) with cardiometabolic health markers. We used data from a large established population-based cohort of middle-aged adults, the 1970 British Cohort Study (BCS70).

2. Methods

This cross-sectional analysis used the age-46-to-48 wave (conducted from July 2016 until July 2018) data of a population-based prospective longitudinal study BCS70, which followed 17,196 participants born in a single week of 1970, in England, Scotland, and Wales, with rationale and methodology described elsewhere[14]. This wave comprised paper-based self-completion questionnaires, computer-assisted personal interviewing, bio-measures, online dietary questionnaires, and accelerometry-based physical activity recording. The present study included data from members giving consent to participate in all the above measurements. The study received ethical approval from NRES Committee South East Coast - Brighton & Sussex (Ref 15/LO/1446).

In total, 7,439 cohort members were invited to the accelerometry study and 6,562 gave consent (88%)[15]. Among those, accelerometry data from 1,670 participants were not usable (*i.e.*, unable to initiate, lost in the post, unable to download/unusable, unable to compute physical activity). Another 136 were excluded due to missing sleep diary data. There were 4,756 participants for the core analyses (Supplementary Figure 1).

A thigh-worn activPAL3 accelerometry (PAL Technologies Ltd., Scotland) recorded time in bed, as a proxy of sleep, and physical activity[14]. At a home visit, a nurse or the participant her/himself fixed the device on the right thigh. The device was waterproofed so participants could wear the monitor continuously to record body posture and stepping speed (cadence) without interruptions. After seven days (or after the device was taken off for any reason), participants mailed it back to the office. Data were processed using the ProcessingPAL software[16]. This program isolated valid waking wear time from sleep (time in bed). The first day of data was discarded, and subsequent days were defined from midnight to midnight. Participants completed a sleep diary (recording the time when they went to bed, fell asleep, woke up, and got out of bed) during the wearing period and returned it with the device. Only cohort members who had at least one valid sleep diary and one accelerometry day were included in the analysis[15,17]. A valid day of sleep diary was defined as that a participant had filled both the time go to bed and wake up time without AM/PM mistaken or missing cells, while a valid device day was defined as at least 10 hours of valid waking wear time. Analogous inclusion criteria have been used in recent major accelerometry studies15,17. In the present study, 62.66% of the participants had full-week data available, while 0.86%/ 7.67% of the participants provided weekend/weekday only.

A nurse conducted home visits to take biological measurements, including body height and mass, blood pressure, blood sample, and information on current medication[14]. Non-fasting blood samples were collected for quantifying glycated hemoglobin (HbA1c), cholesterol profile, triacylglycerols (TG), and c-reactive protein (CRP). Current medication uses were coded using the British National Formulary (BNF) codes. We defined hypertension based on either self-reported physician diagnosis or on BP-regulating drugs or SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg[18] and defined diabetes based on either self-reported physician diagnosis or on blood glucose-regulating drugs or HbA1c $\geq$ 6.5% (48 mmol/mol)[19]. The total-to-HDL cholesterol ratio was computed by dividing total cholesterol by HDL cholesterol[20]. CRP was log-transformed since it displayed a skewed distribution[21].

A proxy of device-based sleep duration, computed by subtracting valid waking wear time from 24 hours, was utilized[16,22]. We also calculated diary-based time in bed (the difference between the time going to bed and getting out of bed) and sleep duration (the difference between the time when falling asleep and waking up). In a recent study, we have shown this algorithm[16] showed acceptable absolute agreement and correlations with diary-derived time in bed and sleep time in BCS70 participants (n = 5,498) (unpublished under-review works). Daily step counts were calculated, while daily MVPA time was derived based on cadence (>100 steps/min) using an algorithm derived from previously validated program[16,23]. Because of the expected non-linear association between sleep duration and health outcomes, we divided participants into three groups (< 7 hr, short sleep; 7-9 hr, medium sleep; > 9 hr, long sleep) with cut-offs derived from previous studies and a suggestive guideline[2,3,5–7,24]. For joint analyses, participants were categorized into two sets of six combinations of sleep duration (three levels mentioned above) and MVPA/step counts (two levels: high and low, based on median cut points: 0.85 hr/d and 9480 steps/d, respectively), where the medium sleep duration and high MVPA/step counts combinations served as the reference group.

