



Sleep duration in middle childhood and age at menarche

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Abstract

Objective: Puberty affects sleep phasing. However, it is unclear if sleep duration earlier in childhood could influence the timing of pubertal events. We aimed to assess the association between middle childhood nighttime sleep duration and age at menarche (AAM).

Methods: In a cohort of 819 premenarcheal Colombian girls who were followed annually for the occurrence of menarche, we estimated adjusted hazard ratios (HR) with 95% confidence intervals (CI) for menarche by categories of recommended sleep duration in middle childhood using Cox models. Analyses were stratified by age at sleep assessment.

Results: Among girls aged 9 to <11 years, compared with girls who slept within recommendations, sleeping above recommendations was related to an adjusted 76% (95% CI: 4%, 198%; p = .04) higher probability of experiencing menarche during follow up. In girls aged ≥ 11 years, compared with girls who slept within recommendations, sleeping under recommendations was related to an adjusted 42% (95% CI: 5%, 93%; p = .03) higher probability of experiencing menarche during follow-up. Sleep duration was not associated with AAM in girls aged <9 years at the time of sleep assessment.

Conclusions: Sleeping above recommendations in girls 9 to <11 years-old and sleeping under recommendations in girls ≥ 11 years-old is associated with earlier menarche.

1 **INTRODUCTION**

Early menarche is a risk factor for chronic disease in adulthood (Canoy et al., 2015) and all-cause mortality (Lozano-Esparza et al., 2021). Both genetic and modifiable environmental factors contribute to age at menarche (AAM) (Anderson et al., 2007). The latter include socioeconomic conditions, family stressors, pollutants, and nutritional status (Villamor & Jansen, 2016).

Sleep duration in children is increasingly recognized as a critical factor in physical and cognitive development; yet little is known about its potential influence on the timing of pubertal events. While it is apparent that pubertal development delays sleep phases which can lead to shortened sleep duration (Foley et al., 2018; Hoyt et al., 2018), whether sleep duration in childhood could influence AAM is unclear. A role of sleep is plausible considering its effects modulating the production of sex

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hormones (Michels et al., 2020) involved in the onset of menses. Also, both childhood sleep duration (Fobian et al., 2018) and earlier AAM (Berentzen et al., 2017) are associated with cardiometabolic disease risk factors in adolescence; hence, childhood sleep duration might be an upstream cause of both timing of menarche and cardiometabolic disease.

The objective of this study was to assess whether shorter nighttime sleep duration in middle childhood is associated with earlier AAM in the Bogotá School Children Cohort (BoSCCo) study.

2 | MATERIALS AND METHODS

2.1 | Study design and population

We conducted a prospective investigation in the context of the BoSCCo study. Details on the cohort design have been previously reported (Villamor et al., 2017). In brief, we recruited 3202 randomly selected children aged 5– 12 years in 2006 from primary public schools in Bogotá, Colombia. At the time of enrollment, we administered a parental questionnaire inquiring on sociodemographic characteristics and performed height and weight measurements on the children using standard techniques.

In-person follow-up visits occurred in June and November 2006, at least once between 2007 and 2009, and at least once between 2011 and 2015. In addition to in-person visits, girls' homes were called on the phone at least once a year. At each in-person or telephonic contact, girls were asked if they had begun menstruation and, if they had, the date of their first menstrual period. Major holidays and school vacation periods were used to aid the girls' recall of the date of menarche if needed.

During the 2007-2009 follow-up, parents of 2308 randomly selected participants completed а selfadministered survey that included questions on the children's nighttime sleep duration on weekdays and weekend days. The question for weekdays was: "Normally, how many hours does the child sleep at night during weekdays? (count the hours and minutes from the time the child falls asleep at night to the time the child awakens in the morning)," with fields for duration in hours and minutes. A second question replaced "weekdays" with "weekend days."

Written informed consent from parents and the children's assent to participate were obtained before enrollment. The study protocol was approved by the Ethics Committee of the National University of Colombia; the University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board approved the use of data from the study.

2.2 | Data analysis

2.2.1 | Outcome

Age at menarche was calculated as date of menarche minus date of birth, in decimal years.

