Insufficient Sleep and Incidence of Dental Caries in Deciduous Teeth among Children in Japan: A Population-Based Cohort Study

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Objectives To examine whether late bedtime and short nighttime sleep duration at age 18 months are associated with risk of caries in deciduous teeth.

Study design Population-based cohort study using health check-up data of 71 069 children born in Kobe City, Japan, who were free of caries at age 18 months and had information on sleep variables at age 18 months and records of dental examinations at age 3 years. Sleep variables were assessed by standardized parent-reported questionnaires, and the incidence of caries in deciduous teeth was defined as the occurrence of at least 1 decayed, missing, or filled tooth assessed by qualified dentists without radiographs. Logistic regression was used to estimate the effects of late bedtime and short sleep duration on dental caries with adjustment for clinical and lifestyle characteristics.

Results Overall, 11 343 (16.0%) cases of caries were observed at age 3 years. aORs for children with late or irregular bedtimes compared with those with bedtimes before 21:00 were 1.26 (95% CI 1.19-1.33), 1.48 (1.38-1.58), 1.74 (1.58-1.92), 1.90 (1.58-2.29), and 1.66 (1.53-1.81) for bedtimes at 21:00, 22:00, 23:00, 0:00, and irregular bedtime, respectively. aORs for children with short or irregular sleep duration compared with those with sleep duration of ≥11 hours were 1.30 (95% CI 1.15-1.47), 1.16 (1.09-1.24), 1.11 (1.05-1.18), and 1.35 (1.25-1.46) for sleep duration of ≤ 8, 9, 10 hours, and irregular sleep duration, respectively.

Conclusions In this exploratory study, late bedtime and short sleep duration were both consistently associated with increased risk of caries in deciduous teeth. *(J Pediatr 2018;198:279-86).*

Untreated dental caries in deciduous teeth, now present in 7.8% of children worldwide,[1] is a major cause of pain and suffering that may affect children and families' quality of life.[2] Although risk factors for dental caries are well-documented,[3] several unique ones might modify its biology in young children who are in the formative stages of development. These involve the implantation of cariogenic bacteria, immaturity of the host defense systems, and behavioral patterns associated with feeding and oral hygiene.[4] In this regard, sleep might be an important factor, given the vulnerability to the adverse effects of insufficient sleep among the pediatric population.

In humans, sleep–wake timing and circadian timing rhythms are synchronized under normal conditions such that sleep is timed to occur during the night.[5] Young children, however, might face environmental demands that may result in a poor fit with the biological limits imposed by their circadian system, as their time to fall asleep at night is largely determined by their parents or caregivers.[6] Possible pathways by which sleep might affect a child's risk for caries include abnormal salivary flow rate caused by alteration in local circadian timing system in the salivary gland[5,7,8] and susceptibility to infection due to impaired immune function.[9-12] Sleep deprivation is associated with diminished salivary flow rate, diminished IgA secretion rate, and elevated levels of salivary amylase activity in rats.[8] Epidemiologic observation also suggests links between short sleep and increased salivary interleukin-6 production[9] and high levels of *Streptococcus mutans* colony counts,[10] and links between late bedtimes and dental caries in deciduous or permanent teeth.[13,14]

We used data from the Kobe Offspring Study[15] to examine whether late bedtime and short nighttime sleep duration at age 18 months is associated with caries in deciduous teeth to determine whether there is a dose–response relationship and to assess whether associations are consistent across various subgroups related to feeding practices and oral hygiene.

Methods

The Kobe Offspring Study[15] was a population-based cohort study using records of municipal health check-ups for children aged 0-3 years in Kobe City, Japan. Kobe City is the sixth largest city in Japan, with a population of about 1.5 million, and is the capital city of Hyogo Prefecture on the southern side of the main island of Japan. The prefectural income per capita was 23 218 USD in 2002,[16] and about 32% of households had an annual income above the average estimates in Japan (ie, 49 095 USD).[17,18] Nearly 93% of the fathers and 19% of the mothers were employed when their children were born, with professional and engineering workers

(27.2%) and clerical workers (37.3%) being the most common jobs, respectively.[19] Among household members aged 20-49 years, 42% had a high school education, 21% had junior college or higher professional school education, and 28% completed college, university, or graduate course.[17]