A questionnaire and an interview were conducted to collect participants' education qualifications, self-assessed general health, impairments/disability, smoking status, and alcohol consumption[14]. The European Statistics on Income and Living Conditions (EU-SILC) definition was used to identify the severity of the physical disability. The abbreviated version of the Alcohol Use Disorders Identification Test - Primary Care Version (AUDIT-PC) was utilized to assess the risk of problematic alcohol drinking. The Oxford WebQ online dietary questionnaire was applied to calculate the calorie intake.

Missing values of covariates (as well as BMI) were imputed by an established procedure of multiple imputation[25]. Twenty linear-regression-based imputations with existing exposures, outcomes, and confounding as predictors were generated on the SAS 9.4 software (SAS Institute, Cary, NC, USA). The similarity of distribution between the imputed dataset and the observed dataset was confirmed by histograms and pooled estimation efficiency (Supplementary Table 1).

Sex, educational attainment, antidepressant use, impairments/disability, smoking status, alcohol consumption (categorical), self-assessed general health, and daily calorie intake (continuous) were utilized to adjust all analyses[26]. BMI, daily sleep duration, or MVPA (continuous) was used for further adjustment when applicable. We also adjusted all models for the number of wear days (continuous), instead of the usual daily waking wear time, because the main exposure (algorithm-derived sleep duration) was derived from daily waking wear time.

A constant was applied to the biochemical variables on certain medication to reduce the potential measurement errors[27], *i.e*., on lipid-regulating drugs (+25% for total cholesterol; −5% for HDL cholesterol; +18% for TG), on BP-regulating drugs (+10 mmHg for both DBP and SBP), and on blood glucose-regulating drugs (+3.2% (11 mmol/mol) for HbA_{1c}).

As recommended in a recent meta-analysis[2], we applied multiple approaches to estimate sleep duration. We initially considered three sleep-related markers (device-based time in bed, diary-based time in bed, and diary-based sleep duration), and carried out preliminary analyses with cardiometabolic markers. We found no appreciable differences in the associations of different sleep estimates with outcomes (Supplementary Table 2), despite the discrepancy in absolute values (Supplementary Table 3). Based on this data-driven approach, we used device-estimated time in bed as the main sleep duration exposure in this study.

We defined exposures as daily sleep duration (categorical) and the two sets of combinations (categorical) based on sleep duration (device-/ diary-based) and MVPA time/step counts. Continuous outcomes were BMI (kg/m^2), HbA_{1c} (mmol/mol), TG (mmol/L), log CRP, SBP (mmHg), and total-to-HDL cholesterol ratio, while dichotomized outcomes were hypertension and diabetes.All statistics were performed on SAS 9.4 software. General linear models were applied to investigate the association between all exposures (and cardiometabolic risk markers with the result shown in least-square means or differences**.** Logistic regression with general linear model parameterization examined the association between categorical exposures and binary outcomes. As there is no agreement on whether BMI is on the mechanistic pathway between

behaviors and cardiometabolic health, we carried out a sensitivity analysis to examine the joint associations without adjustment for BMI. Another logistic regression was conducted with further adjustment for shift work to reduce potential residual confounding due to irregular sleep patterns[3]. To be aligned with the current physical activity guidelines, we performed the joint analyses with MVPA categorization based on the World Health Organization guideline threshold (150 minutes per week) also. Besides total step counts, we also applied physical activity of any intensity (comprising standing, low-intensity physical activity, and MVPA) to the joint analyses to capture a different perspective of total physical activity.

