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A systematic review of the association between sleep health and stress biomarkers in children

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SUMMARY

Sleep is intimately linked with the stress response system. While the evidence for this connection has been systematically reviewed in the adult literature, to our knowledge no studies have examined this relationship in young children. Recent scientific interest in understanding the effects of adverse environments in early childhood, including an emphasis on understanding the role of sleep, highlights the importance of synthesizing the current evidence on the relationship between sleep and the stress response system in early childhood. The aim of this systematic review is to examine the relationship between sleep health and biomarkers of physiologic stress (neuroendocrine, immune, metabolic, cardiovascular) in healthy children ages 0–12 y. Following PRISMA guidelines, we identified 68 empirical articles and critically reviewed and synthesized the results across studies. The majority of studies included school-age children and reported sleep dimensions of duration or efficiency. Overall, evidence of associations between sleep health and stress biomarkers was strongest for neuroendocrine variables, and limited or inconsistent for studies of immune, cardiovascular, and metabolic outcomes. Gaps in the literature include prospective, longitudinal studies, inclusion of children under the age of 5 y, and studies using objective measures of sleep.

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Conflicts of interest

The authors do not have any conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smrv.2021.101494.

Keywords

Biomarkers; Sleep; Sleep health; Stress; Chronic stress; Toxic stress; Systematic review; Physiological stress; Stress response; Pediatrics; Healthy brain and child development study

Introduction

Children who experience chronic stress early in life for economic, environmental, psychosocial, or other reasons are at increased risk for future disease [1]. This increased risk is a result of prolonged activation of primary mediators of the child's stress response system (e.g., glucocorticoids, cytokines, catecholamines) that leads to ‘wear and tear’ on the body and contributes to poor secondary outcomes, such as impaired cardiometabolic functioning, across the lifespan (Fig. 1). Prolonged activation of children's stress response system in the absence of sufficient protective factors is termed ‘toxic stress’ [1,2]. As there is strong evidence linking sleep with the stress response among adults [3], an improved understanding of the relationship between sleep health and physiologic stress in early childhood is needed to direct future research and inform approaches to intervention for children experiencing chronic stress – especially considering the modifiable nature of sleep.

The stress response involves multiple physiologic systems (Fig. 1), and studies of adults and animal models demonstrate the close relationships between these systems and sleep health. For example, sleep has a bidirectional relationship with the hypothalamic-pituitary-adrenal (HPA) axis, a key neuroendocrine regulator of the stress response. Over-activation of the HPA-axis leads to shortened sleep duration, sleep fragmentation, and decreased slow wave sleep, and sleep deficiency exacerbates HPA-axis dysfunction [4]. Cytokines are immune modulators of the stress response system, but interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α) have specific effects on sleep-wake behavior, as documented in electrophysiological, biochemical, and molecular genetic studies [5]. Interleukin-6 (IL-6) modulates sleep-wake behaviors during physiologic disruption, meaning that in the presence of certain pathogens, IL-6 affects sleep-wake behavior, but not in healthy conditions [5]. Increases in blood pressure, insulin, and glucose are detectable within days of sleep deprivation or circadian disruption [3,6], and chronic sleep deficiency alters autonomic nervous system function, increases oxidative stress, and accelerates atherosclerosis [7]. Reviews by Irwin and Opp [8] and Van Reeth et al. [9] and the references in Fig. 1 provide more detail on these relationships from the adult literature.

In 2012, the American Academy of Pediatrics published a seminal report describing an urgent need to support three foundations of health (caregiving, environment, and nutrition) to protect against toxic stress (i.e., prolonged stress response) in childhood, based on scientific evidence that these foundations of health influence lifelong health through physiologic adaptations and disruptions [1]. Sleep health [10] was notably missing from this report despite strong evidence linking sleep and physiologic adaptations and disruptions in the adult literature [11-13]. It was not until 2014 that a definition of ‘sleep health’ was published to emphasize the positive role of sleep in overall health among adults [10]. Buysse identified five dimensions (SATED: Satisfaction, Alertness, Timing, Efficiency,

and Duration) of sleep as important targets for health promotion and prevention activities [10] – emphases historically absent in health promotion messages and strategies [14]. This conceptualization sparked interest in sleep as a potential modifiable target for health promotion and disease prevention. Recently, in 2021, Buysse's definition of sleep health was examined and applied to children in a theoretical review [15]. This reconceptualization of sleep health for pediatric populations maintained Buysse's five dimensions (SATED) of sleep health and added a sixth dimension – behavior (B-SATED) – that includes sleep-related behaviors in children that can support or undermine their sleep, such as regularity of bedtime routine and bedtimes. To advance this field, it is important to improve understanding of the associations between sleep health and physiological changes in early life and factors that may contribute to chronic disease. Thus, the purpose of this systematic review is to identify, evaluate and synthesize the scientific evidence for the relationships between sleep health and physiological biomarkers of the stress response system in early childhood.

Methods

Search strategy

We performed a systematic search of the literature to identify studies that reported associations between sleep health dimensions and biomarkers of physiologic stress in children. We pre-registered our protocol with PROSPERO (CRD42018089780) and conducted the review following PRISMA guidelines [16]. Experienced medical librarians (MCF, JB) consulted on the methodology and ran a medical subject heading (MeSH) analysis of key articles provided by the research team [mesh.med.yale.edu]. In each database we ran scoping searches and used an iterative process to translate and refine the searches (see Appendix A). To maximize sensitivity, we used controlled vocabulary terms and synonymous free-text words to capture the concepts of “physiological stress”, “sleep” and “children”. On January 21, 2018, October 11, 2019, and March 11, 2021, we performed a comprehensive search of MEDLINE (Ovid), Embase (Ovid), APA Psycinfo (Ovid), and CINAHL Complete (EBSCOhost). Articles were limited to the English language. No date limit was applied. All search strategies are provided in Appendix A.

Article selection

We included quantitative, peer-reviewed studies that reported associations between objective and subjective measures of at least one of the six dimensions (B-SATED) of sleep health and biomarkers of physiologic stress among healthy children. A co-first author (MO) is a licensed pediatric nurse practitioner who provides pediatric sleep health care in a large university-based pediatric sleep and was responsible for reviewing the developmental accuracy of the definitions of sleep health dimensions in each article based on clinical guidelines. We defined biomarkers of physiologic stress as primary mediators (neuroendocrine, immune) and secondary outcomes (metabolic, cardiovascular) outlined by Juster et al. [17] and Condon [18]. We did not include studies that only included measures of adiposity (e.g., body mass index) as physiologic stress biomarkers because associations with sleep are well documented [19,20].

We included studies if the mean age of the sample was 12 y or younger, or if results were stratified by age to allow examination of findings in our target age range. We excluded studies of children with diagnosed sleep disorders (e.g., obstructive sleep apnea), developmental or neurological disorders that may influence sleep (e.g., autism, seizure disorders), or were prescribed sleep-altering medications.

Using Covidence software [21], each title and abstract were independently screened by two reviewers (MO, BBI, or EC), and the third reviewer resolved any discrepancies. Two reviewers (MO and EC) independently reviewed the remaining full-text articles for inclusion and exclusion criteria, and any discrepancies were discussed until consensus was reached.

Data extraction and quality assessment

Two members of our group (MO, EC, or EA) reviewed each study with a data extraction form developed for this review. Extracted information included study objectives, hypotheses, design, sample characteristics, sleep and biomarker variables and measures, and study findings and implications. A third reviewer (BBI) compared results for accuracy and resolved discrepancies by referring to the full text. We organized the findings according to the biomarkers within each physiologic system.

We were unable to identify a standard quality checklist adequate for use in this review. Therefore, we evaluated study quality using a modified version of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [22]. Each article was assessed for quality related to the study aims/hypothesis, sample size, sample representativeness, sleep and biomarker measures, missing data, and inferences and conclusions. The complete checklist is presented in Appendix B. Two reviewers (MO, EC, or EA) independently assessed each study for quality and a third reviewer (BBI) resolved discrepancies. We did not exclude any articles based on quality.

Results

As detailed in Fig. 2, we identified 65,485 articles for screening, of which 6262 did not meet inclusion criteria based on the titles and abstracts. We reviewed full texts of the remaining 223 articles and excluded an additional 143 articles, most commonly for the wrong patient population (e.g., adolescent sample; n = 66) or wrong outcomes (e.g., did not examine sleep and biomarker relationship; n = 49). Ultimately, we included 68 studies (Table 1).

The majority of studies were cross-sectional in design (90%). Studies were conducted in the United States (n = 33), 12 European countries (n = 24), Canada (n = 5), Brazil (n = 2), Kuwait (n = 1), China (n = 1), and Australia (n = 1). Publication years ranged from 1977 to 2021, with most published since 2010. Inclusion of metabolic and immune biomarkers increased over time (Fig. 3A). Forty-three percent of studies included participants from multiple racial/ethnic backgrounds, 15% included all non-Hispanic white participants, and 42% did not report race/ethnicity data. Socioeconomic status data were not reported in 84% of studies.

Most studies were conducted with school-aged children (63%). Studies with younger children were fewer and primarily included neuroendocrine measures (Fig. 3B). Sleep duration and efficiency were the most widely studied sleep health dimensions (Fig. 3C).

Study quality

Overall, studies included well-validated biomarkers, and the quality of the aims/hypothesis and inferences/conclusions was high (Appendices B and C). However, few studies provided justifications for the sample size or information on missing data. The quality of sleep measures was mixed, with some studies using well-validated objective sleep measures, such as actigraphy (43%), electroencephalogram (4%: EEG) and polysomnography (7%: PSG), while others relied on non-validated approaches, such as a single parent-report question (15%) or sleep questionnaires that lack evidence of validity (10%), rather than psychometrically sound questionnaires.

Neuroendocrine biomarkers & Children's sleep health

Cortisol

Diurnal cortisol levels.: The majority of neuroendocrine studies measured diurnal cortisol [23-42]—including the cortisol awakening response (CAR), the diurnal slope and total levels of cortisol across the day (e.g., morning and evening cortisol). CAR was negatively associated with sleep duration in preschoolers [35] and school-aged children [33,43], indicating that shorter sleep was associated with a more marked rise in morning cortisol secretion in all but one study [24].

