



ORIGINAL ARTICLE

# Longitudinal association of actigraphy-assessed sleep with physical growth in the first 6 months of life

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## Abstract

**Study Objectives:** Suboptimal sleep is associated with obesity and its sequelae in children and adults. However, few studies have examined the association between sleep and physical growth in infants who experience rapid changes in sleep/wake patterns. We examined the longitudinal association of changes in objectively assessed sleep/wake patterns with changes in growth between ages 1 and 6 months.

**Methods:** We studied 298 full-term infants in the longitudinal Rise & SHINE cohort study. Changes from 1 and 6 months in nighttime sleep duration, wake after sleep onset (WASO), and number of waking bouts  $\geq 5$  min were assessed using ankle actigraphy. Overweight was defined as age- and sex-specific weight for length  $\geq 95$ th percentile. Generalized estimating equation analyses adjusted for infants' and mothers' characteristics.

**Results:** The mean (SD) birth weight was 3.4 (0.4) kg; 48.7% were boys. In multivariable adjusted models, each 1-h increase in nighttime sleep duration between months 1 and 6 was associated with a 26% decrease in the odds of overweight from 1 to 6 months (odds ratio [OR] = 0.74; 95% confidence interval [CI, 0.56, 0.98]). Each 1-unit decrease in number of waking bouts was associated with a 16% decrease in the odds of overweight (OR = 0.84; 95% CI [0.72, 0.98]). Changes in WASO were not associated with the odds of overweight.

**Conclusions:** Greater increases in nighttime sleep duration and more consolidation of nighttime sleep were associated with lower odds of overweight from 1 to 6 months. Adverse sleep patterns as early as infancy may contribute to excess adiposity.

## Statement of Significance

Excess weight in infancy could lead to later obesity and related comorbidities. It is critical to understand determinants of overweight in early life. Adverse sleep patterns are linked to obesity and its sequelae in children and adults. However, little is known on the longitudinal association between sleep and physical growth in infants, who experience rapid changes in sleep/wake patterns. Data from this longitudinal cohort study showed that greater increases in actigraphy-assessed nighttime sleep duration and greater decreases in nighttime sleep fragmentation (measured by number of waking bouts) were associated with lower odds of overweight from 1 to 6 months. Future research collecting data from additional time points more closely is needed.

**Key words:** infant; sleep; physical growth; actigraphy

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## Introduction

The global obesity epidemic spares no age group, even young infants [1, 2]. Obesity has become the most prevalent nutritional disease of children in the United States [3]. Excess weight in early life could lead to later obesity and related comorbidities [1, 4–8]. Thus, it is critical to understand determinants of overweight in infancy, which could inform prevention interventions to help program healthful energy balance over the lifecourse.

A high prevalence of inadequate sleep has paralleled the obesity epidemic [9]. Evidence suggest that short sleep duration is associated with obesity in older children and adults [10–15]. However, relatively little is known about whether similar patterns exist for infants. Suboptimal sleep might be linked to obesity in infants through mechanisms such as discordant feeding practices (e.g. parental feeding to soothe) and reduced energy expenditure. Few prospective studies have reported an association between short sleep duration in infancy and subsequent risk of obesity or accelerated weight gain later in life [16, 17]. To our knowledge, there was only one study that used objective measures of sleep and investigated the contemporaneous relationship between sleep and growth at age 6 months [18].

Accordingly, several major gaps remain. First, the cross-sectional or prospective designs used by the initial investigations on infants did not capture the contemporaneous changes in sleep and physical growth in infants [16–18]. Infants experience rapid changes in their sleep/wake patterns over the first year of life, with the most marked changes happening across the first few months [19]. Total sleep time decreases with age, mostly because of the gradual disappearance of daytime sleep and concentration of sleep during the nighttime [20]. Meanwhile, large declines in nighttime wakefulness occur, as a 24-h circadian rhythm is established and stabilized [19, 21]. Therefore, a rigorous assessment of the relationship between sleep and growth in infancy necessitates a longitudinal design with repeated measurements that capture changes in sleep and growth.

Second, prior research has mainly used subjective measures of sleep from parents' report that routinely overestimate their children's sleep duration, rather than objective measures such as actigraphy that reduce reporting bias and permit continuous, noninvasive assessment over multiple days in the home setting [22]. Third, studies have focused on sleep duration, however, other aspects of sleep (e.g. sleep fragmentation) might also predispose infants to excess weight. In the adult literature, a multidimensional framework is increasingly found to be useful to characterize complementary aspects of sleep health [23]—yet, this framework that addresses sleep duration, continuity, and rhythms has only been applied to studies of infants in a limited manner. Excessive night wakings is among the most common sleep problems during infancy [20, 24]. Research has shown that maternal reports of infant night wakings are associated with later childhood overweight [25]. It is critical to assess components of sleep health, other than duration, so that the physiological impact of sleep disturbances is adequately characterized and targeted interventions could be developed.

The purpose of this study is to examine how changes in objectively assessed sleep are associated with changes in growth in the first 6 months of life. We hypothesized that greater increases in nighttime sleep duration and greater decreases in

sleep fragmentation would be associated with reduced risk of overweight from 1 to 6 months.

