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SYSTEMATIC REVIEW

Sleep timing, sleep consistency, and health in adults: a systematic review[1]

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Abstract: The objective of this systematic review was to examine the associations between sleep timing (e.g., bedtime/wake-up time, midpoint of sleep), sleep consistency/regularity (e.g., intra-individual variability in sleep duration, social jetlag, catch-up sleep), and health outcomes in adults aged 18 years and older. Four electronic databases were searched in December 2018 for articles published in the previous 10 years. Fourteen health outcomes were examined. A total of 41 articles, including 92 340 unique participants from 14 countries, met inclusion criteria. Sleep was assessed objectively in 37% of studies and subjectively in 63% of studies. Findings suggest that later sleep timing and greater sleep variability were generally associated with adverse health outcomes. However, because most studies reported linear associations, it was not possible to identify thresholds for "late sleep timing" or "large sleep variability". In addition, social jetlag was associated with adverse health outcomes, while weekend catch-up sleep was associated with better health outcomes. The quality of evidence ranged from "very low" to "moderate" across study designs and health outcomes using GRADE. In conclusion, the available evidence supports that earlier sleep timing and regularity in sleep patterns with consistent bedtimes and wake-up times are favourably associated with health. (PROSPERO registration no.: CRD42019119534.)

Novelty

- This is the first systematic review to examine the influence of sleep timing and sleep consistency on health outcomes.
- Later sleep timing and greater variability in sleep are both associated with adverse health outcomes in adults.
- Regularity in sleep patterns with consistent bedtimes and wake-up times should be encouraged.

Key words: bedtime, wake-up time, midpoint of sleep, social jetlag, catch-up sleep, sleep variability, sleep regularity, guidelines, public health.

Résumé : L'objectif de cette revue systématique est d'examiner les associations entre la période du sommeil (p. ex. heure de coucher/heure de réveil, point médian du sommeil), la cohérence/régularité du sommeil (p. ex., la variabilité intra-individuelle de la durée du sommeil, le décalage horaire social, le rattrapage du sommeil) et les résultats pour la santé des adultes de 18 ans et plus. Quatre bases de données électroniques ont été consultées en décembre 2018 pour trouver des articles publiés au cours des 10 dernières années. Quatorze résultats pour la santé sont examinés. Un total de 41 articles comportant 92 340 participants distincts de 14 pays répond aux critères d'inclusion. Le sommeil est évalué objectivement dans 37 % des études et subjectivement dans 63 % des études. Les résultats suggèrent que la tardiveté du sommeil et une plus grande variabilité du sommeil sont généralement associées à des résultats de santé négatifs. Toutefois, comme la plupart des études rapportent des associations linéaires, il n'est pas possible d'identifier des seuils de « tardiveté du sommeil » ou de « grande variabilité du sommeil ». De plus, le décalage horaire social est associé à des résultats néfastes pour la santé tandis que le sommeil de rattrapage durant le week-end est associé à de meilleurs résultats pour la santé. D'après la méthode GRADE, la qualité des données probantes varie de « très faible » à « modérée » selon les plans d'étude et les résultats pour la santé. En conclusion, les données probantes disponibles confirment que la hâtiveté du sommeil et la régularité des habitudes du sommeil avec des heures de coucher et des heures de réveil constantes sont favorablement associés à la santé. (Numéro d'enregistrement PROSPERO : CRD42019119534.) [Traduit par la Rédaction]

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Les nouveautés

- Il s'agit de la première revue systématique à examiner l'influence de la période et de la cohérence du sommeil sur les résultats pour la santé.
- La tardiveté du sommeil et une plus grande variabilité du sommeil sont tous deux associés à des résultats de santé défavorables chez les adultes.
- La régularité dans les habitudes de sommeil avec des heures de coucher et de réveil constantes doit être encouragée.

Mots-clés : heure du coucher, heure du réveil, point médian du sommeil, décalage horaire social, sommeil de rattrapage, variabilité du sommeil, régularité du sommeil, directives, santé publique.

Introduction

Sleep is essential for health but most of the research to date has focused on the associations between sleep duration or quality and health outcomes (Hirshkowitz et al. 2015; Watson et al. 2015; Chaput et al. 2016; Ohayon et al. 2017). Much less attention has been devoted to other sleep characteristics such as sleep timing (e.g., bedtime/wake-up time, midpoint of sleep) and sleep consistency/regularity (e.g., intra-individual variability in sleep duration, social jetlag). This is unfortunate because both sleep timing and sleep consistency may be important characteristics of sleep health (Buysse 2014; Chaput 2019; Chaput and Shiau 2019). For example, recent studies have shown that later sleep timing and greater variability in sleep are associated with adverse health outcomes in adults (Abbott et al. 2019; Huang and Redline 2019; Rosique-Esteban et al. 2018; Slavish et al. 2019).

From a public health perspective, better understanding of how sleep timing and sleep consistency affect health is needed to help inform the development of interventions and public health guidelines for healthy sleep. Although many studies have highlighted the importance of sleep duration and sleep quality for health, no study to date has attempted to systematically and comprehensively examine the literature on the associations between sleep timing, sleep consistency, and a wide range of health outcomes in adults. A systematic review could provide a more comprehensive understanding of what is the "optimal sleep timing" and can help quantify the level of sleep variability that is associated with adverse health outcomes. Therefore, the present systematic review aims to examine the associations between sleep timing, sleep consistency, and a broad set of health outcomes in adults aged 18 years and older. Findings from this review will help to better inform public health recommendations for healthy sleep in this population and identify future research needs.

Materials and methods

Protocol and registration

The present systematic review was registered a priori with the International Prospective Register of Systematic Reviews (PROSPERO; Registration No. CRD42019119534; available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42019119534), and was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for reporting systematic reviews and meta-analyses (Moher et al. 2009).

Eligibility criteria

The Participants, Interventions, Comparisons, Outcomes, and Study design (PICOS) framework (Schardt et al. 2007) was followed to identify key study concepts in the research question a priori and to facilitate the search process.

Population

The population of interest was community-dwelling adults aged 18 years and older, including apparently healthy adults, adults with obesity, adults with metabolic syndrome, or adults who have had 1 or more falls in the past year. This also included studies that, among their participant pool, included adults with a chronic condition (e.g., heart disease, diabetes, cancer). Studies including mixed populations, that is, comprising studies with both individuals who met and those who did not meet the eligibility criteria, were included if the results pertaining to the population of interest were reported separately. If results for the population of interest were not reported separately, studies with a mixed population were included if 80% or more of the study population met the inclusion criteria. Exclusion criteria included studies with individuals who were pregnant, residents in long-term care, patients in acute care or a hospital setting, people who were unable to move under their own power, and elite athletes. We also excluded studies that targeted exclusively patients with a sleep disorder or diagnosed disease (e.g., adults with insomnia or type 2 diabetes only) to keep the focus on the general population and not specific clinical populations.

Intervention (exposure)

The interventions or exposures were "sleep timing" and "sleep consistency". Sleep timing refers to the time of day that sleep occurs and is generally reported as bedtime/wake-up time or midpoint of sleep. Sleep consistency refers to the routine or regularity of sleep schedules and can be reported as intra-individual day-to-day variability in bedtimes/wake-up times/sleep duration or weekday-to-weekend variability in bedtimes/wake-up times/sleep duration (e.g., catch-up sleep and social jetlag). Studies were eligible if they used objective (e.g., polysomnography, actigraphy/accelerometry) or subjective (e.g., self-report) measures of sleep timing/consistency (or both). Only studies that quantified sleep timing/consistency were included. For experimental studies, the interventions must have targeted sleep timing/consistency exclusively and not multiple health behaviours (e.g., both sleep and diet). We excluded studies examining the impact of shift working, diurnal preference (morningness/eveningness), or chronotype (e.g., morning lark vs. night owl) because they have previously been extensively reviewed (Taylor and Hasler 2018; Rosa et al. 2019).