All women of childbearing age and children from pregnancy to 3 years of age residing in Kobe City participated in the health check-up program, which consisted of completion of a standardized pregnancy notification form, neonatal health check-ups, advice provided during home visits, and health check-ups for infants at 4, 9, and 18 months and 3 years of age at healthcare centers of ward offices or designated clinics. Information on lifestyle factors was based exclusively on responses to standardized parent-reported questionnaires, which mothers were required to complete at every health check-up. We had access to deidentified data on health check-ups from March 31, 2004, to April 1, 2014 after approval by the Planning and Coordination Bureau of Kobe. Details of the study design have been reported previously.[15] The Ethics Committee of Kyoto University Graduate School and Faulty of Medicine approved the protocol (Approval Number R0923).

Assessment of Sleep

Using a standardized questionnaire, parents reported their young child's habitual wake time and bedtime at 18 months in response to 2 questions: "What time does your child usually wake up?" (7 predefined responses: before 7:00, 7:00, 8:00, 9:00, 10:00, 11:00 and later, and irregular), and "What time does your child usually go to bed?" (7 predefined responses: before 20:00, 20:00, 21:00, 22:00, 23:00, 0:00, and irregular). The 2 former categories were combined to form the reference category (ie, before 21:00) based on the recommended sleep hygiene by the National Sleep Foundation,[20] and late bedtime was defined as 21:00 or later. The child's nighttime sleep duration was calculated as the difference between bedtime and wake time and categorized as ≤8 hours, 9 hours, 10 hours, ≥11 hours, and irregular, with sleep duration of ≥11 hours as reference.

Measurement of Dental Caries

Qualified dentists assessed the oral conditions of the children at 18 months and 3 years through visual examination and not radiography. They classified each tooth into 1 of 7 types: normal, decayed, missing, filled, treated by diammine silver fluoride, observation required, or treated by a dental sealant. We counted teeth treated by diammine silver fluoride as well as decayed teeth as decayed. Incidence of dental caries was defined as the occurrence of at least 1 decayed, missing, or filled tooth. Other records of dental examinations included the caries activity test (CARIOSTAT; Dentsply-Sirona, Tokyo, Japan), a colorimetric test designed to measure the pH decrease caused by microorganisms in the plaque sample obtained from the buccal surfaces (0-4 points, 4 points indicating most active); presence of plaque; abnormal conditions of soft tissues and occlusion; and treatment with fluoride varnish.

Statistical Analyses

The primary outcome was incidence of caries in deciduous teeth at 3 years of age. Secondary outcomes were incidence of caries in mandibular or maxillary anterior teeth or molars. The Cochran–Armitage test for trend was used to assess trends in the incidence of caries. We present risk estimates separately for bedtime and sleep duration, as having a late bedtime does not necessarily equate to short sleep duration, although studies do suggest links between these 2 sleep variables.[20] Also, bedtime correlated modestly with sleep duration in our study (Pearson correlation coefficient, –0.48), and their effects on caries may be confounded and should be handled separately. We used binary logistic regression to estimate ORs and 95% CIs with adjustment for clinical and lifestyle characteristics (Table I). We tested the linearity assumption between the log odds of the outcome and continuous variables by using a scatterplot smoothing method and observed no significant deviations.[21]

In a sensitivity analysis, we further adjusted the following postexposure covariates at age 3 years as covariates: tooth brushing alone (yes/no), tooth brushing by parents before sleep

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Table I. Potential confounders

Background characteristics
- Maternal age at delivery (continuous; y)
- Gestational age (22-27, 28-36, 36-43 wk)
- Maternal alcohol consumption during pregnancy (none, occasional, daily)
- Maternal smoking during pregnancy (yes/no)
- Pre-eclampsia (yes/no)
- Anemia (yes/no)
- Threatened abortion (yes/no)
- First-born child (yes/no)
- Child' sex (boy, girl)
- Birth year (continuous; y)
- Birth weight (continuous; g)
- Birth height (continuous; cm)

Oral hygiene
- Number of teeth at 9 mo (continuous)
- Treated by fluoride varnish (yes/no)
- Tooth brushing by own self (yes/no)
- Tooth brushing by parents before going to bed (yes/no)
- Absence or presence of plaque (yes/no)

