Sleep Health: Journal of the National Sleep Foundation 9 (2023) 801–820

Contents lists available at ScienceDirect

Sleep Health: Journal of the National Sleep Foundation

journal homepage: www.sleephealthjournal.org

The importance of sleep regularity: a consensus statement of the National Sleep Foundation sleep timing and variability panel

Tracey L. Sletten, PhD [a,1], Matthew D. Weaver, PhD [b,c,1], Russell G. Foster, PhD, FRS [d], David Gozal, MD, MBA, PhD (Hon) [e], Elizabeth B. Klerman, MD, PhD [b,c,f], Shantha M.W. Rajaratnam, PhD [a,b,c], Till Roenneberg, PhD [g], Joseph S. Takahashi, PhD [h,i], Fred W. Turek, PhD [j], Michael V. Vitiello, PhD [k], Michael W. Young, PhD [l], Charles A. Czeisler, PhD, MD, FRCP [b,c,*]

[a] Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Clayton, Victoria, Australia
[b] Division of Sleep and Circadian Disorders, Departments of Medicine and Neurology, Brigham and Women's Hospital, Boston, Massachusetts, USA
[c] Division of Sleep Medicine, Harvard Medical School, Boston, Massachusetts, USA
[d] Sleep & Circadian Neuroscience Institute, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK
[e] Joan C. Edwards School of Medicine, Marshall University, Huntington, West Virginia, USA
[f] Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts, USA
[g] Institutes for Occupational, Social, and Environmental Medicine and Medical Psychology, LMU Munich, Munich, Germany
[h] Department of Neuroscience, The University of Texas Southwestern Medical Center, Dallas, Texas, USA
[i] Howard Hughes Medical Institute, The University of Texas Southwestern Medical Center, Dallas, Texas, USA
[j] Center for Sleep and Circadian Biology, Department of Neurobiology, Northwestern University, Evanston, Illinois, USA
[k] Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, Washington, USA
[l] Laboratory of Genetics, The Rockefeller University, New York City, New York, USA

ARTICLE INFO

Article history:
Received 15 February 2023
Received in revised form 21 July 2023
Accepted 25 July 2023

Keywords:
Sleep patterns
Circadian misalignment
Catch-up sleep
Health
Performance

ABSTRACT

Objective: To develop and present consensus findings of the National Sleep Foundation sleep timing and variability panel regarding the impact of sleep timing variability on health and performance.
Methods: The National Sleep Foundation assembled a panel of sleep and circadian experts to evaluate the scientific evidence and conduct a formal consensus and voting procedure. A systematic literature review was conducted using the NIH National Library of Medicine PubMed database, and panelists voted on the appropriateness of 3 questions using a modified Delphi RAND/UCLA Appropriateness Method with 2 rounds of voting.
Results: The literature search and panel review identified 63 full text publications to inform consensus voting. Panelists achieved consensus on each question: (1) is daily regularity in sleep timing important for (a) health or (b) performance? and (2) when sleep is of insufficient duration during the week (or work days), is catch-up sleep on weekends (or non-work days) important for health? Based on the evidence currently available, panelists agreed to an affirmative response to all 3 questions.
Conclusions: Consistency of sleep onset and offset timing is important for health, safety, and performance. Nonetheless, when insufficient sleep is obtained during the week/work days, weekend/non-work day catch-up sleep may be beneficial.

* Corresponding author: Charles A. Czeisler PhD, MD, FRCP, Division of Sleep and Circadian Disorders, 221 Longwood Ave. 438A, Boston, MA 02115, USA.
E-mail address: charles_czeisler@hms.harvard.edu (C.A. Czeisler).
[1] Tracey L. Sletten and Matthew D. Weaver contributed equally.

https://doi.org/10.1016/j.sleh.2023.07.016
2352-7218/

Consensus statement

- Daily regularity in sleep timing is important for health.
- Daily regularity in sleep timing is important for performance.
- When sleep is of insufficient duration during the week (or work days), catch-up sleep on weekends (or non-work days) is important for health.

Introduction

Recommendations for healthy sleep behavior typically focus on the duration of sleep that is optimal for health, well-being, performance, and safety.[1,2] However, components of healthy sleep also include sleep quality, sleep timing, and sleep regularity.[3] The National Sleep Foundation (NSF) established an expert panel in 2014 to conduct a systematic review and develop recommendations for the sleep duration required for optimal health across the lifespan.[1] The NSF sleep duration recommendations derived from that review were consistent with those derived from a subsequent review conducted by the American Academy of Sleep Medicine and the Sleep Research Society.[2] Consensus panels established by the NSF have also provided comprehensive assessments on the duration of sleep associated with driving impairment[4] and on indicators of good sleep quality across the lifespan.[5] An expert review and consensus recommendation on sleep timing, however, has not been previously conducted.

Sleep regularity, or intraindividual variability in sleep timing, and its potential associations with health and performance, have generated increasing attention as key indicators of healthy sleep. Regular sleep timing at the appropriate circadian time is hypothesized to be important for optimal sleep, functioning, and health,[6] yet variability in the timing of sleep and light exposure are common in modern society.[7] While we often consider sleep timing variability to be a consequence of artificial light availability, experimental studies simulating the short photoperiod that occurs during the winter season (ie, 14 hours of darkness/sleep opportunity per day) reveal that variability in sleep latency and duration may have even occurred under such conditions (ie, with more extended darkness and opportunities for sleep) prior to the widespread availability of artificial light,[8] consistent with historical records from that era.[9] In contrast to the stability of exposure to the solar light-dark cycle in that preindustrial era, in modern society variability in the timing of sleep is typically associated with variability in the timing of exposure to light, which can induce circadian misalignment. Growing evidence indicates that circadian misalignment is associated with adverse health outcomes, including metabolic disorders such as obesity and diabetes, cardiovascular disease, immune dysfunction, cancer, and impaired mental health.[10–14] Some data have even suggested that irregular sleep timing may have a greater adverse impact on performance than insufficient sleep.[15,16] As there has been no authoritative consensus statement about the importance of sleep regularity for health, the NSF undertook the process of convening an expert panel to conduct a systematic literature review, discuss and interpret the existing evidence, and formulate consensus statements on the impact of sleep timing variability on health and performance.

Methods

Development of the questions

Societal habits tend to result in sleep deficiency; hence, approximately 70% of US adults fail to attain sufficient sleep on a regular basis.[17] Regularity in sleep duration and timing is rare in the industrialized world,[18] in which the most common pattern of irregularity is a phenomenon called social jetlag (SJL).[19] SJL occurs because societal responsibilities dictate wake times and, thereby, curtail sleep duration on work days; the accumulating sleep deficiency is compensated for by sleeping longer on non-work days.[20] Since some people work on weekends, we will use the terms work days versus non-work days. Due to individual differences (both genetic and behavioral), circadian clocks align themselves at different times with respect to the light-dark (day-night) cycle; these differences are called chronotypes and range from extreme early types (larks), who may sleep between 8 p.m. and 4 a.m., to extreme late types (owls), who may sleep between 4 a.m. and 12 p.m.[20] The broad distribution of chronotypes in industrialized populations is most probably due to changes in light exposure behavior: being exposed to much lower light levels during the day by living indoors, and using electric light after sunset. Under these weak entraining conditions (weak circadian synchronizer), extreme larks become earlier, and all other chronotypes become later in their entrained phase, resulting in a broader chronotype distribution. This has been shown in studies in which the entrained phase of participants was measured under urban (weak) and camping (strong) circadian synchronizer conditions. The SJL concept presumes that sleep-wake behavior on non-work days more faithfully represents the internal phase of different chronotypes than on work days when people interrupt their sleep at an earlier hour with alarm clocks, although social activities may lead to later bedtimes and waketimes than would be aligned with an individuals' chronotype. Thus, on non-work days, later chronotypes sleep later due to their chronotype and longer to compensate for their sleep loss during the work week (catch-up sleep).[20]

In addition, approximately one-quarter of the population in industrialized countries engages in shift work,[21] with this burden of work outside of daylight hours disproportionately falling among minoritized populations.[22] People working shift work schedules are often required to sleep at variable times—1 set of sleep times (usually during the day) when working evening or night shifts, reversion to nighttime sleep on non-work days, and frequent compensatory napping (ie, sleep times during the day). Note that SJL can be considered similar to shift work—working and sleeping on a day shift on work days, which is misaligned with the individual's biological circadian time, and sleeping at later times that are aligned with the individual's circadian time on non-work days. In both cases (shift work and SJL), maximizing sleep duration on non-work days induces less sleep regularity.

Therefore, the literature was reviewed, seeking to answer the following questions.

1a. Is daily regularity in sleep timing important for health?

1b. Is daily regularity in sleep timing important for performance?

2. When sleep is of insufficient duration during the week, is weekend catch-up sleep (WCS) on weekends important for health?

Initially, the following preamble was included for questions 1 and 2: "presuming that sleep is of sufficient duration and at the appropriate biological time." After a subsequent review, the panel revised the question to remove the preamble based on the panel consensus that the available evidence was insufficient to include it. After the preamble was removed, all panel members were provided the opportunity to change their agreement assessment. No changes to the original agreement occurred.

All committee members agreed that the preferred language in this review would be "work days" and "non-work days." This wording is used throughout the manuscript, unless referencing specific nomenclature used in the source article.

Participants and procedures

The NSF assembled a 12-member panel of sleep and circadian experts with scientific and clinical expertise. A systematic review of peer-reviewed original research and systematic literature reviews in the English language was performed using the National Institutes of

Health National Library of Medicine PubMed database. Search terms were agreed upon by the panel (Supplementary Table 1). Exposure terms included MeSH terms and free text terms in the title or abstract related to sleep timing (eg, sleep timing variability, napping, and sleep patterns). Outcome terms included at least 1 sleep, health, safety, or performance outcome (eg, metabolism, cardiovascular, and mental health). Because the objective was to define sleep timing and variability in populations without sleep disorders, we excluded studies of obstructive sleep apnea, insomnia, restless legs syndrome, and narcolepsy. The search was executed on May 20, 2020, without publication date restrictions. Search results were imported to Rayyan software for review.[23]

A team of 8 postdoctoral fellows and junior faculty members reviewed titles and abstracts for inclusion or exclusion. Inclusion criteria were: (a) population without disorders, (b) published in a peer-reviewed journal, (c) human subjects, and (d) English language. It was not feasible for multiple raters to evaluate each potential paper due to the volume of potentially relevant publications. Articles were categorized based on exposure type (eg, sleep timing variability and sleep duration variability) to ensure full-length manuscripts specifically sought to evaluate sleep timing and sleep variability. Full-length texts with exposure types identified as sleep timing variability, sleep regularity, sleep duration variability, circadian misalignment, social jetlag, or catch-up sleep were extracted for further review. Articles related to napping were not included in the full text review subsequent to the initial search to maintain focus on the timing and variability of the primary nocturnal sleep episode. As the impact of polyphasic sleep patterns on health was previously reviewed by the panel,[24] and multiple systematic reviews have evaluated the impact of shift work on health and safety,[14,25–27] articles related to polyphasic sleep and shift work were excluded from this analysis, although statements summarizing those reviews are included in the discussion of this report.

Panel deliberations and consensus voting

Two panel members performed the extraction of the full text articles and independently summarized pertinent study information (eg, sample size, study design, and results) in a tabular format. Each study was discussed, and edits were made in tandem to ensure accuracy. Tables and full text articles were distributed to all panelists to review and confirm extracted information and present to the panel. Panel members assessed the quality of each study, including the risk of bias, using the U.S. Preventive Services Task Force quality ratings that provide a standardized metric of study design and implementation.[28] The size of the cohorts, the number of centers involved in the research, long-term outcomes, statistical tests, and covariates used in statistical adjustments were considered when assigning the rating. All studies were classified as levels I, II-1, II-2, II-3, or III (descriptions of each level in Table 1). Panelists reviewed the scientific literature, discussed scientific evidence, and determined final inclusion decisions for each manuscript during 15 meetings over a 4-month interval.

A modified Delphi RAND Corporation/University of California, Los Angeles Appropriateness Method[29] was applied to develop the consensus statements. Panelists voted via an anonymous electronic survey on the appropriateness of the question on a scale of 1 ("extremely inappropriate") to 9 ("extremely appropriate"). The first round of voting occurred independently. The second round of voting occurred during a virtual meeting. At the virtual meeting, panelists reviewed the overall panel ratings from the first round of voting and discussed the literature. Consensus recommendations were identified as appropriate (median of 7-9), uncertain (median of 4-6), or inappropriate (median of 1-3). An agreement was defined by at least 80% of votes within any of the 3-point ranges. All 12 panel members contributed meaningfully to the development of the research questions and drafting of the final manuscript, and 11 of the 12 panelists voted due to the unavailability of 1 member at the time of voting.