Comparison

Various levels of sleep timing/consistency were used for comparison. However, a comparator or control group was not required for inclusion.

Outcomes

A total of 14 health outcomes were chosen based on the literature, expert input and consensus, and recognition of the importance of including a broad range of health outcomes. Eight health outcomes were identified as *critical* (primary outcomes) by expert agreement (Ross et al. 2020): (*i*) mortality; (*ii*) cardiovascular disease (e.g., coronary artery disease, myocardial infarction, stroke); (*iii*) type 2 diabetes; (*iv*) mental health (e.g., depression, anxiety, psychological distress); (*v*) brain health (e.g., neurodegenerative disease such as Alzheimer's disease or Parkinson's disease); (*vi*) cognitive function (e.g., attention, problem solving, information processing, executive control, learning, memory, decision-making); (*vii*) falls; and (*viii*) accidents/injuries. Six health outcomes were identified as *important* (secondary outcomes) by expert agreement: (*i*) adiposity; (*ii*) biomarkers of cardiometabolic risk (e.g., insulin sensitivity,

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for the identification, screening, eligibility, and inclusion of studies. Reasons for excluding articles were wrong exposure (n = 27), wrong outcome (n = 18), wrong population (n = 8), and wrong intervention (n = 3).

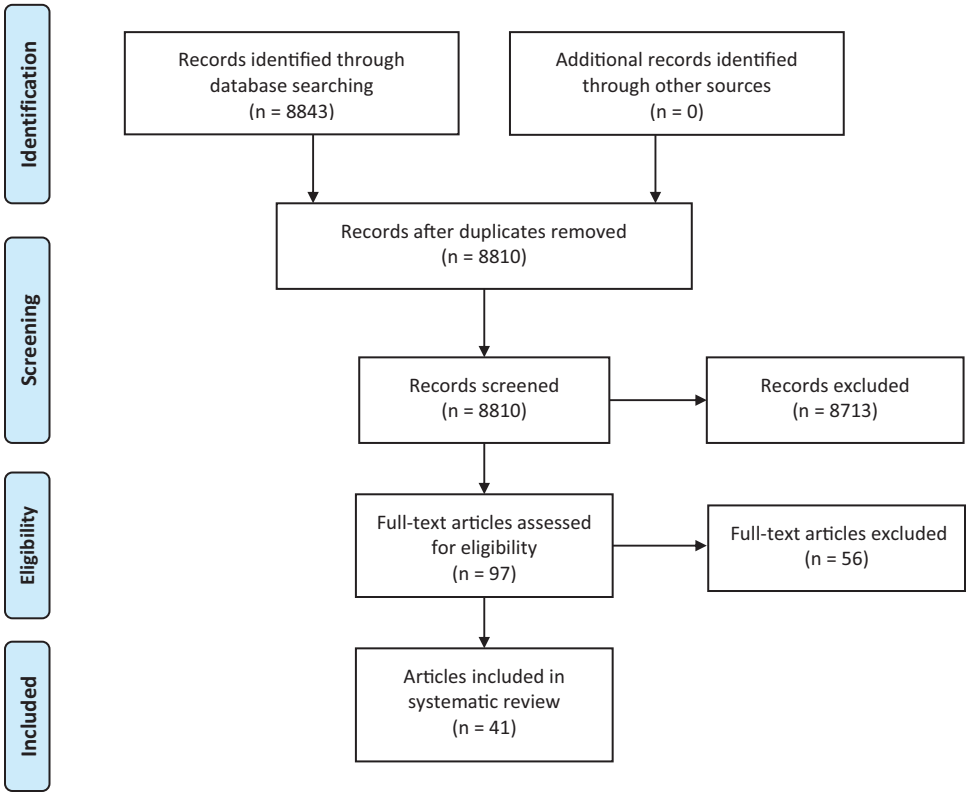

Table 1. Association between sleep timing, sleep variability, and cardiovascular disease in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Cross-sectional study[a]	Serious risk of bias[b]	Only 1 study	No serious indirectness	No serious imprecision	None	771	Intra-individual variability in sleep duration was not significantly associated with heart disease (OR: 1.41, 95% CI: 0.96–2.06) (Slavish et al. 2019)	Very low

Note: Mean age was 53.8 years. Data were collected cross-sectionally only. Sleep was self-reported using a sleep diary for 14 days and intra-individual variability in sleep duration (hours) was calculated using within-person night-to-night variation in total sleep time. The presence of a heart disease was determined by asking participants to indicate whether they had this health condition (yes or no). CI, confidence interval; OR, odds ratio.

[a]Includes 1 cross-sectional study (Slavish et al. 2019).

[b]Only 1 study was published, including self-reported measures of both the exposure and outcome with no psychometric properties reported, so the risk of bias is high. Therefore, the quality of evidence was downgraded from low to very low. Due to the fact that only 1 study was published with this outcome, a meta-analysis was not possible.

glucose tolerance, blood pressure, triglycerides); (*iii*) bone health (e.g., osteoporosis, bone mineral density, fractures); (*iv*) health-related quality of life; (*v*) work productivity (e.g., absenteeism, presenteeism, tests of productivity); and (*vi*) physical activity and sedentary behaviour.

Study designs

All study designs were eligible for inclusion. Only published or in press peer-reviewed studies were included. For longitudinal studies, any follow-up length was allowed as long as sleep timing/consistency was measured at 18 years or older. There were no sample size restrictions.

Information sources and search strategy

A research librarian with expertise in systematic review searching created the electronic search strategy and a second research librarian reviewed it (see Supplement S1[2] for the complete search strategies). The following databases were searched using the Ovid interface: MEDLINE, EMBASE, and PsycINFO. CINAHL was also searched using the EBSCO platform. Searches were conducted the week of December 18, 2018; studies published in the previous 10 years only were searched to manage scope and with a goal to include the most recent body of evidence. Recency in the evidence was also important to help inform the 2020 Canadian 24-hour

[2]Supplementary data are available with the article through the journal Web site at http://nrcresearchpress.com/doi/suppl/10.1139/apnm-2020-0032.

Table 2. Association between sleep timing, sleep variability, and type 2 diabetes in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
3	Cross-sectional study[a]	No serious risk of bias	Serious inconsistency[b]	No serious indirectness	No serious imprecision	None	4342	Each 1-h increment in sleep variability was positively associated with type 2 diabetes (PR: 1.14, 95% CI: 1.01–1.28) (Rosique-Esteban et al. 2018) Intra-individual variability in sleep duration was not significantly associated with type 2 diabetes (OR: 1.53, 95% CI: 0.99–2.34) (Slavish et al. 2019) In older participants (≥61 y), no significant associations were observed between social jetlag and prediabetes/type 2 diabetes. In the younger group (<61 y), the adjusted PRs were 1.39 (95% CI: 1.1–1.9) and 1.75 (95% CI: 1.2–2.5) for prediabetes/type 2 diabetes in adults with 1–2 h and >2 h of social jetlag compared with participants with <1 h of social jetlag (Koopman et al. 2017)	Very low

Note: Mean age ranged between 53.8 years and 65.0 years. Data were collected cross-sectionally only. Sleep was assessed using a wrist-worn accelerometer, self-reported using a sleep diary for 14 days, or self-reported by questionnaire. Type 2 diabetes was defined as previous clinical diagnosis of diabetes, HbA1c ≥ 6.5%, use of antidiabetic medication, fasting plasma glucose >126 mg/dL, or self-reported. CI, confidence interval; OR, odds ratio; PR, prevalence ratio.