Studies assessing sleep duration and the CAR among infants and toddlers were limited in number and had inconsistent results. One study revealed that at 12-weeks (but not 8-weeks), full-term, otherwise healthy infants who had colic and longer sleep duration had a significantly higher CAR [23] than infants without colic. This may reflect associations between developmentally appropriate sleep patterns in infants (e.g., lack of sleep consolidation) that may be worsened by effects of colic on cortisol. Moreover, the exact age at which CAR develops during infancy remains unclear [37]. During toddlerhood, there are robust nap-dependent differences in the CAR that suggest that sleep timing and naps influence a child's diurnal profile [31,40,44]. While the science on naps and cortisol response has advanced since first described by Tennes in 1977 [38] and Larson in 1991 [45], more research is needed to understand the emergence of CAR in infancy and the relationships between naps and CAR.

Several studies included assessments of diurnal cortisol slopes or of cortisol samples taken systematically across the day. Poor sleep efficiency and duration, including more awakenings [30], lower efficiency [36,43], and shorter sleep duration [30,35] was associated with a flatter diurnal cortisol slope. In some studies, these associations were nuanced. For example, short sleep duration was associated with higher morning and evening cortisol levels, but only among children who also experienced insomnia symptoms (e.g., poor sleep efficiency) [29]. In a series of studies among children clustered into groups of ‘poor’, ‘normal’ or ‘good’ sleepers based on multiple objective sleep health dimensions (e.g., duration, efficiency), poor sleep health was associated with increased morning cortisol

secretion [46-48]. These findings may indicate the importance of considering sleep health 'phenotypes' rather than single sleep dimensions. However, the associations between good or poor sleep and cortisol secretion were not statistically significant over time in two of the studies [47,48]. More research is needed to determine whether there is a threshold of sleep deprivation, a sleep health phenotype, and/or a sensitive developmental period (e.g., sensitivity periods in early brain development) associated with higher risk for elevated cortisol levels. Evidence for considering these possibilities stems from the lack of significant associations between sleep duration and diurnal cortisol found in studies that had limited variability in parent-reported sleep duration values between (and within) participants [24,27,34]. Specifically, associations may not be robust or detectable in study samples where, on average, nearly all children are getting adequate sleep.

Cortisol reactivity.: Associations among sleep health dimensions and cortisol reactivity across the first year of life are not fully understood. Infants at age 6 mo who woke more at night (parent report) were more susceptible to the effects of acute stressors (e.g., a heightened salivary cortisol response following a vaccination) at the time of the vaccine and six months later [49,50]. Additional research is needed to fully understand the associations between sleep consolidation and stress reactivity in relation to developmental patterns of sleep consolidation (note: children commonly consolidate their sleep at night by 12 mo of age).

Cortisol responses to stress were lower among school-age children with parent-reported sleep problems (e.g., prolonged sleep latency, frequent night waking, irregular sleep habits), compared to those who reportedly slept well [51]—though the direction of this effect may differ for girls. For example, girls with poor sleep efficiency may have higher rather than lower stress reactivity compared to female peers without difficulty initiating or maintaining sleep [52].

Findings across studies using objective sleep measurement are inconclusive. Raikkonen and colleagues found that children with actigraph-measured sleep efficiency less than 77.5% displayed higher cortisol reactivity following an acute laboratory stressor [43]; but these findings were not replicated in other studies using actigraphy or polysomnography with school-age [24]), kindergarten [46,53], or pre-school age children [47,48].

Cumulative cortisol levels.: Cortisol measured in hair is a novel, longitudinal measure of chronic stress [54]. Flom and colleagues reported that shorter sleep duration in 12 month old children was associated with higher hair cortisol levels [55]. However, hair cortisol was not associated with parent-reported sleep duration [56] or actigraphy [57] in other recent studies of young children.

Immune biomarkers and children's sleep health

C-reactive protein (CRP)—Serum CRP was not associated with sleep duration in six out of seven studies [58-63]. Large sample sizes suggest that these studies were well powered to detect statistically significant effects, but only three used validated sleep measures [60,61,64]. In two studies, *variability* in sleep duration over the course of a week was associated with higher CRP levels in boys and girls [64] and among girls only [61]. Thus,

consistency of sleep timing may have a more important influence on CRP than sleep duration, but replication is needed, especially given the large body of evidence linking sleep duration with CRP in adults [65].

Cytokines: IL-6 and TNF-alpha—Few studies examined relationships among sleep health and pro-inflammatory cytokines. Similar to studies of adults [66], sleep duration was not associated with serum IL-6 [59,61,67] and associations between sleep duration and TNF-α are unclear [59,67]. However, Lavoy and colleagues found sleep efficiency was associated with morning salivary IL-6 levels [68], and El-Sheikh et al. (2007) found associations between multiple dimensions of sleep health (e.g., sleep duration, efficiency, nighttime activity) and salivary IL-6 reactivity in response to a laboratory stressor [69]. This suggests that sleep may influence inflammatory responses to acute stressors, rather than circulating levels during homeostasis, but additional experimental studies are needed.

Metabolic biomarkers and children's sleep health

Insulin and insulin resistance (IR)—In a large cross-sectional study (N = 4525), Rudnicka et al. (2017) found that every one hour longer in sleep duration was associated with a small reduction in fasting insulin (2.88%) and insulin resistance (2.81%; IR, measured by homeostasis model assessment of insulin resistance), including after adjusting for child adiposity [70]. However, the absence of associations between sleep duration and fasting insulin in five other studies suggest that the effect of sleep duration on fasting insulin, if present at all, is very small [58-60,64,71]. Findings from studies of IR suggest that short sleep duration is associated with increased IR, but may be driven by the effects of short sleep on child adiposity. For example, associations between short sleep duration and increased IR were negated after controlling for children's BMI (Cespedes 2014), or present only among children with overweight/obesity [72,73] or obesity-risk alleles [74]. Notably, among adults, chronic sleep loss is thought to represent a novel risk factor for weight gain and IR that can lead to Type 2 diabetes [75].

Glucose—Associations between sleep health dimensions and glucose were examined in very few studies. Increased sleep duration was associated with lower fasting glucose levels in two studies, but effects were small and the quality of sleep measures was mixed [70,76]. In one longitudinal study (N = 6316), self-reported later bedtimes were associated with increased fasting salivary glucose, and glucose mediated a relationship between later bedtimes and increased waist circumference after two years [77]. This suggests that sleep timing may influence glucose levels, and that increased glucose may contribute to the effects of sleep on child adiposity, but replication of these findings is needed.

Leptin—Among school-aged children short sleep duration was associated with an increase in the hormone leptin in four out of five studies [60,70,76,78,79]. Effects detected were generally small, and notably, the direction of this relationship is opposite that found in studies of adults, possibly related to a potential confounding effect of caloric intake and adiposity in adult studies [79]. Additional studies are needed to confirm the direction of the relationship between sleep and leptin, whether and how this relationship changes with age, and if it is evident in earlier childhood.

Alpha-amylase—Associations between sleep health and salivary alpha amylase (sAA), an enzyme regulated by the ANS, were examined in three studies. Infants and toddlers who demonstrated an sAA awakening response had later wake times, but no differences in sleep efficiency, number of awakenings, or total sleep time [25]. Lavoy et al. [68] found self-reported sleep disturbance was associated with increased morning sAA among school-aged children. Raikkonen et al. [43] found that compared to children with average-high sleep efficiency, children with low sleep efficiency displayed higher peak levels of sAA in response to a laboratory stressor [43]. This limited evidence supports the presence of a relationship between sleep and sAA in children, but additional studies are needed to better understand this relationship.

Lipids—Lipid levels were largely not associated with sleep duration, including among studies with large samples sizes and well-validated sleep measures [27,59,60,70,76,80]. Berentzen et al. [81] found that short sleep duration was associated with higher total cholesterol and high-density lipoproteins only among girls [81]. As females often begin puberty before males, and puberty influences lipid levels [82], additional research is needed to understand how hormonal changes may influence the relationship between sleep and metabolic biomarkers among older children.

Spruyt et al. [64] found that variability in sleep duration on school days was associated with higher triglyceride levels among children with obesity (n = 47), but not overweight (n = 16) or normal weight (n = 44) children. This evidence further supports the importance of variability in sleep duration and the potential influence of child adiposity on metabolic outcomes, but again replication is needed.

Cardiovascular biomarkers & children's sleep health

Sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) activity—Sympathovagal imbalance (i.e., increased SNS and decreased PNS activity) was associated with poorer sleep behaviors (night to night variability), poorer sleep efficiency, shorter sleep duration, and later sleep timing [83-85] and mediated a relationship between later sleep timing and obesity among school age children [83]. These findings suggest that, similar to studies of adults [86], poor sleep is associated with poor autonomic function, or an imbalance between SNS and PNS activity. However, associations between sleep health and separate aspects of the SNS or PNS remain unclear. For example, shortened pre-ejection period reactivity (i.e., higher SNS reactivity) in response to a laboratory stressor was associated with poorer sleep efficiency measured by actigraphy [87], but not parent-report [88]. High respiratory sinus arrhythmia, an indicator of PNS activity, was associated with lower sleep activity and higher sleep efficiency, but not sleep duration [89]. Additional research is needed to determine whether mixed findings were related to use of different sleep measures, or if sleep health has a stronger influence on overall autonomic functioning than on SNS or PNS activity alone.

Blood pressure—Studies in this review do not support a statistically significant relationship between sleep duration and blood pressure among school-age children. In five studies with large sample sizes (Ns = 652 to 4525), no associations between blood pressure

and sleep duration [59,70,76,81,90] or a cluster profile of sleep health dimensions [91] were detected. In three others, associations between short sleep duration and higher blood pressure were explained by child adiposity [71,74,92]. This is in contrast to adult literature that suggests extreme sleep periods (very short and very long) are associated with higher blood pressure [93]. The mechanisms of this relationship are not well understood, but activation of the SNS resulting from the sleep deprivation is thought to play a key role in adults [93]. It is unclear whether this mechanism plays a role in early childhood.

