

Accepted Manuscript

Title: Sleep duration and growth outcomes across the first 2 years of life in the GUSTO study

Author: Yi Zhou, Izzuddin M Aris, Sara Shuhui Tan, Shirong Cai, Mya Thway Tint, Gita Krishnaswamy, Michael J Meaney, Keith M Godfrey, Kenneth Kwek, Peter D Gluckman, Yap-Seng Chong, Fabian Yap, Ngee Lek, Joshua J Gooley, Yung Seng Lee

PII: S1389-9457(15)00863-1
DOI: <http://dx.doi.org/doi:10.1016/j.sleep.2015.07.006>
Reference: SLEEP 2836

To appear in: *Sleep Medicine*

Received date: 5-1-2015
Revised date: 9-7-2015
Accepted date: 10-7-2015

Please cite this article as: Yi Zhou, Izzuddin M Aris, Sara Shuhui Tan, Shirong Cai, Mya Thway Tint, Gita Krishnaswamy, Michael J Meaney, Keith M Godfrey, Kenneth Kwek, Peter D Gluckman, Yap-Seng Chong, Fabian Yap, Ngee Lek, Joshua J Gooley, Yung Seng Lee, Sleep duration and growth outcomes across the first 2 years of life in the GUSTO study, *Sleep Medicine* (2015), <http://dx.doi.org/doi:10.1016/j.sleep.2015.07.006>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Sleep duration and growth outcomes across the first 2 years of life in the GUSTO study

Yi Zhou, B.Eng¹, Izzuddin M Aris, PhD², Sara Shuhui Tan, MD¹, Shirong Cai, PhD³, Mya Thway Tint, MBBS M.Sc³, Gita Krishnaswamy, M.Sc⁴, Michael J Meaney, PhD⁵, Keith M Godfrey, MBBS PhD⁶, Kenneth Kwek, MBBS⁷, Peter D Gluckman, MBChB D.Sc^{8,9}, Yap-Seng Chong, MBBS MD^{3,8}, Fabian Yap, MBBS^{1,10}, Ngee Lek, FRCPC¹⁰, Joshua J Gooley, PhD^{1*}, Yung Seng Lee, MBBS PhD^{2,8,11*}

Affiliations:¹Duke-NUS Graduate Medical School, Singapore, ²Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, ³Department of Obstetrics and Gynecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, ⁴Centre for Quantitative Medicine, Duke-NUS Graduate Medical School, Singapore, ⁵Department of Psychiatry, Neurology, and Neurosurgery, McGill University, Montréal, Québec, Canada, ⁶Biomedical Research Centre Medical Research Council Lifecourse Epidemiology Unit, Southampton, UK, NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK, ⁷Department of Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore, ⁸Singapore Institute for Clinical Sciences, Agency for Science and Technology Research (A*STAR), Brenner Centre for Molecular Medicine, Singapore, ⁹Liggins Institute, University of Auckland, Auckland, New Zealand, ¹⁰Department of Paediatrics, Paediatric Endocrinology service, KK Women's and Children's Hospital, Singapore, ¹¹Division of Paediatric Endocrinology and Diabetes, Khoo Teck Puat-National University Children's Medical Institute, National University Hospital, Singapore

Address correspondence to: 1. Joshua J Gooley, Program in Neuroscience & Behavioral Disorders, Duke-NUS Graduate Medical School, 8 College Road, Singapore 169857, Email: joshua.gooley@duke-nus.edu.sg or 2. Lee Yung Seng, Department of Pediatrics, Yong Loo Lin School of Medicine, NUHS Tower Block, level 12, 1E Kent Ridge Road, Singapore 119228, Email: paeleey@nus.edu.sg

Short title: Sleep duration and growth outcomes in early childhood

Abbreviations: BISQ—Brief Infant Sleep Questionnaire, BMI—body mass index, GUSTO—Growing Up in Singapore Towards healthy Outcomes

Key Words: sleep duration; children; growth; body mass index; body length; cohort study

Conflict of Interest: PDG, CYS and KMG have received reimbursement for speaking at conferences sponsored by companies selling nutritional products, and are part of an academic consortium that has received research funding from Abbott Nutrition, Nestle, and Danone. The remaining authors have no conflicts of interest or financial relationships to disclose.

Highlights

- Sleep and growth outcomes were examined in 899 children in an Asian birth cohort.
- Shorter sleep associated with shorter body length in the first 2 years of life.
- Shorter sleep associated with higher BMI in Malay children.
- Shorter sleep associated with higher BMI in infants who slept ≤ 12 h/day at 3 months.