## Methods

### Study design and study participants

The Rise & SHINE (Sleep Health in Infancy & Early Childhood) study is a prospective cohort study investigating associations of infant sleep patterns with growth in early life. Details of the study design have been published [26]. Briefly, healthy mother–infant dyads were recruited between May 2016 and June 2018 from the newborn unit at Massachusetts General Hospital in Boston, USA. After assessing eligibility, four follow-up visits at 1, 6, 12, and 24 months were conducted, collecting information on infants' sleep/wake patterns using actigraphy, weight, and recumbent length, as well as nutritional, parenting, behavioral, and environmental factors. The 1-month visit was considered the baseline as it was the first visit during which we had objectively measured information on infants' sleep/wake patterns. The study was approved by Partners HealthCare Office of Research. Signed informed consent was obtained from all the participating families.

Out of 1459 mother–infant dyads who were eligible and invited, 433 agreed to participate, from which 298 participated in both the 1-month and the 6-month visits and had at least 3 days of valid actigraphy monitoring at both time points. We excluded observations with fewer than three nights of actigraphy data in line with prior work [27]. Research has shown that an actigraphy recording period of 2 days adequately portrayed circadian rhythm in infants [28]. Compared to the nonparticipants, the analytic sample ( $N = 298$ ) had a higher percentage of White and Asian infants, and a higher percentage of infants with college-educated mothers (Supplementary Table S1).

### Main exposures

To objectively assess sleep, a Philips Actiwatch 2 (Philips Healthcare) was placed on infants' left ankle for 7 continuous days while parents recorded infants' sleep/wake episodes on a sleep diary. An older version of the actigraph, Actiwatch AW64, has been validated to assess sleep/wake patterns in infants against polysomnography and direct observation [29, 30]. Agreement rates of 89%–94% were found between actigraphy and polysomnography, with good sensitivity (89%–96%) and modest specificity (39%–76%) [29]. Comparing actigraphy against direct observation, agreement rates of 85%–89% were found, with sensitivity between 88% and 97% and specificity between 32% and 34% [30]. In-house laboratory testing with healthy adults has shown no differences in the performance of the two models [31]. Trained scorers, blinded to other clinical data at a central sleep reading center, denoted rest intervals using the diary, which took precedence in times of disagreement with the actigraph. Sleep data were scored in 30-s epochs as sleep or wake with the Respironics Actiware 6 (Version 6.09, Philips/Respironics) [32]. A validated algorithm was used in which activity count recorded during the measured epoch was modified by the level of activity in the surrounding 2-min time period to yield the final activity count for each epoch [33].

The nighttime and daytime periods were defined as 7:00 pm to 7:59 am and 8:00 am to 6:59 pm, respectively, reflecting the

cutoffs in the expanded version of the validated Brief Infant Sleep Questionnaire [20]. Nighttime (daytime) sleep duration was the average total time spent asleep over nighttime (daytime) periods in hours. Nighttime sleep fragmentation was assessed using two indices: (1) wake after sleep onset (WASO), the average duration of all wake epochs occurring after sleep onset during the nighttime periods; and (2) number of waking bouts, number of episodes of wakefulness recorded by the actigraph showing an area of sustained bouts of wake epochs  $\geq 5$  min during the nighttime periods. The 5-min cutoff was chosen to facilitate comparison with prior research that adopted the same cutoff value [18]. All measures were averaged across measurement days from each visit. The main exposures were changes in the nighttime sleep measures between 1 and 6 months, with daytime and 24-h sleep measures assessed in secondary analyses. We focused on nighttime sleep because we were interested in the maturation of sleep/wake patterns as reflected by nocturnal sleep. In the first few months of life, with the stabilization of a circadian rhythm, infants progressively consolidate their sleep to one main nighttime episode, begin to sleep through the night, and coordinate their sleep with other family members' sleep [19, 20].

### Main outcomes

We measured infant length to the nearest 0.1 cm and weight to the 1 g using calibrated scales. All research staff were trained in anthropometric measurements and inter- and intrarater reliability were continuously evaluated to assure data quality. The primary outcome of interest was a binary indicator of overweight, defined as weight for length (WFL) at or above the 95th percentile of the age- and sex-specific World Health Organization (WHO) growth charts [34], measured at the 1- and 6-month visits. We focused on the dichotomous weight status variable as we were interested in understanding clinically significant changes in weight that are readily interpretable. Prior research has found that infants with overweight or who were at the highest end of the distribution of body mass index were at higher risk of developing obesity later in life compared to other infants [35]. Continuous age- and sex-specific WFL z-scores was examined as a secondary outcome.

### Covariates

In line with prior work, we adjusted for factors important for infants' sleep and growth, including infants' birth weight for gestational age z-score, age at outcome measurement, sex, race/ethnicity, breastfeeding mode (exclusive, partial, none) at 1 and 6 months, sleep at 1 month, as well as mothers' age at delivery and education (less than a bachelor's degree, a bachelor's degree or higher, dichotomized based on variability of responses) [17, 18, 27, 36, 37]. Race/ethnicity was adjusted for as prior work has shown that racial/ethnic differences in sleep emerge in early infancy [27]. Race/ethnicity is a construct that serves as a proxy for disadvantage in social factors, which might shape evolution of sleep patterns in infancy. The race/ethnicity data were collected from parental report and were defined according to Race and Ethnic Standards for Federal Statistics and Administrative Reporting [38].