Discussion

There is emerging evidence that associations between poor sleep and physiologic dysfunction and adaptation reported in the adult literature also exist in early childhood. This highlights the significance of missed opportunities to include sleep health in general health promotion messaging [10] and more specifically in recent efforts to mitigate the effects of toxic stress [3,94]. However, the pediatric literature on sleep health and stress physiology is still in its infancy, and there are a number of major gaps, including very few studies conducted with infants, toddlers, and preschool-age children, and a lack of longitudinal studies and clinical trials to test causal pathways.

Overall, the evidence identified in this review was stronger for relationships between sleep health and biomarkers that represent primary mediators of the stress response than those associated with secondary outcomes of the stress response system. This finding is aligned with the process through which toxic stress ‘gets under the skin,’ first through disrupted HPA-axis and ANS functioning (i.e., primary mediators), and over time, through ‘wear and tear’ on the metabolic and cardiovascular systems (i.e., secondary outcomes). What remains unclear is whether these associations have a cumulative or latent effect on health over the lifespan. Improved understanding of sensitive developmental periods is also needed, as both physiological development of the stress response system and developmental changes in sleep over time add complexity to this research. Prospective studies beginning in early childhood are needed to help answer questions about the directions of associations between sleep health and physiologic stress, especially has these relationships may often be bidirectional.

By examining studies conducted with healthy children, our results were not confounded by the disrupted sleep and stress physiology among children with known sleep problems (e.g., obstructive sleep apnea), underlying chronic disease, or developmental disorders [95]. However, findings in the literature point to an important influence of child adiposity, particularly for cardiovascular and metabolic outcomes, but the direction of relationships remain unclear. In many studies, child adiposity seemed to mediate a relationship between sleep and secondary outcomes [71], while findings of other studies suggest the effects of poor sleep on physiological dysfunction may contribute to child adiposity [77]. Improved understanding of these complex, bidirectional relationships is necessary to identify targets for sleep health interventions, as well as those aimed at preventing childhood obesity. Moreover, prospective, longitudinal studies are needed to determine whether there are subclinical changes in cardiovascular or metabolic biomarkers that are not detected in early childhood yet may have a latent effect on later health outcomes.

Studies included in this review were generally of high quality (Appendices B and C). However, the inclusion of poorly validated sleep measures in 43% of studies limits our ability to interpret study findings and suggests a need for future research using validated sleep measures. Most studies also examined sleep duration and/or efficiency, while the dimensions of sleep behaviors (consistency of bedtime routine and timing), alertness, and satisfaction were largely absent among immune, metabolic, and cardiovascular studies. Findings from this review also support evidence from the adult literature that suggests sleep regularity, rather than sleep duration, may have an important influence on stress physiology [13]. Including valid instruments that measure multiple sleep health dimensions in future studies is necessary to more fully understand the relationship between all six pediatric sleep health dimensions and stress physiology in childhood. Reliance on single parent-report items was surprising considering the importance and availability of valid and reliable parent and child-report sleep questionnaires to measure the sleep dimensions of alertness/sleepiness and satisfaction [96].

Advances in noninvasive methods for measuring physiologic biomarkers, particularly advances in salivary bioscience, offer opportunities to further explore many of the preliminary relationships among sleep health and physiologic biomarkers detected in this review [97]. For example, saliva can be used to measure inflammatory cytokines that have been identified to regulate sleep among adults, including TNF-α and IL-1β [5]. While there are limitations to using and interpreting salivary biomarkers [97], inclusion of noninvasive measures in large, adequately powered studies may help elucidate complex relationships between sleep health and physiologic stress.

Results of this review highlight a lack of racial/ethnic and socioeconomic diversity and transparency among studies. Almost half of the studies in this review did not publish any demographic data on race/ethnicity and very few reported any socioeconomic status data. Increasing racial, ethnic, and socioeconomic diversity in future studies is critical, given known racial inequities in children's sleep health [98,99], disparities in sleep among families living with poverty [100,101], and structural racism as a root cause of toxic stress and health inequities [102].

Our broad search strategy allowed for a comprehensive review of the literature, but the limited evidence for some immune and metabolic biomarkers and the heterogeneity of designs and measures often limited our ability to compare findings across studies. Because we used broad stress terms in our search criteria, it is possible that we missed studies that examined relevant biomarkers but did not conceptualize them as measures of stress. An overall lack of longitudinal studies limited our ability to determine the direction of the associations between sleep and physiologic stress biomarkers. In cross-sectional studies, the timing of data collection procedures was also often unclear, and thus we were unable to compare whether outcomes differed if sleep was measured prior to or following biomarker collection.

Conclusion

Despite substantial evidence in the adult literature, additional research is needed to elucidate the relationship between sleep health and physiologic stress in early childhood. Thoughtful incorporation of physiologic stress biomarkers as well as objective and subjective sleep measures in pediatric sleep research will lead to more comprehensive and nuanced understanding of these complex physiological pathways and inform the development of sleep health promotion interventions. Moreover, such interventions must be informed by evidence derived from health equity research and consider children's sleep in the context of their larger socioecological environment [103].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

* The most important references are denoted by an asterisk.

[1]. Shonkoff JP, Garner AS, Siegel BS, Dobbins MI, Earls MF, McGuinn L, et al.The lifelong effects of early childhood adversity and toxic stress. Pediatrics2012;129(1):e232–46. [PubMed: 22201156]

[2]. Slopen N, Non A, Williams DR, Roberts AL, Albert MAChildhood adversity, adult neighborhood context, and cumulative biological risk for chronic diseases in adulthood. Psychosom Med2014;76(7):481–9. [PubMed: 25077427]

[3]. McEwen BS, Karatsoreos INSleep deprivation and circadian disruption: stress, allostasis, and allostatic load. Sleep Med Clin2015;10(1):1–10. [PubMed: 26055668]

[4]. Buckley TM, Schatzberg AFOn the interactions of the hypothalamic-pituitary-adrenal (HPA) Axis and sleep: normal HPA Axis Activity and circadian rhythm, exemplary sleep disorders. J Clin Endocrinol Metab2005;90(5):3106–14. [PubMed: 15728214]

[5]. Opp MRCytokines and sleep. Sleep Med Rev2005;9(5):355–64. [PubMed: 16102986]

[6]. Rao R, Androulakis IPThe physiological significance of the circadian dynamics of the HPA axis: interplay between circadian rhythms, allostasis and stress resilience. Horm Behav2019;110:77–89. [PubMed: 30862458]

[7]. Tobaldini E, Costantino G, Solbiati M, Cogliati C, Kara T, Nobili L, et al.Sleep, sleep deprivation, autonomic nervous system and cardiovascular diseases. Neurosci Biobehav Rev2017;74:321–9. [PubMed: 27397854]

[8]. Irwin MR, Opp MRSleep health: reciprocal regulation of sleep and innate immunity. Neuropsychopharmacology2017;42(1):129–55. [PubMed: 27510422]

[9]. Van Reeth O, Weibel L, Spiegel K, Leproult R, Dugovic C, Maccari SPHYSIOLOGY OF SLEEP (REVIEW)–Interactions between stress and sleep: from basic research to clinical situations. Sleep Med Rev2000;4(2):201–19.

[10]. Buysse DJSleep health: can we define it? Does it matter?Sleep2014;37(1):9–17. [PubMed: 24470692]

[11]. Juster R-P, McEwen BSSleep and chronic stress: new directions for allostatic load research. Sleep Med2015;16(1):7–8. [PubMed: 25533541]

[12]. McEwen BSSleep deprivation as a neurobiologic and physiologic stressor: allostasis and allostatic load. Metabolism2006;55(Supplement 2):S20–3(0).

[13]. Bei B, Seeman TE, Carroll JE, Wiley JFSleep and physiological dysregulation: a closer look at sleep intraindividual variability. Sleep2017;40(9):zsx109.

[14]. Matricciani L, Paquet C, Galland B, Short M, Olds TChildren's sleep and health: a meta-review. Sleep Med Rev2019;46:136–50. [PubMed: 31121414]

[15]. Meltzer LJ, Williamson AA, Mindell JAPediatric sleep health: it matters, and so does how we define it. Sleep Med Rev2021;57:101425. [PubMed: 33601324]

[16]. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al.The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ2009;339:b2700. [PubMed: 19622552]

[17]. Juster RP, McEwen BS, Lupien SJAllostatic load biomarkers of chronic stress and impact on health and cognition. Neurosci Biobehav Rev2010;35(1):2–16. [PubMed: 19822172]

[18]. Condon EMChronic stress in children and adolescents: a review of biomarkers for use in pediatric research. Biol Res Nurs2018;20(5):473–96. [PubMed: 29865855]

[19]. Chaput JP, Gray CE, Poitras VJ, Carson V, Gruber R, Olds T, et al.Systematic review of the relationships between sleep duration and health indicators in school-aged children and youth. Appl Physiol Nutr Metabol2016;41(6):S266–82.

[20]. Sluggett L, Wagner SL, Harris RLSleep duration and obesity in children and adolescents. Can J Diabetes2019;43(2):146–52. [PubMed: 30266216]

[21]. Covidence systematic review software [Internet]. Veritas Health Innov. Available from: www.covidence.org.