[a]Includes 3 cross-sectional studies (Koopman et al. 2017; Rosique-Esteban et al. 2018; Slavish et al. 2019).

[b]Studies reported mixed findings (the quality of evidence was downgraded from low to very low). Due to heterogeneity in the measurement of sleep and type 2 diabetes, a meta-analysis was not possible.

Movement Guidelines that also integrate sleep (Ross et al. 2020). Reference lists of included studies were also checked. Studies were eligible for inclusion if they were published in English or French. We excluded case studies and grey literature (e.g., book chapters, dissertations, conference abstracts).

Study selection

Bibliographic records were extracted and imported into the Reference Manager Software (Thompson Reuters, San Francisco, Calif., USA) for removal of duplicate references. In level 1 screening, titles and abstracts of potentially relevant articles were screened by 2 independent reviewers using Covidence (Veritas Health Innovation, Melbourne, Australia). In level 2 screening, full-text copies of articles were obtained for those meeting initial screening. Two independent reviewers examined all full-text articles. Any discrepancies were resolved with a discussion and consensus between the 2 reviewers or by a third reviewer if required.

Data extraction

Microsoft Excel was used for data extraction. Data extraction was completed by 1 reviewer and verified by another reviewer. Where multiple models were reported, results from the most fully adjusted models were extracted. Important study features (i.e., author, publication year, country, study design, sample size, age, exposure, comparator, outcome, results, and covariates) were extracted. We also extracted information on whether the studies reported differences by age, sex, race/ethnicity, socioeconomic status, weight status, and/or chronic disease status. Reviewers were not blinded to the authors or journals when extracting data.

Risk of bias and study quality assessment

Using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework (Guyatt et al. 2011), we systematically assessed the quality of primary research contributing to each health outcome by type of study design and assessed the overall quality and risk of bias of the evidence across all health outcomes. Risk of bias assessment was completed for all included studies, by outcome, as described in the Cochrane Handbook (Higgins and Green 2011). GRADE categorizes the quality of evidence into 4 groups ("high", "moderate", "low", and "very low"), and the rating starts at high for randomized studies and at low for all other studies (e.g., nonrandomized experiments or observational studies). The quality of evidence can be upgraded (e.g., due to large magnitude of an effect, presence of a dose–response gradient, or effect of plausible residual confounding) or downgraded if there are serious limitations across studies (e.g., serious risk of bias, inconsistency of relative treatment effects, indirectness, imprecision, or other factors) (Guyatt et al. 2011). The quality of evidence assessment was conducted by the lead author and verified by the larger review team, including systematic review methodology experts. Disagreements were resolved by discussion among the team members, if needed. In an effort to include all available evidence, study quality did not influence eligibility for inclusion.

Synthesis of results

Meta-analyses were planned for each outcome in the event that findings were found to be sufficiently homogenous in terms of statistical, methodological, and clinical characteristics. If studies were deemed not appropriate for meta-analyses, narrative syntheses structured around the health outcomes were planned. Subgroups were defined as adults (18–64 years) and older adults (65 years and more) when possible.

Results

Description of studies

As reported in Fig. 1, a total of 8843 records were identified through database searches. After removing duplicates, a total of 8810 records remained. After titles and abstracts were screened,

Table 3. Association between sleep timing, sleep variability, and mental health in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Longitudinal study[a]	Serious risk of bias[b]	Only 1 study	No serious indirectness	No serious imprecision	None	3806	Multivariate logistic regression analyses revealed that mid-sleep time (<02:00 and ≥04:00 h vs. ≥02:00 and <04:00 h) was not significantly associated with incident clinically significant depression symptoms over 6 y (OR = 1.24, 95% CI: 0.95–1.61, $p = 0.12$). However, early mid-sleep time (<02:00 h) was significantly associated with incident clinically significant depression symptoms over 6 y (OR = 1.58, 95% CI: 1.13–2.20, $p = 0.008$) (Furihata et al. 2017)	Very low
5	Cross-sectional study[c]	Serious risk of bias[d]	Serious inconsistency[e]	No serious indirectness	No serious imprecision	None	9691	No significant association was found between sleep timing and depressive states (Kitamura et al. 2010) Social jetlag was positively correlated with BDI scores ($r = 0.30$, $p < 0.0001$). BDI scores were significantly higher in adults with >2 h of social jetlag than in those with ≤2 h of social jetlag. The association between social jetlag and BDI scores was stronger in the age group 31–40 y compared with the other age groups (18–30 y, 41–50 y, or >50 y) (Levandovski et al. 2011) A significant association was found between delayed sleep–wake schedule and depression among women only (OR: 1.75, 95% CI: 1.28–2.39) (Morita et al. 2015) Late bedtime was significantly associated with an increased prevalence of depressive symptoms (OR: 1.90, 95% CI: 1.16–3.12) for a bedtime of 01:00 h or later vs. 23:00 to 23:59 h. However, the association was no longer significant after adjusting for sleep duration (OR: 1.17, 95% CI: 0.66–2.06) (Sakamoto et al. 2013) Intra-individual variability in sleep duration (for every 1-h increase) was significantly associated with depression (OR: 2.42, 95% CI: 1.62–3.64, $p < 0.01$) and anxiety (OR: 1.77, 95% CI: 1.18–2.65, $p < 0.01$) (Slavish et al. 2019)	Very low

Note: Mean age ranged between 23.0 and 80.1 years. Data were collected cross-sectionally and with a 6-year follow-up for the longitudinal study. Sleep was self-reported using a sleep diary or a questionnaire. Depression symptoms were assessed with the Geriatric Depression Scale, the Center for Epidemiologic Studies Depression Scale, or the Beck Depression Inventory (BDI). Anxiety was assessed using the 20-item State-Trait Anxiety Inventory, Form Y Trait Scale. CI, confidence interval; OR, odds ratio.

[a]Includes 1 longitudinal study (Furihata et al. 2017).

[b]Only 1 study was published, including self-reported measures of sleep with no psychometric properties reported, so the risk of bias is high. Therefore, the quality of evidence was downgraded from low to very low.

[c]Includes 5 cross-sectional studies (Kitamura et al. 2010; Levandovski et al. 2011; Sakamoto et al. 2013; Morita et al. 2015; Slavish et al. 2019).

[d]Sleep was self-reported with no psychometric properties reported so the risk of bias is high.

[e]Studies reported mixed findings. Therefore, the quality of evidence was downgraded from "low" to "very low". Due to heterogeneity in the measurement of sleep and mental health, a meta-analysis was not possible.