ABSTRACT

Objectives: Short sleep duration is thought to be a factor contributing to increased body mass index (BMI) in school-aged children and in adults. Our objective was to determine whether sleep duration associates with growth outcomes during the first two years of life.

Study design: Participants included 899 children enrolled in the Growing up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study. Anthropometric data (weight and body length) and parental reports of sleep duration were collected at 3, 6, 9, 12, 18, and 24 months of age. Mixed model analysis was used to evaluate the longitudinal association of BMI and body length with sleep duration. In subgroup analyses, effects of ethnicity (Chinese, Indian, and Malay) and short sleep at 3 months of age (≤ 12 h per day) were examined on subsequent growth measures.

Results: In the overall cohort, sleep duration was significantly associated with body length ($\beta=0.028$, 95% CI 0.002 to 0.053, $p=0.033$), but not BMI, after adjustment for potential confounding factors. Only in Malay children, shorter sleep was associated with a higher BMI ($\beta=-0.042$, 95% CI -0.071 to -0.012, $p=0.005$) and shorter body length ($\beta=0.079$, 95% CI 0.030 to 0.128, $p=0.002$). Additionally, in children who slept ≤ 12 h per day at 3 months of age, shorter sleep was associated with higher BMI and shorter body length.

Conclusion: The association between sleep duration and growth outcomes begins in infancy. The small but significant relationship between sleep and growth anthropometric measures in early life might be amplified in later childhood.

INTRODUCTION

The rate of childhood obesity has increased substantially over the past few decades. Today, about one third of children worldwide are either overweight or obese¹. In parallel with the global obesity epidemic, there has been a gradual decline in sleep duration over the past several decades, including children in Asia, Europe, and the United States². Numerous studies have demonstrated an inverse correlation between sleep duration and adiposity or obesity risk in children and adults³⁻¹⁰. Possible mechanisms include decreased leptin and increased ghrelin associated with sleep deprivation¹¹, leading to increased caloric intake and reduced energy expenditure, both of which contribute to obesity. Sleep is also thought to be important for growth during child development. Since pulsatile release of human growth hormone occurs during slow-wave sleep¹², it is possible that chronic exposure to short sleep during childhood impacts growth (body length), although this hypothesis has yet to be systematically tested.

The relationship between sleep duration and growth outcomes has been primarily examined in school-aged children and not in younger age groups^{3,6,7,10,13,14}. Also, most prior work was performed in populations that are predominantly Caucasian, even though epidemiologic evidence indicates that sleep duration in children is shorter in East Asian countries¹⁵⁻¹⁷. Similarly, in Singapore it has been reported that 2-year old children sleep about 2 h less per day relative to Swiss children of the same age^{18,19}, but the impact on growth outcomes has not been explored. In the present study, we therefore examined the relationship between sleep duration and growth in Singaporean children during the first 2 years of life. Here, we tested the hypothesis that shorter sleep duration is associated with a higher body mass index (BMI) and shorter body length across early development.

METHODS

Study design and population

The present study was conducted as part of the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study which aims to identify perinatal and early-life factors that impact growth and metabolic health of children raised in Singapore. The GUSTO study methodology has been described in detail elsewhere²⁰. Pregnant women aged ≥ 18 years were recruited in their first trimester from KK Women's and Children's Hospital and the National University Hospital, the two major public hospitals with obstetric services in Singapore. Only women with a homogeneous parental ethnic background who were Chinese, Malay, or Indian were eligible for the study. Women were excluded if they were on chemotherapy, taking psychotropic drugs, or if they had pre-existing diabetes mellitus. A total of 1,247 women with singleton pregnancy were recruited, with children born from 30 November 2009 to 1 May 2011. Informed written consent was obtained from each participant on the day of study enrollment, and procedures were approved by the National Healthcare Group Institutional Review Board (IRB) and the SingHealth Centralized IRB. This study is registered under the Clinical Trials Identifier NCT01174875.

Sleep duration

The Brief Infant Sleep Questionnaire (BISQ) was used to assess infant sleep behavior at 3, 6, 9, 12, 18, and 24 months of age²¹. The BISQ was administered to the main caregiver of the child (mostly mothers) in English, Chinese, Tamil, or Malay. Two items were selected from

the questionnaire responses: 1) “How much time (on average) does your child spend in sleep during the NIGHT?” and 2) “How much time (on average) does your child spend in sleep (naps) during the DAY?” Both responses were reported in hours and minutes. The main exposure parameter in this study was total daily sleep duration, which was calculated as the sum of daytime sleep and nighttime sleep.

