

Association of timing and balance of physical activity and rest/sleep with risk of COVID-19: A UK Biobank study

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Abstract

Behavioural lifestyle factors are associated with cardiometabolic disease and obesity, which are risk factors for COVID-19. We aimed to investigate whether physical activity, and the timing and balance of physical activity and sleep/rest, were associated with SARS-CoV-2 positivity and COVID-19 severity. Data from 91,248 UK Biobank participants with accelerometer data, complete covariate and linked COVID-19 data to 19th July 2020 were included. The risk of SARS-CoV-2 positivity and COVID-19 severity, in relation to overall physical activity, moderate-to-vigorous physical activity (MVPA), balance between activity and sleep/rest, and variability in timing of sleep/rest, was assessed with adjusted logistic regression. Of 207 individuals with a positive test, 124 were classified as having a severe infection. Overall physical activity and MVPA were not associated with severe COVID-19, while a poor balance between activity and sleep/rest was (OR per standard deviation: 0.71 [95% CI: 0.62, 0.81]). This was related to higher daytime activity being associated with lower risk (OR 0.75 [0.61, 0.93]) but higher movement during sleep/rest with higher risk (OR 1.26 [1.12, 1.42]) of severe infection. Greater variability in timing of sleep/rest was also associated with increased risk (OR 1.21 [1.08, 1.35]). Results for testing positive were broadly consistent. In conclusion, these results highlight the importance of not just physical activity, but also quality sleep/rest and regular sleep/rest patterns, on risk of COVID-19. Our findings indicate the risk of COVID-19 was consistently ~1.2 times higher per ~40-minute increase in variability in timing of proxy measures of sleep, indicative of irregular sleeping patterns.

Keywords: accelerometer; sleep variability; sleep timing; lifestyle; pandemic

Abbreviations

MVPA	moderate-to-vigorous physical activity
OR	odds ratio
SD	standard deviation

Introduction

There is evidence that the risk of COVID-19 is higher in people with cardiometabolic diseases [1]. Recent research also suggests that the risk is associated with lifestyle-related factors, including obesity [2] and self-reported slow walking pace [3], a marker of physical fitness.

There has been limited attention on the risk of COVID-19 and behavioural lifestyle factors. Low levels of physical activity are known to be associated with increased risk of cardiometabolic disease, obesity and lower fitness [4]. Further, evidence suggests that irregular sleep timing and increased variability in sleep duration are detrimentally associated with cardiovascular disease risk and markers of cardiometabolic health [5]. This suggests that a balance between active behaviours and quality sleep/rest across the 24-hour day is important for cardiometabolic health. We hypothesise that these behavioural factors may similarly influence the risk of COVID-19.

Our aim was to investigate whether device-measured physical activity, the balance between activity during waking hours and the main sleep/rest period during the day, and the timing of the main sleep/rest and activity periods are associated with the risk of testing positive for SARS-CoV-2 and developing severe COVID-19.

Methods

We used data from UK Biobank (application 36371), a prospective cohort of >500,000 adults aged 40-69 years [6]. Assessments were conducted between March 2006 and July 2010 with data on 24 h movement patterns from Axivity AX3 wrist-worn accelerometers (Axivity, Newcastle, UK) in >100,000 adults gathered between June 2013 and December 2015 [7]. UK Biobank data are linked to national SARS-CoV-2 laboratory test data through Public Health England's Second Generation Surveillance System; data were available from 16th March 2020 to 19th July 2020 and included specimen origin (hospital inpatient vs other): a positive test result for SARS-CoV-2 with hospitalisation was considered as evidence of a severe infection in line with guidance for this dataset [8]. Two SARS-CoV-2 outcomes were used: 1) severe infection with SARS-CoV-2; 2) positive test result for SARS-CoV-2

Analyses were restricted to English centres, individuals with known sleep disorders (identified by ICD10 code G47 in UK Biobank) and those who had died before 16th March 2020 were excluded. Participant characteristics, including body mass index (BMI), sex, ethnicity and self-reported sleep duration were collected at the baseline assessment.

For each participant, accelerometer data (5-second epoch time series) were extracted from UK Biobank [7] and converted to R-format for processing and analysis with GGIR (version 1.11-0, <http://cran.r-project.org>) [9]. Participants were excluded if they failed calibration (including those not calibrated on their own data), had fewer than three days of valid wear (defined as >16 h per day), or wear data were not present for each 15 min period of the 24 h cycle.

Accelerometer outcomes, detailed in **Table 1**, were averaged across valid days and divided into three categories: standard physical activity outcomes; the balance between activity level and sleep/rest; and the variability in timing of activity and sleep/rest.

Statistical analysis

Logistic regression was used to assess associations of a severe infection with SARS-CoV-2 (N=124) with no test or a negative test result (whole cohort, N=91,041) as comparator (model 1) and a positive test result (N=207) with a negative result (N=2009) as comparator (model 2).

For Model 1, participants who tested positive for COVID-19 but were not classified as severe (i.e. they tested positive in the community, N=83) were excluded. This was because it is possible these individuals went on to develop severe COVID-19 but were not retested on hospital admission. Model 1 can be interpreted as the overall population level risk of being admitted to hospital with COVID-19 during the linkage period within UK Biobank. This population level method of assessing risk is commonly reported within COVID-19 risk factor research, and of value here as it enables comparison to the literature in terms of how the risk factors assessed compare to other commonly reported risk factors (e.g. obesity) [3,10].

Model 2 relates specifically to the tested population and can be interpreted as the risk of a positive test in anyone within UK Biobank who has been tested for COVID-19.