### Statistical analyses

For descriptive purposes, we present the overall sample characteristics and by tertiles of changes in nighttime sleep duration between 1 and 6 months. The percentage of overweight infants at 6 months by tertiles of the changes in the three sleep measures are shown.

For the main analyses, we fit a series of prespecified models for the longitudinal outcomes using generalized estimating equations (GEEs), each with an exchangeable working correlation structure [39] to account for the repeated measures within infants. While the specific forms are given in [Supplementary Materials](#), the models were structured to enable estimation of the longitudinal change-in-change effect, while adjusting for sleep at 1 month. The effect estimate associated with the primary exposure of interest (i.e. change in the sleep measure between 1 and 6 months) captures the change in the expected response over time per unit change in the exposure for populations with the same baseline value of the sleep measure. Each person could be thought of as serving as his or her own control. The effect estimate associated with the 1-month sleep measure captures the difference in the expected response at 1 month between two populations that differ in the 1-month sleep exposure by one unit. Thus, the model distinguishes the longitudinal contrast from the cross-sectional contrast [40]. A logistic link function was used when estimating overweight status; an identity link was used when estimating WFL z-scores. A sequential modeling approach was used: Model 1 included the specific change in the sleep measure between 1 and 6 months; Model 2 additionally adjusted for the sleep measure at 1 month; and, Model 3 (the primary model) additionally adjusted for other covariates.

Prespecified sensitivity analyses explored an alternative way to characterize sleep fragmentation: number of waking bouts  $\geq 10$  min to investigate longer intervals of night wakings as they relate to the growth outcomes. We also explored the association between daytime and 24-h sleep duration and growth. We examined models that additionally adjusted for childcare attendance, early introduction of solids before 4 months of age, maternal employment status, and maternal weight gain. We also performed post hoc analyses using logistic and linear regression analyses to examine the associations between changes in sleep from 1 to 6 months with growth outcomes at 6 months.

All regression analyses were conducted in R version 3.5.3 using the gee package [41]. All tests were two sided, with a significance level of 5%.

## Results

### Descriptive results

Sample characteristics are presented in [Table 1](#). The mean (SD) gestational age was 39.5 (1.0) weeks, with a mean (SD) birth weight of 3.4 (0.4) kg. About half were boys. The percentage of infants with overweight was 10.3% at 1 month and 8.8% at 6 months. Among infants who were not overweight at 1 month, 15 (6.0%) became overweight at 6 months, while 21 (75.0%) infants who were overweight became not overweight. At 1 month, the mean (SD) nighttime sleep duration was 7.7 (1.2) h, which increased by 1.1 (1.5) h at 6 months ([Table 1](#); [Figure 1](#)). The mean (SD) WASO was 0.9 (0.5) h at baseline, which slightly increased

**Table 1.** Sample characteristics, overall and across terciles of change in nighttime sleep duration between 1 and 6 months, RISE & SHINE