Growth measures

Growth measures were examined at time points corresponding to administration of the BISQ. Weight was measured to the nearest gram using a calibrated scale (SECA 334 weighing scale; SECA Corp., Hamburg, Germany). Recumbent body length was measured in duplicate to the nearest 0.1 cm from the top of the head to the soles of the feet using a measuring mat (SECA 210 mobile measuring mat; SECA Corp.). BMI was calculated as the weight in kilograms divided by squared body length in meters.

Covariates

Demographic parameters such as ethnicity, maternal education, and household income were collected at the beginning of the study. Parental anthropometric measures were also gathered during pregnancy, and maternal height and BMI at 26 weeks of gestation were used in our analysis. Delivery information and perinatal risk factors included sex of the child, gestational age, birth weight and length, pregnancy smoking status, and maternal gestational diabetes mellitus. Anthropometric measurements of newborns were made within 24 h of birth. Breastfeeding status was documented at every study visit as exclusive, predominant, partial,

or formula-only, which followed the World Health Organization's definitions²². Considering that breastfeeding patterns changed over time, a weighted sum was used (weights: exclusive breastfeeding=1, predominant breastfeeding=0.75, partial breastfeeding=0.5, and formula-only=0) for total breastfeeding duration which took into account the type of breastfeeding and its corresponding duration. Early lifestyle measures in children were also included as covariates such as total media use and outdoor physical activity at 24 months. Daily hours spent watching television or on the computer and handheld devices were collected at 24 months of age for both weekdays and weekends and a weighted average of total media use was calculated. The average number of hours per day spent playing/exercising outdoors was similarly calculated after taking into account weekday and weekend behavior.

Statistical analysis

We first examined maternal and offspring characteristics, as well as exposure and outcome variables, of the three main ethnic groups in Singapore (Chinese, Indian, and Malay). Mean comparisons among groups were performed using one-way ANOVA. A mixed model without random effects was used to examine the relationship between BMI and sleep duration from 3 months to 2 years of age, in order to account for dependence among repeated measures across time points, as well as to maximize usage of longitudinal data. Sleep duration and BMI values at 3, 6, 9, 12, 18, and 24 months were entered into the mixed model, together with covariates described in the previous section. A similar model was used to examine the longitudinal relationship between body length and sleep duration.

In subgroup analyses, we examined the associations of BMI and body length with sleep duration within different ethnic groups after adjusting for covariates. Similarly, children within subgroups with either shorter or longer sleep duration were also examined, with shorter sleep duration defined as ≤ 12 h per day at 3 months of age. This cutoff was chosen because it was the mean sleep duration at the 3-month time point. Additionally, our preliminary analyses suggested stronger ethnic differences in sleep behavior and more variable sleep duration between children at 3 months of age, as compared to later time points. We therefore focused on determining whether sleep duration reported at 3 months was associated with growth outcomes in later development. Data were analyzed using IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp; Armonk, NY).

RESULTS

Of the 1,247 mother-infant pairs recruited at the beginning of the study, 348 subjects were excluded due to missing BISQ or growth data. The remaining 899 subjects had at least one time point with outcome (BMI and body length) and exposure (sleep duration) measures. This group consisted of a greater proportion of mothers with Chinese ethnicity, higher education, and higher household income, as compared to those who were excluded based on missing data (**Supplementary Table 1**). For participants with available sleep and growth data, maternal and offspring characteristics differed substantially across ethnic groups (**Table 1**). As compared to Chinese and Indian mothers, Malay women were of lower socioeconomic status in terms of education and income level, and they had a higher BMI at 26 weeks of gestational age. Breastfeeding duration was also lowest in Malays, and media use at 24

months of age was highest in the Malay group. Across all time points examined, Malay children exhibited shorter body length and higher BMI values than children in the other ethnic groups (**Table 2**).

On average, sleep duration decreased by about an hour (12.08 h to 11.14 h) from 3 months to 24 months of age (**Table 3**). At 3 months, sleep duration was about 1.5 h shorter in Malay children compared to Chinese and Indian children. At 6 months, sleep duration was about an hour longer in Chinese infants compared to the other groups, but these ethnic differences were not present at later time points. Based on mixed model analysis, sleep duration was not associated with BMI for the first 2 years of life, independent of adjustment for covariates (**Table 4**). In contrast, sleep duration was positively associated with body length for the first 2 years of life in both univariate ($\beta=0.039$, 95% CI 0.006 to 0.071, cm/h) and multivariate models ($\beta=0.028$, 95% CI 0.002 to 0.053, cm/h), although the effect size was very small (**Table 4**). Other factors that associated positively with body length during early development included male sex, Chinese or Indian ethnicity, and greater birth length and maternal height.