The physical activity and rest variables listed in **Table 1** were used as independent variables. These variables were standardised prior to entry into the models and the Odds Ratios (OR) per standard deviation (SD) reported for ease of comparison across variables.

In model 2, regressions were adjusted for the following potential confounders selected on current clinical knowledge: age on 16th March 2020, sex, ethnicity, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers and non-cancer illnesses, and number of treatments or medications taken. The model for severity of infection (model 1) was adjusted for key demographic variables only (age, sex and ethnicity) due to the smaller number of outcome events. The activity during waking hours (3, **Table 1**) and amount of movement during sleep/rest (4, **Table 1**) were additionally mutually adjusted for one another and for sleep duration. When assessing the balance between activity and sleep/rest (5, **Table 1**), and the variability in timing of activity and sleep/rest (6-8, **Table 1**), sleep duration was added to the models. Finally, when assessing the variability in timing of activity and sleep/rest (6-8, **Table 1**) overall activity was also added to the models.

Sensitivity analyses

- 1) To allow for differences in sleep duration, we conducted analyses with the average acceleration and timing of the least active 6 hours rather than 8 hours;
- 2) Assuming individuals testing positive in the community to be non-severe, we added them to the comparator group for severe infection with SARS-CoV-2 (severe infection N=124, comparator group N=91,124);
- 3) We did not adjust for BMI in our main analyses as it is potentially on the causal pathway from physical activity to COVID-19 risk. However, we carried out sensitivity analyses for: i) model 1 further adjusted for BMI and number of cancer and non-cancer illnesses (underlying health conditions); and ii) model 2 further adjusted for BMI (initial model already adjusted for underlying health conditions).

4) While we controlled for deprivation and household size, it is difficult to determine risk due to level of exposure. The UK was under lockdown during the period of the study with people requested to stay at home; we ran sensitivity analyses excluding the group likely to have had the greatest exposure to the virus - healthcare workers as they continued working throughout lockdown (UK Biobank codes 2211001-2216012, N=1665, of which 62 were tested (11 positive, 5 severe infection)).

All analyses were carried out in Stata version 16.0 (StataCorp LLC, TX, USA). Statistical significance was set at the alpha level of .05.

Results

Data were available on 91,248 individuals, of whom 2,009 had been tested for COVID-19, 207 had a positive test result and 124 were classified as having a severe infection. Participant characteristics for both models are reported in **Table 2**.

The results of the regression models are shown in **Figure 1 and Table S1** (Supplemental Material 1). Results for severe infection (**Figure 1a**) and positive test results (**Figure 1b**) were broadly consistent. Overall physical activity level and moderate-to-vigorous physical activity (MVPA) were not significantly associated with the risk of testing positive for SARS-CoV-2 or developing severe COVID-19. A higher amount of movement during the main sleep/rest period (least active 8 hours) (OR 1.14-1.26, $p < .05$) and lower activity during waking hours (model 1 only, OR 0.75 [95% CI: 0.61, 0.93], $p = .01$) were associated with increased odds independent of each other (i.e. both were significant in the same model). Consequently, a worse (lower) balance between activity and sleep/rest (i.e. a smaller drop in movement during the main sleep/rest period) was also predictive (OR 0.71-0.86, $p < .05$). Irregular sleeping patterns (greater variability in the start times of activity during waking

hours, amount of movement during the main sleep/rest period , and mid-point of the difference between these times) were consistently associated with significantly greater odds (OR 1.17-1.21, $p < .01$) across both models. Results of unadjusted models were consistent with the adjusted models (Table S1, Supplemental Material 1).

Sensitivity analyses broadly confirmed the associations:

- 1) if the least active 6 hours was as the main sleep/rest period instead of the least active 8 hours;
- 2) if individuals testing positive in the community were assumed to be non-severe and added to the comparator group for severe infection with SARS-CoV-2 (Figure S1, Supplemental Material 2);
- 3) with further adjustment for BMI (Model 1 and 2) and cancer and non-cancer illnesses (Model 1) (Figure S2, Supplemental Material 3);
- 4) when excluding healthcare workers (Figure S3, Supplemental Material 4).

Discussion

The balance and variability in timing of activity and rest were more strongly associated with the risk of testing positive for SARS-CoV-2 or incidence of severe COVID-19 than ‘standard’ measures of activity, i.e. MVPA. This highlights the importance of not just physical activity alone, but also adequate quality sleep/rest. A distinct activity cycle (better balance between activity and rest), reflecting a clear drop in movement during the main sleep/rest period (one third of the day), was associated with a lower risk, independent of self-reported sleep duration. The importance of quality sleep/rest was further evident in the positive association between the level of movement during sleep/rest (the least active

continuous 8 hours) and risk, independent of activity level during waking hours, in all models.

A better balance between activity and the dominant sleep/rest period (by 1 SD of the sample mean) was associated with approximately 30% lower risk of severe COVID-19. This more distinct activity cycle could reflect greater movement during waking hours (16 hours), less movement during the main sleep/rest period (8 hours), or both. For example, a 1 SD higher balance between activity and sleep/rest could reflect the equivalent of 90 minutes extra brisk walking [12]; or lower movement during the main sleep/rest period by 1 SD (i.e. ~2 mg) of the sample mean; or ~45 minutes of brisk walking and lower movement during the main sleep/rest period by ~0.5 SD (i.e. ~1 mg) of the sample mean.

Sleep disruption and physical inactivity can contribute to chronic inflammation [13] and to cardiometabolic disease, which in turn is associated with an increased risk of COVID-19 [1]. Further, as COVID-19 is an acute inflammatory disease, it may exacerbate existing chronic inflammation associated with poor activity and rest behaviours and/or existing cardiometabolic disease. Alongside other risk factors (e.g. psychological stress and genetic predisposition) this may be associated with a ‘cytokine storm’ [13] contributing to the observed increased risk of severe COVID-19.