	Overall	Terciles of change in nighttime sleep duration		
		I	II	III
Range (h)		[-4.43, 0.64]	[0.64, 1.72]	[1.75, 6.65]
N	298	101	98	99
<b>Infant characteristics</b>				
Gestational age (weeks) (mean (SD))	39.5 (1.0)	39.3 (1.1)	39.7 (0.9)	39.6 (1.1)
Birth weight (kg) (mean (SD))	3.4 (0.4)	3.3 (0.5)	3.4 (0.4)	3.3 (0.4)
Birth weight for gestational age z-score (mean (SD))	-0.2 (0.9)	-0.3 (1.0)	-0.1 (0.9)	-0.3 (0.8)
Age at 1-month visit (days) (mean (SD))	36.2 (7.6)	35.8 (7.9)	36.6 (8.8)	36.1 (6.0)
Age at 6-month visit (days) (mean (SD))	194.5 (16.6)	195.9 (16.8)	194.1 (15.7)	193.3 (17.1)
Infant sex: male (%)	48.7	42.6	49.0	54.5
<b>Infant race/ethnicity (%)</b>				
White	41.9	34.7	43.9	47.5
African American	7.7	8.9	8.2	6.1
Asian	17.8	19.8	12.2	21.2
Hispanic/Latino	32.6	36.6	35.7	25.3
<b>Breastfeeding at 1 month (%)</b>				
Exclusive	45.6	43.6	42.9	50.5
None	7.0	6.9	8.2	6.1
Partial	47.3	49.5	49.0	43.4
<b>Breastfeeding at 6 months (%)</b>				
Exclusive	39.3	32.7	44.9	40.4
None	30.9	35.6	28.6	28.3
Partial	29.9	31.7	26.5	31.3
Childcare attendance at 1 month: yes (%)	0.3	1.0	0.0	0.0
Childcare attendance at 6 months: yes (%)	41.2	35.6	42.7	45.5
<b>Mother characteristics</b>				
Maternal age at delivery (years): ≥30 (%)	76.2	72.3	79.6	76.8
Maternal education: ≥Bachelor's degree (%)	73.8	61.4	78.6	81.8
<b>Maternal employment status at 1 month (%)</b>				
Full-time	63.8	59.4	63.3	68.7
Not employed or student	18.8	21.8	18.4	16.2
Part-time	17.4	18.8	18.4	15.2
<b>Maternal employment status at 6 months (%)</b>				
Full-time	54.0	51.5	55.1	55.6
Not employed or student	22.5	23.8	18.4	25.3
Part-time	23.5	24.8	26.5	19.2
<b>Nighttime sleep measures at 1 month</b>				
Sleep duration (h) (mean (SD))	7.7 (1.2)	8.1 (1.0)	7.9 (0.7)	6.6 (1.0)
WASO (h) (mean (SD))	0.9 (0.5)	0.9 (0.4)	0.9 (0.5)	0.9 (0.6)
Waking bouts (mean (SD))	11.0 (2.9)	9.5 (2.4)	10.7 (2.3)	12.9 (2.8)
<b>Nighttime sleep measures at 6 months</b>				
Sleep duration (h) (mean (SD))	8.8 (1.0)	8.2 (1.1)	9.0 (0.7)	9.3 (0.9)
WASO (h) (mean (SD))	1.0 (0.4)	1.0 (0.4)	1.0 (0.3)	1.0 (0.4)
Waking bouts (mean (SD))	7.6 (2.2)	8.2 (2.3)	7.5 (2.0)	7.1 (2.1)
<b>Change in nighttime sleep measures between 1 and 6 months</b>				
Sleep duration (h) (mean (SD))	1.1 (1.5)	-0.5 (1.0)	1.2 (0.3)	2.7 (0.8)
WASO (h) (mean (SD))	0.1 (0.6)	0.1 (0.5)	0.1 (0.6)	0.1 (0.6)
Waking bouts (mean (SD))	-3.3 (3.4)	-1.3 (2.9)	-3.2 (2.5)	-5.7 (3.2)
<b>Growth measures at 1 month</b>				
WFL z-score (mean (SD))	0.3 (1.1)	0.4 (1.1)	0.3 (1.0)	0.3 (1.1)
Overweight <sup>a</sup> : yes (%)	10.3	7.3	11.3	12.2
<b>Growth measures at 6 months</b>				
WFL z-score (mean (SD))	0.3 (1.0)	0.5 (0.9)	0.3 (1.0)	0.2 (1.0)
Overweight <sup>a</sup> : yes (%)	8.8	13.3	7.5	5.3

<sup>a</sup>Overweight was defined as age- and sex-specific WFL percentile ≥95th.

over the 5-month period, likely reflecting the longer nighttime sleep. The number of waking bouts decreased. Nighttime sleep measures at 1 month were negatively correlated with changes in the sleep measures from 1 to 6 months ([Supplementary Table S2](#)). For instance, the longer the nighttime sleep duration at

1 month, the smaller the change in sleep duration between 1 and 6 months.

In bivariate analyses of sleep measures and overweight risk at 6 months, a greater increase in nighttime sleep duration was associated with a lower percentage of overweight at 6 months

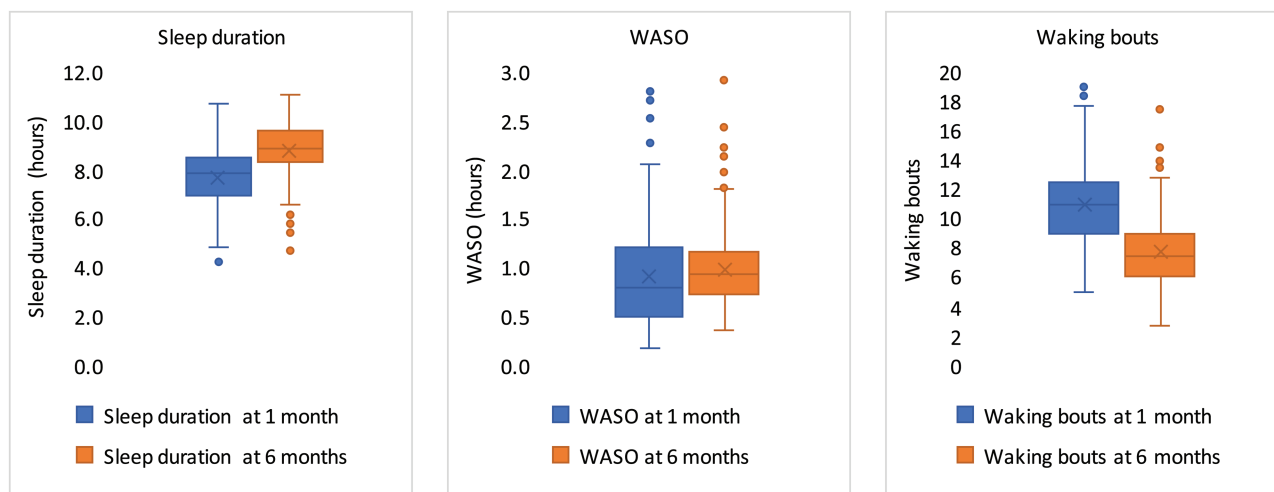


Figure 1. Nighttime sleep measures at 1 month and at 6 months.