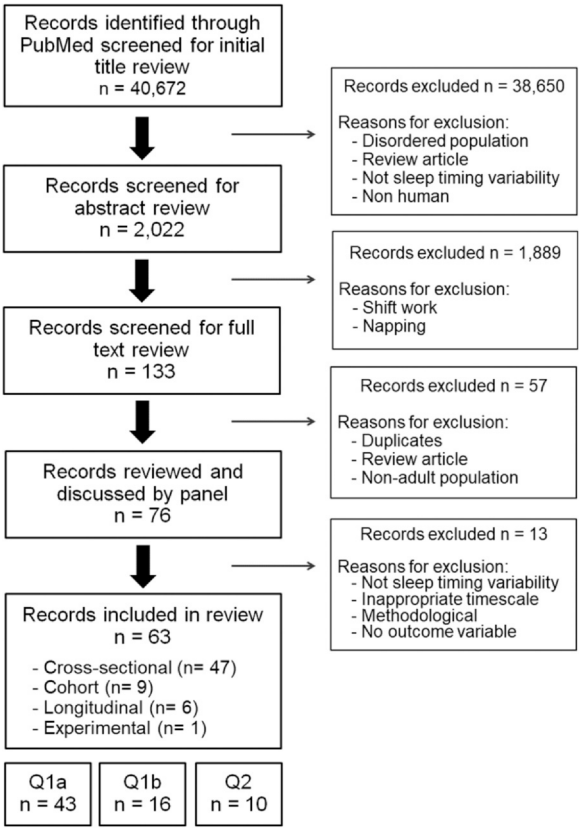

Fig. 1. Flowchart of results from the literature search.

Results

Literature review

The search identified 40,672 potentially relevant publications. After a review of titles, 2022 articles remained. After refining the criteria to exposures directly related to timing and variability of the primary nocturnal sleep episode, 76 articles were identified for full text review, and 63 were ultimately included by the panel. A flowchart of the literature search results is presented in Fig. 1.

Table 1
U.S. Preventive Services Task Force quality ratings[28]

Level	Description
I	Evidence obtained from at least 1 properly designed randomized controlled trial
II-1	Evidence obtained from well-designed controlled trials without randomization
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than 1 center or research group
II-3	Evidence obtained from multiple time series with or without the intervention; dramatic results in uncontrolled trials might also be regarded as this type of evidence
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

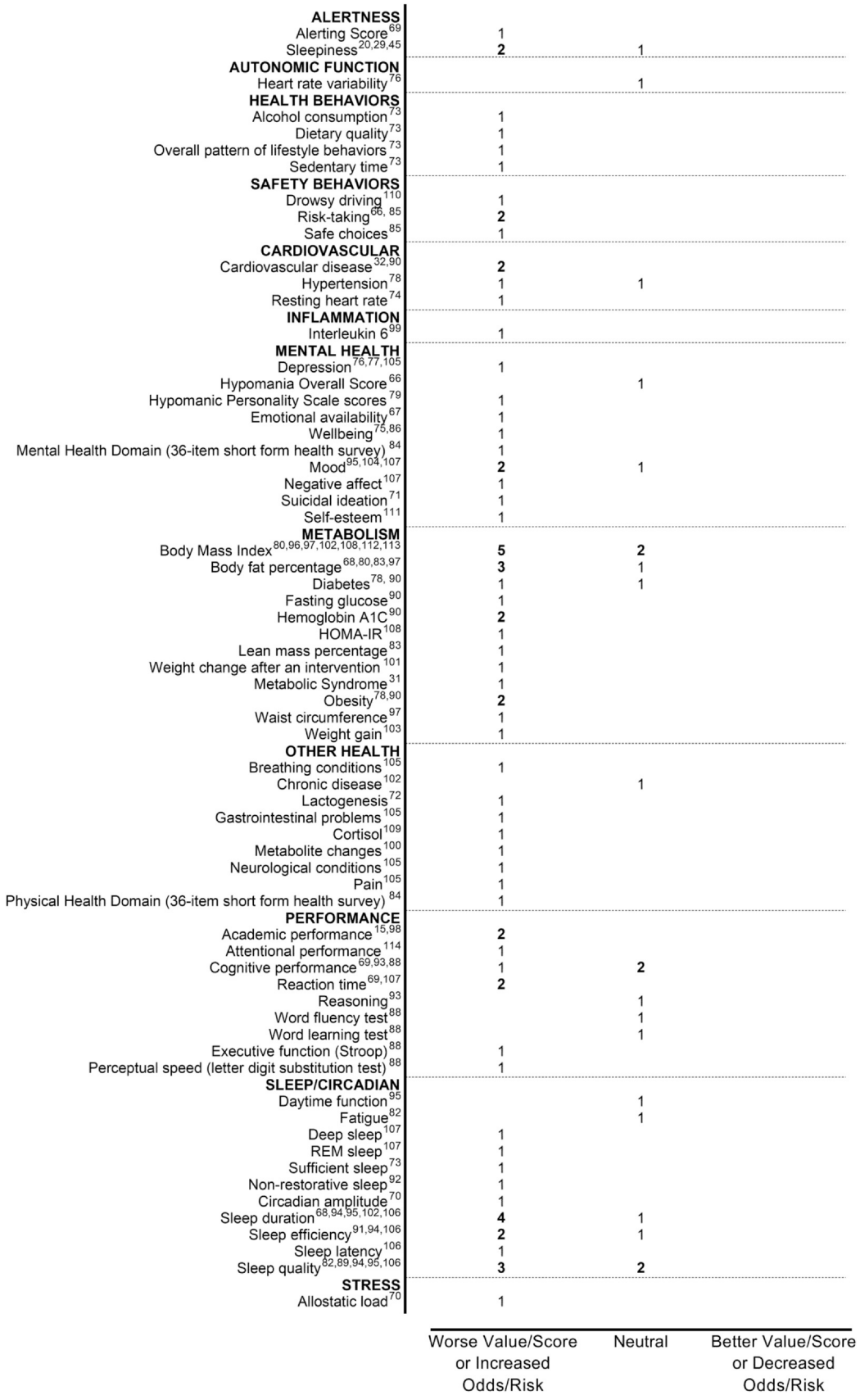

Fig. 2. Summary of associations between sleep timing variability, and health and performance outcomes measured. Numbers indicate the total number of publications in each category. The allostatic load was operationalized as multisystem physiological dysregulation based on 23 biomarkers. HOMA-IR, homeostatic model assessment of insulin resistance.

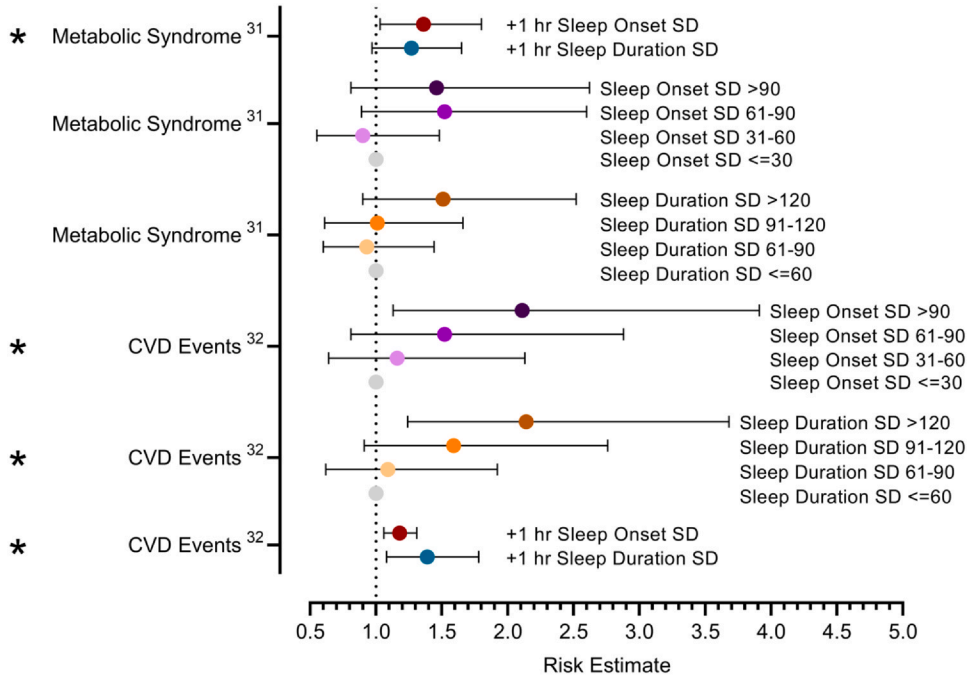

Fig. 3. Summary of findings from 2 of the prospective studies[31,32] with objective sleep assessments and incident, objective outcome assessment. Asterisks indicate statistical significance. CVD, cardiovascular disease; SD, standard deviation of the metric.

The majority of the studies (n = 47) used an observational cross-sectional design. There was substantial variability in the method used to quantify sleep timing variability. Studies implemented the sleep regularity index (SRI), the standard deviation (SD) of total sleep duration, the SD of midpoint sleep time (ie, the time midway between sleep onset and offset times), interdaily stability of sleep-wake times, the sleep timing questionnaire (STQ), and other measures. Studies relevant to question 3 (ie, weekend/non-work day catch-up sleep) were categorized separately; those studies most often characterized the difference between work day and non-work day sleep times or sleep duration.

The most common research outcomes were mood or mental health (n = 15), metabolic outcomes (n = 12), sleep and circadian

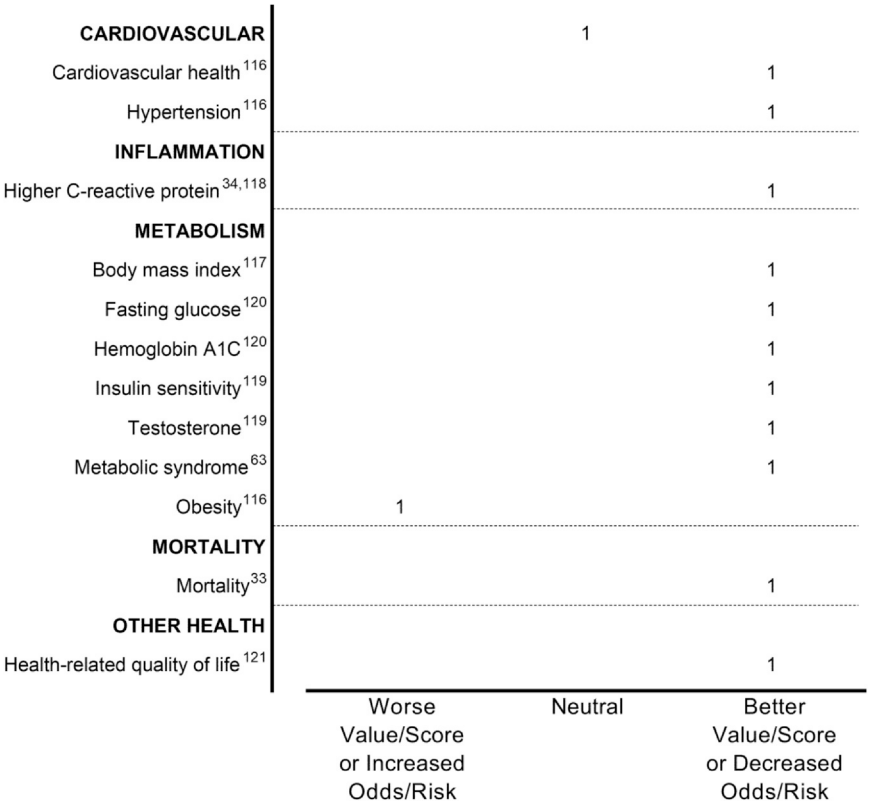

Fig. 4. Summary of associations between catch-up sleep and health outcomes measured. Numbers indicate the total number of publications in each category.