The consistently ~1.2 times higher risk of COVID-19 per ~40-minute increase in variability in timing of sleep/rest, indicative of irregular sleeping patterns, further supports that risk factors for cardiovascular and cardiometabolic disease [4,5] are also risk factors for COVID-19 [2,3].

Limitations

Characteristics of participants, including accelerometer data, were measured prior to the current pandemic. While the analyses were controlled for deprivation and household size, it was not possible to determine level of exposure to infection. However, results were robust when excluding the group likely to have had the highest level of exposure to the virus, healthcare workers. The definition of severe COVID-19 was a positive test from a hospital inpatient, consistent with the definition proposed by the researchers that developed the linkage method [8]; however actual disease severity cannot be confirmed from the linkage data available at the time of analysis. Further, participants in UK Biobank may not be representative of the wider population and testing in the UK has not been universal, making analyses vulnerable to bias. However, participants may not need to be representative when estimating relative risk factor associations, as empirically demonstrated for UK Biobank [14]. As such, our results point to the potential importance of rest and physical activity as predictive of later risk of COVID-19 infection and should be confirmed with current databases from other populations.

Conclusions

This report provides evidence of an association between markers of sleep/rest and physical activity and the risk or severity of COVID-19 infection. Public health studies could incorporate such measures to better identify and protect individuals at high risk of COVID-19 and/or cardiometabolic disease.

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Availability of data and materials: This research has been conducted using the UK Biobank Resource under Application 36371 (<http://www.ukbiobank.ac.uk/>)

Code availability: Accelerometer data were processed using the open-source R-package GGIR (version 1.11-0, <http://cran.r-project.org>)

Ethics approval: Not applicable, secondary data analysis.

Author contributions

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Acquisition, analysis, or interpretation of data: All authors

Drafting of the manuscript: A Rowlands, D Kloecker

Critical revision of the manuscript for important intellectual content: All authors

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Figure legends

Fig 1. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity: a) Model 1. Severe COVID-19 (UK Biobank cohort as comparator); and b) Model 2. Positive test for COVID-19 (negative test result as comparator). Odds ratios expressed per SD of each variable. OR = odds ratio; SD = standard deviation.

Model 2 adjusted for age, sex, ethnicity, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications. Model 1 adjusted for age, sex and ethnicity due to the smaller number of outcome events. Activity during waking hours and movement during sleep/rest mutually adjusted. ‘Activity & sleep/rest’ and ‘Variability in timing of activity and sleep/rest’ variables additionally adjusted for sleep duration. ‘Variability in timing of activity and sleep/rest’ additionally adjusted for overall physical activity.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

Online-Only Supplemental Materials

1. Table S1. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity with risk of COVID-19.
2. Fig S1. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity. Risk of severe COVID-19 (UK Biobank cohort as comparator group, sensitivity analysis with positive test result in the community assumed to be non-severe and added to the comparator group); Odds ratios expressed per standard deviation of each variable. OR = odds ratio.

Adjusted for age, sex and ethnicity. Activity during waking hours and movement during sleep/rest mutually adjusted. 'Activity & sleep/rest' and 'Variability in timing of activity and sleep/rest' variables additionally adjusted for sleep duration.

'Variability in timing of activity and sleep/rest' additionally adjusted for overall physical activity.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

3. Fig S2. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity further adjusted for BMI and underlying health conditions (model 1) and BMI (model 2): a) Model 1. Severe COVID-19 (UK Biobank cohort as comparator); and b) Model 2. Positive test for COVID-19 (negative test result as comparator). Odds ratios expressed per SD of each variable. OR = odds ratio; SD = standard deviation.

Model 2 adjusted for age, sex, ethnicity, BMI, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications. Model 1 adjusted for age, sex, ethnicity, BMI, number of cancer and non-cancer illnesses. Activity during waking hours and

movement during sleep/rest mutually adjusted. ‘Activity & sleep/rest’ and ‘Variability in timing of activity and sleep/rest’ variables additionally adjusted for sleep duration. ‘Variability in timing of activity and sleep/rest’ additionally adjusted for overall physical activity. BMI = body mass index.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

4. Fig S3. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity excluding healthcare workers: a) Model 1. Severe COVID-19 (UK Biobank cohort as comparator); and b) Model 2. Positive test for COVID-19 (negative test result as comparator). Odds ratios expressed per SD of each variable. OR = odds ratio; SD = standard deviation. Model 2 adjusted for age, sex, ethnicity, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications. Model 1 adjusted for age, sex and ethnicity. Activity during waking hours and movement during sleep/rest mutually adjusted. ‘Activity & sleep/rest’ and ‘Variability in timing of activity and sleep/rest’ variables additionally adjusted for sleep duration. ‘Variability in timing of activity and sleep/rest’ additionally adjusted for overall physical activity. BMI = body mass index.
- ^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