(Figure 2). Overweight prevalence was lower among those whose number of waking bouts decreased compared to those whose number of waking bouts increased.

## Main results

Table 2 presents the results from GEE models estimating the associations between changes in nighttime sleep measures and growth outcomes. In unadjusted models, changes in nighttime sleep duration and number of waking bouts were associated with changes in the odds of overweight. In fully adjusted models, a 1-h increase in nighttime sleep duration between months 1 and 6 was associated with a 26% decrease in the odds of overweight from 1 to 6 months (odds ratio [OR] = 0.74; 95% confidence interval [CI], 0.56, 0.98). Change in WASO was not associated with change in the odds of overweight (OR = 1.68; 95% CI [0.92, 3.08]). Fewer number of waking bouts was associated with a lower odds of overweight (OR = 0.84, 95% CI [0.72, 0.98]). For WFL z-scores, change in sleep duration was not associated with the outcome in either unadjusted or adjusted models. Changes in WASO and number of waking bouts were both associated with changes in WFL z-scores in unadjusted models, indicating that worsened sleep fragmentation was associated with greater increases in WFL z-scores. After adjusting for sleep measures at 1 month, the associations were attenuated.

## Sensitivity analyses results

Change in the number of waking bouts  $\geq 10$  min was associated with change in the odds of overweight but not change in WFL z-score. Change in daytime sleep duration was not associated with change in the odds of overweight (OR = 0.79; 95% CI [0.53, 1.18]) from 1 to 6 months. Change in 24-h sleep duration was negatively associated with change in the odds of overweight (OR = 0.78; 95% CI [0.62, 0.99]). Neither change in daytime nor change in 24-h sleep duration was associated with change in WFL z-score. Adjusting for childcare attendance, early introduction of solids before 4 months of age, maternal employment status, and maternal weight gain did not change the main results. When examining the relationships between changes in sleep from 1 to 6 months and growth outcomes at 6 months, we

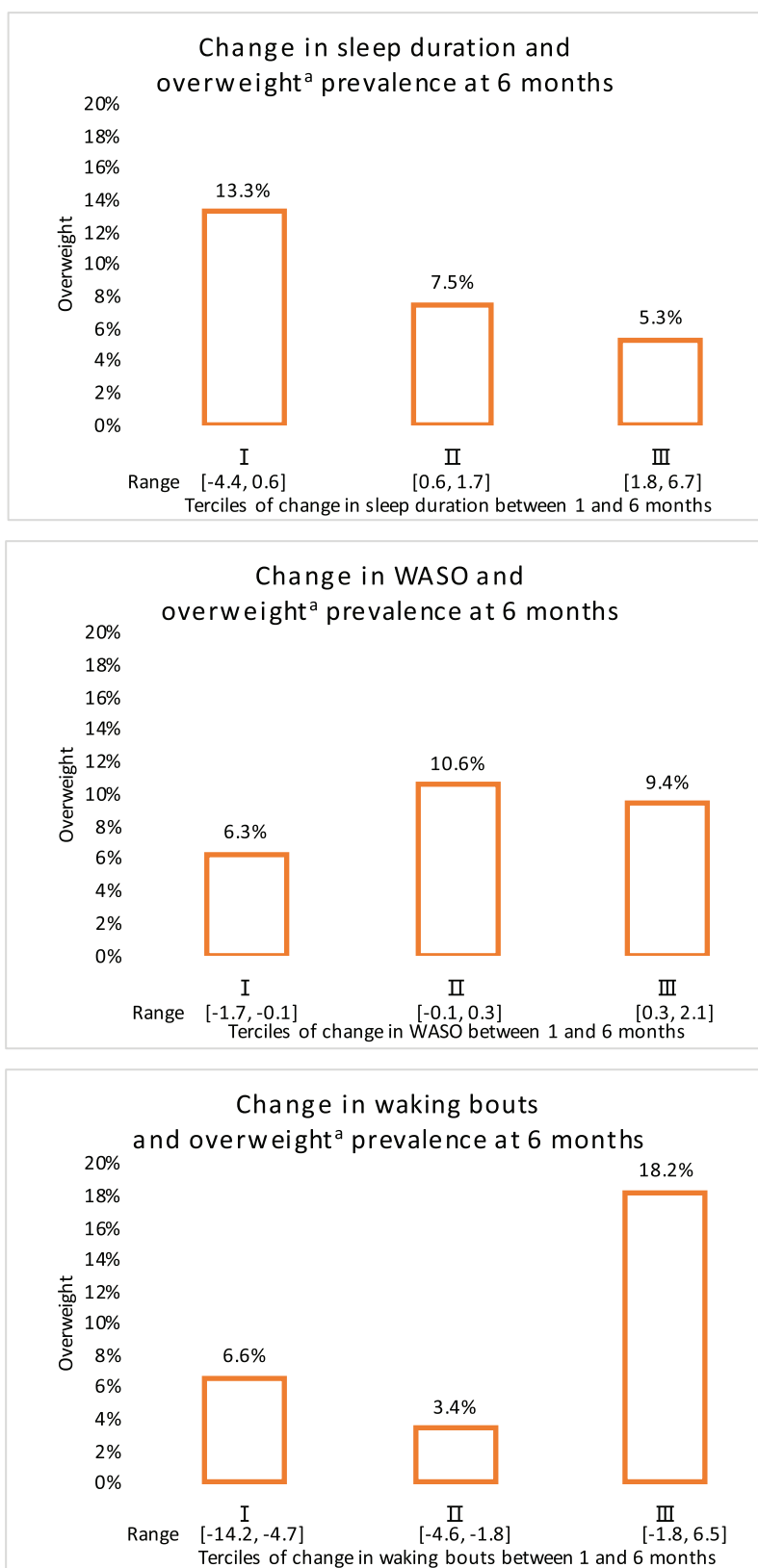
observed that the effect estimates were in the expected direction but were not statistically significant (Supplementary Table S3). For instance, sleep duration was negatively, nonsignificantly, associated with risk of overweight at 6 months (OR = 0.93; 95% CI [0.58, 1.52]).