Table 2
Summary of evidence informing panel recommendations for question 1

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Bae et al. 2014[66]	Cross-sectional	313	61	33.5 ± 9.2	Variability of bed and rise times on weekdays and weekend (sleep timing questionnaire [STQ]) Circadian preference (Composite Scale of Morningness)	Lifetime history of hypomanic symptoms with the Hypomania Checklist-32.	Irregularity of sleep-wake times and evening preference was associated with "irritable/risk-taking" factor score.	III
Bai et al. 2020[67]	Longitudinal	142	100	29.7 ± 5.2	Standard deviation (SD) of bedtime and wake time over 7 days of sleep diaries in mothers (at infant ages 1, 3, and 6 months)	Maternal emotional availability	Mothers with irregular sleep patterns, especially later average bedtimes and greater variability in sleep period across the 3 age points showed poorer parenting quality with infants at bedtime	III
Bailey et al. 2014[68]	Cross-sectional	330	100	20.2 ± 1.5	Sleep duration variability Bedtime variability Wake time variability	Metabolism: body fat percentage, body mass index (BMI), sleep duration, sleep efficiency, and physical activity	Sleep duration and wake time variability were associated with increased body fat% and reduced sleep duration. Sleep variability, most strongly wake time inconsistency, was the most important predictor of body fat percentage.	II-3
Barclay et al. 2020[69]	Cross-sectional	57	61.4	32.4 ± 8.7	Sleep duration variability: within-participant SD in sleep duration across 7 nights.	Alertness: attention network test	Sleep duration variability did not predict orienting score, executive control score, or error rates. Sleep duration variability moderated the association between sleep duration, reaction time, and alerting scores.	II-3
Bei et al. 2017[70]	Prospective cohort	436	60.3	54.1 ± 11.7	Sleep duration variability Bedtime variability Wake time variability intraindividual variability (IIV; day-to-day variability)	Health: cortisol, allostatic load	Sleep timing variability was associated with a flatter cortisol diurnal rhythm and a higher allostatic load, as measured by blood pressure, blood glucose, cortisol, C-reactive protein, interleukin 6, fibrinogen, lipids, heart rate variability, and several other measures.	II-3
Bernert et al. 2017[71]	Prospective cohort	50	72	19.2 ± 1.4	SD of 7-day actigraphic daily sleep onsets and offsets, summed for an overall index of sleep variability. (at baseline, 7 days, and 21 days)	Beck scale for suicide ideation. Pierce suicidal intent scale.	Variability in sleep timing predicted increases in suicidal ideation from 7- to 21-day follow-up. Sleep variability outperformed depressive symptoms in longitudinal prediction of suicidal ideation.	II-2
Buman et al. 2016[30]	Cross-sectional evaluation during a 3-week baseline	20	15	50 ± 9	Strength of circadian periodicity (in overweight or obese US Veterans patients)	Cardiometabolic measures and health-related quality of life (HRQoL)	Circadian periodicity was associated with low-density lipoprotein cholesterol, triglycerides, C-reactive protein, and HRQoL.	II-3
Casey et al. 2019[72]	Cohort	50	100	18-40 (median 23)	Night-to-night variability (NNV): Root mean square of successive differences (SD) in sleep start and end time. In primiparous women: gestational weeks 22 and 32.	Pregnancy health: blood glucose levels, BMI, and gestational disease data from medical charts. Timing of lactogenesis II determined by survey.	Women with greater NNV in sleep start and end time, efficiency, and duration during gestation week 32 had delayed lactogenesis II	II-2

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Duncan et al. 2016[73]	Prospective cross-sectional	1317	52	Median 57 (interquartile range = 20)	Self-report variability in bedtimes and wake times on weekdays and weekends (usual timing) (STQ)	Behaviors: self-report dietary quality, physical activity, alcohol consumption, sitting time, sleep insufficiency, and sociodemographics	Bedtimes that varied by > 30 min associated with lower dietary quality, higher alcohol consumption, higher sitting time, more frequent insufficient sleep, and poorer overall pattern of lifestyle behaviors. Greater variability in wake times, usual bedtimes, and usual wake times were inconsistently associated with lifestyle behaviors.	III
Faust et al. 2020[74]	Prospective cohort	698	40.1	17.9 ± 0.5	Bedtime variability	Cardiovascular: resting heart rate variability	Going to bed even 30 min later than one's usual bedtime resulted in significantly higher resting heart rate throughout sleep and the next day. Bedtimes of at least 1 h earlier were also associated with earlier resting HR throughout sleep but converge with normal heart rate by end of sleep.	II-3
Fischer et al. 2020[75]	Cross-sectional	223	37	19.4 ± 1.5	Composite phase deviation: combines sleep irregularity and sleep mistiming by quantifying: (i) how different the midsleep times are compared to those on the previous day and (ii) how far away midsleep times occur from an individual's preferred sleep timing (chronotype, as measured by midsleep time on weekends (actigraphy)	Self-rated well-being daily on 5 scales: sleepy-alert, sad-happy, sluggish-energetic, sick-healthy, and stressed-calm.	Composite phase deviation for sleep was a significant predictor of average well-being (eg, stressed-calm). Poorest well-being was reported by students for whom both sleep and event schedules were mistimed and irregular.	II-3
Gao et al. 2019[76]	Cross-sectional	42	52.4	22.7 ± 2.7	Interdaily stability of sleep-wake (ISSW) times(weekly sleep-wake regularity from sleep-wake diaries and continuous electrocardiogram) Autonomic function: high-frequency (HF) power	Mood: Weekly Beck Depression Inventory (BDI)-II	Low weekly ISSW predicted subsequent poor mood and worsening mood independently of age, sex, race, sleep duration, and physical activity. No association between ISSW and HF. ISSW-mood association was significantly moderated by nocturnal HF, that is, reported mood was lowest after a week with low ISSW and high HF. After Irregular Weeks with HF-high during sleep, students reported significantly higher BDI and ΔBDI than regular weeks	II-2
Han and Kim, 2020[77]	Cross-sectional	3075	38.7	~19-70 Divided into 10y groups	Sleep duration variability—weekend compared to weekday "When do you usually sleep?"Variance of sleep duration = (weekend duration − weekday duration)/weekday duration × 100. (from a survey question on usual sleep and wake times) Categorized sleep variance into 3 groups based on the degree of the positive and negative values: decreased, increased ≤20%, and increased ≥21%.	Mental health: Depressive symptoms (patient health questionnaire; PHQ-9)	Positive association between sleep duration variance and PHQ-9. Variance in sleep duration affected health regardless of the direction of the change (positive: increased sleep or negative: decreased sleep). Decrease in sleep duration and increase of > 20% in weekends versus weekdays were associated with higher PHQ-9 scores than those who had remained the same sleep duration or with < 20% of increase in sleep duration in weekend.	II-2

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Hausler et al. 2020[78]	Cross-sectional	2598	Presented separately for disorder groups	Middle- to older-age. Ages provided split between disorder groups	Several measures of sleep duration variability from 14 days actigraphy (ie, NNV, range between shortest and longest sleep duration, and range between average weekday and weekend sleep duration)	Cardiometabolic: cardiovascular risk factors including obesity, diabetes, and hypertension.	Subjects with highest sleep duration variability - measured as NNV, range between shortest and longest sleep duration, and range between average weekday and weekend sleep duration were more likely to be obese. These associations robust in most but not all sensitivity analyses, and no associations between sleep duration variability measures and diabetes or hypertension were found.	II-2
Hensch et al. 2019[79]	Cross-sectional	771 (actigraphy) 1766 (Pittsburgh sleep quality index [PSQI])	48.2 (actigraphy) 47.3 (PSQI)	M = 70.3 (actigraphy) M = 69.6 (PSQI)	7-day actigraphy: NNV in sleep onset and offset time (and duration). Operationalized by intraindividual SD across a single subject's multiple nights.	Mental health: hypomanic personality scale as measure of vulnerability to bipolar disorder	Higher hypomanic personality scale scores associated with greater intraindividual sleep variability (sleep onset time), more disturbed sleep, and more daytime sleepiness. Core hypomanic features were especially associated with self-reported sleep impairments.	II-3
Hooker et al. 2020[80]	Cross-sectional correlation	103	64	26.7 ± 7	Day-to-day SD in midsleep time	Behaviors and body composition	Variations in activity, caloric intake, and sleep were unrelated.	II-2
Huang and Redline, 2019[31]	Cross-sectional	2003	50-57 mean (presented separately for categories of sleep regularity)	69-79 mean (presented separately for categories of sleep regularity)	7-day actigraphy at exam 5 and were prospectively followed throughout exam 6. Sleep regularity was quantified by the 7-day SD of actigraphy-assessed sleep duration and sleep onset timing.	Metabolic abnormalities defined by: 1) the National Cholesterol Education Program Adult Treatment Panel III criteria and 2) a data-driven clustering of metabolic factors.	Every 1-h increase in the sleep duration SD was associated with 27% higher odds of metabolic syndrome Every 1-h increase in the sleep timing SD was associated with 23% higher odds of metabolic syndrome. Remained significant with additional adjustment for sleep-related factors including sleep duration. In the prospective analysis (n = 970), the corresponding fully adjusted odds ratio (OR) was 1.27 for sleep duration and 1.36 for sleep timing. Compared with the cluster of few metabolic changes, every 1-h increase in sleep variability was associated with almost doubled odds for the cluster characterized by incidence of multiple metabolic abnormalities (OR 1.97 for sleep duration and OR 2.10 for sleep timing).	II-2
Huang et al. 2020[32]	Longitudinal	1992	53-55 across groups	Sleep duration SD: < 90 min 69.1 ± 9, > =90 min 69.4 ± 9.5, sleep onset timing: < 90 min 69.4 ± 9.1, > 90 min 68.8 ± 9.60	SD of 7-days sleep duration and sleep onset timing (actigraphy).	Cardiovascular: Fatal or nonfatal cardiovascular disease (CVD) event	CVD across categories of sleep duration SD were 1.00 (reference) for < =60 min, 1.09 (0.62-1.92) for 61-90 min, 1.59 (0.91-2.76) for 91-120 min, and 2.14 (1.24-3.68) for > 120 min. Similarly, compared with participants with a sleep timing SD < = 30 min, the hazard ratios (95% confidence intervals) for CVD were 1.16 (0.64-2.13) for 31-60 min, 1.52 (0.81-2.88) for 61-90 min, and 2.11 (1.13-3.91) for > 90 min Compared with sleep-onset timing SD ≤ 30 min, the hazard ratios for CVD after adjusting for CVD risk factors and sleep-related factors were 1.16 for 31-60 min, 1.52 for 61-90 min, and 2.11 for > 90 min, with 18% higher risk for every 1-h increase in sleep-onset timing SD.	II-2

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Hysing et al. 2015[81]	Cross-sectional	10,220	53.3	17.9 ± 0.8	Bedtime difference (weekdays/weekends) > 2 h	Behaviors: frequency of self-harm	Large differences in sleep timing between weekdays and weekends were associated with increased frequency of self-harm.	III
Kang and Chen, 2009[82]	Cross-sectional	160	49.4	20.3 ± 1.9	Subjective rating of irregular bedtime frequency, grouped as low, medium, high based on 2-week sleep log.	Alertness: sleep quality (PSQI) Daytime sleepiness (Epworth sleepiness scale) Fatigue (fatigue severity scale)	Increase in bedtime schedule irregularity associated with decrease in average sleep time/day. Irregular bedtime frequency and average sleep time per day were correlated with PSQI scores but not with Epworth sleepiness scale or fatigue severity scale scores. A significant positive correlation between irregular bedtime frequency and PSQI scores was evident in the intermediate and HF groups as compared to low-frequency group.	III
Kim et al. 2015[83]	Cross-sectional	191	100	83.4 ± 2.6	Night-to-night sleep pattern variability across all nights of recording was assessed using SDs. Sleep and physical activity were monitored via accelerometer (ActiGraph GT3X+) during at least 5 consecutive 24-h periods.	Metabolism: Body composition using dual-energy X-ray absorptiometry.	Bedtime variability range: 4-129 min (mean 32 min). Night-to-night bedtime, sleep duration, and sleep timing midpoint variability correlated with percentage body fat and percentage lean mass. Significant associations of night-to-night bedtime variations and inconsistent sleep-wake patterns with all body composition indices (adjusted for mean nightly sleep duration, self-reported nap duration, and daily physical activity).	II-2
Kimura et al. 2000[84]	Cross-sectional	299	50.8	20-60+	Single question, generally regular versus not regular.	Physical health: self-administered questionnaires using the SF-36 and questions on lifestyle	Regular sleep showed the highest significance in MANCOVA of 8 domains. Drinking alcohol and regular sleep was closely related to physical health status. In the mental component summary and related domains, the important factors were regularity of sleep, not living alone, eating breakfast, interest in art, and drinking alcohol.	III
Lau et al. 2019[85]	Longitudinal	201 (baseline n)	63.2	20.1 ± 1.5	Sleep timing variability: SD of sleep onset time, wakeup time, and midsleep time (average of bedtime and wakeup time) during the 5/6 nights at T1/T2 before the assessment session on days 6/7.	Behaviors: risk-related decision-making measured in-vivo by the risky gains task (RGT)	Variable sleep timing was cross-sectionally correlated with making more risky choices at baseline and fewer safe choices after loss at follow-up.	II-3
Lemola et al. 2013[86]	Cross-sectional	441	45 (white), 27 (African American)	57.7 ± 11.8 and 54.9 ± 10.3	Sleep duration variability (actigraphy): "day-to-day variability of sleep duration was calculated as the mean referenced variation (individual SD of sleep duration across the 7 days of measurement divided by the individual average of sleep duration, coefficient of variation."	Mental health, including satisfaction, positive affect, depression, anxiety, etc.	More variable total sleep time (TST) was the most consistent predictor of lower well-being.	II-3

