# Sleep Duration and Telomere Length in Children

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**Objective** To test the association between sleep duration and telomere length in a pediatric population.

**Study design** We analyzed cross-sectional data for 1567 children from the age 9 study wave of the Fragile Families and Child Wellbeing Study, a population-based birth cohort of children born between 1998 and 2000 in large American cities (population >200 000). We measured telomere length using quantitative polymerase chain reaction, and children's typical nightly sleep duration was reported by their primary caregivers. Using linear regression, we estimated the association between sleep duration and telomere length both in unadjusted models and adjusting for a number of covariates.

**Results** We found that children with shorter sleep durations have shorter telomeres than children with longer sleep durations. Each hour less of nightly sleep duration is associated with having telomeres that are 0.015 log-kilobases per chromosome shorter ($P < .05$). We found no difference in this association by race, sex, or socioeconomic status.

**Conclusions** We provide preliminary evidence that children with shorter sleep durations have shorter telomeres. This finding is consistent with a broader literature indicating that suboptimal sleep duration is a risk for increased physiological stress and impaired health. Future research should address the limitations of our study design by using longitudinal study designs and telomere measurements, measuring sleep duration via polysomnography or actigraphy, and assessing the intermediate biological mechanisms of the link between sleep and telomere dynamics. *(J Pediatr 2017;187:247-52).*

Inadequate nightly sleep duration is linked to morbidities[1-3] and mortality,[4-6] as well as a number of physiological sequelae, including inflammation, oxidative stress, increased sympathetic tone, and neuroendocrine dysregulation.[7] Although little of this research has considered pediatric populations, short sleep duration in childhood is associated with changes in hypothalamic–pituitary–adrenocortical system activity,[8] autonomic nervous system activity,[9] and metabolic regulation.[10] This type of stress-altered hypothalamic–pituitary–adrenocortical activity is known to correlate with telomere length.[11,12] Telomeres are repetitive DNA sequences (in humans, $TTAGGG_n$) and associated proteins that cap the end of chromosomes. With each cycle of chromosomal replication and cellular division, the telomere becomes shorter, except in specialized cells expressing telomerase.[13] This means that telomere length gradually decreases with age in most cells, although the rate of telomere attrition varies across humans in part because of between-person differences in hypothalamic–pituitary–adrenocortical activation, which is associated with shorter telomere length.[11,12] Thus, distal social or experiential predictors of physiological stress—that is, difficult life experiences[14-16]—may also be associated with an accelerated rate of telomere attrition. Identifying factors that predict telomere length or attrition disparities may indicate opportunities for clinical intervention, even if the biological mechanisms by which the experience becomes associated with telomere length are unknown. Telomere length may be a particularly useful biomarker when assessing health in pediatric populations, because disparities in telomere length emerge before the manifestation of chronic health conditions in adulthood. In adults, shorter sleep duration has been shown to be one of these adverse life experiences; shorter sleep duration is associated with shorter telomere length in adults.[17-21] However, no study has tested whether the same association is found in children. Therefore, we used DNA collected from a diverse, population-based sample of 1567 9-year-old American children born between 1998 and 2000 to assess the association between children's typical nightly sleep duration (reported by primary caregivers) and telomere length. We hypothesized that children who have shorter nightly sleep durations would have shorter telomeres than their peers who sleep for more hours each night.

## Methods

We analyzed cross-sectional data from 1567 children in the age 9 study wave of the Fragile Families and Child Wellbeing Study, a population-based birth cohort of children born between 1998 and 2000 in large American cities (population >200 000). Interviews with mothers and fathers were conducted at the child's birth and again when the child was 1, 3, 5, and 9 years of age. At 9 years of age, the child's

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primary caregiver (a parent or other adult) also provided information about the child. Because only 13 of the children in our analytic sample had primary caregivers who were not their mothers, for brevity we refer to data from these primary caregivers as being mother reported. DNA from saliva was collected from mothers and children when children were 9 years of age, during an assessment in the home. The Institutional Review Boards of Princeton University and Columbia University approved data collection. Of the 2482 children for whom telomere length is available, our analysis is based on a complete case analysis of the 1567 children who also had data on all necessary predictors. Neither telomere length nor sleep duration differed significantly between included and excluded cases.