[22]. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JPThe Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol2008;61(4):344–9. [PubMed: 18313558]

[23]. Brand S, Furlano R, Sidler M, Schulz J, Holsboer-Trachsler EOh, baby, please don't cry!': in infants suffering from infantile colic hypothalamic-pituitary-adrenocort ical axis activity is related to poor sleep and increased crying intensity. Neuropsychobiology2011;64(1):15–23. [PubMed: 21577009]

[24]. Brand S, Mikoteit T, Kalak N, Sadeghi Bahmani D, Lemola S, Gerber M, et al.Cortisol impacted on explicit learning encoding, but not on storage and retrieval, and was not associated with sleep patterns-results from the trier social stress test for children (TSST-C) among 9-y old children. Front Psychol2018;9:2240. [PubMed: 30519204]

[25]. Bright MA, Frick JE, Out D, Granger DAIndividual differences in the cortisol and salivary α-amylase awakening responses in early childhood: relations to age, sex, and sleep. Dev Psychobiol2014;56(6):1300–15. [PubMed: 24604597]

[26]. Bright MA, Granger DA, Frick JEDo infants show a cortisol awakening response?Dev Psychobiol2012;54(7):736–43. [PubMed: 22006547]

[27]. Carissimi A, Martins AC, Dresch F, da Silva LC, Zeni CP, Hidalgo MPSchool start time influences melatonin and cortisol levels in children and adolescents - a community-based study. Chronobiol Int2016;33(10):1400–9. [PubMed: 27579611]

[28]. El-Sheikh M, Buckhalt JA, Keller PS, Granger DAChildren's objective and subjective sleep disruptions: links with afternoon cortisol levels. Health Psychol2008;27(1):26–33. [PubMed: 18230010]

[29]. Fernandez-Mendoza J, Vgontzas AN, Calhoun SL, Vgontzas A, Tsaoussoglou M, Gaines J, et al.Insomnia symptoms, objective sleep duration and hypothalamic-pituitary-adrenal activity in children. Eur J Clin Invest2014;44(5):493–500. [PubMed: 24635035]

[30]. Flom M, St John AM, Meyer JS, Tarullo ARInfant hair cortisol: associations with salivary cortisol and environmental context. Dev Psychobiol2017;59(1):26–38. [PubMed: 27472986]

*[31]. Gribbin CE, Watamura SE, Cairns A, Harsh JR, Lebourgeois MKThe cortisol awakening response (CAR) in 2- to 4-y-old children: effects of acute nighttime sleep restriction, wake time, and daytime napping. Dev Psychobiol2012;54(4):412–22. [PubMed: 21953381]

[32]. Kiel EJ, Hummel AC, Luebbe AMCortisol secretion and change in sleep problems in early childhood: moderation by maternal overcontrol. Biol Psychol2015;107:52–60. [PubMed: 25766262]

[33]. Lemola S, Perkinson-Gloor N, Hagmann-von Arx P, Brand S, Holsboer-Trachsler E, Grob A, et al.Morning cortisol secretion in school-age children is related to the sleep pattern of the preceding night. Psychoneuroendocrinology2015;52(1):297–301. [PubMed: 25553389]

*[34]. Marceau K, Abel EA, Duncan RJ, Moore PJ, Leve LD, Reiss D, et al.Longitudinal associations of sleep duration, morning and evening cortisol, and BMI during childhood. Obesity2019;27(4):645–52. [PubMed: 30816633]

*[35]. Saridjan NS, Kocevska D, Luijk MP, Jaddoe VW, Verhulst FC, Tiemeier HThe prospective association of the diurnal cortisol rhythm with sleep duration and perceived sleeping problems in preschoolers: the Generation R Study. Psychosom Med2017;79(5):557–64. [PubMed: 28570434]

[36]. Scher A, Hall WA, Zaidman-Zait A, Weinberg JSleep quality, cortisol levels, and behavioral regulation in toddlers. Dev Psychobiol2010;52(1):44–53. [PubMed: 19921708]

[37]. Stalder T, Baumler D, Miller R, Alexander N, Kliegel M, Kirschbaum CThe cortisol awakening response in infants: ontogeny and associations with development-related variables. Psychoneuroendocrinology2013;38(4):552–9. [PubMed: 22920911]

[38]. Tennes K, Vernadakis ACortisol excretion levels and daytime sleep in one-year-old infants. J Clin Endocrinol Metab1977;44(1):175–9. [PubMed: 833255]

[39]. Thorpe KJ, Pattinson CL, Smith SS, Staton SLMandatory naptimes in childcare do not reduce children's cortisol levels. Sci Rep2018;8(1):4545. [PubMed: 29540702]

*[40]. Tribble RC, Dmitrieva J, Watamura SE, LeBourgeois MKThe cortisol awakening response (CAR) in toddlers: nap-dependent effects on the diurnal secretory pattern. Psychoneuroendocrinology2015;60:46–56. [PubMed: 26116959]

[41]. Ward TM, Gay C, Alkon A, Anders TF, Lee KANocturnal sleep and daytime nap behaviors in relation to salivary cortisol levels and temperament in preschool-age children. Attend Child Care2008;9(3):244–53.

[42]. Watamura SE, Sebanc AM, Gunnar MRRising cortisol at childcare: relations with nap, rest, and temperament. Dev Psychobiol2002;40(1):33–42. [PubMed: 11835149]

[43]. Raikkonen K, Matthews KA, Pesonen AK, Pyhala R, Paavonen EJ, Feldt K, et al.Poor sleep and altered hypothalamic-pituitary-adrenocortical and sympatho-adrenal-medullary system activity in children. J Clin Endocrinol Metab2010;95(5):2254–61. [PubMed: 20194713]

[44]. Tervahartiala K, Karlsson L, Pelto J, Kortesluoma S, Hyttinen S, Ahtola A, et al.Toddlers' diurnal cortisol levels affected by out-of-home, center-based childcare and at-home, guardian-supervised childcare: comparison between different caregiving contexts. Eur Child Adolesc Psychiatr2020;29(9):1217–29.

[45]. Larson MC, Gunnar MR, Hertsgaard LThe effects of morning naps, car trips, and maternal separation on adrenocortical activity in human infants. Child Dev1991;62(2):362–72. [PubMed: 2055127]

[46]. Hatzinger M, Brand S, Perren S, Stadelmann S, von Wyl A, von Klitzing K, et al.Electroencephalographic sleep profiles and hypothalamic-pituitary-adrenocortical (HPA)-activity in kindergarten children: early indication of poor sleep quality associated with increased cortisol secretion. J Psychiatr Res2008;42(7):532–43. [PubMed: 17645894]

[47]. Hatzinger M, Brand S, Perren S, Von Wyl A, Stadelmann S, von Klitzing K, et al.In pre-school children, sleep objectively assessed via sleep-EEGs remains stable over 12 months and is related to psychological functioning, but not to cortisol secretion. J Psychiatr Res2013;47(11):1809–14. [PubMed: 24011863]

[48]. Hatzinger M, Brand S, Perren S, Von Wyl A, Stadelmann S, von Klitzing K, et al.In pre-school children, sleep objectively assessed via actigraphy remains stable over 12 months and is related to

psychological functioning, but not to cortisol secretion. J Psychiatr Res2014;55:22–8. [PubMed: 24814637]

[49]. Beijers R, Riksen-Walraven JM, de Weerth CCortisol regulation in 12-month-old human infants: associations with the infants' early history of breastfeeding and co-sleeping. Stress2013;16(3):267–77. [PubMed: 23116166]

[50]. Lucas-Thompson R, Goldberg WA, Germo GR, Keller MA, Davis EP, Sandman CASleep arrangements and night waking at 6 and 12 months in relation to infants' stress-induced cortisol responses. Infant Child Dev2009;18(6):521–44.

*[51]. Capaldi Ii VF, Handwerger K, Richardson E, Stroud LRAssociations between sleep and cortisol responses to stress in children and adolescents: a pilot study. Behav Sleep Med2005;3(4):177–92. [PubMed: 16190809]

[52]. Pesonen AK, Kajantie E, Heinonen K, Pyhala R, Lahti J, Jones A, et al.Sex-specific associations between sleep problems and hypothalamic-pituitary-adrenocortical axis activity in children. Psychoneuroendocrinology2012;37(2):238–48. [PubMed: 21742441]

[53]. Hatzinger M, Brand S, Perren S, Stadelmann S, von Wyl A, von Klitzing K, et al.Sleep actigraphy pattern and behavioral/emotional difficulties in kindergarten children: association with hypothalamic-pituitary-adrenocortical (HPA) activity. J Psychiatr Res2010;44(4):253–61. [PubMed: 19762039]

[54]. Russell E, Koren G, Rieder M, Van Uum SHair cortisol as a biological marker of chronic stress: current status, future directions and unanswered questions. Psychoneuroendocrinology2012;37(5):589–601. [PubMed: 21974976]

[55]. Flom M, St. John AM, Meyer JS, Tarullo ARInfant hair cortisol: associations with salivary cortisol and environmental context. Dev Psychobiol2017;59(1):26–38. [PubMed: 27472986]

[56]. Bates RA, Singletary B, Yacques A, Justice LSleep and stress in mother–toddler dyads living in low-income homes. Dev Psychobiol2020. n/a(n/a).

[57]. Eythorsdottir DY, Frederiksen P, Larsen SC, Olsen NJ, Heitmann BLAssociations between objective measures of physical activity, sleep and stress levels among preschool children. BMC Pediatr2020;20(1):258. [PubMed: 32460881]

[58]. Carson V, Tremblay MS, Chaput JP, Chastin SFAssociations between sleep duration, sedentary time, physical activity, and health indicators among Canadian children and youth using compositional analyses. Appl Physiol Nutr Metabol2016;41(6 Suppl 3):S294–302.

*[59]. Cespedes EM, Rifas-Shiman SL, Redline S, Gillman MW, Pena MM, Taveras EMLongitudinal associations of sleep curtailment with metabolic risk in mid-childhood. Obesity2014;22(12):2586–92. [PubMed: 25234485]

[60]. Navarro-Solera M, Carrasco-Luna J, Pin-Arboledas G, Gonzalez-Carrascosa R, Soriano JM, Codoner-Franch PShort sleep duration is related to emerging cardiovascular risk factors in obese children. J Pediatr Gastroenterol Nutr2015;61(5):571–6. [PubMed: 25988561]

[61]. Nielsen MS, Quist JS, Chaput JP, Dalskov SM, Damsgaard CT, Ritz C, et al.Physical activity, sedentary time, and sleep and the association with inflammatory markers and adiponectin in 8- to 11-y-old Danish children. J Phys Activ Health2016;13(6):733–9.

[62]. Zhou M, Lalani C, Banda JA, Robinson TNSleep duration, timing, variability and measures of adiposity among 8- to 12-y-old children with obesity. Obes Sci Prac2018;4(6):535–44.

[63]. Nguyen-Rodriguez ST, Gallo LC, Isasi CR, Buxton OM, Thomas KS, Sotres-Alvarez D, et al.Adiposity, depression symptoms and inflammation in hispanic/latino youth: results from HCHS/SOL youth. Ann Behav Med : Pub Soc Behav Med2020;54(7):529–34.