2.2.2 | Exposure

Nighttime sleep duration in middle childhood was calculated as the weighted average of the weekday (weight, 5/7) and weekend day (weight, 2/7) reported sleep hours. Sleep duration in hours and minutes was categorized per the American Academy of Sleep Medicine age-specific recommendations (Paruthi et al., 2016) as under, within, or above. Cut points (hours) for each group were, respectively, <9, 9–12, or >12 for girls 6–12 years-old, and <8, 8–10, or >10 for those aged ≥13 years.

2.2.3 | Covariates

Children's height- and body mass index (BMI, kg/m^2)for-age Z scores at enrollment were calculated according to the WHO growth reference for children and adolescents (de Onis et al., 2007). Maternal AAM was recalled age of first menstrual cycle and parity was the number of previous live births. Socioeconomic status was categorized from 1 (lowest) to 4 (highest in the sample) per the local government's classification.

2.2.4 | Statistical analysis

Of the 1635 girls enrolled, 1141 underwent sleep duration assessment in middle childhood. We excluded 276 who were postmenarcheal and 46 who had been loss to follow-up by the time of sleep assessment; thus, the analytic sample size was 819. Compared with girls excluded from analyses, those included were, on average, younger and had shorter stature, later AAM, and more highly educated mothers (Table S1). One hundred girls (12%) had not experienced menarche by their last follow-up contact.

We investigated the associations between sleep duration categories and AAM with use of time-to-event techniques. These methods adequately account for rightcensoring of the outcome since not all girls had menarche during follow-up. Because menarche is a late pubertal event and puberty can affect sleep duration, estimates among the oldest girls could be prone to reverse causation bias; hence, all analyses were stratified by age (y) at

Sleep duration in middle childhood	n	Median age at menarche (years) ^a	Unadjusted estimates		Adjusted estimates ^c	
			HR ^b	95% CI	HR	95% CI
<9 years-old						
Under	80	12.4	0.99	0.73, 1.33	1.04	0.74, 1.48
Within	133	12.3	1.00		1.00	
Above	6	13.2	0.65	0.40, 1.04	0.72	0.39, 1.03
9 to <11 years-old						
Under	150	12.5	1.14	0.91, 1.42	1.05	0.81, 1.36
Within	184	12.4	1.00		1.00	
Above	8	12.0	1.77	1.01, 3.11	1.76	1.04, 2.98
≥11 years-old						
Under	113	12.9	1.41	1.08, 1.83	1.42	1.05, 1.93
Within	137	13.3	1.00		1.00	
Above	8	13.5	1.11	0.63, 1.95	1.16	0.65, 2.08

TABLE 1 Age at menarche in school-age girls from Bogotá, Colombia and sleep duration in middle childhood stratified by age at sleep duration assessment.

^aFrom Kaplan–Meier survival probabilities.

^bHazard ratios from Cox proportional hazards models with age at menarche as the outcome. The robust sandwich covariance matrix estimate was specified in the model. Complete case analysis (n = 219 in <9 years-old group; n = 342 in 9 to <11 years-old group; n = 258 in \geq 11 years-old group).

^cAdjusted for child's height and BMI-for-age Z score, socioeconomic status, and mother's age at menarche and parity. Complete case analysis (n = 167 in <9 years-old group; n = 283 in 9 to <11 years-old group; n = 229 in ≥11 years-old group).

sleep assessment (<9, 9 to <11, or \geq 11). We estimated unadjusted median ages at menarche by sleep duration categories from Kaplan-Meier cumulative probabilities and hazard ratios (HR) with 95% confidence intervals (CI) from Cox proportional hazard models. In these models, menarche was the dichotomous outcome with age in decimal years as the time scale. Girls who did not experience menarche during follow-up were censored at the last contact. Models were adjusted for sociodemographic characteristics that were related to the exposure (Zhu et al., 2022) without being its consequence, or that were known independent predictors of AAM (Villamor et al., 2017). These included height- and BMI-for-age Z scores, socioeconomic status, and mother's AAM and parity. The robust sandwich covariance matrix estimate was specified in each model to account for correlations among siblings. HR > 1 indicate an earlier menarche compared with the reference category, whereas HR < 1indicate a later menarche.