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Lim et al. 2012[87]	Cross-sectional	700	75	82.4 ± 7.2	Up to 11-day actigraphy to determine rest fragmentation (kRA; metric of the fragmentation of periods of sustained rest).	Alertness: performance in 5 cognitive domains	Greater fragmentation of both rest and activity was associated with lower levels of cognitive performance, and this association was independent of total amounts of rest or activity.	II-3
Luik et al. 2015[88]	Cross-sectional	1723	53.5	62 ± 9.4	Actigraphic stability and fragmentation of 24-h rhythm over 7 days (interdaily stability and intra-daily variability).	Alertness: cognitive functioning: word learning test, word fluency test, letter digit substitution task, and Stroop color word test (Stroop).	Persons with less stable 24-h rhythms and more fragmented rhythms performed worse on the letter digit substitution task and Stroop. (Tasks that draw on perceptual speed and executive functioning)	II-3
Lund et al. 2010[89]	Cross-sectional	1125	62.7	17-24	Self-reported bedtime and TST for bedtime delay on weekends and weekend oversleep.	Sleep quality: PSQI	Bedtime delay and weekend oversleep did not predict PSQI.	III
Lunsford-Avery et al. 2018[90]	Cross-sectional	1978	54	68.7 ± 9.2	Sleep regularity index (SRI)	Cardiometabolic risk (multiethnic study of atherosclerosis)	Sleep irregularity associated with delayed sleep timing, increased daytime sleep, and sleepiness and reduced light exposure. SRI independent of sleep duration. Greater sleep irregularity correlated with 10-y risk of cardiovascular disease, greater obesity, hypertension, fasting glucose, hemoglobin A1C, and diabetes status. Greater sleep irregularity was associated with increased perceived stress and depression, psychiatric factors integrally tied to cardiometabolic disease.	II-2
Manber et al. 1996[91]	Longitudinal and prospective (experimental)	39 (20 sleep only and 19 in regularity groups)	69.2	18.8 ± 1.0	SD of bedtime and wake time over 4 time points (baseline, T1, T2, follow-up)	Alertness: subjective sleepiness	Regular sleep associated with improvements in alertness and improved sleep efficiency	I
Matsumoto et al. 2017[92]	Cross-sectional	9788	78	53.6 ± 13.4	Self-report: “are your awakening and bedtime regular?”	Alertness: subjective nonrestorative sleep: "do you get adequate rest during sleep?"	Irregular sleep schedule associated with nonrestorative sleep (OR: 2.02). Numerous variables associated with nonrestorative sleep.	III
McCrae et al. 2012[93]	Cross-sectional	72	1.66% when 1 = male, 2 = female	70.2 ± 7.1	NNV in sleep time and wake time (14 days sleep diaries, within person SD over 14 days)	Alertness: processing speed (symbol digit) and reasoning (letter series)	NNV in either TST or TWT was not associated with either cognitive measure.	III
Monk et al. 2011[94]	Cross-sectional	654	44.5	74.7 ± 6.0	Stability of bedtime from the STQ, stability of rise time from STQ binary splits for the stability of bedtimes and stability of rise times, with stability defined as scoring 1 (0-15 min).	Sleep: PSQI, time in bed, time spent asleep, and sleep efficiency from STQ.	Stability in bedtimes and stability in rise times were associated with better sleep quality. For bedtime and rise time stability, the direction of effect was similar but mostly weaker.	III

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Murray et al. 2019[95]	Cross-sectional	170	53.5	29.8 ± 10.7	SRI (DSWPD patients)	Sleep timing and quality variables, daytime function, sleep-related daytime impairment, mood, and insomnia symptom severity	Higher SRI was associated with earlier sleep and longer TST but did not relate to sleep quality, daytime function, or mood outcomes. SRI mediated the effects of sleep onset time and phase angle on daytime function. Sleep quality, daytime function, or mood outcomes.	II-3
Nicholson et al. 2021[96]	Prospective cohort	307	84.7	18.9 ± 0.9	Day-to-day variability (absolute number of minutes) Weekday-to-weekend sleep duration difference, day-to-day differences, and overall SD	body weight	Weekend-to-weekday variability associated with higher BMI, greater sleep variability reported by overweight, or obese individuals	II-3
Ogilvie et al. 2016[97]	Cross-sectional	2146	53.7	68.6 ± 9.2	7-day actigraphy: NNV in sleep duration using the within person between-night SD of sleep duration and modeled in approximate quartiles (≤48, 48-70, 70-99, and 99-262)	BMI waist circumference Total body fat	Those in the highest quartile of sleep variability had a 5% higher prevalence of general obesity and a 6% higher prevalence of abdominal obesity compared to those in the lowest quartile. BMI was 1-2 units larger among those with high sleep variability relative to those who had low sleep variability. Those with high sleep variability had a waist circumference 2.5-5 cm larger and body fat 2-3 kg more than those who had low sleep variability. No significant interactions were found between sleep variability and the adiposity outcomes.	II-2
Okano et al. 2019[98]	Cross-sectional	88	51.5	Mean = 18.19	Sleep via Fitbit charge HR sleep inconsistency defined as the SD of the participant's daily sleep duration in minutes so that a larger SD indicated greater sleep inconsistency.	Academic performance: an overall score defined as the sum of 8 quizzes and 3 midterms	Greater consistency of sleep correlated with better grades. There was a significant negative correlation between sleep inconsistency and overall score, indicating that the greater inconsistency in sleep duration was associated with a lower overall score. Sleep measures accounted for nearly 25% of the variance in academic performance.	II-3
Okun et al. 2011[99]	Prospective cross-sectional	222	67	73.7 ± 7.1	Mean values and intraindividual variability in bedtime, wake time, and TST (from sleep diaries)	Inflammation: self-report caffeine and alcohol use, exercise, and daytime napping (from sleep diaries). Interleukin 6 from morning blood samples.	Greater variability in wake time and time in bed was associated with higher IL-6 among good sleepers relative to caregivers and older adults with insomnia. Good sleepers who consumed moderate amounts of alcohol had the lowest concentrations of IL-6 compared with the other 3 groups who consumed alcohol. Insomnia subjects, but not good sleepers, showed increased concentrations of IL-6 associated with caffeine use. Caregivers showed increased concentrations of TNF-α with alcohol use relative to good sleepers. Greater variability in bedtime, later wake times, and longer time in bed was associated with higher TNF-α regardless of group.	II-3

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Papandreou et al. 2019[100]	Cross-sectional	236	71.9-86.6 in each sleep group	20-65	Sleep variability: intraparticipant SD of the sleep duration. Two groups based on sleep duration and variability quintiles: "low sleep duration or variability" (1st-2nd quintile) and "high sleep duration or variability" (4th-5th quintile).	159 circulating metabolites	Ten metabolites, including acyl-carnitines, phosphatidylcholine, lyso-phosphatidylcholine, sucrose, glutamic acid, and triacylglycerol, were significantly associated with high sleep variability (4th plus 5th quintiles). The area under the curve was 0.69 and 0.63 in the multimetabolite score for high sleep duration and sleep variability, respectively. The variance in sleep duration explained by metabolites was 7%. No metabolites were selected for prediction of sleep variability (continuous).	II-3
Papandreou et al. 2020[101]	Pre-post intervention (+cross-sectional)	1986	47	65 ± 5	Accelerometry-derived sleep variability in elderly with overweight/obesity and metabolic syndrome	Changes in average weight, BMI, and waist circumference attained after 12-month interventions	The adjusted difference in 12-month changes in weight and BMI in participants in the third tertile of sleep variability was 0.5 kg and 0.2 kg/m2, respectively, as compared with participants in the first tertile.	II-2
Paterson et al. 2018[102]	Cross-sectional	311	49.8	Over 64 years. Frequencies provided in categories of age	Regularity of bed and rise time: "in the last 7 days, how much did your sleep and wake times vary from day to day?" (categorical responses selected)	Sleep duration calculated from participants' recall of bed and rise times in the 24 h preceding survey administration	Sleep schedules with variability in bed and rise times of > 60 min were associated with increased odds of reporting sleep duration below 7 h per night.	III
Phillips et al. 2017[16]	Cross-sectional	61	47.5	20.2 ± 1.3	SRI (30 days sleep diaries) Most and least regular quintiles	Academic performance (self-reported GPA) Circadian phase (salivary DLMO) Light exposure patterns	DLMO occurred later; the daily sleep propensity rhythm peaked later; and light rhythms had lower amplitude in irregular compared to regular sleepers. A mathematical model showed irregular versus regular group differences in circadian timing were likely primarily due to their different patterns of light exposure. A positive correlation between academic performance and SRI.	III
Roane et al. 2015[103]	Cross-sectional	132	54	18.6 ± 0.4	Mean and variability scores for sleep duration (TST, TSTv), bedtime (BT, BTv), and wake time (WT, WTv) (9 weeks actigraphy).	Metabolism: MEQ (chronotype) and CES-D (depressed mood) at week 9, and self-reported weight/height (weeks 1 and 9).	A sex-by-TSTv interaction was found. Ethnicity, TST, TSTv, and BTv accounted for 31% of the variance in weight change for males; TSTv was the most significant contributor.	II-2
Sano et al. 2015[104]	Cross-sectional	68	27.9	20.1 ± 1.5	Sleep regularity in last 1-5 days (SRI). Value of 0-1 using cross correlation of sleep/wake episodes	Mood evaluated using visual nonnumeric scales (later scored as 0: sad, 100: happy).	Sleep regularity and sleep duration predicted daily happy-sad mood with 65%-80% accuracy.	II-2

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Slavish et al. 2019[105]	Cross-sectional	771	50.7	53.8 ± 19.8	IIV in TST, circadian midpoint (14 days sleep diaries)	Health/mental health: medical conditions (eg, heart disease, cancer, high blood pressure, breathing problems, diabetes, and gastrointestinal problems), mental health symptoms (depression: BDI, anxiety: State-Trait Anxiety Inventory)	IIV in TST was related to increased odds of having neurological, breathing, and gastrointestinal problems, as well as pain and depression; all results held controlling for mean sleep and adjusting for false discovery rate. IIV in sleep quality and sleep efficiency was not associated with odds of having any medical or mental health conditions after adjusting for false discovery rate. IIV in circadian midpoint or mean circadian midpoint not associated with health conditions.	II-2
Soehner et al. 2011[106]	Cross-sectional	62	66.1	31.5 ± 5.9	STQ assessed duration, timing, and stability of sleep separately for work-week nights (Sunday-Thursday) and for weekend nights (Friday and Saturday).	Alertness: habitual sleep latency and minutes awake after sleep onset (from STQ). Subjective sleep quality (PSQI) Sleep duration (from STQ) Daytime sleepiness (Epworth sleepiness scale)	Stable weekday rise time correlated with better self-reported sleep quality and shorter sleep-onset latency. A more regular weekend bedtime was associated with a shorter sleep latency. A more stable weekend rise time was related to longer weekday sleep duration and lower daytime sleepiness. Increased overall regularity in rise time was associated with better subjective sleep quality, shorter sleep-onset latency, and higher weekday sleep efficiency. Morning orientation was related to increased regularity in both bedtimes and rise times.	II-3
Taub, 1978[107]	Between-subjects	36 (2 groups of n = 18)	0	18-24	Irregular sleepers or control subjects Control group: slept naturally from 12 to 8 00 am for 7-8 h. Irregular sleepers: retiring and awakening times varied by about 2-4 h	Alertness/mood: auditory reaction time and subjective mood. Sublingual temperature Pulse rate 30 min after awakening in (a) morning, at (b) noon, (c) afternoon, and (d) early evening following an EEG-recorded 12-8 00 am sleep night.	Irregular sleepers compared with the control group had lower levels of pulse rate and body temperature, but longer reaction times. Negative affect (deactivation-sleep, depression, general deactivation, and inertfatigued) were greater and positive mood states (cheerful, energetic, and general activation—less in the irregular sleepers. The irregular sleepers averaged less stage 4, and REM, but more stage 2 and transitions between sleep stages.	II-2
Taylor et al. 2016[108]	Longitudinal (5 y)	n= 338	100	52.1 ± 2.1	Mean bedtime Bedtime variability Bedtime delay Bedtime advance (from diary reported bedtimes)	Metabolism: BMI and insulin resistance (homeostatic model assessment-insulin resistance, HOMA-IR) at 2 time points.	Greater variability in bedtime and greater bedtime delay were associated with higher HOMA-IR. Greater bedtime advance was associated with higher BMI. Prospectively, greater bedtime delay predicted increased HOMA-IR at time 2. Results were partially explained by shifted sleep timing on weekends.	II-2
Van Lenten and Doane, 2016[109]	Cross-sectional	76	76	18.5 ± 0.4	Sleep duration variability (SD measured by actigraphy)	Cortisol	Increasing sleep duration variability was associated with lower average levels of waking cortisol and flattened diurnal cortisol slope.	II-3