*[64]. Spruyt K, Molfese DL, Gozal DSleep duration, sleep regularity, body weight, and metabolic homeostasis in school-aged children. Pediatrics2011;127(2):e345–52. [PubMed: 21262888]

[65]. Meier-Ewert HK, Ridker PM, Rifai N, Regan MM, Price NJ, Dinges DF, et al.Effect of sleep loss on C-Reactive protein, an inflammatory marker of cardiovascular risk. J Am Coll Cardiol2004;43(4):678–83. [PubMed: 14975482]

[66]. Irwin MR, Olmstead R, Carroll JESleep disturbance, sleep duration, and inflammation: a systematic review and meta-analysis of cohort studies and experimental sleep deprivation. Biol Psychiatr2016;80(1):40–52.

[67]. Gump BB, Gabrikova E, Bendinskas K, Dumas AK, Palmer CD, Parsons PJ, et al.Low-level mercury in children: associations with sleep duration and cytokines TNF-alpha and IL-6. Environ Res2014;134:228–32. [PubMed: 25173056]

[68]. LaVoy EC, Palmer CA, So C, Alfano CABidirectional relationships between sleep and biomarkers of stress and immunity in youth. Int J Psychophysiol2020;158:331–9. [PubMed: 33130179]

[69]. El-Sheikh M, Buckhalt JA, Granger DA, Erath SA, Acebo CThe association between children's sleep disruption and salivary interleukin-6. J Sleep Res2007;16(2):188–97. [PubMed: 17542949]

[70]. Rudnicka AR, Nightingale CM, Donin AS, Sattar N, Cook DG, Whincup PH, et al.Sleep duration and risk of Type 2 diabetes. Pediatrics2017;140(3).

[71]. Derks IP, Kocevska D, Jaddoe VW, Franco OH, Wake M, Tiemeier H, et al.Longitudinal associations of sleep duration in infancy and early childhood with body composition and cardiometabolic health at the age of 6 y: the Generation R study. Child Obes2017;13(5):400–8. [PubMed: 28604071]

[72]. Peplies J, Börnhorst C, Günther K, Fraterman A, Russo P, Veidebaum T, et al.Longitudinal associations of lifestyle factors and weight status with insulin resistance (HOMA-IR) in preadolescent children: the large prospective cohort study IDEFICS. Int J Behav Nutr Phys Activ2016;13:1–12.

[73]. Pacheco SR, Miranda AM, Coelho R, Monteiro AC, Braganca G, Loureiro HCOverweight in youth and sleep quality: is there a link?Arch Endocrinol Metabol2017;61(4):367–73.

[74]. Prats-Puig A, Grau-Cabrera P, Riera-Perez E, Cortes-Marina R, Fortea E, Soriano-Rodriguez P, et al.Variations in the obesity genes FTO, TMEM18 and NRXN3 influence the vulnerability of children to weight gain induced by short sleep duration. Int J Obes2013;37(2):182–7.

[75]. Spiegel K, Knutson K, Leproult R, Tasali E, Van Cauter ESleep loss: a novel risk factor for insulin resistance and Type 2 diabetes. J Appl Physiol2005;99(5):2008–19. [PubMed: 16227462]

*[76]. Li L, Fu J, Yu XT, Li G, Xu L, Yin J, et al.Sleep duration and cardiometabolic risk among Chinese school-aged children: do adipokines play a mediating role?Sleep2017;40(5):1.

*[77]. Alqaderi H, Redline S, Tavares M, Goodson JEffect of late bedtime on salivary glucose and abdominal obesity in children. Sleep Biol Rhythm2017;15(3):227–33.

[78]. Boeke CE, Storfer-Isser A, Redline S, Taveras EMChildhood sleep duration and quality in relation to leptin concentration in two cohort studies. Sleep: J Sleep Sleep Disord Res2014;37(3):613–20.

[79]. Hart CN, Carskadon MA, Considine RV, Fava JL, Lawton J, Raynor HA, et al.Changes in children's sleep duration on food intake, weight, and leptin. Pediatrics2013.

[80]. Hjorth MF, Sjodin A, Dalskov SM, Damsgaard CT, Michaelsen KF, Biltoft-Jensen A, et al.Sleep duration modifies effects of free ad libitum school meals on adiposity and blood pressure. Appl Physiol Nutr Metabol2016;41(1):33–40.

[81]. Berentzen NE, Smit HA, Bekkers MB, Brunekreef B, Koppelman GH, De Jongste JC, et al.Time in bed, sleep quality and associations with cardiometabolic markers in children: the Prevention and Incidence of Asthma and Mite Allergy birth cohort study. J Sleep Res2014;23(1):3–12. [PubMed: 24118590]

[82]. Eissa MA, Mihalopoulos NL, Holubkov R, Dai S, Labarthe DRChanges in fasting lipids during puberty. J Pediatr2016;170:199–205. [PubMed: 26706233]

[83]. Jarrin DC, McGrath JJ, Poirier PAutonomic dysfunction: a possible pathophysiological pathway underlying the association between sleep and obesity in children at-risk for obesity. J Youth Adolesc2015;44(2):285–97. [PubMed: 25480401]

[84]. Michels N, Clays E, De Buyzere M, Vanaelst B, De Henauw S, Sioen IChildren's sleep and autonomic function: low sleep quality has an impact on heart rate variability. Sleep: J Sleep Sleep Disord Res2013;36(12):1939–46.

*[85]. Erath SA, Tu KMThe parenting context of children's sleep. Sleep Develop: Fam Socio-Cult Consider2011.

[86]. Mellman TA, Bell KA, Abu-Bader SH, Kobayashi INeighborhood stress and autonomic nervous system activity during sleep. Sleep2018;41(6):zsy059.

[87]. Bagley EJ, El-Sheikh MRelations between daytime pre-ejection period reactivity and sleep in late childhood. J Sleep Res2014;23(3):335–8. [PubMed: 24372764]

[88]. Martikainen S, Pesonen A-K, Jones A, Feldt K, Lahti J, PyhaLa R, et al.Sleep problems and cardiovascular function in children. Psychosom Med2013;75(7):682–90. [PubMed: 23873712]

[89]. Elmore-Staton L, El-Sheikh M, Vaughn B, Arsiwalla DDPreschoolers' daytime respiratory sinus arrhythmia and nighttime sleep. Physiol Behav2012;107(3):414–7. [PubMed: 22842009]

[90]. Carson V, Chaput JP, Janssen I, Tremblay MSHealth associations with meeting new 24-hour movement guidelines for Canadian children and youth. Prev Med2017;95:7–13. [PubMed: 27923668]

[91]. Matricciani L, Paquet C, Fraysse F, Grobler A, Wang Y, Baur L, et al.Sleep and cardiometabolic risk: a cluster analysis of actigraphy-derived sleep profiles in adults and children. Sleep2021.

[92]. Wells J, Hallal P, Reichert F, Menezes A, Araujo C, Victora CSleep patterns and television viewing in relation to obesity and blood pressure: evidence from an adolescent Brazilian birth cohort. Int J Obes2008;32(7):1042–9.

[93]. Wang Y, Mei H, Jiang Y-R, Sun W-Q, Song Y-J, Liu S-J, et al.Relationship between duration of sleep and hypertension in adults: a meta-analysis. J Clin Sleep Med : Off Publ Am Acad Sleep Med2015;11(9):1047–56.

[94]. Juster R-P, McEwen BSSleep and chronic stress: new directions for allostatic load research. Sleep Med2015;16(1):7–8. [PubMed: 25533541]

[95]. Medic G, Wille M, Hemels MEShort- and long-term health consequences of sleep disruption. Nat Sci Sleep2017;9:151–61. [PubMed: 28579842]

[96]. Lewandowski AS, Toliver-Sokol M, Palermo TMEvidence-based review of subjective pediatric sleep measures.J Pediatr Psychol2011;36(7):780–93. [PubMed: 21227912]

[97]. Granger DA, Taylor MK, editors. Salivary bioscience: foundations of interdisciplinary saliva research and applications. Switzerland AG: Springer International Publishing; 2020.

[98]. Guglielmo D, Gazmararian JA, Chung J, Rogers AE, Hale LRacial/ethnic sleep disparities in US school-aged children and adolescents: a review of the literature. Sleep Health2018;4(1):68–80. [PubMed: 29332684]

[99]. Smith JP, Hardy ST, Hale LE, Gazmararian JARacial disparities and sleep among preschool aged children: a systematic review. Sleep Health2019;5(1):49–57. [PubMed: 30670165]

[100]. Patel NP, Grandner MA, Xie D, Branas CC, Gooneratne N"Sleep disparity" in the population: poor sleep quality is strongly associated with poverty and ethnicity. BMC Publ Health2010;10(1):475.

[101]. Whinnery J, Jackson N, Rattanaumpawan P, Grandner MAShort and long sleep duration associated with race/ethnicity, sociodemographics, and socioeconomic position. Sleep2014;37(3):601–11. [PubMed: 24587584]

[102]. McEwen CA, McEwen BSSocial structure, adversity, toxic stress, and intergenerational poverty: an early childhood model. Annu Rev Sociol2017;43(1):445–72.

[103]. Owens J, Ordway MRSleep among children. In: DT D, I K, S R, editors. The social Epidemiology of sleep. Oxford, UK: Oxford University Press; 2019.

[104]. Sanford LD, Suchecki D, Meerlo PStress, arousal, and sleep. In: Meerlo P, Benca RM, Abel T, editors. Sleep, neuronal plasticity and brain function. Berlin, Heidelberg: Springer Berlin Heidelberg; 2015. p. 379–410.

[105]. Fisher BE, Rinehart SStress, arousal, psychopathology and temperament: a multidimensional approach to sleep disturbance in children. Pers Indiv Differ1990;11(5):431–8.