Table 4. Association between sleep timing, sleep variability, and brain health in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Longitudinal study[a]	No serious risk of bias	Only 1 study	No serious indirectness	No serious imprecision	None	2238	Having late mid-sleep time was associated with a higher risk of cognitive decline when compared with average mid-sleep time (OR: 0.61, 95% CI: 0.41–0.90) (Suh et al. 2018)	Low
1	Cross-sectional study[b]	Serious risk of bias[c]	Only 1 study	No serious indirectness	No serious imprecision	None	771	Intra-individual variability in sleep duration (for every 1-h increase) was significantly associated with neurological problems (OR: 2.68, 95% CI: 1.37–5.22, $p < 0.01$) (Slavish et al. 2019)	Very low

Note: Mean age ranged between 53.8 and 68.1 years. Data were collected cross-sectionally and with a 4-year follow-up for the longitudinal study. Sleep was assessed with a questionnaire or by a sleep diary for 14 days. Incidence of mild cognitive impairment or dementia was assessed using neuropsychological tests by geriatric psychiatrists and the presence of a neurological disease (e.g. Parkinson's disease) was determined by asking participants to indicate whether they had this health condition (yes or no). CI, confidence interval; OR, odds ratio.

[a]Includes 1 longitudinal study (Suh et al. 2018).

[b]Includes 1 cross-sectional study (Slavish et al. 2019).

[c]Only 1 study was published, including self-reported measures of sleep with no psychometric properties reported, so the risk of bias is high. Therefore, the quality of evidence was downgraded from low to very low. Due to the fact that only 1 study was published for each study design, a meta-analysis was not possible.

97 full-text articles were obtained for further review and 41 articles met the inclusion criteria. Reasons for excluding articles were wrong exposure (n = 27), wrong outcome (n = 18), wrong population (n = 8), and wrong intervention (n = 3). Some studies were excluded for multiple reasons. See Supplement S2[2] for the complete list of full-text articles excluded.

Characteristics of studies sorted by outcome are summarized in Supplementary Table S1[2]. Data across studies involved 92 340 unique participants from 14 countries. The study designs were randomized trials (n = 2), longitudinal studies (n = 4), cross-sectional studies (n = 33), or longitudinal studies that also reported cross-sectional analyses (n = 2). Sleep was assessed objectively (polysomnography or actigraphy/accelerometry) in 37% of studies (n = 15) and subjectively (self-report) in 63% of studies (n = 26). None of the studies that used an objective sleep measure reported associations with a subjective sleep measure in addition to the objective one. Midpoint of sleep was the main sleep timing variable and day-to-day sleep duration variability was the main sleep consistency variable reported. It was determined by the review team that a meta-analysis was not possible because of high levels of heterogeneity across studies (see Supplementary Table S1[2]), and narrative syntheses were employed instead.

Data synthesis

Critical outcomes

Mortality

No studies examined the association between sleep timing/consistency and mortality in adults.

Cardiovascular disease

One cross-sectional study examined the association between sleep timing/consistency and cardiovascular disease in adults (Table 1 and Supplementary Table S1[2]). Slavish et al. (2019) showed that intra-individual variability in sleep duration was not significantly associated with heart disease (odds ratio (OR): 1.41, 95% confidence interval (CI): 0.96–2.06). The quality of evidence was downgraded from low to very low because of a serious risk of bias.

Type 2 diabetes

A total of 3 cross-sectional studies examined the association between sleep timing/consistency and type 2 diabetes in adults (Table 2 and Supplementary Table S1[2]). One study showed that greater sleep variability was associated with type 2 diabetes (Rosique-Esteban et al. 2018), 1 study reported null findings (Slavish et al. 2019), and 1 study reported that social jetlag was associated with type 2 diabetes only in adults aged 60 years or younger (Koopman et al. 2017). The quality of evidence for all 3 studies was downgraded from low to very low because of serious inconsistency in the findings.

Mental health

A total of 6 studies (1 longitudinal and 5 cross-sectional) examined the association between sleep timing/consistency and mental health in adults (Table 3 and Supplementary Table S1[2]). All studies for this outcome reported on depressive symptoms. The longitudinal study showed that the midpoint of sleep was not significantly associated with incident clinically significant depression symptoms over 6 years but early mid-sleep time (earliest octile of the midsleep time, <02:00 h) was (Furihata et al. 2017). The quality of evidence was downgraded from low to very low because of a serious risk of bias. Among the 5 cross-sectional studies, 3 reported that sleep variability, later bedtime and/or social jetlag were associated with depression (Levandovski et al. 2011; Sakamoto et al. 2013; Slavish et al. 2019), 1 reported that later sleep timing was associated with depression among women but not men (Morita et al. 2015), and 1 reported no association between sleep timing and depressive symptoms (Kitamura et al. 2010). The quality of evidence for these 5 cross-sectional studies was downgraded from low to very low because of a serious risk of bias and serious inconsistency in the findings.

Brain health

Two observational studies (1 longitudinal and 1 cross-sectional) examined the association between sleep timing/consistency and brain health in adults (Table 4 and Supplementary Table S1[2]). The longitudinal study showed that having a late midpoint of sleep (after 03:00 h) was associated with a higher risk of cognitive decline when compared with average midsleep time (Suh et al. 2018). The quality of evidence remained at low for the longitudinal study. The cross-sectional study reported that greater sleep variability was associated with neurological problems (Slavish et al. 2019). The quality of evidence was downgraded from low to very low because of a serious risk of bias.

Table 5. Association between sleep timing, sleep variability, and cognitive function in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
7	Cross-sectional study[a]	No serious risk of bias	Serious inconsistency[b]	No serious indirectness	No serious imprecision	None	775	Better learning, assessed by performance on trained items, was associated with earlier bedtimes ($r = -0.32$, $p = 0.01$). However, midpoint of sleep and intraindividual variability in bedtimes, sleep duration, and midpoint of sleep were not significantly associated with retention of learning or knowledge transfer (all $p > 0.20$) (Gao et al. 2019) Earlier sleep timing was associated with significantly fewer attentional lapses at postpartum weeks 9 and 12. A more stable sleep midpoint was associated with significantly fewer attentional lapses at postpartum weeks 2 and 5–13. Across the first 12 postpartum weeks, women with earlier or more stable sleep periods had less daytime impairment than women with later or more variable sleep midpoints. Postpartum women with earlier sleep midpoints also showed less severe decrements in performance across time, which has been attributed to cumulative impacts of sleep disturbance (McBean and Montgomery-Downs, 2013) Low sleep duration variability predicted better attentional performance. For students with low sleep duration variability, less sleep was associated (B = –0.25) with reduced ability to ignore irrelevant cues and redirect attention to target locations. In other words, consistently low sleep duration was associated with compromises in attention (Whiting and Murdock, 2016) Postural control performance (multisensory integration) was consistently better on Monday, after free sleep over the weekend, when compared with tests performed on Friday, which was after a work week (Umemura et al. 2018) Bedtimes and wake-up times were not independent predictors of "excellent" school performance in the fully adjusted model (BaHammam et al. 2012) FSE grades significantly correlated with mid-sleep time during the pre-exam period and the semester period (Spearman's rho of 0.54 and 0.41, respectively), with earlier sleep timing associated with better academic achievement (Genzel et al. 2013) Night-to-night variability in sleep duration was not associated with processing speed or reasoning (McCrae et al. 2012)	Very low

Note: Mean age ranged between 20.1 and 70.2 years. Sleep was assessed by actigraphy or with a sleep diary. Cognitive function was assessed through different tests, including an educational learning task to measure performance on trained and knowledge-transfer test problems, psychomotor vigilance reaction time tests, attentional capture tasks with cue-target intervals, postural control performance with the Biodex Balance System (multisensory integration), self-reported grades to assess academic performance, and processing speed and reasoning tests. FSE, final semester exam.