(*continued on next page*)

Table 2 (*continued*)

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Watling et al. 2020[110]	Cross-sectional	137	58.4	19.8 ± 2.9	STQ: habitual bedtime (good nighttime) and habitual wake time (good morning time) for week nights and weekend nights. Stability of habitual bedtime and wake time measured on an arbitrary scale of 1-11, with higher scores representing greater instability.	Alertness: reports of continuing to drive while sleepy. Reports of experiencing a sleep-related close call.	STQ sleep stability associated with continuing to drive while sleepy	II-2
Wong et al. 2013[111]	Prospective cohort study	930	76.7	21.7 ± 2.2	Social jetlag (duration variability) STQ consisted of 14 items in assessing an individual's habitual sleep-wake patterns in a recent normal week. Sleep duration on school days and holidays are separately assessed. Weekday/ weekend sleep discrepancy is calculated by subtracting the hours of sleep in school days from holidays.	Academic function, physical and psychological health	Sleep was shorter on weekdays compared to weekends (2.3 h, SD: 1.9). Higher social jetlag was associated with worse self-esteem.	II-3
Xu et al. 2018[112]	Cross-sectional	471	51.3	50.7 ± 12.1 (females) 48.6 ± 12.7 (males)	Habitual sleep duration and nightly sleep duration variation from Fitbit charge HR wristbands (SD of sleep duration).	BMI Blood pressure Obesity-related clinical blood laboratory measurements: diabetes markers, lipids, liver function, kidney function, red blood cells, and white blood cell counts.	Larger sleep duration variation was significantly and independently associated with increased BMI.	II-2
Yamaguchi et al. 2013[113]	Prospective cohort	1368	31.9	35-69	Subjective sleep-wake regularity for the past year by asking whether the time of falling asleep at night and waking in the morning was mostly regular or irregular.	Daily intake of total energy, proteins, fat, and carbohydrates. BMI. Intake frequency of staple foods.	Poor sleep-wake regularity associated with low intake energy ratio of proteins, high intake energy ratio of carbohydrates, skipping intake of the staple foods at breakfast, and excessive intake amount of the staple foods at lunch and dinner. Poor sleep-wake regularity associated with higher BMI.	III
Zhang et al. 2020[114]	Cohort	56	53.6	44.0 ± 3.6	Sleep duration and sleep midpoint difference between weekend and weekdays (1-week actigraphy)	Alertness: brain oxygenation from functional magnetic resonance imaging at resting state and during a visual attention task	Longer weekend sleep duration (relative to weekdays) was associated with better attentional performance & greater deactivation of the default mode network, and greater resting-state functional connectivity between the anterior default mode network and occipital cortex. Later weekend sleep timing was associated with worse performance on the visual attention task and lower occipital activation.	II-3
Zhu et al. 2020[115]	Longitudinal (correlational)	56	55.4	60.7 ± 6.8	SD of sleep duration and midsleep time from 8 days of sleep diaries, in adults with type 2 diabetes.	Glycemic control (hemoglobin A1C)	Larger variability in sleep duration and midsleep were significantly related to higher A1C levels. A 10-min increase in sleep duration variability was related to a 0.28% increase in A1C.	II-3

delayed sleep-wake phase disorder (DSWPD); grade point average (GPA); dim light melatonin onset (DLMO); multivariate analysis of covariance (MANCOVA).

outcomes (n = 11), performance (n = 9), and other health outcomes (n = 9). (Figs. 2-4).

Question 1: (a) is daily regularity in sleep timing important for health? and (b) is daily regularity in sleep timing important for performance?

Regardless of the exposure or outcome, all included studies reported a neutral or negative association between sleep timing variability and the outcome of interest (Fig. 2), with the majority of the studies reporting that increased sleep variability was associated with adverse outcomes.

There were 54 papers relevant to this question (Table 2). Of these, 50 demonstrated at least 1 outcome variable that was significantly worsened in association with increased sleep timing variability. No significant difference in at least 1 outcome was reported in 12 papers, and no papers reported decreased risk. One study detailed an association between the strength of circadian periodicity (repeating patterns of the rest-activity cycle) with a series of cardiometabolic outcomes and health-related quality of life but did not indicate a direction of effect.[30] Of the 82 variables that were found to have a significant association with increased sleep timing variability, 63 reported adverse health effects, 11 reported adverse alertness or performance outcomes, 4 reported adverse health-related behaviors, and 4 reported adverse safety-related behaviors.

Two prospective studies deployed objective assessments of sleep to examine the impact of sleep regularity on metabolism[31] and cardiovascular events.[32] These studies provide support for a dose-response relationship between irregularity (measured by SD of sleep onset timing and sleep duration) and risk of these conditions (Fig. 3).

Question 2: when sleep is of insufficient duration during the week (or work days), is catch-up sleep on weekends (or non-work days) important for health?

The review identified 9 articles that examined catch-up sleep with short sleep on work nights associated with extended sleep on nights ending on non-work days (Table 3). Studies that compared individuals who continued to obtain short sleep on non-work nights (n = 8) demonstrated that individuals who obtained short sleep on work nights and experienced extended catch-up sleep on non-work nights were at decreased odds of experiencing multiple negative health outcomes, including inflammation, adverse metabolic outcomes, and mortality (Fig. 4).

A longitudinal study of participants less than 65 years of age demonstrated that those obtaining consistently short sleep (≤5 hours) had an increased risk of mortality, whereas individuals who curtailed sleep during the week combined with longer catch-up sleep on the weekends had no difference in mortality compared to those who consistently slept for a longer duration (short-medium/long versus medium-medium or medium-long sleep).[33] Data from other studies revealed that, among individuals sleeping ≤6 hours during the week, those obtaining 1-2 hours more sleep on the weekend (than during weekdays) had more favorable serum high-sensitivity C-reactive protein levels than those who did not extend their sleep on the weekends, identifying a potential protective effect for longer WCS durations.[34]

Panel deliberations and consensus voting

The panel achieved consensus for all 3 questions/statements with the 80% agreement threshold achieved (Table 4). The median appropriateness rating was in the appropriate range for each statement. The highest appropriateness rating (rating = 9) was reached for question 1a, that is, daily regularity in sleep timing is important for health. The lowest acceptable appropriateness rating (rating = 8) was achieved for question 2, that is, catch-up sleep is important for health.

Discussion

Our review found that, across a wide variety of health and performance outcomes (eg, mortality, inflammation, cognitive performance, metabolic indicators, breastfeeding, and mental health), increased sleep timing variability was associated with adverse health and performance outcomes. This is consistent with a prior review that reported greater variability in sleep (ie, less consistency in sleep timing or duration) was associated with adverse health outcomes in the general population.[35] Many of the associations described in these studies are consistent with the literature on people performing shift work, such as the association between sleep regularity and cardiovascular disease,[32] though this review excluded studies exclusively focused on shift work populations.

Variability in sleep timing in modern society is nearly always associated with variability in the timing of light exposure, timing of meals, and activity. It, thus, remains unknown whether the adverse health and performance associations described herein are due to variability in the timing of sleep itself or variability in the timing of these associated environmental and behavioral factors. Variability in the ensemble of environmental and behavioral factors associated with variability in sleep timing can induce circadian disruption and circadian misalignment. Based on experiments in laboratory animals, circadian disruption leads to impaired immune responses[36,37] and reduced lifespan.[38–40] For example, the survival of laboratory animals with cardiomyopathic heart disease is reduced if the animals are exposed to light at adverse circadian phases.[41]

The majority of studies in this review demonstrate that regularity of sleep is important for health and performance. When sleep deficiency has accumulated, often on work days, a number of studies suggest that the common human pattern of extending sleep on non-work days ("catch-up" sleep) can be beneficial. While some medical practitioners and researchers recommend that people maintain consistent bedtimes and wake times on all days of the week,[42,43] notwithstanding accumulating sleep deficiency, this consensus panel concluded that sleep deficiency should instead be minimized by extending sleep on non-work days for up to 1-2 h and/or obtaining naps when feasible. While there are costs to health and performance associated with the decision to seek more hours of sleep (given the consequence of reduced sleep timing regularity), the tradeoff may often be beneficial though the studies informing this question did not directly test the costs versus benefits of this tradeoff. Interventional studies designed to directly test this question are needed, particularly given early evidence of an adverse association between sleeping in on weekends and academic performance.[15] Catch-up sleep on non-working days may not fully ameliorate the sleep deficiency accumulated on work days, and it can take up to several days to recover from just 1 hour of lost sleep.[8,44] Therefore, although 1 or 2 nights of catch-up sleep can be helpful (and are recommended), some degree of sleep deficiency often remains. Moreover, the potentially adverse circadian consequences resulting from sleep extension on non-work days should be considered when individuals may awaken on a catch-up non-work day well after sunrise and would, thus, be exposed to a reduced duration of morning light within the window required to induce a circadian phase advance.[45] This may result in a later circadian phase and consequent difficulty awakening (with potential performance and safety decrements) with early wake times required on subsequent work or school days.

While the reviewed literature incorporated various outcome measures of health and performance, there was no consensus among studies on how to quantify sleep timing variability. Studies quantified sleep timing variability in a number of different ways, including the SD of either sleep duration, sleep onset, midpoint, or offset; the SRI;[16] the STQ[46]; or other self-reported sleep regularity assessments. Additional sleep timing variability assessments were also developed

Table 3
Summary of evidence informing panel recommendations for question 2

Reference	Study Design	Sample size	Sex (% F)	Age	Exposure	Outcome	Major findings	Risk of bias
Åkerstedt et al. 2019[33]	Prospective cohort study	38,015	67-58 across groups	Mean 44-62 across groups	Differential between weekday and weekend sleep duration	Mortality	Short, but not long, weekend sleep was associated with increased mortality in those < 65 y.	II-2
Cabeza de Baca et al. 2019[116]	Cross-sectional	22,082	100	72.1 ± 6.0	"Sleep debt" defined as the difference between self-reported total weekday and weekend sleep hours of at least 2 h	Ideal cardiovascular health	Subjects with sleep debt were more likely to be obese and have hypertension and poorer ideal cardiovascular health.	III
Han et al. 2020[34]	Cross-sectional	5506	59.2 (weekend catch-up sleep [WCS]) 55.1 (non-WCS)	19 y or older, grouped into 10 y ranges	WCS defined as weekend sleep duration > 1 h longer than weekday sleep duration.	Inflammation: serum high-sensitivity C-reactive protein level categorized into quartiles.	Adults with WCS were less likely to show the highest hsCRP level (versus the lowest level) compared with those without WCS. This association was significant only for those with weekday sleep duration of 6 h or lower. Longer WCS (≥3 h) was not associated with hsCRP levels.	II-3
Im et al. 2017[117]	Cross-sectional	2156	58	43 ± 14.5	Sleep duration, WCS, and chronotype	Obesity/body mass index	WCS was associated with lower average body mass index. Later chronotype was associated with higher body mass index.	II-3
Jung et al. 2019[118]	Cross-sectional	3304	47.3	20 y or older	Weekend catch-up sleep (CUS): [average weekend daily duration – average weekday daily duration]. Categorized into 4 groups based on duration of CUS.	Inflammation: Serum high-sensitivity C-reactive protein levels.	At least 1-h and less than 2 h of weekend CUS reduced the risk of elevated high-sensitivity C-reactive protein levels.	II-3
Killick et al. 2015[119]	Randomized crossover trial (laboratory imposed)	19	0	28.6 ± 2	Simulated WCS: randomized to 3 weekend nights of 10 h time in bed, 6 h time in bed, or 10 h time in bed with slow-wave suppression.	Metabolism: insulin sensitivity and other metabolic outcomes	10 h of WCS was associated with higher insulin sensitivity and other favorable metabolic outcomes.	I
Kong et al. 2017[120]	Cross-sectional	3508	41	53.9 ± 8.7	Differences of sleep duration during weekdays and weekends in patients with type 2 diabetes	Metabolism: indices of glycemic control (glycated hemoglobin [HbA1c] and fasting plasma glucose)	Sleep duration difference between weekdays and weekends was associated with both HbA1c and fasting plasma glucose in a curvilinear manner. Sleep duration of about 1 h more during weekends when compared to weekdays was associated with beneficial effect in HbA1c.	II-3
Oh et al. 2019[121]	Cross-sectional	4871	55.7	Weekend CUS: 40.6 ± 0.4 Non-CUS: 48.4 ± 0.5	Weekend CUS versus non-CUS groups based on sleep questionnaires	HRQoL from European quality of life scale-5 dimensions questionnaire	Weekend CUS behavior was associated with better HRQoL than non-CUS. Especially, participants with short weekday sleep duration and late chronotypes showed significantly better HRQoL.	II-2
Son et al. 2020[63]	Cross-sectional	1453 766 CUS, 687 non-CUS	61% F in non-CUS group	3 categories: 20-39, 40-65, > 65 y.	Weekend CUS divided into 4 categories: ≤0, 0-1, 1-2, and ≥2 h	Metabolic syndrome: more than 3 of the 5 criteria met: 1) abdominal obesity; 2) high blood pressure; 3) hypertriglyceridemia 4) low serum high-density lipoprotein level; and 5) impaired blood glucose.	Weekend CUS 1-2 h associated with reduced odds of metabolic syndrome. In a population sleeping less than 6 h on average, weekend CUS ≥ 1 h and < 2 h was associated with a reduced risk of metabolic syndrome. Stratified analyses revealed that this association was present among those aged 20-39 and 40-65 y, and there may be a benefit to CUS > 2 h in younger age groups.	II-3