Lifestyle factors
- Exposure to tobacco smoke at 4 months (none, exposed to only household smoking, exposed to tobacco smoke)
- Age of introduction of solids (continuous; mo)
- Weaning at 9 mo (yes/no)
- Bottle-feeding at 9 mo (yes/no)
- Bottle-feeding at 18 mo (yes/no)
- Breastfeeding at 18 mo (yes/no)
- Eating sweets irregularly (yes/no)
- Frequency of eating sweets (1, 2, or ≥3 times per day)
- Daily juice consumption (yes/no)
- Use of babysitter or nursery at 4 mo
- Use of babysitter or nursery at 18 mo (yes/no)
- Mental status of the mother (continuous; 1-5 scores)
- Support by family, friends, and neighbors (yes/no)

Common comorbidities at 18 mo
- Atopic dermatitis (yes/no)
- Asthma (yes/no)
- Asthmatic bronchitis (yes/no)
- Food allergy (yes/no)
- Varicella (yes/no)
- Pneumonia (yes/no)
- Severe diarrhea (yes/no)
- History of familiar allergenic disease (yes/no)

(yes/no), eating sweets irregularly (yes/no), frequency of eating sweets (1, 2, or ≥3 times per day), daily juice consumption (yes/no), and use of babysitter or nursery (yes/no). A second sensitivity analysis further controlled for bedtime (before 21:00, 21:00, 22:00, 23:00, 0:00, and irregular) and sleep duration (≤8 hours, 9 hours, 10 hours, ≥11 hours, and irregular) at 3 years to examine whether insufficient sleep at 18 months is merely a risk factor for later sleep problem and that concurrent sleep may be the biologically relevant exposure window affecting dental caries.

We next did subgroup analyses among prespecified baseline characteristics. These included child's sex, birth order, plaque status, bottle-feeding and breastfeeding status, tooth brushing by parents before going to bed, regularity and frequency of eating sweets, and daily juice consumption. Interactions between covariates and bedtime and sleep duration were computed by testing whether the coefficients on the interaction terms are jointly equal to zero.

Missing values for covariates were prevalent for maternal age at delivery (30.2%), maternal alcohol consumption during pregnancy (31.2%), maternal smoking during pregnancy (31.3%), treated by fluoride varnish at 18 months (12.7%), birth height (12.4%), number of teeth at 9 months (11.7%), firstborn (8.7%), and gestational age (6.2%). All the other covariates had less than 5% missing data. We estimated missing values for covariate using multiple imputation before their inclusion in the multivariable models. Results from 20 multiple imputation cycles were imputed by imputation chained equations (ICE) program and combined with the MICOMBINE commands of STATA Software version 14.0 (2017; StataCorp LP, College Station, Texas).[22] The outcome and sleep variables, and all covariates considered to be potential confounders, were used to perform the multiple imputation. All reported P values were 2-sided, and a P value of <.05 was considered statistically significant.

Results

Of the 145 318 children in the Kobe Offspring Study, 84 292 were born between March 1, 2004, and December 31, 2010, and received the 18-month-old health check-ups. Of these children, 77 636 also had complete information on sex and parent-reported bedtime and wake time at 18 months and were free of caries at 18 months. Information on dental examinations was further available for 71 069 (84.3% of children received the 18-month-old health check-up) children (**Figure**; available at www.jpeds.com). Significant differences were observed in mother's age, child's sex, gestational week, and birth weight between those included and excluded, including bedtime and sleep duration at 18 months. The differences were, however, generally small (**Table II**; available at www.jpeds.com).

Among the 71 069 children, 48 943 (68.9%) had late bedtimes (ie, 21:00 or later) and 5709 (8.0%) had irregular bedtimes (**Table III**). Children with late bedtimes were more often girls and first-born and had mothers who were more often smokers during pregnancy. They also were more often exposed to secondhand smoking at age 4 months. More than 99% of

children received fluoride varnish at 18 months; children with late bedtimes had their teeth brushed less frequently by themselves or by parents before going to bed, ate sweets more frequently and irregularly, and drank juice every day. They were also more likely to have bottle-feeding (**Table III**). Abnormalities at delivery, gestational age, birth weight, and comorbidities at age 18 months did not differ significantly across the 6 groups. Short nighttime sleep duration of ≤8 hours was observed in 2353 (3.3%) children, and the distribution of the covariates by categories of nighttime sleep duration displayed a similar pattern to that of bedtime (**Table IV**; available at www.jpeds.com).