## Discussion

In this longitudinal study of objectively assessed changes in sleep and growth in the first 6 months of life, we found greater increases in nighttime sleep duration and greater decreases in number of nighttime waking bouts were associated with lower odds of overweight from 1 to 6 months. Specifically, each 1-h increase in nighttime sleep duration was associated with a 26% decrease in the adjusted odds of overweight from 1 to 6 months. Each 1-unit decrease in number of waking bouts was associated with a 16% decrease in the adjusted odds of overweight from 1 to 6 months. Changes in nighttime WASO were not associated with odds of overweight from 1 to 6 months. Each 1-h increase in 24-h sleep duration was associated with a 22% decrease in the adjusted odds of overweight from 1 to 6 months. These data show that associations previously observed in later life extend to early infancy.

Our results related to sleep duration and infant overweight are in broad agreement with those of prior studies on older children and adults (e.g. [42–45]), and are in agreement with those of prior studies relating short sleep during infancy to subsequent obesity (e.g. [16,17]). Our longitudinal result is in line with the cross-sectional finding reported by Tikotzky et al. that short sleep duration was associated with higher WFL ratio [18]. Our results on the relationship between sleep fragmentation and infant overweight also agree with prior studies of adults documenting that greater sleep fragmentation is associated with higher risk of obesity [46]. Very little research has looked into the relationship among infants. For an exception, Tikotzky et al. reported a positive, insignificant correlation between objectively measured number of night wakings and body size [18].

Our unique contribution to the literature is that we examined the change-in-change relationship between sleep patterns and growth, using longitudinal, objective measures of sleep in the naturalistic setting that removed reporting bias. The



**Figure 2.** Unadjusted relationships of changes in nighttime sleep measures and overweight prevalence at 6 months. <sup>a</sup>Overweight was defined as age- and sex-specific WFL percentile  $\geq 95$ th.

change-in-change approach (i.e. change in the expected growth outcome over time per unit change in the sleep measure) is of particular importance in that infants' sleep/wake patterns

undergo dramatic changes during the developmentally critical period from 1 to 6 months, which are best described by modeling changes in both sleep and growth.

**Table 2.** Effect estimates from GEE relating changes in nighttime sleep measures to changes in overweight risk and WFL z-score between 1 and 6 months, RISE & SHINE

	Overweight <sup>a</sup>						WFL z-score					
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]	Beta	[95% CI]	Beta	[95% CI]	Beta	[95% CI]
Sleep duration (h)	0.71**	[0.56, 0.90]	0.73*	[0.57, 0.95]	0.74*	[0.56, 0.98]	-0.05	[-0.11, 0.01]	-0.04	[-0.10, 0.02]	-0.04	[-0.11, 0.04]
WASO (h)	1.47	[0.97, 2.22]	1.67	[0.96, 2.91]	1.68	[0.92, 3.08]	0.19*	[0.04, 0.33]	0.15	[-0.03, 0.32]	0.14	[-0.04, 0.31]
Waking bouts	1.17*	[1.02, 1.35]	1.16*	[1.00, 1.34]	1.19*	[1.02, 1.39] <sup>b</sup>	0.03*	[0.00, 0.05]	0.02	[-0.01, 0.04]	0.03	[-0.003, 0.06]

Model 1 included only the specific change in the nighttime sleep measure between 1 and 6 months. Model 2 additionally included the nighttime sleep measure at 1 month. Model 3 additionally controlled for infant birth weight for gestational age z-score, age at outcome measurement, sex, race/ethnicity, breastfeeding mode, maternal age, and maternal education. Statistically significant results were bolded.

<sup>a</sup>Overweight was defined as age- and sex-specific WFL percentile  $\geq 95$ th.

<sup>b</sup>Equivalent to 0.84 [0.72, 0.98] when looking at the OR [95% CI] associated with a 1-unit decrease in waking bouts.

\* $p < 0.05$ .

\*\* $p < 0.01$ .