In subgroup analyses based on ethnicity, sleep duration was negatively associated with BMI only in Malay children with each additional hour of sleep corresponding to a 0.042 kg/m² (95% CI -0.071 to -0.012, $p=0.005$) decrease in BMI (**Table 5**). Additionally, sleep duration was positively associated with body length in Malay subjects ($\beta=0.079$, 95% CI 0.030 to 0.128, cm/h, $p=0.002$). Since average sleep duration was significantly less in Malay children in the first few months after delivery (**Table 5**), we considered the possibility that the relationship between sleep duration and growth outcomes might be related to the greater

number of shorter sleepers in the Malay group. To examine this, we performed a subgroup analysis by sleep duration, in which children were categorized as shorter sleepers (≤ 12 h) or longer sleepers (>12 h) based on parent-reported sleep behavior at 3 months of age (**Table 5**). Based on this definition, approximately two-thirds of Malay children were shorter sleepers (67.7%), whereas fewer than half of Chinese and Indian infants had shorter sleep duration (46.1% and 45.7%, respectively). In the shorter sleeper subgroup, sleep duration was negatively associated with BMI ($\beta=-0.036$, 95% CI -0.065 to -0.008, $\text{kg/m}^2/\text{h}$, $p=0.013$) and positively associated with body length ($\beta=0.070$, 95% CI 0.025 to 0.116, cm/h , $p=0.003$), after adjustment for covariates. When analyzed further by ethnic subgroups, these relationships for BMI and body length remained significant in Chinese and Malay shorter sleepers (**Table 5**). In contrast to the shorter sleepers, the same analyses repeated on subgroups with longer-duration sleep did not show a significant association between sleep duration and BMI or body length.

DISCUSSION

Previous studies conducted in older children showed that sleep duration was negatively associated with BMI and body fat³⁻¹⁰. Sleep duration in childhood could have long-term consequences, as shorter sleep duration in children aged 5 to 11 years was associated with higher BMI values in adulthood in a prospective birth cohort study ($\beta=-0.99$, assessed at 32 years of age)⁵. Moreover, based on a recent meta-analysis of 11 pediatric studies, a pooled odds ratio of 1.89 was observed for being overweight in children with short-duration sleep³. These studies suggest that sleep duration is an important contributing factor to metabolic

health, which is also supported by studies in adult populations¹¹. In the present study, sleep duration did not associate with BMI in the full sample, which could be attributed to the much younger age of our study participants. By comparison, a weak but significant association between sleep duration and BMI was observed in Malay participants, after controlling for differences in demographic and lifestyle factors. It is possible that the higher proportion of shorter sleepers in the Malay subgroup accounted for this observation given that both Chinese and Malay children who slept ≤ 12 h at 3 months of age showed a significant negative association between sleep duration and BMI. For children with sleep durations exceeding 12 h, there was no association with BMI, suggesting a possible ceiling effect when sufficient sleep is achieved.

In the present study, sleep duration associated positively with body length during the first 2 years of life, after adjusting for factors known to influence growth outcomes. Prior related work on body height has focused primarily on the relationship between sleep disordered breathing and growth in children aged 2-6 years with adenotonsillar hypertrophy²³. Following adenotonsillectomy, there is an improvement in sleep and an increase in height. The effects of sleep disordered breathing on growth are thought to be mediated, at least in part, through disruption of slow-wave sleep when growth hormone is preferentially secreted¹². While it might be predicted that shorter-duration sleep in healthy children would associate with shorter height, a weak negative association was observed between sleep duration and height in English and Scottish children aged 5 to 11 years whose sleep behavior was assessed by questionnaire²⁴. Additional studies are therefore needed to establish whether sleep duration impacts the rate of growth across childhood.

Although our study included several strengths, including enrollment of subjects across three major ethnic groups in Asia, multiple measures of sleep and growth outcomes over the first 2 years of development, and adjustment for known confounders, there were also limitations that should be considered. Firstly, the majority of children (84.2%) did not have sleep duration data at all six time points. Thus, while our sampling frequency of sleep behavior was higher compared to other birth cohort studies, the response rate was also lower and our sample size was relatively small at each time point (3,234 responses were collected over 6 time points). The amount of missing data precluded accurate determination of growth trajectories and growth velocities on a per-individual basis. Therefore, we did not examine whether the rate of growth varied with changes in sleep duration across the first 2 years of life. Another limitation of our study is that information on growth percentiles was not available for the three major ethnic groups examined in Singapore. Since the sample sizes for the ethnic groups studied were too small to generate robust longitudinal growth percentiles, it was not possible to normalize growth parameters by ethnicity. The effect size, as measured by the beta coefficient, was also relatively small for sleep duration on growth outcomes, as compared to other factors such as sex and ethnicity. Finally, we would like to highlight that sleep duration data collected by questionnaires are prone to parental estimation errors, and more reliable estimates of sleep behavior could potentially be obtained using objective measures, e.g. actigraphy or polysomnography.