3. Results

As shown in Supplementary Table 4, participants with medium sleep duration (7-9 hr/d) were more likely to attain postgraduate academic qualifications, wear the device for more days (better compliance), report better self-rated general health, have lower impairments/disability, have less antidepressant use, and have a lower prevalence of obesity. Participants with short sleep duration (< 7 hr/d) had a higher prevalence of diabetes (6.82% vs. 3.26% among those with short and medium sleep duration, respectively). Being male and current smoking showed a negative correlation with sleep duration. Participants with long sleep duration had lower step counts compared to those with medium and short sleep duration. However, alcohol consumption, sleep quality, and prevalent hypertension were unrelated to sleep duration.

As shown in Table 1 and Supplementary Table 5-6, in the multivariable-adjusted analyses (including physical activity), short sleep was associated with higher BMI compared to medium and long sleep. Short sleep was associated with a lower total-to-HDL cholesterol ratio, while long sleep duration was associated with a higher ratio compared to medium sleep. Participants with short sleep had significantly higher odds for prevalent diabetes (adjusted for MVPA time/step counts: 1.56 [1.01, 2.41] and 1.57 [1.02, 2.43], respectively) (Supplementary Table 7) compared to those with the medium sleep.

The participant's distribution of combinations of sleep duration and MVPA time was similar to the combinations of sleep duration and step counts (Supplementary Table 8). Joint association showed that,

187 regardless of sleep duration, participants with either low MVPA time or step counts had higher BMI
188 compared to the reference group (Table 2; Supplementary Table 9). Participants with long sleep and low
189 MVPA time/step counts had higher total-to-HDL cholesterol ratio compared to the reference group
190 (differences from the reference group: low MVPA: 0.27 [0.08, 0.45]; low step counts: 0.31 [0.12, 0.49]).
191 The association of inadequate sleep duration with BMI and total-to-HDL cholesterol ratio was attenuated
192 after physical activity stratification in joint analyses.

193 As shown in Figure 1 and Supplementary Table 10, independent of MVPA time, participants with short
194 sleep had higher odds for prevalent diabetes (low MVPA time and high MVPA time: 2.04 [1.09, 3.82] and
195 2.07 [1.04, 4.15], respectively) compared to the reference group. Low MVPA time was associated with
196 higher odds for hypertension only in medium and long sleep groups. Participants with short sleep and low
197 step counts had higher odds for both prevalent hypertension and diabetes (1.34 [1.06, 1.69] and 1.98 [1.07,
198 3.68], respectively) compared to the reference group.

199 In the sensitivity analysis, the joint associations of MVPA and sleep duration with both conditions were
200 slightly enhanced without adjustment for BMI yet were largely attenuated after further adjustment for shift
201 work. However, participants with short sleep had higher odds for both conditions, independent of step
202 counts, after adjustment for shift work (Supplementary Table 10).Only 9.31% of participants did not meet
203 the WHO MVPA guidelines. By applying guideline-based categorization, the results showed a similar trend
204 as the main analyses, although the adverse effects of low MVPA level on HbA_{1c} and prevalent diabetes
205 were highlighted (Supplementary Table 11). With a median-of physical activity of any intensity of 1.92
206 hr/d, results were similar to the ones in the main analysis (Supplementary Table 12).

207 **4. Discussion**

208 The present study is, to our knowledge, among the first investigations to examine the joint associations of
209 thigh-worn-device-measured physical activity and sleep with cardiometabolic health. Short sleep duration
210 was associated with higher BMI, lower total-to-HDL cholesterol ratio, and higher prevalent diabetes, while

long sleep duration was associated with a higher total-to-HDL cholesterol ratio. Regardless of sleep duration, participants with low MVPA time/step counts had higher BMI compared to those with medium sleep duration with high MVPA time/step counts; those with long sleep duration and low MVPA time/step counts had a higher total-to-HDL cholesterol ratio. Participants with short sleep duration and low step counts had higher odds for both prevalent hypertension and diabetes, while participants with short sleep duration had higher odds for prevalent diabetes, independent of MVPA time.