Table 1. Accelerometer outcome variables for physical activity and sleep/rest

	Outcome	Unit	Abbreviation	Interpretation
Physical activity				
1	Average acceleration over 24 h day	mg	overall physical activity	Proxy for total physical activity
2	Moderate-to-vigorous physical activity in 1-min bouts ^a	min	MVPA	Purposeful activity (e.g. walking) accumulated in 1-min bouts
Activity and sleep/rest				
3	Average acceleration over most active continuous 16 h	mg	activity during waking hours	Overall intensity of movement during the most active 16 h of the day as a proxy for waking hours. Greater values present a higher level of physical activity within this window.
4	Average acceleration over least active continuous 8 h ^b	mg	movement during sleep/rest	Overall intensity of movement during the least active 8 h of the day sleep/rest as a proxy for the sleep window (main rest period). Lower values represent a more restful window of recovery.
5	The intensity of the most active 16 h expressed as % of average acceleration over the 24 h day	%	balance between activity and sleep/rest	A proxy for the balance between activity and rest/sleep in a 24 h day. A value of 100% would mean no distinction between activity and sleep/rest (i.e. no drop in movement levels during the main sleep/rest period). As the value gets closer to 150% it indicates an increasingly distinct activity/rest cycle with two thirds of the day active and one third resting.
Variability in timing of activity and sleep/rest				
6	Variability (SD) in the start time of the most active continuous 16 h	min	variability in timing of activity	Proxy for variability in time of sleep offset (wake)
7	Variability (SD) in the start time of the least active continuous 8 h ^b	min	variability in timing of sleep/rest	Proxy for variability in time of sleep onset

8	Variability (SD) in the mid-point of the time difference between the start of the most active continuous 16 h and least active continuous 8 h ^b	min	variability in sleep/rest mid-point	Proxy for variability in mid-sleep time
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h = hour; mg = milli-gravitational units; SD = standard deviation

^a Accelerometer cut-point for classification of MVPA = 100 mg [11]

^b To allow for differences in the duration of sleep, we conducted sensitivity analyses assessing the impact of the average acceleration and timing of the least active 6 h rather than 8 h.

Table 2: Characteristics of UK Biobank participants by COVID-19 positive and severity