3 | RESULTS

Mean \pm *SD* age at the time of sleep duration assessment was 10.1 \pm 1.6 years. The proportion of girls in sleep duration categories under, within, and above recommendations was 42%, 55%, and 3%, respectively. Estimated median (IQR) AAM was 12.6 (11.9, 13.4) years. Sleep duration was not associated with AAM in girls aged <9 years at the time of sleep assessment (Table 1). Among girls aged 9 to <11 years, compared with girls who slept within recommendations, sleeping above recommendations was related to an adjusted 76% (95% CI: 4%, 198%; p = .04) higher probability of experiencing menarche at any time of follow up (Table 1). In girls aged \geq 11 years, compared with girls who slept within recommendations, sleeping under recommendations was related to an adjusted 42% (95% CI: 5%, 93%; p = .03) higher probability of experiencing menarche during follow-up (Table 1).

4 | DISCUSSION

In this longitudinal study of Colombian schoolgirls, sleeping above recommendations at 9 to <11 years and sleeping under recommendations at \geq 11 years was associated with earlier menarche. These associations were independent of child, maternal, and household factors.

Previous investigations had focused on the role of puberty on sleep duration; our inquiry on the potential effect of sleep duration on the timing of a pubertal event is a novel contribution. In our study, the direction of the association between sleep duration and earlier menarche depended on age at assessment of sleep. At ages 9 to <11 years, long sleep duration was related to earlier menarche. Long sleep duration could influence AAM by modulating the synthesis of sex hormones. High estradiol levels are associated with earlier AAM (Fassler et al., 2019). In adult women, longer sleep duration was associated with increased estradiol concentrations (Michels et al., 2020). Whether longer sleep may be involved in triggering onset of menses by increasing estradiol concentrations is an intriguing possibility. Another potential mechanism in the association between long sleep duration and AAM is melatonin release by the pineal gland. Abnormalities and dysfunctions of the pineal gland have been associated with precocious puberty (Patel et al., 2020). Thus, melatonin, an important regulator in the sleep-wake cycle, may act as an upstream factor in the association between sleep duration and AAM (Claustrat & Leston, 2015). We noted that this association pertained to only 8 girls in the oversleep category: thus, the results could also be due to chance.

In contrast with the findings among girls aged 9 to <11 years, short sleep duration in the \geq 11 years-old group was related to earlier menarche, consistent with findings from a cross-sectional study (Bo et al., 2019). Despite our study's longitudinal design, we cannot rule out reverse causation as a possible explanation because, even among premenarcheal girls, puberty may have already started by age 11 years and puberty shortens sleep (Foley et al., 2018; Hoyt et al., 2018).

The strengths of this study include the prospective nature of data collection which precludes differential misclassification of exposure. In addition, we were able to control for a number of relevant confounders. Some limitations should also be noted. First, it is difficult to determine the directionality of the association due to the timing of sleep ascertainment; sleep duration measured in older girls may be a consequence of puberty onset. Second, there is a lack of variability in measured sleep duration resulting in a small sample of girls in the oversleep category. Third, generalizability may be an issue. Because only pre-menarcheal girls could be included in the analyses, excluded post-menarcheal girls were the oldest at enrollment and/or had earlier AAM. Thus, results may not be applicable to older girls or girls with earlier AAM. Fourth, AAM is an imperfect proxy for the timing of puberty onset since the interval between these events may vary between girls. Although menarche generally occurs 2-3 years after the larche, the first measurable physical manifestation of puberty (Cabrera et al., 2014); it may vary with respect to the disinhibition of the hypothalamic-pituitary-gonadal axis, which is the prime pubertal event and could only be reliably identified using hormonal biomarkers. Hence, quantification of changes in sex hormone concentrations is warranted in future studies. Finally, non-differential misclassification of sleep

duration from recall bias could have attenuated estimates of association.

In conclusion, sleeping above recommendations in girls 9 to <11 years-old and sleeping under recommendations in girls \geq 11 years-old is associated with earlier menarche. Further studies on sleep duration and timing of pubertal events involving assessments prior to puberty onset are warranted.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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