Inadequate sleep duration is associated with obesity, cardiometabolic disease, and mortality[2–5]. In this study, participants with short sleep duration had higher odds for prevalent diabetes, higher BMI, and lower total-to-HDL cholesterol ratio; those with long sleep duration had higher total-to-HDL cholesterol ratio (Table 1, Supplementary Table 5-7). Inadequate sleep duration has been linked to lower energy expenditure and glucose homeostasis disruption, leading to insulin resistance and alterations in hunger hormones, such as leptin and ghrelin[28]. In two recent meta-analyses, both short and long sleep durations were associated with increased risks of cardiometabolic events and type 2 diabetes[3,5]. A 12-year longitudinal study of 20,432 healthy adults suggested those who slept for ≤ 6 hr/d had a 15% higher risk of CVD incidence and a 23% higher risk of coronary heart disease incidence compared to people who slept for 7-8 hours[29]. In a meta-analysis[4], inadequate sleep (≤ 5 or ≥ 9 hr/d) was associated with high blood pressure. The same author suggested physical activity reduction might explain the biological mechanism between prolonged sleep duration and hypertension.

Inadequate sleep duration was associated with shorter physical activity duration[30,] while low physical activity and Inadequate sleep duration are risk factors for both CVD and type 2 diabetes[8]. Our results indicated people with insufficient sleep duration had higher odds for prevalent diabetes despite high daily MVPA time (Figure 1, Supplementary Table 10). Participants with low sleep duration and low step counts had higher odds for both prevalent hypertension and diabetes. Aligned with the present study (Table 2; Supplementary Table 9), Zuo et al. (2012) found that individuals with both low physical activity and short sleep duration had the highest odds of insulin resistance compared to other combinations[10]. The previous

cross-sectional analysis suggested cardiometabolic risk markers were associated with reallocation of 30 min/d of sedentary time with either sleep (2.2% lower insulin and 2.0% lower β-cell function), light-intensity activity (1.9% lower TG, 2.4% lower insulin, and 2.2% lower β-cell function), or MVPA (2.4% smaller waist circumference, 4.4% higher HDL cholesterol, 8.5% lower TG, 1.7%lower glucose, 10.7% lower insulin, and 9.7% higher insulin sensitivity), indicating MVPA may be the most potent health-enhancing, time-dependent behavior, with additional benefit conferred from sleep duration when reallocated from sedentary time[31].

The 2018 U.S. Physical Activity Guidelines Advisory Committee evidence review[13] suggested daily step counts could be used as a viable metric for assessing the association of physical activity of any intensity with mortality, incident CVD and type 2 diabetes. The linear association between step counts with the above health outcomes contrasted with the negative curvilinear relationship of MVPA for these same outcomes. Step counts capture an overall physical activity profile especially in inactive population with low MVPA as a very low amount of physical activity has shown its health benefits. Our results offered preliminary evidence supporting such an assumption. The synergetic effect of physical activity and sleep duration with prevalence of hypertension and diabetes was more visible when step counts were applied than MVPA time (Figure 1, Supplementary Table 10).

The primary strengths of this study are the large sample size and detailed device-derived measurements. By using a posture-based activity monitor, we could assess habitual physical activity and sleep, in a more precise, less biased way than using self-report. The cross-sectional design limits the ability to establish a causal relationship, although we have made any effort to address reverse causality by adjusting models for impairments/disability and self-assessed general health; longitudinal studies are warranted to support the reliability and generalizability of our study findings. Since we applied a distribution-specific cut point (median) for physical activity in a specific cohort of the same age group, the generalizability of volume-specific study findings could be compromised. Although we have taken into account both MVPA and step counts in our analyses to reflect an overall physical activity profile, studies addressing the joint effect of

261 sleep and other types of physical activity (e.g., low-intensity physical activity) based on compositional data
262 analysis and analogous approaches will shed further light on the joint associations of sleep and physical
263 activity.