Suboptimal infant sleep might increase energy intake and overweight risk by promoting discordant feeding practices (e.g. parental feeding to soothe, early introduction of solid foods) adopted by some parents to promote infant sleep, which are known risk factors for childhood overweight [47, 48]. On the other hand, poor sleep patterns might promote infant eating dysregulation [49]. Sleep loss has been associated with lower levels of eating self-regulation and increased risk of overeating in older children [50]. For infants who rely on parents for feeding, it is possible that sleep-deprived infants might have compromised ability to know when they were full and might signal excess appetite to parents, who might overfeed them. Moreover, suboptimal infant sleep might lead to tiredness and reduced activity during daytime, which would increase overweight risk.

Similar although less significant associations were seen for continuous measures of WFL z-scores with sleep. The more significant associations for the dichotomous overweight measure may reflect the associations of sleep duration and sleep fragmentation on a more extreme phenotype, rather than influencing growth in a continuous fashion.

The study has limitations. First, the relatively small representation of African American individuals and families with lower socioeconomic status in the Boston area where we enrolled participants raises questions about the generalizability of the findings to these groups. Second, although our analyses controlled for a series of covariates important for both sleep and growth, there might be residual confounding bias. For instance, breastfeeding has been associated with both sleep and growth [36, 37]. Our analyses controlled for breastfeeding mode (exclusive, partial, none) but not breastfeeding duration, which could have nuanced implications for the relationships between sleep and growth. There could still be concern that at least 3 days of actigraphy data might not be sufficient to assess sleep reliably. Additionally, the observational nature of the data constrained our ability to identify causality. Future experimental studies are needed to elucidate the mechanisms. Another limitation is that the study by design did not have additional time points between 1 and 6 months to capture trajectories of sleep and growth. Given the substantial changes that can occur during this period of life, future research collecting data from additional time points more closely within the period is needed.

## Conclusion

Our results showed that increased nighttime sleep duration and decreased nighttime sleep fragmentation were associated with lower odds of overweight from 1 to 6 months. Once present, obesity is hard to treat, as entrenched behaviors and metabolic forces tend to resist weight loss [51]. Thus, it is important that parents and caregivers begin prevention efforts as early as possible [1]. Infants engage in sleep activities more than in any other activity and adequate sleep plays fundamental roles in healthy growth. Sufficient and consolidated sleep could be part of the obesity prevention approach in infancy.

## Supplementary Material

Supplementary material is available at *SLEEP* online.

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## References

- Gillman MW. Fetal and infant origins of obesity. In: Kopelman PG, Caterson I, William Dietz w, eds. *Clinical Obesity in Adults and Children*. Malden, MA: John Wiley & Sons, Ltd; 2010:92–102.