[106]. Keller PS, Kouros CD, Erath SA, Dahl RE, El-Sheikh MLongitudinal relations between maternal depressive symptoms and child sleep problems: the role of parasympathetic nervous system reactivity. J Child Psychol Psychiatry2014;55(2):172–9. [PubMed: 24117807]

[107]. Larson MC, White BP, Cochran A, Donzella B, Gunnar MDampening of the cortisol response to handling at 3 months in human infants and its relation to sleep, circadian cortisol activity, and behavioral distress. Dev Psychobiol1998;33(4):327–37. [PubMed: 9846236]

[108]. Richard CA, Mosko SSMother-infant bedsharing is associated with an increase in infant heart rate. Sleep2004;27(3):507–11. [PubMed: 15164907]

[109]. Stalder T, Bäumler D, Miller R, Alexander N, Kliegel M, Kirschbaum CThe cortisol awakening response in infants: ontogeny and associations with development-related variables. Psychoneuroendocrinology2013;38(4):552–9. [PubMed: 22920911]

[110]. Watamura SE, Donzella B, Kertes DA, Gunnar MRDevelopmental changes in baseline cortisol activity in early childhood: relations with napping and effortful control. Dev Psychobiol2004;45(3):125–33. [PubMed: 15505801]

Practice points

- Promoting sleep health may have physiologic benefits
- Singular focus on sleep duration recommendations may not be adequate in health promotion messaging.
- Detection of young children's physiologic stress response in relation to sleep is more evident within the HPA-axis, then in secondary outcomes (metabolic, cardiovascular).

Research agenda

- Incorporate multiple sleep health dimensions and sleep assessment measures that adequately differentiate between them.
- Increase sample representation in pediatric sleep research (socioeconomic, race/ethnicity, age, sex).
- Follow existing robust protocols for biomarker collection.
- Design longitudinal studies beginning in early life to examine sleep health and physiologic stress biomarkers during critical developmental periods.

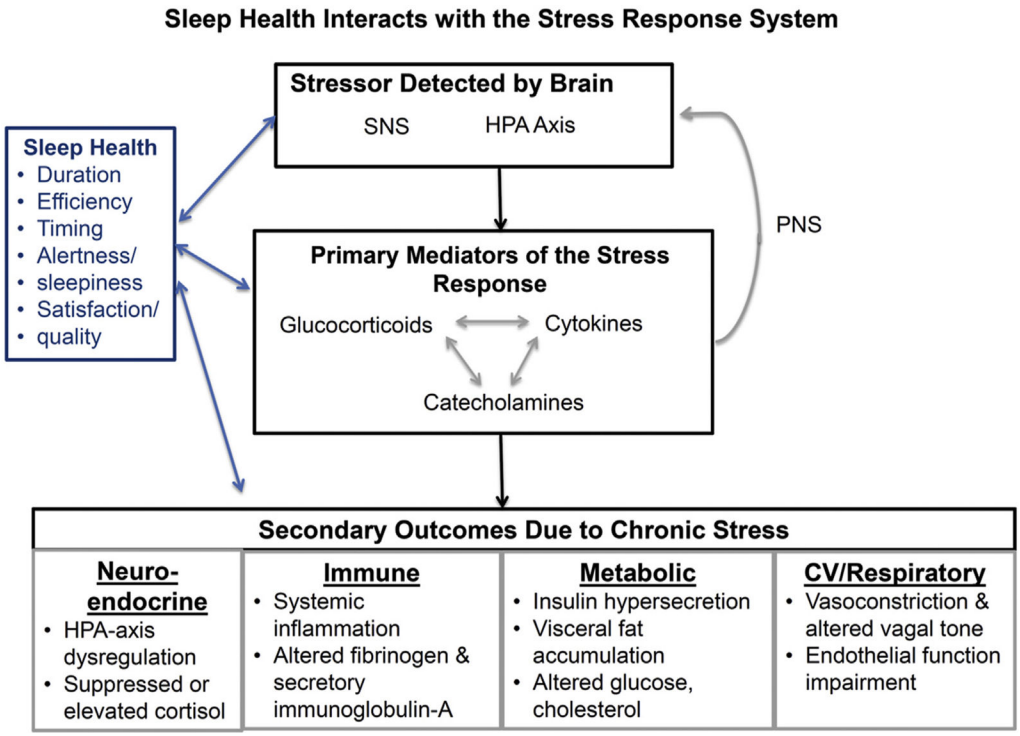

Fig. 1.

Overview of stress response system and suggested connection with sleep health based on adult studies. In the physiological response to stress, activation of the sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal (HPA) axis leads to release of glucocorticoids, catecholamines, and cytokines. These primary mediators act as part of a complex, non-linear network in the “fight or flight” response to stress. The parasympathetic nervous system (PNS) also plays a regulatory role as part of a negative feedback loop. Over time, prolonged release of primary mediators causes wear and tear on physiological systems and contributes to secondary outcomes, including but not limited to the examples provided (Condon, 2018; Juster et al., 2010). Evidence from adult studies suggests that sleep health interacts with multiple components of the stress response system, including a bidirectional relationship with the HPA axis and regulation by inflammatory cytokines [5,9,12,86,94,104].

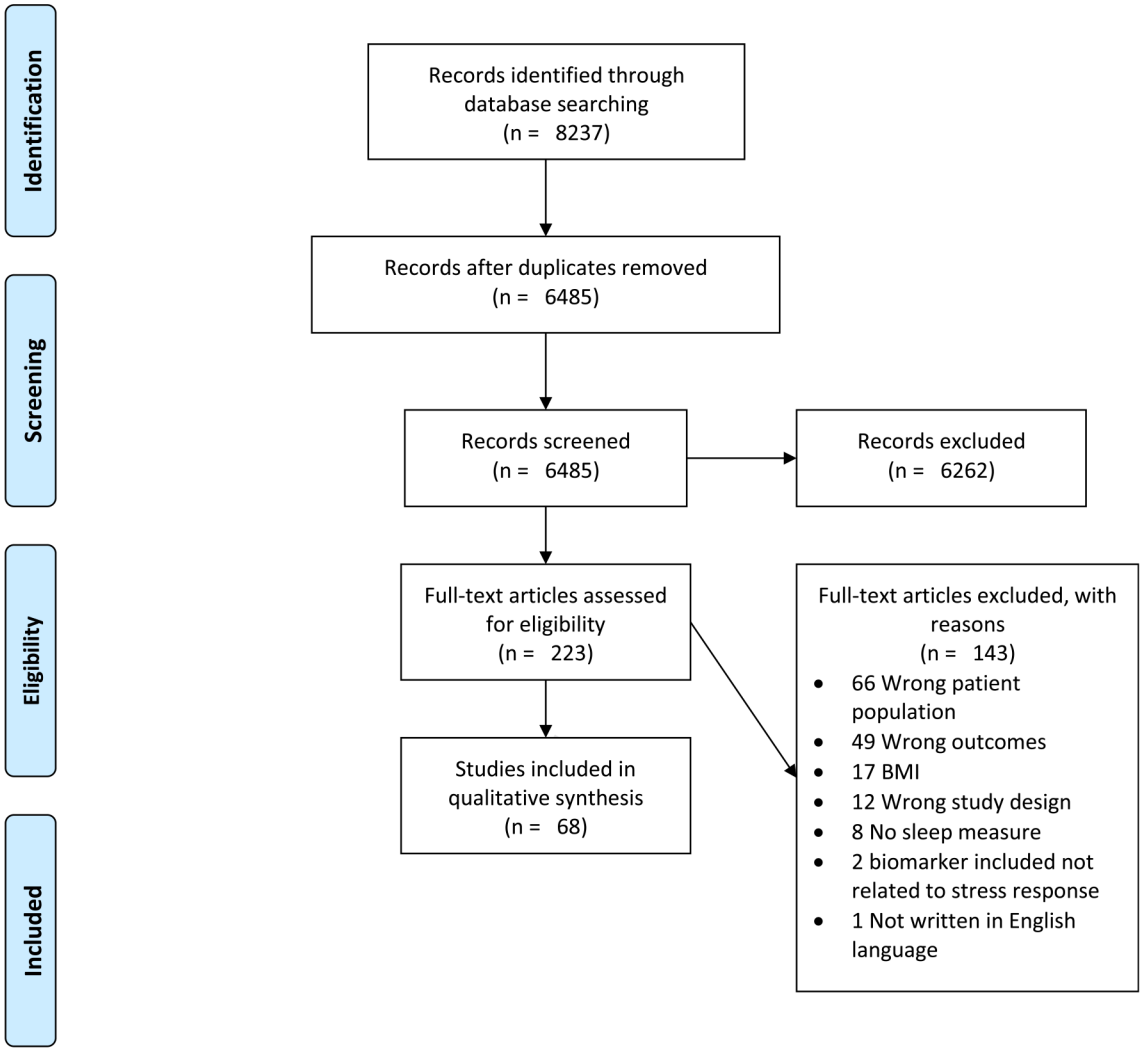

Fig. 2.

PRISMA flow diagram.

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

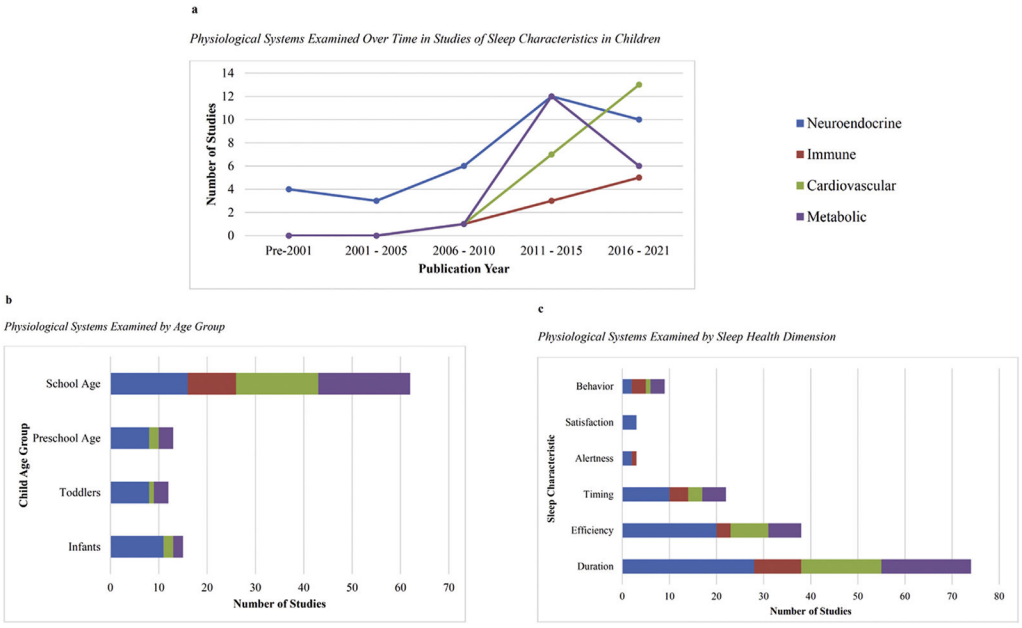

Fig. 3.