264 ## 5. Conclusion

265 This study adds to the evidence base of joint associations between physical activity and sleep with
266 cardiometabolic health. We found low MVPA and step counts were both associated with higher BMI
267 regardless of sleep duration. Among participants with long sleep duration, low physical activity was
268 associated with a higher total-to-HDL cholesterol ratio. Higher physical activity levels may favorably
269 modify the detrimental association between inadequate sleep duration with BMI, blood lipids, hypertension,
270 and diabetes. Our results suggested physical activity of any intensity could be beneficial to people who
271 sleep less than the recommended amount.

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276 resource: https://beta.ukdataservice.ac.uk/datacatalogue/studies/study?id=8547#!/access-data. The open R-
277 package "ProcessingPAL" applied in the current study is available online: https://github.com/UOL-
278 COLS/ProcessingPAL/releases.

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283 ## Disclosure of potential conflicts of interest

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Figure 1. The joint association of physical activity and the prevalence of hypertension [1] and (b) diabetes [2] within each sleep duration category after multiple imputations.

Values are shown in odds ratios compared to the combination of medium sleep duration, and high MVPA/step counts with the value in bold denoting significant differences.Models were adjusted for sex, education, total wearing days, antidepressant drug use, self-rated health, disability/limitation, smoking, alcohol consumption, daily energy intake, and BMI.

[1] Hypertension was defined from either self-reported diagnosis or on BP-regulating drugs or SBP ≥ 140 mmHg or DBP ≥ 90 mmHg.

[2] Diabetes was defined from either self-reported diagnosis or on blood glucose-regulating drugs or HbA_{1c} ≥ 6.5% (48 mmol/mol).

Table 1 — Associations of daily sleep duration with cardiometabolic risk markers (imputated results).

	Daily sleep duration [a]		
	Short (<7 hr/d)	Medium (7-9 hr/d)	Long (>9 hr/d)
BMI (kg/m^2)	**27.63**	26.79	26.40
(n=4,756)	**(27.08, 28.18)**	(26.33, 27.26)	(25.89, 26.91)
HbA_{1c} (mmol/mol) [b]	37.03	36.33	36.32
(n=3,917)	(36.11, 37.95)	(35.55, 37.11)	(35.46, 37.18)
TG (mmol/L)	1.76	1.89	1.96
(n=2,253)	(1.56, 1.96)	(1.72, 2.07)	(1.77, 2.16)
Log CRP	0.11	0.14	0.15
(n=2,226)	(0.04, 0.18)	(0.08, 0.19)	(0.09, 0.22)
Systolic BP (mmHg)	125.41	125.71	125.88
(n=4,722)	(123.83, 126.98)	(124.38, 127.04)	(124.40, 127.36)
Total-to-HDL cholesterol	**3.85**	4.05	**4.18**
ratio (n=3,948)	**(3.70, 4.00)**	(3.93, 4.18)	**(4.04, 4.32)**

Values are shown in the least squared means as the value in bold means a significant difference compared to the medium group.Models were adjusted for sex, education, total wearing days, antidepressant drug use, self-rated health, disability/limitation, smoking, alcohol consumption, daily energy intake, and daily MVPA time. Except for BMI, all models were further adjusted for BMI.

[a] The algorithm-derived sleep duration was used.

[b] A constant was added to the variable for those on current medication, *i.e*., on lipid-lowering drugs (+25% for total cholesterol; −5% for HDL cholesterol; +18% for TG), on BP lowing drugs (+10 mmHg for DBP and SBP, respectively), and on oral medication for diabetes (+3.2% (11 mmol/mol) for HbA_{1c}).

Table 2. The joint association of physical activity and the cardiometabolic risk markers within each sleep duration category after multiple imputations.