Table 4
Results of expert panel voting from 11 panel members

Question	Median appropriateness rating (range)	Agreement threshold (80%)	Decision
1a	9 (7-9)	Agree	Appropriate
1b	8 (8-9)	Agree	Appropriate
2	8 (7-9)	Agree	Appropriate

Consensus recommendations were identified as appropriate (median of 7-9), uncertain (median of 4-6), or inappropriate (median of 1-3). An agreement was defined by at least 80% of votes within any of the 3-point ranges.

after our review.[47] The dependence of these metrics on the type of data gathered, the number of days of data collected, sample size, and the research question was evaluated by Fischer et al.[48] Given the increasing acknowledgment of the importance of sleep regularity for health, development of a gold standard measure of sleep variability is needed. The panel recommends that 1 common metric is used consistently to facilitate comparisons within the literature, with the addition of other metrics chosen by each investigator. Consensus will be required for this common metric, especially since the characteristics of the metrics differ.[48] The panel identifies, however, that metrics of day-to-day variability such as the increasingly deployed SRI are prioritized over less precise survey methods of sleep patterns on work days versus non-work days. The metric recommended for research studies also needs to be easily translated for public health recommendations.

The panel determined there was insufficient evidence to quantify via a single fixed number how much variability in sleep timing is associated with increased risk. Of relevance, an SD of 1 hour in sleep onset timing was found to be associated with a 23% increased risk of metabolic syndrome[31] and an 18% increase in cardiovascular risk.[32]

Sleep timing variability is an area of intense research focus. Additional studies published after the panel's search was finalized were circulated among the panel members. None of the subsequent findings are inconsistent with the panel recommendations. Additional evidence supports a relationship between lower sleep regularity and higher body mass index,[49,50] less favorable hemoglobin A1c, obesity, weight gain, metabolic syndrome, increased inflammatory biomarkers including white blood cell count, elevated blood pressure, depressed mood, increased nonsuicidal self-injury, higher all-cause mortality,[51] and adverse behavioral health of adolescents. A recent review of sleep regularity and cardiometabolic outcomes is aligned with the conclusions of the panel, finding that lower regularity was associated with a variety of adverse outcomes, including metabolic syndrome. Sleep regularity may be lower among non-White adults compared to White adults, suggesting that sleep regularity may be a driver of sleep health disparities.[52,53] Further evidence also supports the panel recommendations regarding catch-up sleep, with 1 recent report of an association between WCS and alleviation of nonalcoholic fatty liver disease,[54] though other controlled studies of catch-up sleep were mixed, with some evidence suggesting that 2 days of catch-up sleep did not restore insulin sensitivity to levels that were observed prior to sleep accumulation of sleep deficiency.[55–57] The abovementioned review also found that higher SJL, which may or may not include catch-up sleep, was associated with glycemic dysregulation, adiposity, type 2 diabetes, and metabolic syndrome. These findings are consistent with those of others who have detailed an association between higher SJL and greater body mass index.[19,58–62]

We specifically sought to identify studies that informed the question, "When sleep is of insufficient duration during the work week, is WCS important for health?" This catch-up sleep differs from the prior questions by considering when the duration of sleep obtained during the work week may be inadequate. One study of a population of adults averaging less than 6 hours of sleep per night during the week found a protective association between catch-up sleep and metabolic syndrome, with 1-2 hours of catch-up sleep on the weekend associated with reduced odds of metabolic syndrome.[63] Another study found an association between extending sleep on the weekend and lower adiposity, while increased variability (using the SRI metric) was not associated with adiposity, suggesting that catch-up sleep was beneficial despite the reduced regularity in this context.[64] As our daily patterns have shifted during and possibly after the COVID-19 pandemic, emerging evidence suggests that increased freedom in daily routines has enabled increases in sleep regularity,[65] potentially allowing for behavioral adjustments to sleep-wake patterns that are associated with a multitude of adverse outcomes.

Limitations

The evidence reviewed by the panel was limited to articles captured by the search criteria within the PubMed database. Some publications emerging after the search was conducted may be omitted though the panel sought to identify new publications up until the submission of the manuscript. Some relevant articles in the time before keywords were abstracted, which reported that the timing of sleep in sufficient detail may not have been identified. For example, Johns et al.[15] conducted a relevant study and published their findings in 1976. While not captured by our search, the study found that medical students who woke earlier on the weekday and weekend, resulting in less SJL but potentially greater sleep deficiency, had better exam scores compared to those who slept later on the weekend (ie, catch-up sleep).[15] In addition, the quality of articles was limited, with most observational designs relying on self-reported data, limiting the ability of panelists to interpret causal relationships. More robust research is clearly needed. Most studies examining sleep timing variability did not control for sleep duration in their analyses or whether sleep was obtained at an appropriate biological time. Future research should facilitate a separate examination of the specific impacts of sleep timing variability versus sleep duration variability, as reported by Huang et al.,[32] in addition to the combined impacts. This review focused on variability in the timing of the primary nocturnal sleep episode and did not include studies related to napping behavior or the health effects of shift work.

Conclusions

The overwhelming body of evidence led the panel to conclude that sleep regularity is important for health and performance. Regular schedules were associated with improved outcomes across multiple dimensions of health and performance, including alertness, health and safety behaviors, cardiovascular health, metabolic health (including fasting glucose, hemoglobin A1C, and metabolic syndrome), inflammation, mental health (including depression, mood, and suicidal ideation), academic performance, cognitive performance, sleep duration, and sleep quality. The odds of all these adverse outcomes were found to be increased on irregular schedules compared to regular schedules, consistent with data indicating that increased SJL (ie, 1 source of sleep timing variability) is associated with worse health outcomes.

Irregular schedules were not associated with improved outcomes in any study. Based on the preponderance of the evidence currently available, the panel, therefore, concluded that, to the extent that it is feasible, individuals should seek to optimize sleep timing regularity. However, when sleep duration is inadequate during work days, 1-2 hours of catch-up sleep on non-work days may be beneficial.

Funding

This project was supported by the National Sleep Foundation.

Credit author statement

The National Sleep Foundation conceived the study and convened the panel. All authors contributed to the design of the search and agreed on the questions to be answered. All authors contributed to the summary and interpretation of the data. TLS and MDW wrote the original draft. All authors read, edited, and approved the final manuscript. CAC chaired the panel and supervised the project as a whole.

Acknowledgments

We are grateful for logistical support and coordination from Katherine Draghi, Meredith Ellison, Anita Roach, Erin Koffel, and the National Sleep Foundation. We also thank Bryan Baxter, Lauren Booker, Ivy Mason, Megan Mulhall, Rebecca Robbins, and Melissa St. Hilaire for assistance with the literature review.

Declaration of conflict of Interest

Dr. Weaver reports consulting with the Fred Hutchinson Cancer Center, the National Sleep Foundation (NSF), and the University of Pittsburgh, and grant support from the Centers for Disease Control and the National Institutes of Health.

Dr. Sletten and Dr. Weaver report personal fees from the NSF during the conduct of the study.

Dr. Klerman reports grants from the National Institutes of Health, other from Federal Aviation Administration; grants from Havard University; grants from the Massachusetts Insitute of Technology, during consulting for the American Academy of Sleep Medicine Foundation, Circadian Therapeutics, NSF, Sleep Research Society Foundation, Yale University Press and travel support from European Biological Rhythms Society. Dr Klerman's partner owns Chronsulting.

Dr. Takahashi is an Investigator in the Howard Hughes Medical Institute, and a co-founder and an SAB member of Synchronicity Pharma.

Dr. Rajaratnam has unpaid appointments at the Cooperative Research Centre for Alertness, Safety and Productivity, Australia, and the Sleep Health Foundation. Dr. Rajaratnam is also supported by grants from Vanda Pharmaceuticals, Philips Respironics, Cephalon, Rio Tinto, BHP Billiton, and Shell. Dr. Rajaratnam has received other support from Optalert, Compumedics, Teva Pharmaceuticals, and Circadian Therapeutics, through his institution. He is a member of the NSF Sleep Timing Variability Consensus Panel, for which he was paid an honorarium through his institution.

Dr. Czeisler serves as the incumbent of an endowed professorship provided to the Harvard Medical School by Cephalon, Inc. and reports institutional support for a Quality Improvement Initiative from Delta Airlines and Puget Sound Pilots; education support to the Harvard Medical School Division of Sleep Medicine and support to Brigham and Women's Hospital from Jazz Pharmaceuticals PLC, Inc., Philips Respironics, Inc., Optum, and ResMed, Inc.; research support to Brigham and Women's Hospital from Axome Therapeutics, Inc., Dayzz Ltd., Peter Brown and Margaret Hamburg, Regeneron Pharmaceuticals, Sanofi SA, Casey Feldman Foundation, Summus, Inc., Takeda Pharmaceutical Co., Ltd., the Abbaszadeh Foundation, and the CDC Foundation; educational funding to the Sleep and Health Education Program of the Harvard Medical School Division of Sleep Medicine from ResMed, Inc., Teva Pharmaceuticals Industries, Ltd., and Vanda Pharmaceuticals; personal royalty payments on sales of the Actiwatch-2 and Actiwatch-Spectrum devices from Philips Respironics, Inc; personal consulting fees from Axsome, Inc., the Bryte Foundation, Deep, Inc., and Vanda Pharmaceuticals; honoraria from the Associated Professional Sleep Societies, LLC, for the Thomas Roth Lecture of Excellence at SLEEP 2022 from the Massachusetts Medical Society for a New England Journal of Medicine Perspective article, the National Council for Mental Wellbeing, and the NSF for serving as the Chair of the Sleep Timing and Variability Consensus Panel, lecture fees from Teva Pharma Australia PTY Ltd., Merck, Sharpe and Dohme, Oregon Health Sciences University, and Emory University and for serving as an Advisory Board Member for the Institute of Digital Media and Child Development, the Klarman Family Foundation, and the UK Biotechnology and Biological Sciences Research Council. Dr. Czeisler has received personal fees for serving as an expert witness on a number of civil matters, criminal matters, and arbitration cases, including those involving the following commercial and government entities: Amtrak; Bombardier, Inc.; C&J Energy Services; Dallas Police Association; Delta Airlines/Comair; Enterprise Rent-A-Car; FedEx; Greyhound Lines, Inc./Motor Coach Industries/FirstGroup America; PAR Electrical Contractors, Inc.; Puget Sound Pilots; the San Francisco Sheriff's Department; Schlumberger Technology Corp.; Union Pacific Railroad; United Parcel Service; and Vanda Pharmaceuticals. Dr. Czeisler has received travel support from Merck, Sharpe and Dohme; equity interest in Vanda Pharmaceuticals, Whoop, Inc., and Signos, Inc.; and institutional educational gifts to the Brigham and Women's Hospital from Johnson & Johnson, Mary Ann, and Stanley Snider via Combined Jewish Philanthropies, Alexandra Drane, DR Capital, Harmony Biosciences, LLC, San Francisco Bar Pilots, Whoop, Inc., Harmony Biosciences LLC, Eisai Co., Ltd., Idorsia Pharmaceuticals Ltd., Sleep Number Corp., Apnimed, Inc., Avadel Pharmaceuticals, Bryte Foundation, f.lux Software, LLC, and the Stuart F. and Diana L. Quan Charitable Fund. Dr. Czeisler's interests were reviewed and are managed by the Brigham and Women's Hospital and Mass General Brigham in accordance with their conflict-of-interest policies.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.sleh.2023.07.016.