Variable	Severity of infection (in UK Biobank), model 1			Test result, model 2		
	Negative/not tested	Severe	Total	Negative	Positive	Total
Participants (N)	91041	124	91165	1802	207	2009
Age at COVID-19 diagnosis	68.1 (61.0-73.2)	69.6 (58.7-75.5)	68.1 (61.0-73.2)	70.5 (62.6-75.3)	64.9 (56.2-73.4)	70.1 (61.6-75.2)
Sex (female)	51908 (57.0%)	52 (41.9%)	51960 (57.0%)	949 (52.7%)	103 (49.8%)	1052 (52.4%)
Ethnicity						
White European	87951 (98.4%)	115 (95.8%)	88066 (98.4%)	1725 (98.0%)	191 (95.0%)	1916 (97.7%)
South Asian	684 (0.8%)	2 (1.7%)	686 (0.8%)	22 (1.3%)	3 (1.5%)	25 (1.3%)
Black/Afro-Caribbean	760 (0.9%)	3 (2.5%)	763 (0.9%)	13 (0.7%)	7 (3.5%)	20 (1.0%)
Townsend deprivation index	-2.5 (-3.8--0.2)	-2.5 (-3.6-0.6)	-2.5 (-3.8--0.2)	-2.3 (-3.7-0.3)	-2.3 (-3.6-0.5)	-2.3 (-3.7-0.3)
Number in household	2.0 (2.0-3.0)	2.0 (2.0-3.0)	2.0 (2.0-3.0)	2.0 (2.0-3.0)	2.0 (2.0-4.0)	2.0 (2.0-3.0)
^a Fruit and vegetable score	4.3 (3.0-6.0)	4.3 (2.7-6.0)	4.3 (3.0-6.0)	4.3 (3.0-6.0)	4.0 (2.7-6.0)	4.3 (3.0-6.0)
^b Red meat score	1.5 (1.5-2.5)	2.0 (1.5-3.0)	1.5 (1.5-2.5)	1.5 (1.5-2.5)	2.0 (1.5-2.5)	1.5 (1.5-2.5)
Smoking status						
Never	52357 (57.7%)	56 (45.2%)	52413 (57.6%)	889 (49.4%)	107 (51.2%)	996 (49.7%)
Previous	32328 (35.6%)	54 (43.5%)	32382 (35.6%)	754 (41.9%)	79 (38.2%)	833 (41.5%)
Current	6119 (6.7%)	14 (11.3%)	6133 (6.7%)	155 (8.6%)	21 (10.1%)	176 (8.8%)
Alcohol intake frequency	1.5 (0.5-3.5)	1.5 (0.5-3.5)	1.5 (0.5-3.5)	1.5 (0.5-3.5)	1.5 (0.5-3.5)	1.5 (0.5-3.5)
Number of self-reported cancers	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Number of self-reported non-cancer illnesses	1.0 (0.0-2.0)	2.0 (1.0-3.0)	1.0 (0.0-2.0)	2.0 (1.0-3.0)	1.0 (0.0-3.0)	2.0 (1.0-3.0)
Number of treatments/medications taken	1.0 (0.0-3.0)	2.0 (1.0-5.0)	1.0 (0.0-3.0)	2.0 (1.0-4.0)	2.0 (0.0-4.0)	2.0 (1.0-4.0)
Body mass index (BMI) (kg·m ⁻²)	26.0 (23.6-28.9)	27.3 (24.1-31.9)	26.0 (23.6-28.9)	26.8 (24.2-30.2)	27.3 (24.1-31.1)	26.9 (24.2-30.3)
Self-reported sleep duration (h)	7.0 (7.0-8.0)	7.0 (7.0-8.0)	7.0 (7.0-8.0)	7.0 (6.0-8.0)	7.0 (6.0-8.0)	7.0 (6.0-8.0)
Physical activity						
Overall physical activity (mg)	27.4 (22.7-33.0)	26.9 (21.3-32.8)	27.4 (22.7-33.0)	25.8 (21.1-31.0)	26.8 (21.9-32.1)	25.9 (21.1-31.1)
Moderate to vigorous PA accumulated in 1-min bouts (min)	42.1 (24.7-65.2)	36.0 (19.4-55.4)	42.0 (24.7-65.2)	34.6 (18.5-55.5)	36.9 (22.2-57.3)	35.0 (18.8-55.9)
Activity and sleep/rest						
Activity during waking hours (16 h) (mg)	39.0 (32.2-47.1)	38.2 (29.8-45.9)	39.0 (32.2-47.1)	36.5 (29.8-44.5)	38.1 (30.5-45.5)	36.7 (29.9-44.6)
Amount of movement during sleep (8 h) (mg)	3.8 (3.1-4.9)	4.2 (3.3-5.8)	3.8 (3.1-4.9)	3.9 (3.2-4.9)	4.2 (3.3-5.7)	3.9 (3.2-5.0)
^c Amount of movement during sleep (6 h) (mg)	2.8 (2.4-3.2)	3.0 (2.6-3.7)	2.8 (2.4-3.2)	2.8 (2.5-3.3)	3.0 (2.5-3.6)	2.8 (2.5-3.4)
Balance between activity and sleep/rest (%)	142.5 (140.4-144.0)	141.1 (138.0-143.4)	142.5 (140.4-144.0)	141.9 (139.4-143.6)	141.4 (138.6-143.2)	141.8 (139.4-143.6)
Timing of activity and sleep/rest						
Start time of most active 16h per day (hh:mm)	7:05 (6:34-7:37)	7:04 (6:34-7:47)	7:05 (6:34-7:37)	7:07 (6:34-7:38)	7:02 (6:28-7:43)	7:07 (6:34-7:38)
Variability in timing of activity (SD, min)	37.6 (25.0-55.1)	46.4 (31.5-68.4)	37.6 (25.0-55.1)	38.2 (26.4-56.5)	46.7 (31.4-70.8)	38.8 (26.6-57.6)
Start time of least active 8h per day (hh:mm)	23:04 (22:34-23:35)	23:02 (22:28-23:41)	23:04 (22:34-23:35)	23:07 (22:34-23:37)	23:02 (22:28-23:43)	23:05 (22:33-23:37)
Variability in timing of sleep/rest (8 h, SD, min)	37.7 (25.0-55.4)	46.7 (30.4-67.1)	37.6 (25.0-55.1)	38.3 (26.5-56.5)	47.1 (31.0-71.2)	39.1 (26.7-57.7)
^c Start time of least active 6h per day (hh:mm)	00:08 (23:34-00:43)	00:08 (23:34-00:58)	00:08 (23:34-00:43)	00:10 (23:34-00:48)	00:07 (23:34-00:53)	00:08 (23:34-00:48)
^c Variability in timing of sleep/rest (6h, SD, min)	53.1 (38.0-70.6)	56.6 (40.3-80.8)	53.1 (38.0-70.6)	53.2 (38.9-72.0)	57.2 (40.7-81.8)	53.5 (39.3-72.6)
Mid-point of difference between start of least active 8h and most active 16h (hh:mm)	3:04 (2:34-3:36)	3:02 (2:29-3:41)	3:04 (2:34-3:36)	3:07 (2:34-3:38)	3:02 (2:28-3:43)	3:06 (2:34-3:38)
Variability in sleep/rest mid-point (8h, SD, min)	37.6 (25.0-55.1)	46.7 (30.6-68.1)	37.6 (25.0-55.1)	38.3 (26.4-56.5)	47.1 (30.6-71.8)	38.8 (26.6-57.6)
^c Mid-point of difference between start of least active 6h and most active 16h (hh:mm)	3:36 (3:05-4:09)	3:38 (3:04-4:22)	3:36 (3:05-4:09)	3:38 (3:04-4:13)	3:36 (3:04-4:10)	3:38 (3:04-4:13)
^c Variability in sleep/rest mid-point (6h, SD, min)	39.3 (28.0-54.9)	43.1 (30.1-70.1)	39.3 (28.0-54.9)	40.5 (28.8-55.5)	46.1 (29.8-69.8)	40.9 (28.9-56.5)

Continuous variables are reported as median (interquartile range), categorical variables as number (percentage)

h = hour; mg = milli-gravitational units; SD = standard deviation

^aNumber of portions reported per day

^bNumber of portions reported per week

^cTo allow for differences in the duration of sleep, we conducted sensitivity analyses assessing the impact of the average acceleration and timing of the least active 6 h rather than 8 h

Table S1: Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity with risk of COVID-19.

Variable	Unadjusted		Adjusted					
	^a Model 1		^b Model 2		^a Model 1		^b Model 2	
	severe COVID-19 (UK Biobank cohort as comparator)		positive test for COVID-19 (negative test result as comparator)		severe COVID-19 (UK Biobank cohort as comparator)		positive test for COVID-19 (negative test result as comparator)	
	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value
Physical activity								
Overall physical activity	0.83 (0.69, 1.01)	.06	1.08 (0.94, 1.25)	.28	0.85 (0.70, 1.04)	.11	0.93 (0.79, 1.09)	.40
Moderate to vigorous PA	0.81 (0.66, 0.99)	.04	1.11 (0.96, 1.28)	.17	0.81 (0.66, 1.01)	.06	1.00 (0.84, 1.18)	.98
^cActivity and rest								
^d Activity during waking hours (16 h)	0.81 (0.66, 0.98)	.03	1.06 (0.92, 1.23)	.39	0.75 (0.61, 0.93)	.01	0.88 (0.74, 1.05)	.15
^d Movement during sleep/rest (L8 h)	1.21 (1.09, 1.34)	<.001	1.20 (1.08, 1.34)	<.001	1.26 (1.12, 1.42)	<.001	1.14 (1.00, 1.30)	.04
Balance between activity and sleep/rest	0.68 (0.60, 0.77)	<.001	0.87 (0.77, 0.98)	.02	0.71 (0.62, 0.81)	<.001	0.86 (0.75, 0.98)	.03
^{c,e}Variability in timing of activity and rest								
Variability in timing of activity	1.21 (1.10, 1.33)	.001	1.24 (1.11, 1.37)	<.001	1.18 (1.07, 1.31)	.001	1.18 (1.05, 1.32)	.006
Variability in timing of sleep/rest	1.20 (1.09, 1.32)	.002	1.27 (1.13, 1.41)	<.001	1.18 (1.06, 1.31)	.002	1.18 (1.04, 1.33)	.007
Variability in sleep/rest mid-point	1.23 (1.11, 1.36)	.001	1.25 (1.13, 1.39)	<.001	1.21 (1.08, 1.35)	.001	1.17 (1.04, 1.35)	.003