CONCLUSION

We demonstrated that sleep duration associates weakly with anthropometric measures in early life. During the first 2 years of development, shorter sleep duration associated with higher BMI values in Malay participants and in the subgroup of children who slept ≤ 12 per day at 3 months of age. Additionally, shorter sleep was associated with shorter body length. Building on prior work conducted in older children, our results suggest that sleep duration might begin to influence body weight and length from infancy. Future work should examine the impact of sleep duration on growth trajectories and velocities as our cohort matures longitudinally.

ACKNOWLEDGEMENTS

We are extremely grateful to families who participated in the GUSTO study, and the entire GUSTO Study Group team of investigators. Specifically, the authors would like to thank Dr. Yiong Huak Chan for providing consultation on our statistical analyses. The authors also appreciate the support of the Duke-NUS/SingHealth Academic Medicine Research Institute and the editing assistance of Taara Madhavan. The GUSTO birth cohort study is funded by the National Research Foundation (NRF), Prime Minister's Office, Singapore, through its "Translational Clinical Research (TCR) Flagship Program on Developmental Pathways to Metabolic Disease" (DevOS), with fund-administration by the National Medical Research Council (NMRC), Ministry of Health - NMRC/TCR/004-NUS/2008. Additional support was provided by the Singapore Institute for Clinical Sciences (SICS), under the Agency for Science, Technology and Research (A*STAR); and the Duke-NUS Signature Research Program funded by A*STAR and the Ministry of Health, Singapore.

SUPPLEMENTARY MATERIALS

Supplementary Table 1. Demographic characteristics for subjects who were included in the analysis versus those who excluded due to missing growth or sleep data.

Accepted Manuscript

REFERENCES

1. Bethell C, Simpson L, Stumbo S, Carle AC, Gombojav N. National, state, and local disparities in childhood obesity. *Health affairs* 2010;29:347-56.
2. Matricciani L, Olds T, Petkov J. In search of lost sleep: secular trends in the sleep time of school-aged children and adolescents. *Sleep Med Rev* 2012;16:203-11.
3. Cappuccio FP, Taggart FM, Kandala N-B, et al. Meta-Analysis of Short Sleep Duration and Obesity in Children and Adults. *Sleep* 2008;31:619-26.
4. Carter PJ, Taylor BJ, Williams SM, Taylor RW. Longitudinal analysis of sleep in relation to BMI and body fat in children: the FLAME study. *British Medical Journal* 2011;342:d2712.
5. Landhuis CE, Poulton R, Welch D, Hancox RJ. Childhood sleep time and long-term risk for obesity: a 32-year prospective birth cohort study. *Pediatrics* 2008;122:955-60.
6. Magee L, Hale L. Longitudinal associations between sleep duration and subsequent weight gain: a systematic review. *Sleep Med Rev* 2012;16:231-41.
7. Marshall NS, Glozier N, Grunstein RR. Is sleep duration related to obesity? A critical review of the epidemiological evidence. *Sleep Med Rev* 2008;12:289-98.
8. Reilly JJ, Armstrong J, Dorosty AR, et al. Early life risk factors for obesity in childhood: cohort study. *British Medical Journal* 2005;330:1357.
9. Taveras EM, Rifas-Shiman SL, Oken E, Gunderson EP, Gillman MW. Short sleep duration in infancy and risk of childhood overweight. *Arch Pediatr Adolesc Med* 2008;162:305-11.
10. Tikotzky L, De Marcas G, Har-Toov J, Dollberg S, Bar-Haim Y, Sadeh A. Sleep and physical growth in infants during the first 6 months. *Journal of sleep research*

2010;19:103-10.

11. Spiegel K, Tasali E, Penev P, van Cauter E. Brief Communication: Sleep Curtailment in Healthy Young Men Is Associated with Decreased Leptin Levels, Elevated Ghrelin Levels, and Increased Hunger and Appetite. *Ann Intern Med* 2004;141:846-50.
12. Sassin JF, Parker DC, Mace JW, Gotlin RW, Johnson LC, Rossman LG. Human Growth Hormone Release: Relation to Slow-Wave Sleep and Sleep-Waking Cycles. *Science* 1969;165:513-5
13. Taveras EM, Rifas-Shiman SL, Oken E, Gunderson EP, Gillman MW. Short sleep duration in infancy and risk of childhood overweight. *Arch Pediatr Adolesc Med* 2008;162:305-11.
14. Agras WS, Hammer LD, McNicholas F, Kraemer HC. Risk factors for childhood overweight: a prospective study from birth to 9.5 years. *The Journal of pediatrics* 2004;145:20-5.
15. Steptoe A, Peacey V, Wardle J. Sleep Duration and Health in Young Adults. *Archives of Internal Medicine* 2006;166:1689-92.
16. Olds T, Blunden S, Petkov J, Forchino F. The relationships between sex, age, geography and time in bed in adolescents: A meta-analysis of data from 23 countries. *Sleep Medicine Reviews* 2010;14:371–8.
17. Mindell JA, Sadeh A, Wiegand B, How TH, Goh DYT. Cross-cultural differences in infant and toddler sleep. *Sleep Medicine* 2010;11:274–80.
18. Aishworiya R, Chan P, Kiing J, Chong SC, Laino AG, Tay SK. Sleep behaviour in a sample of preschool children in Singapore. *Ann Acad Med Singapore* 2012;41:99-104.