## Measures

**Telomere Length.** We measured telomere length using saliva provided when the child was approximately 9 years of age. Prior research using this data has described in detail how absolute telomere length is measured using a quantitative real-time polymerase chain reaction assay.[22] In brief, samples were measured in triplicate and averaged. Reference DNA samples derived from cell lines not expressing or expressing telomerase were included in each plate, and to minimize plate-to-plate variation telomere length was normalized using the geometric mean of these reference DNA samples. The coefficient of variation of a standard was 11%. These analyses exclude the 1% tails of shortest and longest telomeres, because extreme values could represent mismeasurement or oral pathology. Telomere length was log-transformed to approximate a normal distribution. Mother's telomere length, used as a covariate, was measured and logged in the same manner. This approach to measuring telomere length in buccal cells has been compared directly with telomere length measures from peripheral mononuclear blood cells. Although buccal cell telomere lengths are longer than peripheral mononuclear blood cell telomere lengths, telomere length in the 2 cell types is highly correlated.[22] Telomeres shorten at equivalent rates across a range of tissues.[23]

**Sleep Duration.** The predictor of interest was the child's average nightly sleep duration, which we treated as a continuous variable. Mothers reported how many hours their child typically slept per night during the week. In the analytic sample, hours of sleep at 9 years of age ranges from 4 to 14. To adjust for implausible sleep durations, we removed the handful of cases with very short (<6 hours; n = 2) or long (>12 hours; n = 5) nightly sleep durations using listwise deletion, an approach similar to prior research using this data.[24]

**Covariates.** Our analysis accounted for a wide range of factors known to be associated with either children's telomere lengths or children's nightly sleep duration.[25] Child characteristics used as covariates included the age in months, low birth weight (<2500 g), and sex (recorded at birth). Pubertal development at 9 years of age was reported by mothers in a series of questions on the child's experience of 5 physical puberty changes: a height growth spurt, hair growth, skin changes, a deepening voice (boys), facial hair growth (boys), breast growth (girls), or menarche (girls). Mothers indicated the extent to which the child had begun to experience each of these changes with response categories of "no" (coded 1), "yes, barely" (coded 2), "yes, definitely" (coded 3), or "development is completed" (coded 4); for menarche, responses were "no" (coded 1) and "yes" (coded 4). The responses to all of these questions were averaged to compute a pubertal development score ranging from 1 to 4. The child's body mass index was computed from weight and height measurements taken by the interviewer during the home visit portion of the age 9 interview. Finally, mothers reported if the child had ever been diagnosed with attention deficit hyperactivity disorder/attention deficit disorder or autism.

Additional covariates included characteristics of the child's parents. Mother's race/ethnicity, nativity, age, educational attainment, household income, relationship with the child's biological father, and household composition were assessed at the time of the child's birth. Mother's race/ethnicity was self-reported and included categories for white (non-Hispanic), black (non-Hispanic), Hispanic, and some other race/ethnicity. Nativity measures whether or not the mother was born in the United States. Mother's age and father's age were self-reported. Maternal education is a categorical variable for less than high school education, high school diploma or graduate equivalency diploma, some college education, and a college graduate or higher. Household income was reported by the mother. Additionally, mothers were asked at the child's birth if they were married to or cohabiting with the child's biological father and how many other children already lived in their home. We also included the mother's telomere length (measured at the 9-year interview) as a covariate, to account for a portion of the sizable heredity in telomere length as well as to capture the effects the environments in which both mothers and children were embedded in the child's first nine years of life. Finally, to account for the city-based clustering of the baseline sample, we included a series of dummy variables indicating the city in which the child was born and clustered standard errors by sample city.

## Statistical Analyses

Using unadjusted and adjusted linear regression models, we examined to what extent children's sleep durations were associated with their telomere lengths. Model 1 assessed the unadjusted association between sleep duration and log-telomere length. Model 2 adjusted this estimate for child's age at the 9-year interview as well as parental ages at the child's birth. Model 3 added a set of covariates including mother's log-telomere length, child and family characteristics, and the city in which the child was born. We also conducted sensitivity analyses to assess whether race, sex, or socioeconomic status moderated these associations and whether there was a nonlinear association between sleep duration and telomere length. All analyses were conducted using R (R Foundation for Statistical Computing, Vienna, Austria),[26] and we considered results with $P < .05$ to be significant.