^a Adjusted analysis adjusted for: adjusted for age, sex and ethnicity

^b Adjusted analysis adjusted for: age, sex, ethnicity, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications

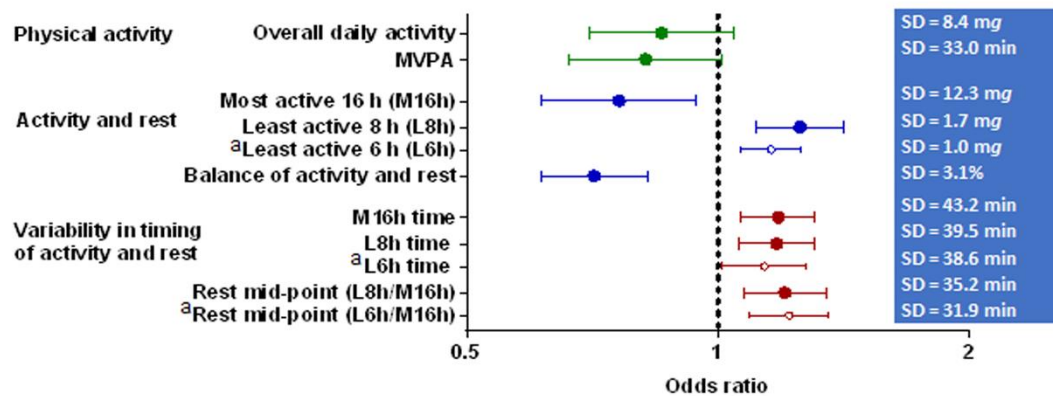
^c Adjusted analysis: In addition, adjusted for sleep duration

^d Adjusted analysis: In addition, mutually adjusted for each other

^e Adjusted analysis: In addition, adjusted for overall physical activity

Odds ratios expressed per standard deviation of each variable

a) Model 1



b) Model 2

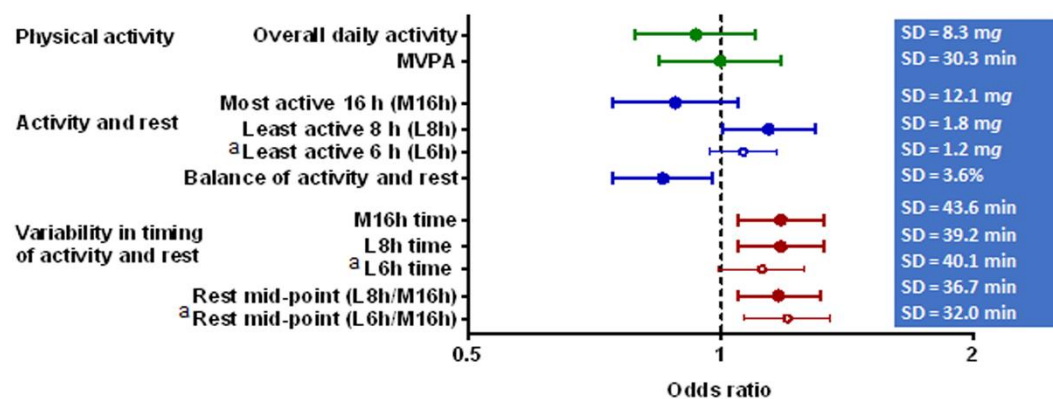


Fig 1. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity: a) Model 1. Severe COVID-19 (UK Biobank cohort as comparator); and b) Model 2. Positive test for COVID-19 (negative test result as comparator). Odds ratios expressed per SD of each variable. OR = odds ratio; SD = standard deviation.

Model 2 adjusted for age, sex, ethnicity, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications. Model 1 adjusted for age, sex and ethnicity due to the smaller number of outcome events. Activity during waking hours and movement during sleep/rest mutually adjusted. 'Activity & sleep/rest' and 'Variability in timing of activity and sleep/rest' variables additionally adjusted for sleep duration. 'Variability in timing of activity and sleep/rest' additionally adjusted for overall physical activity.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

a) Model 1 - comparator group = all non-severe COVID (includes those not tested, those testing negative, those testing positive but not classed as severe)