[a]Includes 7 cross-sectional studies (BaHammam et al. 2012; McCrae et al. 2012; Genzel et al. 2013; McBean and Montgomery-Downs 2013; Whiting and Murdock 2016; Umemura et al. 2018; Gao et al. 2019).

[b]Mixed findings reported, so the quality of evidence was downgraded from "low" to "very low" because of serious inconsistency. Due to heterogeneity in the measurement of sleep and cognitive function, a meta-analysis was not possible.

Table 6. Association between sleep timing, sleep variability, and accidents and injuries in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Cross-sectional study[a]	Serious risk of bias[b]	Only 1 study	No serious indirectness	No serious imprecision	None	253	Drivers who reported a >2-h change in sleep duration before the accident were not significantly more likely to be involved in single-vehicle accidents compared with ≤2 h (OR: 4.89, 95% CI: 0.78–30.59) (Lucidi et al. 2013)	Very low

Note: Mean age was 44.0 years. Data were collected cross-sectionally only. Sleep variability was self-reported through an interview. Diurnal car accidents notified between 07:00 and 10:00 h to the regional Rescue Service with a formal request for an ambulance on the accident site was the outcome variable. CI, confidence interval; OR, odds ratio.

[a]Includes 1 cross-sectional study (Lucidi et al. 2013).

[b]Only 1 study was published, including self-reported measures of sleep with no psychometric properties reported, so the risk of bias is high. Therefore, the quality of evidence was downgraded from "low" to "very low". Due to the fact that only 1 study was published with this outcome, a meta-analysis was not possible.

Cognitive function

A total of 7 cross-sectional studies examined the association between sleep timing/consistency and cognitive function in adults (Table 5 and Supplementary Table S1[2]). Among them, 5 generally reported that sleep variability and/or later sleep timing were associated with adverse cognitive function (Genzel et al. 2013; McBean and Montgomery-Downs 2013; Whiting and Murdock 2016; Umemura et al. 2018; Gao et al. 2019) while 2 reported null findings (BaHammam et al. 2012; McCrae et al. 2012). The quality of evidence was downgraded from low to very low because of serious inconsistency.

Falls

No studies examined the association between sleep timing/consistency and falls in adults.

Accidents and injuries

Only 1 study examined the association between sleep timing/consistency and accidents/injuries in adults (Table 6 and Supplementary Table S1[2]). This cross-sectional study (Lucidi et al. 2013) showed that there was no significant difference in the likelihood of single-vehicle accidents when comparing drivers who reported a change in sleep duration of more than 2 h before the accident to those with a change in sleep duration of less than 2 h. The quality of evidence was downgraded from low to very low because of a serious risk of bias.

Important outcomes

Adiposity

A total of 11 studies (3 longitudinal and 8 cross-sectional studies) examined the association between sleep timing/consistency and adiposity in adults (Table 7 and Supplementary Table S1[2]). Among the longitudinal studies, 2 reported that greater variability in sleep was associated with weight gain (Kobayashi et al. 2013; Roane et al. 2015) while 1 study reported null findings (Taylor et al. 2016). The quality of evidence remained at low for the longitudinal studies. Among the 8 cross-sectional studies, 3 studies reported that greater sleep variability or later sleep timing were associated with higher adiposity (Kim et al. 2015; Taylor et al. 2016; Sasaki et al. 2018), 2 studies reported null findings (Baron et al. 2011; Rosique-Esteban et al. 2018), 1 study reported that weekend catch-up sleep was associated with lower body mass index (BMI) (Im et al. 2017), 1 study reported that social jetlag was associated with obesity (Parsons et al. 2015), and 1 study reported that social jetlag was not associated with overweight/obesity (Zhang et al. 2018). The quality of evidence was downgraded from low to very low because of serious inconsistency.

Biomarkers of cardiometabolic risk

A total of 14 studies (1 randomized trial, 2 longitudinal studies, and 11 cross-sectional studies) examined the association between sleep timing/consistency and biomarkers of cardiometabolic risk in adults (Table 8 and Supplementary Table S1[2]). The randomized trial showed no effect of sleep timing on acute insulin response to glucose, disposition index, or insulin sensitivity (Pizinger et al. 2018). The quality of evidence was downgraded from high to moderate because of serious imprecision. The longitudinal studies reported that sleep variability and later sleep timing were associated with higher cardiometabolic risk (Taylor et al. 2016; Huang and Redline 2019). The quality of evidence remained at low for the longitudinal studies. Among the 11 cross-sectional studies, 3 studies reported that greater sleep variability or later sleep timing were associated with higher cardiometabolic risk (Taylor et al. 2016; Knutson et al. 2017; Huang and Redline 2019), 4 studies reported null findings (Bei et al. 2017; Buxton et al. 2018; Abbott et al. 2019; Slavish et al. 2019), 1 study reported that weekend catch-up sleep was associated with lower cardiometabolic risk (Hwangbo et al. 2013), and 3 studies reported that social jetlag was associated with higher cardiometabolic risk (Rutters et al. 2014; Parsons et al. 2015; Wong et al. 2015). The quality of evidence remained at low for the cross-sectional studies.

Bone health

Two cross-sectional studies examined the association between sleep timing/consistency and bone health in adults (Table 9 and Supplementary Table S1[2]). The cross-sectional studies reported that later sleep timing was associated with osteopenia (Lucassen et al. 2017) and osteoporosis (Wang et al. 2015). The quality of evidence was downgraded from low to very low due to a serious risk of bias.

Health-related quality of life

Only 1 study examined the association between sleep timing/consistency and health-related quality of life in adults (Table 10 and Supplementary Table S1[2]). This cross-sectional study (Oh et al. 2019) showed that catch-up sleep was associated with better health-related quality of life. The quality of evidence was downgraded from low to very low because of a serious risk of bias.

Work productivity

No studies examined the association between sleep timing/consistency and work productivity in adults.

Physical activity and sedentary behaviour

A total of 4 studies (1 randomized trial and 3 cross-sectional studies) examined the association between sleep timing/consistency

Table 7. Association between sleep timing, sleep variability, and adiposity in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
3	Longitudinal study[a]	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	21 586	Greater variability in sleep duration was independently associated with an increase in BMI (β coefficient = 0.31, 95% CI: 0.01–0.61, $p < 0.05$) (Kobayashi et al. 2013) Variability in sleep duration ($r = 0.32$) and wake-up time ($r = 0.27$) were significantly correlated with weight gain. In hierarchical regression analyses, greater variability in sleep duration was a significant predictor of weight gain for males ($r = 0.53$, $p < 0.001$), but not for females ($r = 0.09$, $p = 0.24$). Greater bedtime variability was also a significant predictor of weight gain for males ($r = 0.35$, $p = 0.005$) but not for females ($r = –0.08$, $p = 0.52$) (Roane et al. 2015) Associations between sleep timing and variability with BMI were not statistically significant (Taylor et al. 2016)	Low
8	Cross-sectional study[b]	No serious risk of bias	Serious inconsistency[c]	No serious indirectness	No serious imprecision	None	15 804	$n = 3$ studies reported that greater sleep variability or later sleep timing was associated with higher adiposity (Kim et al. 2015; Taylor et al. 2016; Sasaki et al. 2018) $n = 2$ studies reported null findings between sleep variability or sleep timing and adiposity (Baron et al. 2011; Rosique-Esteban et al. 2018) $n = 1$ study reported that weekend catch-up sleep was associated with lower BMI (Im et al. 2017) $n = 1$ study reported that social jetlag was associated with obesity (Parsons et al. 2015) $n = 1$ study reported that social jetlag was not associated with overweight/obesity (Zhang et al. 2018)	Very low

Note: Mean age ranged between 18.6 and 83.4 years. Data were collected cross-sectionally and up to 9 years. Sleep was assessed by wrist actigraphy, daily sleep diaries or self-reported by questionnaire. Adiposity was assessed by objectively measured or self-reported height and weight to calculate body mass index (BMI) or by dual-energy X-ray absorptiometry. Outcomes included change in BMI, weight change, percent body fat, fat mass index, and obesity (BMI ≥30, ≥28, or ≥25 kg/m^2). CI, confidence interval.