2. Ogden CL, et al. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA*. 2014;**311**(8):806–814.
3. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics*. 1998;**101**(3 Pt 2):518–525.
4. Ben-Shlomo Y, et al. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*. 2002;**31**(2):285–293.
5. Freedman DS, et al. Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. *Pediatrics*. 2001;**108**(3):712–718.
6. Zheng M, et al. Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. *Obes Rev*. 2018;**19**(3):321–332.
7. Taveras EM, et al. Weight status in the first 6 months of life and obesity at 3 years of age. *Pediatrics*. 2009;**123**(4):1177–1183.
8. Ong KK, et al. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr*. 2006;**95**(8):904–908.
9. Institute of Medicine (US) Committee on Sleep Medicine and Research. Chapter 1: Introduction. In: Colten HR, Altevogt BM, eds. *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem*. Washington DC: National Academies Press (US); 2006.
10. Cappuccio FP, et al. Meta-analysis of short sleep duration and obesity in children and adults. *Sleep*. 2008;**31**(5):619–626. doi:10.1093/sleep/31.5.619
11. Van Cauter E, et al. Sleep and the epidemic of obesity in children and adults. *Eur J Endocrinol*. 2008;**159**(Suppl 1):S59–S66.
12. Buxton OM, et al. Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States. *Soc Sci Med*. 2010;**71**(5):1027–1036.
13. Wu Y, et al. Short sleep duration and obesity among children: a systematic review and meta-analysis of prospective studies. *Obes Res Clin Pract*. 2017;**11**(2):140–150.
14. Patel SR, et al. Short sleep duration and weight gain: a systematic review. *Obesity (Silver Spring)*. 2008;**16**(3):643–653.
15. Lowry R, et al. Association of sleep duration with obesity among US high school students. *J Obes*. 2012;**2012**:476914.
16. Bell JF, et al. Shortened nighttime sleep duration in early life and subsequent childhood obesity. *Arch Pediatr Adolesc Med*. 2010;**164**(9):840–845.
17. Taveras EM, et al. Short sleep duration in infancy and risk of childhood overweight. *Arch Pediatr Adolesc Med*. 2008;**162**(4):305–311.
18. Tikotzky L, et al. Sleep and physical growth in infants during the first 6 months. *J Sleep Res*. 2010;**19**(1 Pt 1):103–110.
19. Henderson JM, et al. The consolidation of infants' nocturnal sleep across the first year of life. *Sleep Med Rev*. 2011;**15**(4):211–220.
20. Sadeh A, et al. Sleep and sleep ecology in the first 3 years: a web-based study. *J Sleep Res*. 2009;**18**(1):60–73.
21. Joseph D, et al. Getting rhythm: how do babies do it? *Arch Dis Child Fetal Neonatal Ed*. 2015;**100**(1):F50–F54.
22. Spruyt K, et al. The underlying interactome of childhood obesity: the potential role of sleep. *Child Obes*. 2012;**8**(1):38–42.
23. Buysse DJ. Sleep health: can we define it? Does it matter? *Sleep*. 2014;**37**(1):9–17. doi:10.5665/sleep.3298
24. Sadeh A, et al. Parenting and infant sleep. *Sleep Med Rev*. 2010;**14**(2):89–96.
25. Alamian A, et al. Infant sleep problems and childhood overweight: effects of three definitions of sleep problems. *Prev Med Rep*. 2016;**4**:463–468.
26. Ash T, et al. Emergence of racial/ethnic differences in infant sleep duration in the first six months of life. *Sleep Med X*. 2019;**1**:100003.
27. Yu X, et al. Emergence of racial/ethnic and socioeconomic differences in objectively measured sleep-wake patterns in early infancy: results of the Rise & SHINE study. *Sleep*. 2021;**44**(3). doi:10.1093/sleep/zsaa193
28. Thomas KA, et al. Circadian research in mothers and infants: how many days of actigraphy data are needed to fit cosinor parameters? *J Nurs Meas*. 2008;**16**(3):201–206.
29. So K, et al. Actigraphy correctly predicts sleep behavior in infants who are younger than six months, when compared with polysomnography. *Pediatr Res*. 2005;**58**(4):761–765.
30. Sung M, et al. Validation of actigraphy for determining sleep and wake in preterm infants. *Acta Paediatr*. 2009;**98**(1):52–57.
31. Respiration P. *Equivalence of Activity Recordings and Derived Sleep Statistics*. Andover, MA: Philips Healthcare; 2009.
32. Sadeh A. Assessment of intervention for infant night waking: parental reports and activity-based home monitoring. *J Consult Clin Psychol*. 1994;**62**(1):63–68.
33. Chen X, et al. Racial/ethnic differences in sleep disturbances: the Multi-Ethnic Study of Atherosclerosis (MESA). *Sleep*. 2015;**38**(6):877–888. doi:10.5665/sleep.4732
34. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatr Oslo Nor 1992 Suppl*. 2006;**450**:76–85.
35. Baird J, et al. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ*. 2005;**331**(7522):929.
36. Johnson L, et al. Associations between infant feeding and the size, tempo and velocity of infant weight gain: SITAR analysis of the Gemini twin birth cohort. *Int J Obes (Lond)*. 2014;**38**(7):980–987.
37. Galbally M, et al. Breastfeeding and infant sleep patterns: an Australian population study. *J Paediatr Child Health*. 2013;**49**(2):E147–E152.
38. Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity. Published online October 30, 1997. <https://www.federalregister.gov/documents/1997/10/30/97-28653/revisions-to-the-standards-for-the-classification-of-federal-data-on-race-and-ethnicity>. Accessed March 29, 2021.
39. Diggle P, et al. *Analysis of Longitudinal Data*. 2nd ed. Oxford, NY: Oxford University Press; 2002.
40. Diggle P, et al. *Analysis of Longitudinal Data*. 2nd ed. USA: Oxford University Press; 2013.
41. R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing; 2020. <https://www.R-project.org/>. Accessed June 18, 2018.
42. Bonuck K, et al. Sleep-disordered breathing, sleep duration, and childhood overweight: a longitudinal cohort study. *J Pediatr*. 2015;**166**(3):632–639.
43. Halal CSE, et al. Short sleep duration in the first years of life and obesity/overweight at age 4 years: a birth cohort study. *J Pediatr*. 2016;**168**:99–103.e3.
44. Magee L, et al. Longitudinal associations between sleep duration and subsequent weight gain: a systematic review. *Sleep Med Rev*. 2012;**16**(3):231–241.
45. Agrad WS, et al. Risk factors for childhood overweight: a prospective study from birth to 9.5 years. *J Pediatr*. 2004;**145**(1):20–25.



46. Chen J, et al. Weekly sleep trajectories and their associations with obesity and hypertension in the Hispanic/Latino population. *Sleep*. 2018;**41**(10). doi:[10.1093/sleep/zsy150](https://doi.org/10.1093/sleep/zsy150)
47. Clayton HB, et al. Prevalence and reasons for introducing infants early to solid foods: variations by milk feeding type. *Pediatrics*. 2013;**131**(4):e1108–e1114.
48. Stifter CA, et al. Parent use of food to soothe infant/toddler distress and child weight status. An exploratory study. *Appetite*. 2011;**57**(3):693–699.
49. Hughes SO, et al. Executive functioning, emotion regulation, eating self-regulation, and weight status in low-income preschool children: how do they relate? *Appetite*. 2015;**89**:1–9.
50. Burt J, et al. Sleep and eating in childhood: a potential behavioral mechanism underlying the relationship between poor sleep and obesity. *Sleep Med*. 2014;**15**(1):71–75.
51. Rosenbaum M, et al. The physiology of body weight regulation: relevance to the etiology of obesity in children. *Pediatrics*. 1998;**101**(3 Pt 2):525–539.