	Daily sleep duration [a]					
	Short (<7 hr/d)		Medium (7-9 hr/d)		Long (>9 hr/d)	
	Low MVPA	High MVPA	Low MVPA	High MVPA	Low MVPA	High MVPA
BMI (kg/m^2)	**2.26**	0.69	**1.35**		**1.01**	-0.32
(n=4,756)	**(1.39, 3.14)**	(-0.17, 1.55)	**(0.81, 1.88)**		**(0.31, 1.70)**	(-1.11, 0.47)
HbA_{1c} (mmol/mol) [b]	1.08	0.16	-0.2		0.12	-0.31
(n=3,917)	(-0.41, 2.57)	(-1.22, 1.55)	(-1.08, 0.68)		(-1.04, 1.27)	(-1.62, 1.00)
TG (mmol/L)	-0.15	-0.04	0.08		0.18	0.04
(n=2,253)	(-0.47, 0.18)	(-0.37, 0.29)	(-0.12, 0.28)	reference	(-0.08, 0.44)	(-0.27, 0.35)
Log CRP	0.00	-0.04	0.02		0.07	-0.02
(n=2,226)	(-0.11, 0.11)	(-0.15, 0.07)	(-0.05, 0.09)		(-0.02, 0.16)	(-0.12, 0.09)
Systolic BP (mmHg)	0.13	-0.19	0.43		0.91	-0.31
(n=4,722)	(-2.39, 2.64)	(-2.61, 2.24)	(-1.09, 1.96)		(-1.06, 2.89)	(-2.57, 1.94)
Total-to-HDL cholesterol	0.01	-0.28	0.15		**0.27**	0.16
ratio (n=3,948)	(-0.23, 0.25)	(-0.50, -0.05)	(0.00, 0.29)		**(0.08, 0.45)**	(-0.05, 0.38)
	Low step counts	High step counts	Low step counts	High step counts	Low step counts	High step counts
BMI (kg/m^2)	**2.32**	0.81	**1.45**		**0.99**	-0.22
(n=4,756)	**(1.42, 3.23)**	(0.00, 1.63)	**(0.91, 1.99)**		**(0.30, 1.68)**	(-1.03, 0.59)
HbA_{1c} (mmol/mol)	1.19	0.16	-0.23		0.08	-0.31
(n=3,917)	(-0.38, 2.76)	(-1.17, 1.48)	(-1.11, 0.64)		(-1.06, 1.21)	(-1.65, 1.04)
TG (mmol/L)	-0.07	-0.09	0.11		0.15	0.12
(n=2,253)	(-0.42, 0.28)	(-0.40, 0.22)	(-0.09, 0.31)	reference	(-0.11, 0.41)	(-0.20, 0.44)
Log CRP	0.01	-0.02	0.04		0.06	0.02
(n=2,226)	(-0.11, 0.13)	(-0.12, 0.08)	(-0.03, 0.11)		(-0.03, 0.15)	(-0.09, 0.13)
Systolic BP (mmHg)	0.30	0.14	0.96		1.06	0.04
(n=4,722)	(-2.35, 2.94)	(-2.18, 2.45)	(-0.56, 2.49)		(-0.89, 3.01)	(-2.27, 2.34)
Total-to-HDL cholesterol	0.03	-0.21	**0.21**		**0.31**	0.16
ratio (n=3,948)	(-0.22, 0.28)	(-0.43, 0.00)	**(0.07, 0.35)**		**(0.12, 0.49)**	(-0.06, 0.38)

Values are shown in differences in the least squared means compared to the combination of medium sleep duration, and high MVPA/step counts with the value in bold denoting significant differences. Models were adjusted for sex, education, total wearing days, antidepressant drug use, self-rated health, disability/limitation, smoking, alcohol consumption, and daily energy intake. Except for BMI, all models were further adjusted for BMI.

[a] The algorithm-derived sleep duration was used.

[b] A constant was added to the variable for those on current medication, *i.e.*, on lipid-lowering drugs (+25% for total cholesterol; −5% for HDL cholesterol; +18% for TG), on BP lowing drugs (+10 mmHg for DBP and SBP, respectively), and on oral medication for diabetes (+3.2% (11 mmol/mol) for HbA_{1c}).