[a]Includes 3 longitudinal studies (Kobayashi et al. 2013; Roane et al. 2015; Taylor et al. 2016).

[b]Includes 8 cross-sectional studies (Baron et al. 2011; Kim et al. 2015; Parsons et al. 2015; Taylor et al. 2016; Im et al. 2017; Rosique-Esteban et al. 2018; Sasaki et al. 2018; Zhang et al. 2018).

[c]Mixed findings reported, so the quality of evidence was downgraded from "low" to "very low" because of serious inconsistency. Due to heterogeneity in the measurement of sleep and adiposity, a meta-analysis was not possible.

Table 8. Association between sleep timing, sleep variability, and biomarkers of cardiometabolic risk in adults.

No. of studies	Design	Quality Assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Randomized trial[a]	No serious risk of bias	Only 1 study	No serious indirectness	Serious imprecision[b]	None	5	Participants underwent a 2-phase randomized crossover inpatient study differing in sleep times: normal (00:00–08:00 h) or late (03:30–11:30 h). There was no effect of sleep timing on acute insulin response to glucose, disposition index, or insulin sensitivity (all $p > 0.90$) (Pizinger et al. 2018)	Moderate
2	Longitudinal study[c]	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	1211	Every 1-h increase in the sleep duration SD was associated with 27% (95% CI: 0.97–1.65) higher odds of incident metabolic syndrome, and every 1-h increase in the sleep timing SD was associated with 36% (95% CI: 1.03–1.80) higher odds of incident metabolic syndrome (Huang and Redline 2019) Greater bedtime delay at baseline predicted increased HOMA-IR at follow-up ($\beta = 0.152$, $p < 0.01$). Associations were not statistically significant with the other sleep timing indicators (Taylor et al. 2016)	Low
11	Cross-sectional study[d]	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	24 597	$n = 3$ studies reported that greater sleep variability or later sleep timing was associated with higher cardiometabolic risk (Taylor et al. 2016; Knutson et al. 2017; Huang and Redline 2019) $n = 4$ studies reported null findings between sleep variability or sleep timing with cardiometabolic risk (Bei et al. 2017; Buxton et al. 2018; Abbott et al. 2019; Slavish et al. 2019) $n = 1$ study reported that weekend catch-up sleep was associated with lower cardiometabolic risk (Hwangbo et al. 2013) $n = 3$ studies reported that social jetlag was associated with higher cardiometabolic risk (Rutters et al. 2014; Parsons et al. 2015; Wong et al. 2015)	Low

Note: Mean age ranged between 25.1 and 69.6 years. The intervention study comprised 3 days and there were up to 6.3 years of follow-up for the longitudinal studies. Sleep was assessed by polysomnography, actigraphy, daily sleep diaries or self-reported by questionnaire. Cardiometabolic risk was assessed through insulin sensitivity (insulin-modified frequently sampled intravenous glucose tolerance test), metabolic syndrome (National Cholesterol Education Program Adult Treatment Panel III criteria), insulin resistance (homeostasis model assessment of insulin resistance; HOMA-IR), glucose and insulin concentrations, oral glucose tolerance test, systolic and diastolic blood pressure, hypertension status, resting heart rate, lipid profile, HbA1c, allostatic load (23 biomarkers from 7 systems), and cardiometabolic risk score (Framingham risk score). CI, confidence interval.

[a]Includes 1 randomized crossover trial (Pizinger et al. 2018).

[b]Only 1 study was published, including only 5 participants (pilot study) and limited power to detect differences, so the risk of imprecision is high. Therefore, the quality of evidence was downgraded from "high" to "moderate".

[c]Includes 2 longitudinal studies (Taylor et al. 2016; Huang and Redline 2019).

[d]Includes 11 cross-sectional studies (Hwangbo et al. 2013; Rutters et al. 2014; Parsons et al. 2015; Wong et al. 2015; Taylor et al. 2016; Bei et al. 2017; Knutson et al. 2017; Buxton et al. 2018; Abbott et al. 2019; Huang and Redline 2019; Slavish et al. 2019). Due to heterogeneity in the measurement of sleep and cardiometabolic risk, a meta-analysis was not possible.

Table 9. Association between sleep timing, sleep variability, and bone health in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
2	Cross-sectional study[a]	Serious risk of bias[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	7425	One hour later sleep timing was associated with osteopenia (OR: 1.51, 95% CI: 1.08–2.11) (Lucassen et al. 2017) Osteoporosis risk was significantly higher in post-menopausal women with bedtimes ≥0:00 h compared with those whose bedtimes were <0:00 h (OR: 1.69, 95% CI: 1.39–2.13) (Wang et al. 2015)	Very low

Note: Mean age ranged between 55.5 and 58.3 years. Data were collected cross-sectionally. Sleep was self-reported by questionnaire in both studies. In the first study, bone mineral density was assessed using dual-energy X-ray absorptiometry and osteopenia was defined as a T-score between –1 and –2.5. In the second study, calcaneal quantitative ultrasound was used to estimate bone mineral density and a T-score of <–2.5 was defined as osteoporosis. CI, confidence interval; OR, odds ratio.

[a]Includes 2 cross-sectional studies (Wang et al. 2015; Lucassen et al. 2017).

[b]Sleep was self-reported with no psychometric properties reported so the risk of bias is high. Therefore, the quality of evidence was downgraded from "low" to "very low". Due to heterogeneity in the measurement of sleep and bone health, a meta-analysis was not possible.

and physical activity/sedentary behaviour in adults (Table 11 and Supplementary Table S1[2]). The randomized trial reported mixed findings (McNeil et al. 2016) and the quality of evidence was downgraded from high to moderate because of serious imprecision. The 3 cross-sectional studies reported that later sleep timing and social jetlag were associated with lower physical activity and higher sedentary behaviour (Rutters et al. 2014; Shechter and St-Onge 2014; Duncan et al. 2016). The quality of evidence remained at low for the cross-sectional studies.

Summary of findings

A high-level summary of findings by health outcome can be found in Table 12. Overall, 31 (63%) studies showed that sleep variability, social jetlag, and later sleep timing were associated with adverse health outcomes; 14 (29%) showed null findings; and 4 (8%) showed mixed findings. Among the 3 studies that examined catch-up sleep, all of them (100%) found that weekend catch-up sleep was associated with positive health outcomes. The overall quality of evidence ranged from very low to moderate.

Variation of effect by sociodemographic characteristics and health status

An objective of this review was to examine if the associations between sleep timing/consistency and health outcomes differed by age, sex, race/ethnicity, socioeconomic status, weight status, and/or chronic disease status by looking at subgroup analyses and/or effect modification. We found that 73% of studies did not report this information; 17% of studies found some variation of effect (mainly by age and/or sex and generally found stronger associations in younger adults and women, for example); and 10% of studies reported no variation of effect for age, sex, race/ethnicity, and/or chronic disease status.