19. Iglowstein I, Jenni OG, Molinari L, Largo RH. Sleep Duration From Infancy to Adolescence: Reference Values and Generational Trends. *Pediatrics* 2003;111:302-7.
20. Soh SE, Tint MT, Gluckman PD, et al. Cohort Profile: Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study. *International journal of epidemiology* 2014;43:1401-9.
21. Sadeh A. A Brief Screening Questionnaire for Infant Sleep Problems Validation and Findings for an Internet Sample. *Pediatrics* 2004;113.
22. The World Health Organization. Indicators for assessing infant and young child feeding practices: Part 1. WHO Press; 2008.
23. Bonuck KA, Freeman K, Henderson J. Growth and growth biomarker changes after adenotonsillectomy: systematic review and metaanalysis. *Archives of disease in childhood* 2009;94:83-91.
24. Gulliford MC, Price CE, Rona RJ, Chinn S. Sleep habits and height at ages 5 to 11. *Archives of disease in childhood* 1990;65:119-22.

TABLES

Table 1. Maternal and offspring characteristics. Data are shown as mean (SD) or %.

Mothers	Chinese (n = 507)	Indian (n = 155)	Malay (n = 237)	Total (n = 899)	p-value
Highest education obtained (%)					
Below "A" level/diploma	31.01%	27.03%	68.58%	40.19%	<0.001
Household income (%)					
Below S\$4000 per month	32.27%	50.35%	70.31%	45.67%	<0.001
Anthropometrics at 26 weeks gestation					
Weight (kg)	62.95 (9.61)	67.99 (11.60)	69.40 (14.13)	65.51 (11.67)	<0.001
Height (cm)	158.93 (5.67)	157.73 (5.44)	157.15 (5.71)	158.26 (5.69)	<0.001
BMI (kg/m ²)	24.68 (4.04)	26.97 (5.45)	27.81 (5.81)	25.90 (5.01)	<0.001
Perinatal risk factors					
Smoking during pregnancy (%)	1.79%	1.31%	5.11%	2.58%	0.017
Gestational diabetes (%)	19.13%	20.00%	10.13%	16.91%	0.005
Intrauterine growth retardation (%)	1.97%	5.16%	1.27%	2.34%	0.032
Offspring					
Birth information					
Male (%)	53.45%	48.39%	54.43%	52.84%	0.462
Gestational age (weeks)	38.82 (1.33)	38.71 (1.62)	38.52 (1.26)	38.72 (1.37)	0.023
Birth weight (kg)	3.13 (0.43)	3.05 (0.51)	3.13 (0.43)	3.12 (0.45)	0.126
Birth length (cm)	48.87 (2.27)	48.82 (2.19)	48.38 (2.07)	48.73 (2.21)	0.014
Birth BMI (kg/m ²)	13.08 (1.29)	12.74 (1.52)	13.31 (1.28)	13.08 (1.34)	<0.001
NICU stay (%)	2.76%	2.58%	3.38%	2.89%	0.869
Lifestyle risk factors					
Breastfeeding duration (months)	3.51 (3.49)	3.18 (3.27)	1.92 (2.71)	3.03 (3.33)	<0.001
Total media use at 24 months (h/day)	1.81 (1.89)	2.11 (2.24)	2.77 (2.58)	2.11 (2.19)	<0.001
Physical activity at 24 months (h/day)	0.80 (0.78)	0.92 (0.79)	0.73 (0.78)	0.80 (0.78)	0.053

Table 2. Growth outcomes in children. Data are shown as mean (SD).