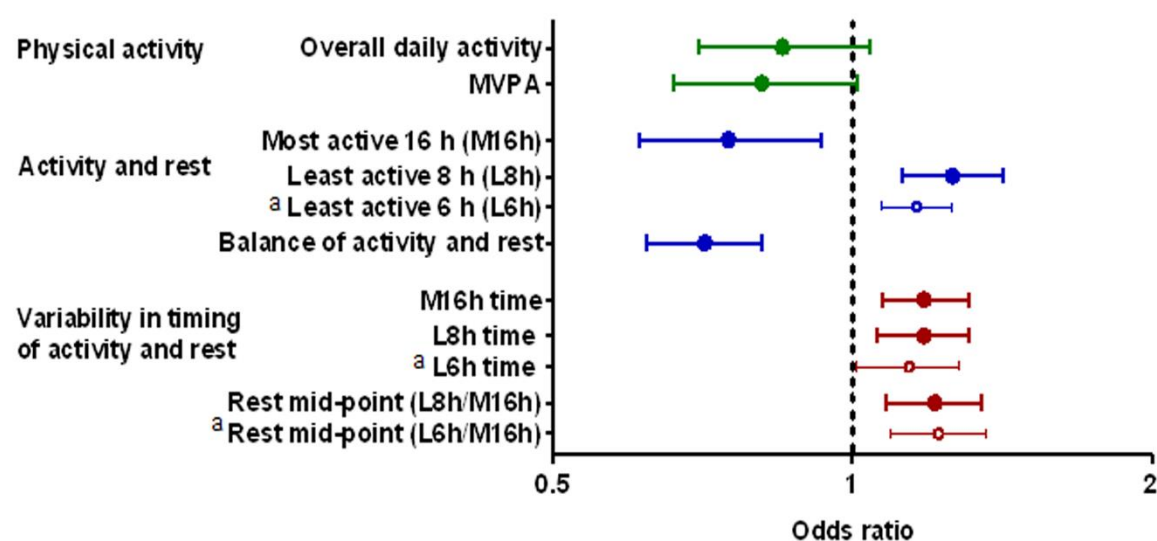
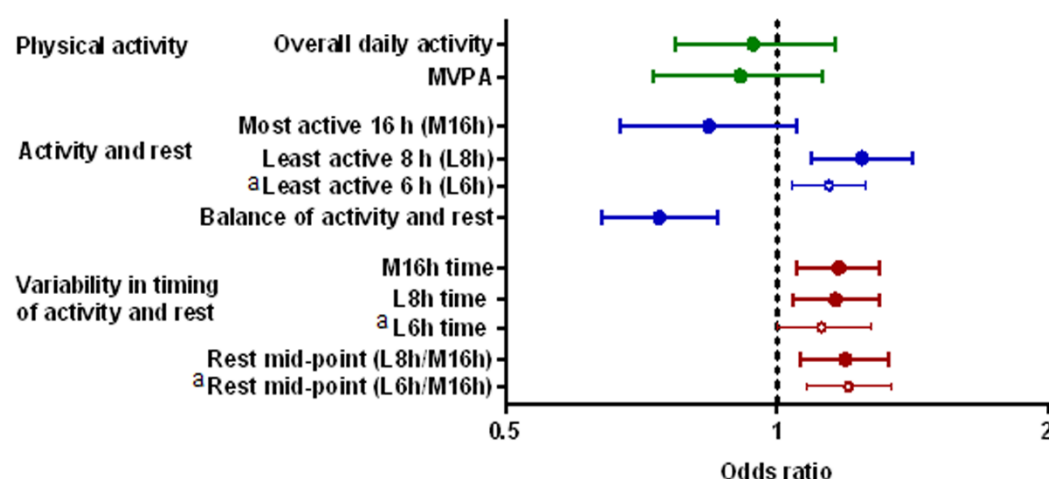


Fig S1. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity. Risk of severe COVID-19 (UK Biobank cohort as comparator group, sensitivity analysis with positive test result in the community assumed to be non-severe and added to the comparator group); Odds ratios expressed per standard deviation of each variable. OR = odds ratio.

Adjusted for age, sex and ethnicity. Activity during waking hours and movement during sleep/rest mutually adjusted. 'Activity & sleep/rest' and 'Variability in timing of activity and sleep/rest' variables additionally adjusted for sleep duration. 'Variability in timing of activity and sleep/rest' additionally adjusted for overall physical activity.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

a) Model 1 - further adjusted for BMI and number of cancer and non-cancer illnesses