Discussion

This systematic review synthesized peer-reviewed scientific evidence from 41 manuscripts examining the associations between sleep timing, sleep consistency/regularity, and health outcomes in adults aged 18 years and older. The overall quality of evidence ranged from very low to moderate across study designs and outcomes. Collectively, later sleep timing and more sleep variability were generally associated with adverse health outcomes. However, the evidence currently available on sleep timing and consistency does not support the development of quantifiable targets on what was constitutes "late sleep timing" or "large sleep variability" because most studies reported linear associations only. Additionally, the present systematic review showed that social jetlag was associated with adverse health outcomes while weekend catch-up sleep was protective in the few studies that considered this exposure (n = 3). Overall, this comprehensive assessment of available evidence supports the concept that earlier sleep timing is favourably associated with health while regularity in sleep with consistent bedtimes and wake-up times is beneficial for health outcomes among adults.

More studies of the studies in this systematic review examined cardiometabolic health (n = 14) and adiposity (n = 11), and fewer studies examined our other outcomes of interest. No studies examined the relationships between sleep timing/consistency and mortality, falls, or work productivity. Also, only 1 study looked at cardiovascular disease, accidents/injuries, and health-related quality of life. Future studies will need to cover a broader range of outcomes to deepen our understanding of this topic area. For example, the 1 study on cardiovascular disease had a 95% CI that barely crossed one (OR: 1.41, 95% CI: 0.96–2.06) and, therefore, reported null findings (Slavish et al. 2019). More studies are definitively needed to confirm such findings. The imbalance between the number of studies reporting on critical health outcomes (n = 20) versus important ones (n = 32) also reminds us that it is easier to publish studies with outcomes such as adiposity and cardiometabolic risk instead of mortality or cardiovascular disease. Higher quality studies with hard outcomes are needed in this field of research to better inform public health guidelines. In addition, future studies should use statistical approaches that provide a more detailed exploration of the dose–response relationship between sleep timing/consistency and health outcomes as such approaches may provide clear cut-offs that could be used for public health guidelines.

Day-to-day variability in sleep is increasingly recognized as an important feature of sleep health beyond mean sleep (Chaput and Shiau 2019). A recent systematic review showed that the correlates most consistently associated with greater intra-individual variability in sleep/wake patterns were younger age, non-White race/ethnicity, living alone, physical health conditions, higher BMI, weight gain, bipolar and unipolar depression symptomatology, stress, and evening chronotype (Bei et al. 2016). While the underlying mechanisms remain to be elucidated, sleep schedule irregularity can give rise to sleep disturbances because of misalignment between sleep-wake timing and the circadian system (Irish et al. 2015). The resultant reduction in sleep and its continuity could lead to metabolic and health impairments. However, the extent to which this effect is independent of total sleep duration is not fully

Table 10. Association between sleep timing, sleep variability, and health-related quality of life in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Cross-sectional study[a]	Serious risk of bias[b]	Only 1 study	No serious indirectness	No serious imprecision	None	4871	The proportions of "have problems" response in each EQ-5 D dimension were significantly higher in the non-catch-up sleep group. The EQ-5 D index score was also higher (better) in the catch-up sleep group compared with the non-catch-up sleep group (0.975 ± 0.001 vs. 0.958 ± 0.001, $p < 0.001$). In multivariate logistic regression analyses, the OR for having problems in the dimensions of usual activities (OR: 1.63, 95% CI: 1.07–2.47) and anxiety/depression (OR: 1.45, 95% CI: 1.11–1.90) were significantly higher in the non-catch-up sleep group (Oh et al. 2019)	Very low

Note: Mean age was 44.5 years. Data were collected cross-sectionally. Sleep was self-reported by questionnaire. Health-related quality of life was assessed using the Korean version of the European quality of life scale-5 dimensions (EQ-5 D). CI, confidence interval; OR, odds ratio.

[a]Includes 1 cross-sectional study (Oh et al. 2019).

[b]Sleep was self-reported with no psychometric properties reported so the risk of bias is high. Therefore, the quality of evidence was downgraded from "low" to "very low". Due to the fact that only 1 study was published with this outcome, a meta-analysis was not possible.

clear. For example, associations between greater bedtime variability and insulin resistance were seen even after adjusting for sleep duration in the study by Taylor et al. (2016) while sleep timing, without concomitant sleep restriction, did not affect insulin sensitivity and glucose tolerance in the experimental study by Pizinger et al. (2018). More studies are needed in this area to better elucidate the underlying mechanisms and define normal sleep variability and timing.

Social jetlag is increasingly studied in the literature and reflects the variability in circadian timing across work days and non-work days. It is generally measured as the difference in the midpoint of sleep (in hours) between weekdays and weekends (free days). Findings from the present review support the view that social jetlag is associated with adverse effects on health. The discrepancy between circadian and social clocks is highly prevalent; 69% of adults report at least 1 h of social jetlag, and it is known to disturb physiological processes (Koopman et al. 2017). Future studies will need to better quantify what is considered "bad" social jetlag for clinical and public health guidelines.

Weekend catch-up sleep is another indicator of sleep variability (i.e., weekend-to-weekday sleep duration variability). Although only 3 studies were included in this review, they all showed that weekend catch-up sleep was favourably associated with health outcomes. This suggests that although it would be better to obtain sufficient sleep on all 7 days of the week, catching-up on weekday sleep debt on the weekend appears to be better than not doing it. Recovering a sleep debt by extending sleep over the weekend is a compensatory behaviour that needs further investigations before evidence-based public health recommendations can be made. It is also interesting to note the apparent contradiction that both catch-up sleep and sleep regularity improve health. To catch up sleep, changes in bedtime and/or wake-up time are necessary. It will be important for future studies to shed some light on this issue and determine whether catch-up sleep on a chronic basis is really a healthy habit or not.

There are very few studies that explore whether associations between sleep timing/consistency and health outcomes vary as a function of age, sex, race/ethnicity, socioeconomic status, weight status and/or chronic disease status. Unfortunately, 73% of studies did not conduct subgroup analyses nor report effect modification data, making it difficult to know whether the findings observed can be generalized to all community-dwelling adults. Those studies that did report on subgroup analyses or effect modification reported inconsistent findings. Specifically, 17% of studies found some variation of effect (mainly by age and/or sex), with generally stronger associations in younger adults and in women while 10% of studies reported that there were no modifications of the effect for age, sex, race/ethnicity, and/or chronic disease status. Future studies should thus conduct subgroup analyses when possible to help determine whether the associations observed can be applied broadly to the adult population for public health guidance.

Results synthesized in the present systematic review can have important public health implications. Irregular sleep is a highly prevalent form of chronic circadian disruption in today's society (Huang and Redline 2019) and our findings suggest it may be a modifiable risk factor for several important health indicators. Beyond sleep duration and quality, findings from this review show that sleep timing and sleep regularity are also important components of sleep hygiene. Future studies should endeavour to provide practical quantitative cut-offs so that the general public can have a benchmark to aim for. With advances in wearable health technologies that monitor sleep patterns, measures of sleep timing and regularity can be readily derived and tracked. In the meantime, encouraging consistency in sleep schedules and reducing sleep variability should be recommended for healthy sleep.

A number of limitations of this review should be highlighted. First, the high level of heterogeneity across studies precluded

Table 11. Association between sleep timing, sleep variability, and physical activity and sedentary behaviour in adults.