References

1. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health.* 2015;1(1):40–43.
2. Watson NF, Badr MS, Belenky G, et al. Recommended amount of sleep for a healthy adult: a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society. *Sleep.* 2015;38(6):843–844.
3. Buysse DJ. Sleep health: can we define it? does it matter? *Sleep.* 2014;37(1):9–17.
4. Czeisler CA, Wickwire EM, Barger LK, et al. Sleep-deprived motor vehicle operators are unfit to drive: a multidisciplinary expert consensus statement on drowsy driving. *Sleep Health.* 2016;2(2):94–99.
5. Ohayon M, Wickwire EM, Hirshkowitz M, et al. National Sleep Foundation's sleep quality recommendations: first report. *Sleep Health.* 2017;3(1):6–19.
6. Sletten TL, Cappuccio FP, Davidson AJ, Van Cauter E, Rajaratnam SMW, Scheer F. Health consequences of circadian disruption. *Sleep.* 2020;43(1):1–3.
7. Dillon HR, Lichstein KL, Dautovich ND, Taylor DJ, Riedel BW, Bush AJ. Variability in self-reported normal sleep across the adult age span. *J Gerontol B Psychol Sci Soc Sci.* 2015;70(1):46–56.
8. Klerman EB, Barbato G, Czeisler CA, Wehr TA. Can people sleep too much? effects of extended sleep opportunity on sleep duration and timing. *Front Physiol.* 2021;12:792942.
9. Ekirch AR. *At Day's Close: Night in Times Past.* New York: WW Norton & Company; 2006.
10. Qian J, Scheer F. Circadian System And Glucose Metabolism: Implications For Physiology And Disease. *Trends Endocrinol Metab.* 2016;27(5):282–293.
11. Chellappa SL, Vujovic N, Williams JS, Scheer F. Impact of circadian disruption on cardiovascular function and disease. *Trends Endocrinol Metab.* 2019;30(10):767–779.
12. Murray JM, Sletten TL, Magee M, et al. Prevalence of circadian misalignment and its association with depressive symptoms in delayed sleep phase disorder. *Sleep.* 2017;40(1).
13. Abbott SM, Malkani RG, Zee PC. Circadian disruption and human health: A bidirectional relationship. *Eur J Neurosci.* 2020;51(1):567–583.

14. Iarc Monographs Vol 124 group. Carcinogenicity of night shift work. *Lancet Oncol.* 2019;20(8):1058–1059.
15. Johns MW, Dudley HA, Masterton JP. The sleep habits, personality and academic performance of medical students. *Med Educ.* 1976;10(3):158–162.
16. Phillips AJK, Clerx WM, O'Brien CS, et al. Irregular sleep/wake patterns are associated with poorer academic performance and delayed circadian and sleep/wake timing. *Sci Rep.* 2017;7(1):3216.
17. Sheehan CM, Frochen SE, Walsemann KM, Ailshire JA. Are U.S. adults reporting less sleep?: findings from sleep duration trends in the National Health Interview Survey, 2004-2017. *Sleep.* 2019;42(2):1–8.
18. Di H, Guo Y, Daghlas I, et al. Evaluation of sleep habits and disturbances among US adults, 2017-2020. *JAMA Netw Open.* 2022;5(11):e2240788.
19. Roenneberg T, Allebrandt KV, Merrow M, Vetter C. Social jetlag and obesity. *Curr Biol.* 2012;22(10):939–943.
20. Roenneberg T, Pilz LK, Zerbini G, Winnebeck EC. Chronotype and social jetlag: a (self-) critical review. *Biology (Basel).* 2019;8(3):80300542019.
21. Yong LC, Li J, Calvert GM. Sleep-related problems in the US working population: prevalence and association with shiftwork status. *Occup Environ Med.* 2017;74(2):93–104.
22. Saenz R. A demographic profile of US workers around the clock. *Population Reference Bureau.* 2008https://www.prb.org/resources/a-demographic-profile-of-u-s-workers-around-the-clock/.
23. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev.* 2016;5(1):210.
24. Weaver MD, Sletten TL, Foster RG, et al. Adverse impact of polyphasic sleep patterns in humans: report of the National Sleep Foundation sleep timing and variability consensus panel. *Sleep Health.* 2021;7(3):293–302.
25. Straif K, Baan R, Grosse Y, et al. Carcinogenicity of shift-work, painting, and firefighting. *Lancet Oncol.* 2007;8(12):1065–1066.
26. Rivera AS, Akanbi M, O'Dwyer LC, McHugh M. Shift work and long work hours and their association with chronic health conditions: a systematic review of systematic reviews with meta-analyses. *PLoS One.* 2020;15(4):e0231037.
27. Costa G. Shift Work and Occupational. In: Theorell T, ed. *Handbook of Socioeconomic Determinants of Occupational Health. Handbook Series in Occupational Health Sciences.* Springer, Cham; 2020. https://doi.org/10.1007/978-3-030-05031-3_3-1
28. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001;20(3 Suppl):21–35.
29. Fitch K, Bernstein S, Aquilar M, et al. *The RAND/UCLA Appropriateness Method User's Manual.* Santa Monica, CA, USA: The RAND Corporation,; 2001.
30. Buman MP, Hu F, Newman E, Smeaton AF, Epstein DR. Behavioral periodicity detection from 24h wrist accelerometry and associations with cardiometabolic risk and health-related quality of life. *Biomed Res Int.* 2016;2016:4856506.
31. Huang T, Redline S. Cross-sectional and prospective associations of actigraphy-assessed sleep regularity with metabolic abnormalities: the multi-ethnic study of atherosclerosis. *Diabetes Care.* 2019;42(8):1422–1429.
32. Huang T, Mariani S, Redline S. Sleep irregularity and risk of cardiovascular events: the multi-ethnic study of atherosclerosis. *J Am Coll Cardiol.* 2020;75(9):991–999.
33. Akerstedt T, Ghilotti F, Grotta A, et al. Sleep duration and mortality - does weekend sleep matter? *J Sleep Res.* 2019;28(1):e12712.
34. Han KM, Lee HJ, Kim L, Yoon HK. Association between weekend catch-up sleep and high-sensitivity C-reactive protein levels in adults: a population-based study. *Sleep.* 2020;43(8).
35. Chaput JP, Dutil C, Featherstone R, et al. Sleep timing, sleep consistency, and health in adults: a systematic review. *Appl Physiol Nutr Metab.* 2020;45(10 (Suppl. 2)):S232–S247.
36. Castanon-Cervantes O, Wu M, Ehlen JC, et al. Dysregulation of inflammatory responses by chronic circadian disruption. *J Immunol.* 2010;185(10):5796–5805.
37. Brager AJ, Ehlen JC, Castanon-Cervantes O, et al. Sleep loss and the inflammatory response in mice under chronic environmental circadian disruption. *PLoS One.* 2013;8(5):e63752.
38. Boomgarden AC, Sagewalker GD, Shah AC, et al. Chronic circadian misalignment results in reduced longevity and large-scale changes in gene expression in Drosophila. *BMC Genomics.* 2019;20(1):14.
39. Pittendrigh CS, Minis DH. Circadian systems: longevity as a function of circadian resonance in *Drosophila melanogaster*. *Proc Natl Acad Sci U S A.* 1972;69(6):1537–1539.
40. Inokawa H, Umemura Y, Shimba A, et al. Chronic circadian misalignment accelerates immune senescence and abbreviates lifespan in mice. *Sci Rep.* 2020;10(1):2569.
41. Penev PD, Kolker DE, Zee PC, Turek FW. Chronic circadian desynchronization decreases the survival of animals with cardiomyopathic heart disease. *Am J Physiol.* 1998;275(6):H2334–2337.
42. Allen SL, Howlett MD, Coulombe JA, Corkum PV. ABCs of sleeping: a review of the evidence behind pediatric sleep practice recommendations. *Sleep Med Rev.* 2016;29:1–14.
43. Neubauer DN. Sleep problems in the elderly. *Am Fam Physician.* 1999;59(9):2551.
44. Kitamura S, Katayose Y, Nakazaki K, et al. Estimating individual optimal sleep duration and potential sleep debt. *Sci Rep.* 2016;6(1):35812.
45. Porcheret K, Wald L, Fritschi L, et al. Chronotype and environmental light exposure in a student population. *Chronobiol Int.* 2018;35(10):1365–1374.
46. Monk TH, Buysse DJ, Kennedy KS, Pods JM, DeGrazia JM, Miewald JM. Measuring sleep habits without using a diary: the sleep timing questionnaire. *Sleep.* 2003;26(2):208–212.
47. Dzierzewski JM, Donovan EK, Sabet SM. The sleep regularity questionnaire: development and initial validation. *Sleep Med.* 2021;85:45–53.
48. Fischer D, Klerman EB, Phillips AJK. Measuring sleep regularity: theoretical properties and practical usage of existing metrics. *Sleep.* 2021;44(10):zsab103.
49. Wong PM, Barker D, Roane BM, Van Reen E, Carskadon MA. Sleep regularity and body mass index: findings from a prospective study of first-year college students. *Sleep Adv.* 2022;3(1):zpac004.
50. Jaiswal SJ, Quer G, Galarnyk M, Steinhubl SR, Topol EJ, Owens RL. Association of sleep duration and variability with body mass index: sleep measurements in a large US population of wearable sensor users. *JAMA Intern Med.* 2020;180(12):1694–1696.
51. Omichi C, Koyama T, Kadotani H, et al. Irregular sleep and all-cause mortality: a large prospective cohort study. *Sleep Health.* 2022;8(6):678–683.
52. Chung J, Goodman M, Huang T, Bertisch S, Redline S. Multidimensional sleep health in a diverse, aging adult cohort: concepts, advances, and implications for research and intervention. *Sleep Health.* 2021;7(6):699–707.
53. Chung J, Goodman M, Huang T, et al. Racial-ethnic differences in actigraphy, questionnaire, and polysomnography indicators of healthy sleep: the multi-ethnic study of atherosclerosis. *Am J Epidemiol.* 2021:kwab232.
54. Seo Y, Sung GH, Lee S, Han KJ. Weekend catch-up sleep is associated with the alleviation of non-alcoholic fatty liver disease. *Ann Hepatol.* 2022;27(3):100690.
55. Broussard JL, Wroblewski K, Kilkus JM, Tasali E. Two nights of recovery sleep reverses the effects of short-term sleep restriction on diabetes risk. *Diabetes Care.* 2016;39(3):e40–41.
56. Depner CM, Melanson EL, Eckel RH, et al. Effects of ad libitum food intake, insufficient sleep and weekend recovery sleep on energy balance. *Sleep.* 2021;44(11):zsab136.
57. Ness KM, Strayer SM, Nahmod NG, Chang AM, Buxton OM, Shearer GC. Two nights of recovery sleep restores the dynamic lipemic response, but not the reduction of insulin sensitivity, induced by five nights of sleep restriction. *Am J Physiol Regul Integr Comp Physiol.* 2019;316(6):R697–R703.
58. Parsons MJ, Moffitt TE, Gregory AM, et al. Social jetlag, obesity and metabolic disorder: investigation in a cohort study. *Int J Obes.* 2015;39(5):842–848.
59. Mathew GM, Hale L, Chang A-M. Social jetlag, eating behaviours and BMI among adolescents in the USA. *Br J Nutr.* 2020;124(9):979–987.
60. Stoner L, Castro N, Signal L, et al. Sleep and adiposity in preadolescent children: the importance of social jetlag. *Childhood Obesity.* 2018;14(3):158–164.
61. Li TM, Pien LC, Cheng WJ. Direction and magnitude of social jetlag are associated with obesity: results from a sample of hospital employees. *Chronobiol Int.* 2022;39(9):1242–1248.
62. Roenneberg T, Allebrandt KV, Merrow M, Vetter C. Social jetlag and obesity. *Curr Biol.* 2012;22(10):939–943.
63. Son SM, Park EJ, Cho YH, et al. Association between weekend catch-up sleep and metabolic syndrome with sleep restriction in Korean adults: a cross-sectional study using KNHANES. *Diabetes Metab Syndr Obes.* 2020;13:1465–1471.
64. Glasgow TE, Adams EL, Ksinan A, et al. Sleep onset, duration, or regularity: which matters most for child adiposity outcomes? *Int J Obes.* 2022;46(8):1502–1509.
65. Ramírez-Contreras C, Zerón-Rugerio MF, Izquierdo-Pulido M. Life before and after COVID-19: the 'new normal' benefits the regularity of daily sleep and eating routines among college students. *Nutrients.* 2022;14(2):351.
66. Bae M, Lee K, Baek JH, et al. Lifetime experiences of hypomanic symptoms are associated with delayed and irregular sleep-wake cycle and seasonality in non-clinical adult samples. *Compr Psychiatry.* 2014;55(5):1111–1115.
67. Bai L, Whitesell CJ, Teti DM. Maternal sleep patterns and parenting quality during infants' first 6 months. *J Fam Psychol.* 2020;34(3):291–300.
68. Bailey BW, Allen MD, LeCheminant JD, et al. Objectively measured sleep patterns in young adult women and the relationship to adiposity. *Am J Health Promot.* 2014;29(1):46–54.
69. Barclay NL, Rowley S, Robson A, Akram U, Myachykov A. Sleep duration, sleep variability, and impairments of visual attention. *Q J Exp Psychol (Hove).* 2020;73(6):868–880.
70. Bei B, Seeman TE, Carroll JE, Wiley JF. Sleep and physiological dysregulation: a closer look at sleep intraindividual variability. *Sleep.* 2017;40(9):zsx109.
71. Bernert RA, Hom MA, Iwata NG, Joiner TE. Objectively assessed sleep variability as an acute warning sign of suicidal ideation in a longitudinal evaluation of young adults at high suicide risk. *J Clin Psychiatry.* 2017;78(6):e678–e687.
72. Casey T, Sun H, Burgess HJ, et al. Delayed lactogenesis II is associated with lower sleep efficiency and greater variation in nightly sleep duration in the third trimester. *J Hum Lact.* 2019;35(4):713–724.
73. Duncan MJ, Kline CE, Rebar AL, Vandelanotte C, Short CE. Greater bed- and wake-time variability is associated with less healthy lifestyle behaviors: a cross-sectional study. *Z Gesundh Wiss.* 2016;24(1):31–40.
74. Faust L, Feldman K, Mattingly SM, Hachen D, N VC. Deviations from normal bedtimes are associated with short-term increases in resting heart rate. *NPJ Digit Med.* 2020;3:39.
75. Fischer D, McHill AW, Sano A, et al. Irregular sleep and event schedules are associated with poorer self-reported well-being in US college students. *Sleep.* 2020;43(6):zsz300.
76. Gao L, Li P, Hu C, et al. Nocturnal heart rate variability moderates the association between sleep-wake regularity and mood in young adults. *Sleep.* 2019;42(5):zsz034.
77. Han KT, Kim SJ. Instability in daily life and depression: the impact of sleep variance between weekday and weekend in South Korean workers. *Health Soc Care Community.* 2020;28(3):874–882.