Physiological systems examined A) over time in studies of sleep health in children, B) by age group, and C) by sleep characteristic.

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Table 1

Summary of studies included in systematic review.

First Author, Year	Design	N (%Female)	Age Group	Sleep Health	Sleep Measure	Key Findings by Physiologic System
Alqaderi et al., 2017 [77]	L	6316 (61)	SA	T	SI	**M:** Later bedtimes associated with ↑ salivary glucose (β = 0.9, 95%CI = 0.14,1.7).
Bagley et al., 2014 [87]	CS	235 (48)	SA	D, E	ACT	**CV:** Lower sleep efficiency (b = 0.24, p < 0.01), higher sleep activity (b = −0.54, p < 0.001), more frequent waking (b = −0.06, p < 0.05) associated with ↑ SNS reactivity in response to laboratory challenge.
Bates et al., 2020 [56]	L	94 (57)	T	E	PRQ-V	**M:** Difficulty falling asleep or staying asleep not associated with toddler's hair cortisol levels at two time points one year apart (r = −0.05, p = 0.68 and r = −0.21, p = 0.09)
Beijers et al., 2013 [49]	L	193 (47)	I	E	SD	**NE:** Night waking from age 0–6 mo, but not 12 mo, associated with ↑ cortisol reactivity.
Berentzen et al., 2014 [81]	CS	1481 (51)	SA	D, B	SRQ-NV	**CV:** Time in bed, sleep–wake pattern, and night-time awakenings N/A with SBP/DBP. **M:** Shorter sleep duration associated with ↑ total cholesterol (β = 0.16, 95%CI 0.01,0.31) and HDL (β = 0.08, 95%CI 0.01,0.14) among girls.
Boeke et al., 2014 [78]	L	655 (32)	P, SA	D	SI	**M:** Chronic sleep curtailment from 6 mo to 7 y associated with ↑ leptin (β = 0.084, 95%CI 0.014,0.154) among girls at age 7. Stronger among girls with overweight/obesity.
Brand et al., 2011 [23]	CS	16 (63)	I	D, E	ACT SD	**NE:** Prolonged sleep duration associated with ↑ cortisol across the day (r = 0.54, p < 0.05).
Brand et al., 2018 [24]	CS	39 (38)	SA	D, E	EEG	**NE:** CAR N/A with sleep duration, sleep efficiency, awakenings or sleep onset latency. Wake after sleep onset positively associated with cortisol AUC.
Bright et al., 2014 [25]	CS	47 (36)	I, T	D, E, T	ACT	**NE:** 43% of 12-month olds, 50% of 18-month-olds, 42% of 24-month-olds demonstrated CAR. 18-month-olds who displayed CAR had greater sleep efficiency than those who did not. **M:** Children who demonstrated sAA awakening response had later wake time but N/A with sleep duration or efficiency.
Bright et al., 2012 [26]	CS	32 (59)	I, T	T	SD	**NE:** Infants <1 y exhibited greater change from AM to post-nap waking (r = −0.32, p = 0.08) than older infants.
Capaldi et al., 2005 [51]	CS	31 (52)	SA	D, E, A	PRQ-V	**NE:** Poor sleep health (e.g., sleepiness, prolonged sleep latency) associated with cortisol during a stress test (r = −0.80, p < 0.05)
Carissimi et al., 2016 [27]	CS	80 (59)	SA	D, T	SR	**NE:** Sleep duration, bedtime, wake-time) N/A with morning, afternoon or night cortisol levels.
Carson et al., 2016 [58]	CS	4169 (49)	SA	D	SI	**I:** Time spent in sleep relative to other movement behaviors (e.g., sedentary time, physical activity) N/A with CRP. **CV:** Time spent in sleep relative to other movement behaviors negatively associated with SBP (−0.04, p = 0.027). **M:** Sleep duration N/A with fasting insulin, HDL, triglycerides.
Carson et al., 2017 [90]	CS	4157 (49)	SA	D	SI	**CV:** Meeting Canadian guidelines for sleep duration (9–11 h/night) N/A with SBP/DBP.
Cespedes et al., 2014 [59]	CS, L	652 (47)	SA	D	SI	**I:** Chronic sleep curtailment (lower sleep duration) from 6 months to 7 y N/A with age 7 CRP, IL-6, or TNF-α. **CV:** Chronic sleep curtailment N/A with age 7 SBP. **M:** Chronic sleep curtailment associated with ↑ fasting insulin and IR at age 7, but not after controlling for BMI. Sleep curtailment N/A with HDL or triglycerides.

First Author, Year	Design	N (%Female)	Age Group	Sleep Health	Sleep Measure	Key Findings by Physiologic System
Derks et al., 2017 [71]	L	5161 (50)	I, T, P & SA	D	SI	**CV:** Sleep duration at age 2 months associated with SBP at age 6 y, but not after controlling for BMI. **M:** Sleep duration at age 6 months associated with HDL at age 6 y but N/A with fasting insulin, total cholesterol and triglycerides.
El-Sheikh et al., 2007 [69]	CS	64 (56)	SA	D, E, A	ACT PRQ-V	**I:** Greater WASO and ↑ nighttime activity associated with ↓ IL-6 reactivity ($\beta = -0.73$; $p \leq 0.05$). Longer sleep duration and higher sleep efficiency associated with ↑ IL-6 reactivity among boys ($\beta = 0.27$; $p \leq 0.05$).
El-Sheikh et al., 2008 [28]	CS	64 (56)	SA	D, C, S, T	ACT PRQ-V	**NE:** Afternoon cortisol levels associated with ↓ sleep duration and efficiency and ↑ minutes awake after sleep onset, sleep satisfaction, sleepiness and late-night bedtimes.
Elmore-Staton et al., 2012 [89]	CS	29 (31)	P	D, E	ACT	**CV:** High RSA associated with lower sleep activity ($r = -108.52$, $p < 0.01$) and higher sleep efficiency ($r = 72.54$, $p < 0.01$) but not sleep duration.
Erath & Tu, 2015 [85]	CS	339 (54)	SA	D, E, T	ACT	**CV:** Higher RSA withdrawal in response to stress task associated with ↑ sleep efficiency ($\beta = 0.23$; $p < 0.001$) and sleep duration ($\beta = 0.22$; $p < 0.001$), but only among children with higher skin conductance level reactivity.
Eythorsdottir et al., 2020 [57]	CS	77 (38)	T, P, SA	D, E	ACT	**NE:** Sleep duration, sleep efficiency, and sleep latency N/A with hair cortisol
Fernandez-Mendoza et al., 2014 [29]	CS	327 (54)	SA	D, E	PSG PRQ-V	**NE:** Children with insomnia symptoms and short sleep duration had higher morning cortisol (1.38 ± 0.08 μg/dL) than short sleep duration, 'normal' sleep duration, and insomnia symptom groups.
Fisher et al., 1990 [105]	CS	79 (47)	SA	S	PRQ-NV	**NE:** Cortisol higher following stress task among children with increased awakenings ($\beta = 0.29$, p-0.01).
Flom et al., 2017 [55]	CS	111 (NR)	I	D, E	PRQ-V	**NE:** ≥10 h sleep duration associated with ↓ hair cortisol ($d = -0.638$, $p = 0.012$). Steeper salivary cortisol diurnal slopes associated with ↑ sleep duration ($d = 1.619$, $p < 0.001$)and ↓sleep disruption ($r = -.295$, $p = 0.016$).
Gribbin et al., 2012 [31]	CS	7 (71)	P	D, T	PSG ACT SD	**NE:** Cortisol AUC differed by sleep timing (night sleep, and morning, afternoon, evening nap) and highest after night sleep.
Gump et al., 2014 [67]	CS	100 (43)	SA	D, E	ACT SD	**I:** Sleep duration associated with TNF-α ($\beta = 0.38$, $p < 0.001$).
Hartet al., 2013 [79]	L	37 (43)	SA	D, E	ACT	**M:** ↑ sleep duration associated with ↓ fasting leptin ($d = 0.52$, $p = 0.04$).
Hatzinger et al., 2008 [46]	CS	67 (48)	P	D, E	EEG PRQ-NV	**NE:** Poor sleepers (per sleep onset latency, total sleep time, others) had lower mean cortisol levels than good and normal sleepers ($F = 8.24$, $p < 0.001$) and lower CAR than good sleepers ($f = 5.83$, $p < 0.01$).
Hatzinger et al., 2010 [53]	L	82 (40)	P, SA	E, D	ACT	**NE:** ↑ cortisol associated with extended sleep onset latency ($F = 3.98$, $p = 0.049$) and low sleep efficiency ($F = 13.76$, $p = 0.000$)
Hatzinger et al., 2014 [48]	CS/L	82 (40)	SA	E, D	ACT SD	**NE:** Sleep efficiency associated with ↑ morning cortisol (prolonged sleep latency; $r = 0.25$; number of awakenings $r = 0.33$ and WASO: $r = 0.29$) in CS analysis but not one year later.
Hatzinger et al., 2013 [47]	CS/L	67 (48)	SA	E, D	PSG	**NE:** Sleep efficiency associated with ↑morning cortisol (prolonged sleep latency; $r = 0.29$ and WASO: $r = 0.43$) in CS analysis but not one year later.
Hjorth et al., 2016 [80]	L; Trial	530 (49)	SA	D	ACT SD	**M:** Sleep duration N/A with lipids or IR.