No. of studies	Design	Quality assessment					No. of participants	Absolute effect	Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other			
1	Randomized trial[a]	No serious risk of bias	Only 1 study	No serious indirectness	Serious imprecision[b]	None	18	Relative moderate-intensity physical activity time was greater in the delayed bedtime session vs. control and advanced wake-time sessions (26.6% ± 19.9% vs. 16.1% ± 10.6% and 17.5% ± 11.8%, $p = 0.01$), whereas vigorous-intensity physical activity time was greater following advanced wake-time vs. delayed bedtime (2.7% ± 3.0% vs. 1.3% ± 2.4%, $p = 0.004$). No differences in sedentary time were observed between sessions (McNeil et al. 2016)	Moderate
3	Cross-sectional study[c]	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	1484	Later bedtime (coefficient = –1.62 and 3.94, respectively), later wake-up time (coefficient = –1.68 and 3.81, respectively), and later midpoint of sleep (coefficient = –1.70 and 3.99, respectively) were significantly associated with less time spent in MVPA and increased time in sedentary activity (Shechter and St-Onge 2014) Later wake-up times were associated with fewer minutes of physical activity (β = 0.995, 95% CI: 0.99–1.00, $p = 0.03$). The associations between bedtimes or variability in bedtimes or wake-up times with physical activity were not significant. Having bedtimes that varied by >30 min was associated with higher sitting time (β = 1.07, 95% CI: 1.01–1.13, $p = 0.01$). Other associations between sleep and sitting time were not significant (Duncan et al. 2016) Participants with ≥2 h of social jetlag were more physically inactive compared with participants who had ≤1 h of social jetlag (7.6 ± 2.5 vs. 8.7 ± 1.4, $p < 0.05$) (Rutters et al. 2014)	Low

Note: Mean age ranged between 23.0 and 57.0 years. The sleep restriction trial comprised 1 day and included 3 sessions: (1) control (habitual sleep); (2) 50% sleep restriction with an advanced wake-up time; and (3) 50% sleep restriction with a delayed bedtime. Sleep was assessed by polysomnography, actigraphy, or self-reported by questionnaire. Physical activity and sedentary behaviours were assessed by accelerometry or by questionnaire. CI, confidence interval; MVPA, moderate-to-vigorous physical activity.

[a]Includes 1 randomized crossover study (McNeil et al. 2016).

[b]Only 1 study was published, including a small sample of healthy and active adults with good sleep. Furthermore, the assessment of sleep and outcomes was only conducted for 1 night and 36-h post-intervention in each condition, which does not account for day-to-day variations (so the risk of imprecision is high). Therefore, the quality of evidence was downgraded from "high" to "moderate".

[c]Includes 3 cross-sectional studies (Rutters et al. 2014; Shechter and St-Onge 2014; Duncan et al. 2016). Due to heterogeneity in the measurement of sleep and physical activity and sedentary behaviour, a meta-analysis was not possible.

Table 12. High-level summary of findings by outcome.

Outcome	No. of studies	Quality of evidence	Summary of findings
Critical			
Mortality	0	NA	NA
Cardiovascular disease	1	Very low	Variability in sleep duration was not associated with heart disease
Type 2 diabetes	3	Very low	*n* = 1 study reported that sleep variability was associated type 2 diabetes *n* = 1 study reported null findings *n* = 1 study reported that social jetlag was associated with type 2 diabetes in younger adults only
Mental health	6	Very low	*n* = 3 studies reported that sleep variability, later bedtime, and social jetlag were associated with depression *n* = 1 study reported that later sleep timing was associated with depression among women only *n* = 1 study reported null findings *n* = 1 study reported mixed findings
Brain health	2	Very low to low	*n* = 2 studies reported that sleep variability and later bedtime were associated with adverse brain health outcomes
Cognitive function	7	Very low	*n* = 5 studies reported that sleep variability and later sleep timing were associated with adverse cognitive function *n* = 2 studies reported null findings
Falls	0	NA	NA
Accidents and injuries	1	Very low	*n* = 1 study reported that sleep variability was associated with car accidents
Important			
Adiposity	11	Very low to low	*n* = 6 studies reported that sleep variability, later sleep timing and social jetlag were associated with adiposity *n* = 4 studies reported null findings *n* = 1 study reported that weekend catch-up sleep was associated with lower adiposity
Biomarkers of cardiometabolic risk	14	Low to moderate	*n* = 8 studies reported that sleep variability, later sleep timing, and social jetlag were associated with higher cardiometabolic risk *n* = 5 studies reported null findings *n* = 1 study reported that weekend catch-up sleep was associated with lower cardiometabolic risk
Bone health	2	Very low	*n* = 2 studies reported that later sleep timing was associated with osteopenia and osteoporosis
Health-related quality of life	1	Very low	*n* = 1 study reported that catch-up sleep was associated with better health-related quality of life
Work productivity	0	NA	NA
Physical activity and sedentary behaviour	4	Low to moderate	*n* = 3 studies reported that later sleep timing and social jetlag were associated with lower physical activity and higher sedentary behaviour *n* = 1 study reported mixed findings

Note: The number of studies is more than *N* = 41 because some papers had more than one outcome measure and/or study design. NA, not applicable.

conducting meta-analyses. Second, the available evidence largely comprised cross-sectional studies and 63% of studies relied on self-reported sleep. More longitudinal and experimental studies that use objective measures of sleep over a longer period of time are needed. It is important to note, however, that polysomnography, actigraphy, diary, and questionnaires all represent fundamentally different strategies for estimating sleep; they are all useful but measure different things. For this reason, they are difficult to compare. Third, three-quarters of studies did not report possible modification of effect by age, sex, race/ethnicity, socioeconomic status, weight status, or chronic disease status. It is thus difficult to determine whether the effects observed apply broadly to all adults in the general population. Fourth, this review excluded studies that targeted clinical populations exclusively as well as those about shiftworking, diurnal preference (morningness/eveningness), or chronotype to keep the emphasis on studies that quantified sleep timing/consistency. Fifth, this review only included articles published in English or French and conducted over the past 10 years. However, excluding non-English publications from evidence syntheses does not impact conclusions according to a recent meta-epidemiologic study (Nussbaumer-Streit et al. 2020). Finally, the risk of publication bias (i.e., an overrepresentation of studies with significant findings) cannot be discarded.

Conclusion

Overall, our findings support the notion that later sleep timing and greater sleep variability are both associated with adverse health outcomes. However, the available evidence is unable to provide clear targets to achieve. Thus, earlier sleep timing and regularity in sleep with consistent bedtimes and wake-up times are advised to promote health benefits.

Conflict of interest statement

T.J.S. reports grants from the Public Health Agency of Canada during the conduct of the study, personal fees from the Public Health Agency of Canada, and the PEI Public Schools Branch. V.J.P. reports personal fees from the Canadian Society for Exercise Physiology during the conduct of the study and is a Canadian Agency for Drugs and Technology in Health (CADTH) employee. The current work was unrelated to her employment, and CADTH had no role in the funding, design, or oversight of the work reported. M.E.K. reports personal fees and nonfinancial support from the Canadian Society for Exercise Physiology during the conduct of the study. A.R.-W. reports personal fees from ProQuest LLC outside of the submitted work. J.C. reports grants from Canopy Growth, Rana, Philipps/Respironics, Merck, and Eisai outside the

submitted work. The remaining authors declare that they have no conflicts of interest.

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