b) Model 2 - further adjusted for BMI

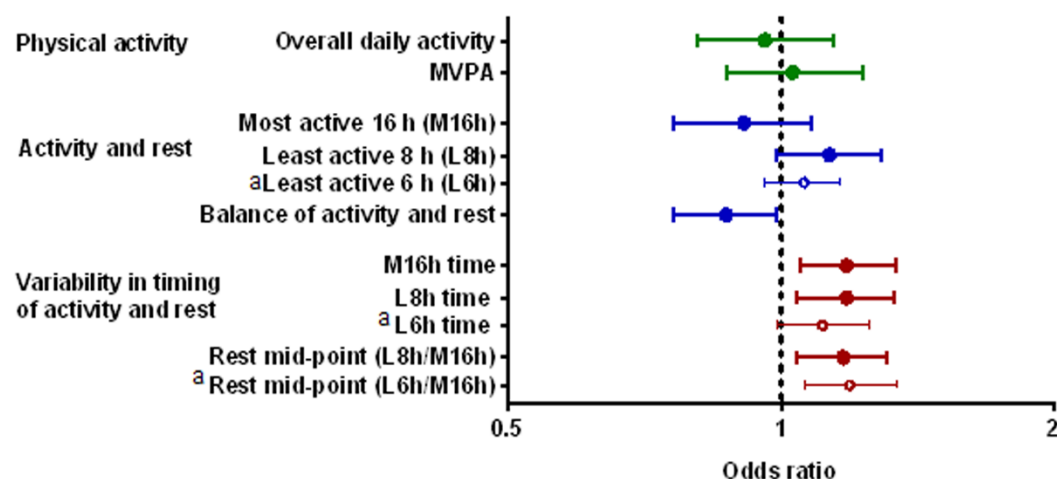
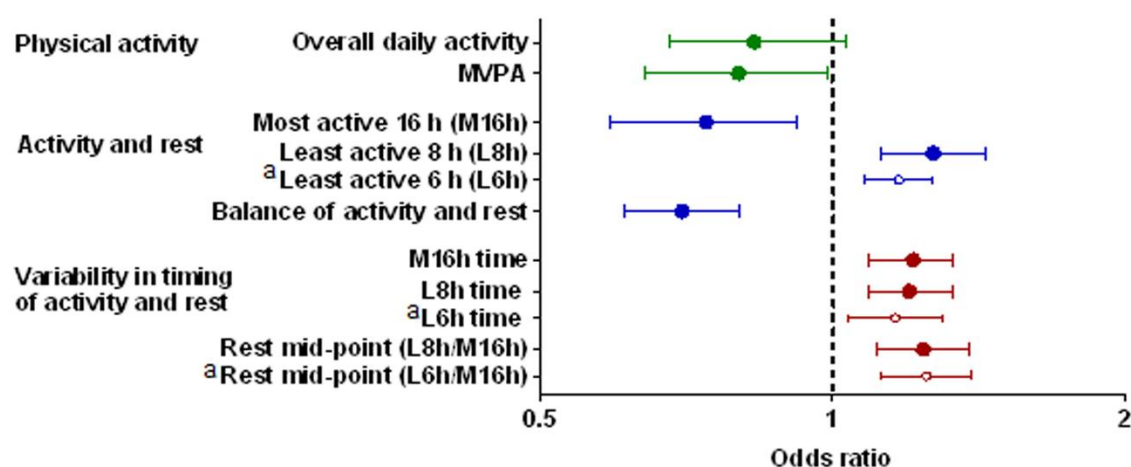


Fig S2. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity further adjusted for BMI and underlying health conditions (model 1) and BMI (model 2): a) Model 1. Severe COVID-19 (UK Biobank cohort as comparator); and b) Model 2. Positive test for COVID-19 (negative test result as comparator). Odds ratios expressed per SD of each variable. OR = odds ratio; SD = standard deviation.

Model 2 adjusted for age, sex, ethnicity, BMI, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications. Model 1 adjusted for age, sex, ethnicity, BMI, number of cancer and non-cancer illnesses. Activity during waking hours and movement during sleep/rest mutually adjusted. 'Activity & sleep/rest' and 'Variability in timing of activity and sleep/rest' variables additionally adjusted for sleep duration. 'Variability in timing of activity and sleep/rest' additionally adjusted for overall physical activity. BMI = body mass index.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).

a) Model 1 - excluding health-workers



b) Model 2 - excluding health-workers

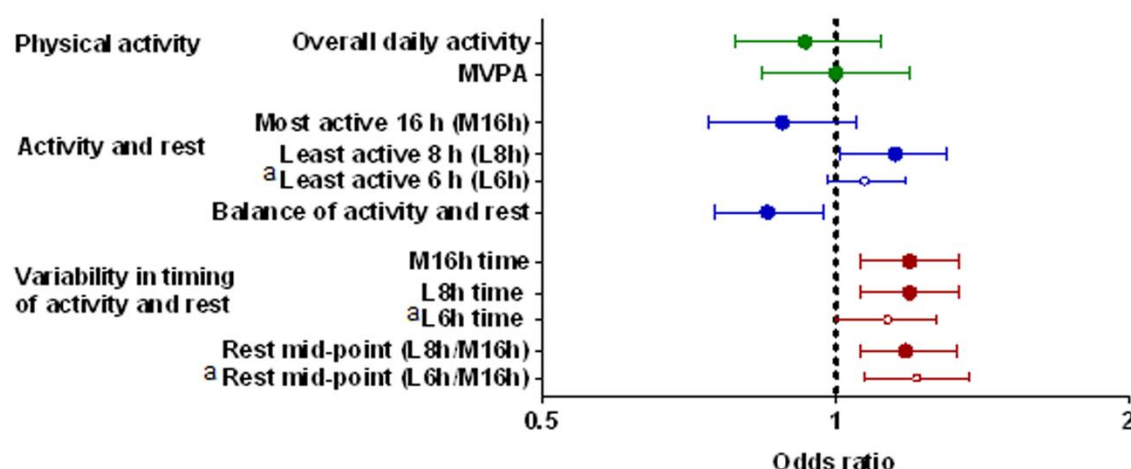


Fig S3. Association of physical activity, the balance between activity and sleep/rest, and variability in the timing of sleep/rest and activity excluding healthcare workers: a) Model 1. Severe COVID-19 (UK Biobank cohort as comparator); and b) Model 2. Positive test for COVID-19 (negative test result as comparator). Odds ratios expressed per SD of each variable. OR = odds ratio; SD = standard deviation.

Model 2 adjusted for age, sex, ethnicity, Townsend Deprivation Index, number of people in household, fruit/vegetable consumption, red meat consumption, smoking status, alcohol intake, number of self-reported cancers & non-cancer illnesses, and number of treatments/medications. Model 1 adjusted for age, sex and ethnicity. Activity during waking hours and movement during sleep/rest mutually adjusted. 'Activity & sleep/rest' and 'Variability in timing of activity and sleep/rest' variables additionally adjusted for sleep duration. 'Variability in timing of activity and sleep/rest' additionally adjusted for overall physical activity. BMI = body mass index.

^a Sensitivity analyses using the least active 6 hours rather than 8 hours (open circles).