Age and growth outcomes		Chinese (<i>n</i> = 507)	Indian (<i>n</i> = 155)	Malay (<i>n</i> = 237)	Total (<i>n</i> = 899)	<i>p</i> -value
3 months	Weight (kg)	6.31 (0.78)	5.82 (0.68)	6.01 (0.77)	6.15 (0.79)	<0.001
	Length (cm)	61.45 (2.49)	60.91 (2.20)	60.01 (2.34)	60.98 (2.48)	<0.001
	BMI (kg/m ²)	16.69 (1.50)	15.65 (1.42)	16.66 (1.58)	16.51 (1.55)	<0.001
6 months	Weight (kg)	7.81 (0.94)	7.53 (0.87)	7.67 (0.97)	7.73 (0.94)	0.005
	Length (cm)	67.43 (2.72)	67.39 (2.54)	66.15 (2.66)	67.10 (2.73)	<0.001
	BMI (kg/m ²)	17.15 (1.56)	16.55 (1.50)	17.53 (1.84)	17.14 (1.65)	<0.001
9 months	Weight (kg)	8.64 (1.00)	8.57 (0.99)	8.56 (1.03)	8.61 (1.01)	0.550
	Length (cm)	71.98 (2.92)	71.99 (2.66)	70.64 (2.89)	71.64 (2.93)	<0.001
	BMI (kg/m ²)	16.65 (1.45)	16.51 (1.45)	17.12 (1.54)	16.75 (1.49)	<0.001
12 months	Weight (kg)	9.38 (1.05)	9.46 (1.20)	9.29 (1.12)	9.37 (1.09)	0.354
	Length (cm)	75.78 (3.10)	76.30 (2.89)	74.22 (2.94)	75.48 (3.12)	<0.001
	BMI (kg/m ²)	16.31 (1.31)	16.20 (1.40)	16.81 (1.50)	16.42 (1.40)	<0.001
18 months	Weight (kg)	10.69 (1.24)	11.01 (1.52)	10.64 (1.38)	10.73 (1.33)	0.025
	Length (cm)	82.24 (3.33)	83.29 (3.45)	81.14 (3.21)	82.10 (3.39)	<0.001
	BMI (kg/m ²)	15.78 (1.50)	15.89 (1.55)	16.02 (1.46)	15.86 (1.50)	0.175
24 months	Weight (kg)	11.94 (1.50)	12.16 (1.72)	11.92 (1.60)	11.97 (1.57)	0.318
	Length (cm)	88.00 (3.66)	88.47 (3.68)	86.39 (3.21)	87.64 (3.63)	<0.001
	BMI (kg/m ²)	15.39 (1.32)	15.39 (1.52)	15.86 (1.48)	15.52 (1.41)	0.001

Table 3. Total daily sleep duration in the first two years of life. Data are shown as mean (SD).

Age and sleep duration (h)	Chinese	Indian	Malay	Total	<i>p</i> -value
3 months (n=643)	12.49 (3.84)	12.43 (4.36)	10.96 (3.55)	12.08 (3.91)	<0.001
6 months (n=719)	12.17 (2.65)	11.22 (2.95)	11.12 (3.08)	11.75 (2.85)	<0.001
9 months (n=547)	11.78 (2.38)	11.74 (2.49)	11.30 (2.84)	11.67 (2.51)	0.170
12 months (n=515)	11.69 (1.87)	12.09 (2.54)	11.32 (2.48)	11.66 (2.13)	0.047
18 months (n=411)	11.60 (1.95)	11.47 (1.76)	11.58 (2.12)	11.57 (1.97)	0.917
24 months (n=399)	11.23 (2.01)	11.19 (2.06)	10.92 (2.18)	11.14 (2.06)	0.414

Table 4. Longitudinal mixed model analysis for BMI and body length versus sleep duration from 3 to 24 months of age, with adjustment for covariates. Values show estimates of fixed effects with 95% confidence intervals. * $p < 0.05$ and ** $p < 0.01$.