First Author, Year	Design	N (%Female)	Age Group	Sleep Health	Sleep Measure	Key Findings by Physiologic System
Jarrin et al., 2015 [83]	CS	564 (44)	SA	D, T	PRQ-V SD	**CV:** Shorter sleep duration (β = −0.05, p = 0.030) and later sleep timing (β = 0.05, p = 0.042) associated with ↑ sympathovagal imbalance.
Keller et al., 2014 [106]	L	271 (47)	SA	D, E	ACT	**CV:** Higher RSA withdrawal in response to stress task associated with longer sleep duration (*b* = −1.63, p < 0.01) among children of non-depressed mothers, and less sleep activity (*b* = −0.25, p < 0.01) among children of depressed and non-depressed mothers.
Kiel et al., 2015 [32]	L	51 (38–51)	T, P	E	PRQ-NV	**NE:** Blunted cortisol secretion predicted ↑ sleep problems at high levels of parental critical control (β = 0.40, p = 0.031). Cortisol N/A with sleep efficiency problems.
Larson et al., 1991 [45]	CS	24 (54)	I	T, D	SD	**NE:** ↓ cortisol associated with morning naps but N/A with nap timing or duration.
Larson et al., 1998 [107]	CS	86 (51)	I	D	SD	**NE:** Early-morning peak cortisol ↑ among infants who did not wake/signal for their parent overnight compared to those who did.
Lavoy et al., 2020 [68]	CS	55 (53)	SA	D, E	ACT, SRQ-V	**NE:** WASO associated with ↑ single morning measure salivary cortisol (β = 0.313) **I:** Sleep efficiency associated with ↑ IL-6 (β = 0.450). Sleep duration associated with ↑ IL-1β (β = 0.463). **M:** Sleep disturbance associated with ↑ sAA (β = 0.400).
Lemola et al., 2015 [33]	CS	113 (34)	SA	D, E	EEG	**NE:** Morning cortisol secretion negatively associated with sleep duration and slow wave sleep.
Li et al., 2017 [76]	CS	2142 (74)	SA	D	SI	**CV:** Sleep duration N/A with BP. **M:** Sleep duration associated with leptin (β = −0.054, p = 0.039) and fasting glucose (β = −0.055, p < 0.001). Sleep duration N/A with HDL, insulin, IR, or triglycerides after controlling for leptin.
Lucas–Thompson et al., 2009 [50]	L	92 (47)	I	E	SD	**NE:** Infants with more night-wakings had ↑ cortisol reactivity to laboratory stressor at 6 months but not 12 months.
Marceau et al., 2019 [34]	L	361 (NR)	SA	D	SD	**NE:** Sleep duration N/A with morning cortisol levels at age 6, 7, and 9 y.
Martikainen et al., 2013 [88]	CS	285 (53)	SA	E	PRQ-V	**CV:** Sleep problems (e.g., disorders of initiating sleep, sleep-wake transitions) N/A with HRV in response to stress task.
Matricciani et al., 2021 [91]	CS	1043 (50)	SA	D, E, T	ACT	**CV:** Sleep profiles N/A with SBP or DBP **M:** Children with “short sleep” cluster profile had ↑ metabolic syndrome severity score (i.e., index including glucose, HDL) compared to “overall good sleep” profile.
Michels et al., 2013 [84]	CS, L	334 (47)	SA	D, E	SD, ACT	**CV:** Sleep duration N/A with HRV. Frequent awakenings, long latency, low sleep efficiency associated with ↑ sympathovagal imbalance.
Navarro-Solera et al., 2015 [60]	CS	90	SA	D	PRQ-V	**I:** Sleep duration N/A with CRP. **CV:** SBP ↑ among children with short sleep duration compared to recommended sleep group. **M:** Sleep duration N/A fasting insulin, leptin, glucose, total cholesterol, HDL, or triglycerides.
Nguyen-Rodriguez et al., 2020 [63]	CS	1287 (49)	SA	D	SRQ-NV	**I:** Sleep duration not associated with CRP
Nielsen et al., 2016 [61]	CS	787	SA	D, B	ACT SD	**I:** Sleep duration variability associated with ↑ CRP among girls (β = 0.003; 95% CI = 0.001,0.005). Sleep duration and sleep duration variability N/A with IL-6.
Pacheco et al., 2017 [73]	CS	82	SA	D, E	Lab PSG	**M:** Poor sleep efficiency associated with increased HOMA-IR (r = 0,37, p = 0.03) among children with overweight/obesity.
Peplies et al., 2016 [72]	L	1730	P & SA	D	SI	**M:** Children with less than recommended sleep duration 1.8 times more likely to have IR. Sleep duration N/A with IR in a subsample (n = 1253) of normal weight children.

First Author, Year	Design	N (%Female)	Age Group	Sleep Health	Sleep Measure	Key Findings by Physiologic System
Pesonen et al., 2012 [52]	CS	284	SA	D, E, A	ACT PRQ-V	**NE:** Problems with sleep efficiency and sleepiness associated with ↓diurnal cortisol and ↓cortisol responses to stress task in boys. Problems with sleep efficiency associated with ↑cortisol responses to stress task. N/A with sleep duration.
Prats-Puig et al., 2013 [74]	CS	297	SA	D	SRQ-NV	**CV:** Shorter sleep duration associated with ↑SBP only among children with obesity-risk alleles. **M:** Sleep duration associated with ↓IR only among children with obesity-risk allele (β = −0.171,95% CI = −0.276,−0.066).
Raikkonen et al., 2010 [43]	CS	276–282	SA	D, E	ACT	**NE:** Children with short sleep duration displayed higher CAR than average sleepers. Children with low sleep efficiency had [cortisol reactivity and AUC in response to stress task. **M:** Children with low sleep efficiency had ↑sAA in response to stress task.
Richard et al., 2004 [108]	CS	35	I	E	PSG	**CV:** HR 5.5%–8.8% higher during each stage of sleep on bedsharing nights compared to solitary night. No difference in HR during waking hours.
Rudnicka et al., 2017 [70]	CS	4525	SA	D	SI ACT	**CV:** Sleep duration N/A with BP. **M:** One hour longer sleep duration associated with ↓fasting glucose (0.24%), leptin (3.03%), insulin (2.88%) and IR (2.81%). Sleep duration N/A with lipids.
Saridjan et al., 2017 [35]	CS/L	364	I, T, P, SA	D,	PRQ-NV	**NE:** Flatter slopes and more positive CAR associated with shorter sleep duration at 14 months. AUC at 14 months N/A with sleep duration from 14 to 36 months.
Scher et al., 2010 [36]	CS	27	T	D, E	ACT	**NE:** Higher sleep efficiency scores associated with ↓awakening cortisol and ↓nocturnal rise from bedtime to awakening. Variability in sleep efficiency associated with ↑variability in bedtime cortisol.
Spruyt et al., 2011 [64]	CS	308	SA	D, B	ACT	**I:** Short sleep duration associated with ↓ CRP (r = −0.63, p < 0.05). **M:** Variability in sleep duration associated with ↑ triglyceride levels among children with obesity (r = 0.31; p < 0.05).
Stalder et al., 2013 [109]	CS	33	I	D, T, B	ACT	**NE:** CAR detected in 32 infants and on 86.9% of study days. Cortisol on awakening positively associated with number of naps.
Tennes et al., 1977 [38	CS	20	I	T	SD	**NE:** Naps >1 h associated with ↓cortisol regardless of time of day.
Tervahartiala et al., 2020 [44]	CS	213 (41)	T	T	SD	**NE:** Nap timing in the morning and afternoon associated with diurnal cortisol changes. Afternoon naps associated with increased cortisol.
Thorpe et al., 2018 [39]	CS; Trial	43	P	D	ACT SD	**NE:** Cortisol declines from post-naptime to bedtime, but not among children who did not nap.
Tribble et al., 2015 [40]	CS	28	T	D, T	ACT	**NE:** Cortisol rise following morning (b = 11.00, p < 0.001) and afternoon naps (b = 4.97, p < 0.01). Morning nap associated with most robust post-nap rise (b = 10.21, p < 0.001).
Ward et al., 2008 [41]	CS	38	P	S	ACT SD PRQ-V	**NE:** Children with disruptive behaviors at naptime had ↑ afternoon cortisol and less decrease from morning to afternoon compared with non-problem nappers.
Watamura et al., 2004 [110]	CS	77	T	D, T	SD	**NE:** Greater variability in cortisol at wake-up and midmorning among 12, 18, and 24-month olds than among 30- and 36-month-olds.
Watamura et al., 2002 [42]	CS	35	P	D, B	SD	**NE:** Afternoon cortisol levels higher in center-based childcare than at home, and NA with nap duration or behaviors (day to day nap v. no nap).
Wells et al., 2008 [92]	CS	4452	SA	D	SI	**CV:** Short sleep duration associated with ↑SBP, but not after controlling for activity patterns/ obesity.

First Author, Year	Design	N (%Female)	Age Group	Sleep Health	Sleep Measure	Key Findings by Physiologic System
Zhou et al., 2018 [62]	CS	188	SA	B, D, T,	ACT SD	**I, M:** Sleep duration, timing, and variability N/A with cardiometabolic risk factor clustering score (BMI, BP, cholesterol, triglycerides, CRP, IR).

CS=Cross sectional; L = longitudinal.

SA = school-aged; P = preschool; T = toddlers; I-Infants.

B=Behaviors; S=Satisfaction; A = Alertness; T = Timing; E = Efficiency; D = Duration.

ACT = actigraphy; SI= Single Item; SD = sleep diary; PRQ-V = parent-report questionnaire-validated; PRQ-NV = parent report-not validated; SRQ-V = self-report questionnaire-validated; SRQ-NV = self-report questionnaire-not validated.

↑ = increased/higher; ↓ = decreased/lower; N/A = not associated.

CAR, Cortisol awakening response; AM, morning; AUC, area under the curve; WASO, wake after sleep onset; CRP, c-reactive protein, IL, interleukin, TNF-a; tumor necrosis factor alpha; SNS, sympathetic nervous system; SBP, systolic blood pressure; DBP, diastolic blood pressure; RSA, respiratory sinus arrhythmia, HRV, heart rate variability, BMI, body mass index; HDL, high-density lipoproteins; sAA, salivary alpha-amylase; IR, insulin resistance.

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