78. Hausler N, Marques-Vidal P, Haba-Rubio J, Heinzer R. Association between actigraphy-based sleep duration variability and cardiovascular risk factors - results of a population-based study. *Sleep Med.* 2020;66:286–290.
79. Hensch T, Wozniak D, Spada J, et al. Vulnerability to bipolar disorder is linked to sleep and sleepiness. *Transl Psychiatry.* 2019;9(1):294.
80. Hooker SA, Oswald LB, Reid KJ, Baron KG. Do physical activity, caloric intake, and sleep vary together day to day? exploration of intraindividual variability in 3 key health behaviors. *J Phys Act Health.* 2020;17(1):45–51.
81. Hysing M, Sivertsen B, Stormark KM, O'Connor RC. Sleep problems and self-harm in adolescence. *Br J Psychiatry.* 2015;207(4):306–312.
82. Kang JH, Chen SC. Effects of an irregular bedtime schedule on sleep quality, daytime sleepiness, and fatigue among university students in Taiwan. *BMC Public Health.* 2009;9:248.
83. Kim M, Sasai H, Kojima N, Kim H. Objectively measured night-to-night sleep variations are associated with body composition in very elderly women. *J Sleep Res.* 2015;24(6):639–647.
84. Kimura T, Ogushi Y, Haruki Y, Okada Y. Is interest in art effective in health-related quality of life? results of a cross-sectional survey on lifestyle and health promotion. *Tokai J Exp Clin Med.* 2000;25(3):141–149.
85. Lau EYY, Wong ML, Rusak B, et al. The coupling of short sleep duration and high sleep need predicts riskier decision making. *Psychol Health.* 2019;34(10):1196–1213.
86. Lemola S, Ledermann T, Friedman EM. Variability of sleep duration is related to subjective sleep quality and subjective well-being: an actigraphy study. *PLoS One.* 2013;8(8):e71292.
87. Lim AS, Yu L, Costa MD, et al. Increased fragmentation of rest-activity patterns is associated with a characteristic pattern of cognitive impairment in older individuals. *Sleep.* 2012;35(5):633–640B.
88. Luik AI, Zuurbier LA, Hofman A, Van Someren EJ, Ikram MA, Tiemeier H. Associations of the 24-h activity rhythm and sleep with cognition: a population-based study of middle-aged and elderly persons. *Sleep Med.* 2015;16(7):850–855.
89. Lund HG, Reider BD, Whiting AB, Prichard JR. Sleep patterns and predictors of disturbed sleep in a large population of college students. *J Adolesc Health.* 2010;46(2):124–132.
90. Lunsford-Avery JR, Engelhard MM, Navar AM, Kollins SH. Validation of the sleep regularity index in older adults and associations with cardiometabolic risk. *Sci Rep.* 2018;8(1):14158.
91. Manber R, Bootzin RR, Acebo C, Carskadon MA. The effects of regularizing sleep-wake schedules on daytime sleepiness. *Sleep.* 1996;19(5):432–441.
92. Matsumoto T, Tabara Y, Murase K, et al. Combined association of clinical and lifestyle factors with non-restorative sleep: the Nagahama study. *PLoS One.* 2017;12(3):e0171849.
93. McCrae CS, Vatthauer KE, Dzierzewski JM, Marsiske M. Habitual sleep, reasoning, and processing speed in older adults with sleep complaints. *Cognit Ther Res.* 2012;36(2):156–164.
94. Monk TH, Buysse DJ, Billy BD, et al. Circadian type and bed-timing regularity in 654 retired seniors: correlations with subjective sleep measures. *Sleep.* 2011;34(2):235–239.
95. Murray JM, Phillips AJK, Magee M, et al. Sleep regularity is associated with sleep-wake and circadian timing, and mediates daytime function in delayed sleep-wake phase disorder. *Sleep Med.* 2019;58:93–101.
96. Nicholson LM, Egbert AH, Moreno JP, Bohnert AM. Variability of sleep and relations to body weight among first-year college students. *Int J Behav Med.* 2021;28(2):227–237.
97. Ogilvie RP, Redline S, Bertoni AG, et al. Actigraphy measured sleep indices and adiposity: the multi-ethnic study of atherosclerosis (MESA). *Sleep.* 2016;39(9):1701–1708.
98. Okano K, Kaczmarzyk JR, Dave N, Gabrieli JDE, Grossman JC. Sleep quality, duration, and consistency are associated with better academic performance in college students. *NPJ Sci Learn.* 2019;4:16.
99. Okun ML, Reynolds 3rd CF, Buysse DJ, et al. Sleep variability, health-related practices, and inflammatory markers in a community dwelling sample of older adults. *Psychosom Med.* 2011;73(2):142–150.
100. Papandreou C, Camacho-Barcia L, Garcia-Gavilan J, et al. Circulating metabolites associated with objectively measured sleep duration and sleep variability in overweight/obese participants: a metabolomics approach within the SATIN study. *Sleep.* 2019;42(5):zsz030.
101. Papandreou C, Bullo M, Diaz-Lopez A, et al. High sleep variability predicts a blunted weight loss response and short sleep duration a reduced decrease in waist circumference in the PREDIMED-plus trial. *Int J Obes (Lond).* 2020;44(2):330–339.
102. Paterson JL, Reynolds AC, Dawson D. Sleep schedule regularity is associated with sleep duration in older australian adults: implications for improving the sleep health and wellbeing of our aging population. *Clin Gerontol.* 2018;41(2):113–122.
103. Roane BM, Seifer R, Sharkey KM, et al. What role does sleep play in weight gain in the first semester of university? *Behav Sleep Med.* 2015;13(6):491–505.
104. Sano A, Yu AZ, McHill AW, et al. Prediction of happy-sad mood from daily behaviors and previous sleep history. *Annu Int Conf IEEE Eng Med Biol Soc.* 2015;2015:6796–6799.
105. Slavish DC, Taylor DJ, Lichstein KL. Intraindividual variability in sleep and comorbid medical and mental health conditions. *Sleep.* 2019;42(6):zsz052.
106. Soehner AM, Kennedy KS, Monk TH. Circadian preference and sleep-wake regularity: associations with self-report sleep parameters in daytime-working adults. *Chronobiol Int.* 2011;28(9):802–809.
107. Taub JM. Behavioral and psychophysiological correlates of irregularity in chronic sleep routines. *Biol Psychol.* 1978;7(1–2):37–53.
108. Taylor BJ, Matthews KA, Hasler BP, et al. Bedtime variability and metabolic health in midlife women: the SWAN sleep study. *Sleep.* 2016;39(2):457–465.
109. Van Lenten SA, Doane LD. Examining multiple sleep behaviors and diurnal salivary cortisol and alpha-amylase: within- and between-person associations. *Psychoneuroendocrinology.* 2016;68:100–110.
110. Watling CN, Shaw LM, Watling H. Sleep-impaired emotional regulation, impaired cognition, and poor sleep health are associated with risky sleepy driving in young adults. *Traffic Inj Prev.* 2020;21(2):133–138.
111. Wong ML, Lau EY, Wan JH, Cheung SF, Hui CH, Mok DS. The interplay between sleep and mood in predicting academic functioning, physical health and psychological health: a longitudinal study. *J Psychosom Res.* 2013;74(4):271–277.
112. Xu X, Conomos MP, Manor O, Rohwer JE, Magis AT, Lovejoy JC. Habitual sleep duration and sleep duration variation are independently associated with body mass index. *Int J Obes (Lond).* 2018;42(4):794–800.
113. Yamaguchi M, Uemura H, Katsuura-Kamano S, et al. Relationship of dietary factors and habits with sleep-wake regularity. *Asia Pac J Clin Nutr.* 2013;22(3):457–465.
114. Zhang R, Tomasi D, Shokri-Kojori E, Wiers CE, Wang GJ, Volkow ND. Sleep inconsistency between weekends and weekdays is associated with changes in brain function during task and rest. *Sleep.* 2020;43(10).
115. Zhu B, Kapella MC, Zhao X, Fritschi C. Intra-individual variability in sleep is related to glycaemic control in adults with type 2 diabetes. *J Adv Nurs.* 2020;76(4):991–998.
116. Cabeza de Baca T, Chayama KL, Redline S, et al. Sleep debt: the impact of weekday sleep deprivation on cardiovascular health in older women. *Sleep.* 2019;42(10):zsz149.
117. Im HJ, Baek SH, Chu MK, et al. Association between weekend catch-up sleep and lower body mass: population-based study. *Sleep.* 2017;40(7):zsx089.
118. Jung SW, Lee KJ, Lee JH. Does weekend catch-up sleep affect high-sensitivity C-reactive protein levels among korean workers?: a cross-sectional study using KNHANES. *J Occup Environ Med.* 2019;61(9):e367–e373.
119. Killick R, Hoyos CM, Melehan KL, Dungan 2nd GC, Poh J, Liu PY. Metabolic and hormonal effects of 'catch-up' sleep in men with chronic, repetitive, lifestyle-driven sleep restriction. *Clin Endocrinol (Oxf).* 2015;83(4):498–507.
120. Kong AP, Choi KC, Zhang J, et al. Curvilinear associations of sleep patterns during weekdays and weekends with glycemic control in type 2 diabetes: the Hong Kong Diabetes Registry. *Acta Diabetol.* 2017;54(2):151–162.
121. Oh YH, Kim H, Kong M, Oh B, Moon JH. Association between weekend catch-up sleep and health-related quality of life of Korean adults. *Medicine (Baltimore).* 2019;98(13):e14966.