	BMI (kg/m ²) (n=799§)		Body length (cm) (n=797§)	
	Univariate model	Multivariate model	Univariate model	Multivariate model
Sleep duration (h/day)	-0.009 (-0.026, 0.007)	-0.014 (-0.030, 0.001)	0.039 (0.006, 0.071)*	0.028 (0.002, 0.053)*
Sex (male)	0.520 (0.340, 0.701)**	0.399 (0.227, 0.570)**	1.814 (1.462, 2.166)**	1.437 (1.155, 1.720)**
Ethnicity (Chinese)	-0.373 (-0.585, -0.162)**	-0.250 (-0.475, -0.025)*	1.438 (1.008, 1.868)**	1.122 (0.762, 1.482)**
Ethnicity (Indian)	-0.660 (-0.944, -0.375)**	-0.622 (-0.900, -0.345)**	1.354 (0.779, 1.929)**	1.085 (0.635, 1.535)**
Maternal education (Below “A” level/diploma)	-0.007 (-0.194, 0.181)	-0.107 (-0.320, 0.105)	-1.003 (-1.383, -0.624)**	-0.370 (-0.720, -0.020)*
Household income (Below \$4000/month)	-0.072 (-0.256, 0.113)	-0.055 (-0.259, 0.149)	-0.971 (-1.342, -0.600)**	0.003 (-0.340, 0.334)
Pregnancy smoking (no)	-0.288 (-0.852, 0.275)	-0.444 (-0.966, 0.079)	0.887 (-0.344, 2.118)	-0.091 (-0.969, 0.788)
Gestational diabetes (no)	0.079 (-0.170, 0.328)	0.077 (-0.156, 0.309)	0.111 (-0.403, 0.625)	0.151 (-0.229, 0.532)
Birth weight (kg)	0.889 (0.689, 1.089)**	0.929 (0.692, 1.167)**	NA†	NA†
Birth length (cm)	NA†	NA†	0.515 (0.439, 0.590)**	0.427 (0.353, 0.501)**
Gestational age (weeks)	0.008 (-0.063, 0.079)	-0.142 (-0.218, -0.065)**	0.250 (0.105, 0.394)**	-0.164 (-0.287, -0.042)**
Maternal BMI (kg/m ²)	0.037 (0.019, 0.055)**	0.017 (-0.001, 0.036)	NA†	NA†
Maternal height (cm)	NA†	NA†	0.134 (0.102, 0.166)**	0.091 (0.065, 0.116)**
Breastfeeding duration (months)	0.004 (-0.023, 0.032)	0.018 (-0.009, 0.046)	0.016 (-0.040, 0.071)	-0.059 (-0.104, -0.013)*
Total media use at 24 months (h/day)	0.057 (0.015, 0.098)**	0.042 (0.002, 0.082)*	-0.028 (-0.116, 0.060)	0.024 (-0.044, 0.091)
Physical activity at 24 months (h/day)	0.056 (-0.061, 0.173)	0.024 (-0.088, 0.136)	0.220 (-0.022, 0.462)	0.047 (-0.139, 0.233)
Age 3 months‡	0.925 (0.774, 1.076)**	0.953 (0.802, 1.104)**	-26.69 (-26.97, -26.41)**	-26.69 (-26.97, -26.40)**
Age 6 months‡	1.626 (1.484, 1.767)**	1.646 (1.505, 1.787)**	-26.65 (-20.91, -20.38)**	-20.64 (-20.91, -20.38)**
Age 9 months‡	1.185 (1.043, 1.327)**	1.200 (1.059, 1.342)**	-16.04 (-16.30, -15.77)**	-16.02 (-16.29, -15.75)**
Age 12 months‡	0.813 (0.684, 0.942)**	0.826 (0.697, 0.955)**	-12.11 (-12.37, -11.85)**	-12.11 (-12.37, -11.84)**
Age 18 months‡	0.212 (0.094, 0.331)**	0.218 (0.099, 0.338)**	-5.39 (-5.62, -5.15)**	-5.37 (-5.61, -5.13)**

§The sample size is smaller than the starting sample ($n=899$) due to the built-in modeling mechanism of the mixed model to exclude subjects with incomplete/insufficient longitudinal data for the model to give an accurate estimation of fixed effects.

†The respective variable is not applicable to the analysis, since only birth weight and maternal BMI are relevant for infant BMI, and only birth length and maternal height are relevant for infant body length.

‡The reference is 24 months of age.

Table 5. Longitudinal mixed model analysis of BMI and body length versus sleep duration, assessed in different ethnic subgroups and by sleep duration at 3 months of age, after adjustment for covariates. * $p < 0.05$ and ** $p < 0.01$.

Subgroup and measures		Chinese	Indian	Malay	Overall
By ethnic group, BMI vs. sleep duration	β	-0.006	0.002	-0.042**	-0.014
	n	445	137	217	799
By ethnic group, body length vs. sleep duration	β	-0.006	-0.011	0.079**	0.028*
	n	445	137	216	797
Shorter sleepers (≤ 12 h/day), BMI vs. sleep duration	β	-0.044*	-0.061	-0.048*	-0.036*
	n	150	44	104	298
Shorter sleepers (≤ 12 h/day), body length vs. sleep duration	β	0.062*	0.108	0.081*	0.070**
	n	150	44	104	298
Longer sleepers (> 12 h/day), BMI vs. sleep duration	β	0.008	-0.036	-0.043	-0.009
	n	175	50	49	274
Longer sleepers (> 12 h/day), body length vs. sleep duration	β	0.024	-0.001	-0.034	0.006
	n	174	50	49	273