Overall, 11 343 (16.0%) children developed dental caries at age 3 years, with 11 211 related to decayed teeth. The risk of caries increased with bedtime becoming later in a dose–response manner, and children with irregular bedtime also had a greater risk of caries (**Table V**). Compared with children with earlier bedtime (before 21:00), children with later (22:00 or later) and irregular bedtime had a > 40% increased odds of caries. The multivariable aORs were 1.26 (95% CI 1.19-1.33), 1.48 (1.38-1.58), 1.74 (1.58-1.92), 1.90 (1.58-2.29), and 1.66 (1.53-1.81) for bedtimes at 21:00, 22:00, 23:00, 0:00, and irregular bedtime, respectively. Similar associations were observed for different sites (mandibular or maxillary, anterior teeth, or molars). Sensitivity analyses indicated that these associations were robust against the influence of behavior patterns including bedtime at age 3 years. Among the covariates adjusted, exposure to tobacco smoke at 4 months (OR 1.58, 95% CI 1.46-1.72), prolonged breastfeeding at 18 months (2.08, 1.98-2.19), eating sweets irregularly (1.23, 1.17-1.29) or twice or more times per day (1.63, 1.56-1.71), drinking juice daily (1.51, 1.45-1.58), and plaque present at 18 months (1.47, 1.40-1.54) were all significantly associated with a risk of caries at 3 years (**Table VI**; available at www.jpeds.com).

The risk of caries also increased with sleep duration becoming shorter, but the associations were less pronounced than those of bedtime (**Table VII**). Compared with children with nighttime sleep duration of ≥11 hours, children with shorter (≤8 hours) and irregular sleep duration had a 30% increased risk of caries. The multivariable aORs were 1.30 (95% CI 1.15-1.47), 1.16 (1.09-1.24), 1.11 (1.05-1.18), and 1.35 (1.25-1.46) for sleep durations of ≤8 hours, 9 hours, 10 hours, and irregular sleep duration, respectively. Similar associations were observed for mandibular anterior teeth or molars and maxillary molars but not for maxillary anterior teeth. These associations also were robust against the influence of behavior patterns including sleep duration at age 3 years. Covariates that were significantly associated with a risk of caries were similar to those observed in the model for bedtime (**Table VI**).

Associations between bedtime and caries were generally similar across subgroups stratified according to child's sex, plaque status, tooth brushing by parents before sleep, breastfeeding status, and regularity of eating sweets and for sleep duration, birth order and daily juice consumption (**Tables VIII and IX**; available at www.jpeds.com). The largest differences across strata were observed for bottle-feeding status, with stronger associations observed among children without

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Table III. Characteristics of 71 069 children by categories of bedtime at age 18 months

Characteristics	Categories of bedtime at age 18 months					
	Before 21:00	21:00	22:00	23:00	0:00	Irregular
Number of children	16 417	30 458	14 061	3616	808	5709
Background characteristics						
Maternal age at delivery, y,* mean (SD)	31.7 (4.1)	31.7 (4.5)	31.2 (5.0)	30.4 (5.6)	30.3 (5.7)	30.5 (5.5)
Maternal age ≥35 y*	2415 (20.6)	5015 (23.3)	2277 (23.5)	537 (22.5)	111 (22.0)	839 (22.0)
Gestational wk[†]						
22-27	25 (0.2)	36 (0.1)	16 (0.1)	7 (0.2)	1 (0.1)	10 (0.2)
28-36	1029 (6.7)	1703 (6.0)	766 (5.8)	225 (6.7)	47 (6.2)	317 (5.9)
36-43	14 321 (93.1)	26 876 (93.9)	12 389 (94.1)	3141 (93.1)	714 (93.7)	5020 (93.9)
Maternal alcohol consumption during pregnancy*						
Occasional	1970 (17.2)	3776 (17.9)	1629 (17.2)	372 (16.0)	67 (13.7)	664 (17.8)
Daily	63 (0.6)	125 (0.6)	72 (0.8)	15 (0.6)	3 (0.6)	30 (0.8)
Maternal smoking during pregnancy*	1447 (12.6)	3223 (15.3)	1941 (20.5)	561 (24.0)	127 (26.0)	885 (23.7)
Pre-eclampsia[†]	283 (1.8)	646 (2.2)	360 (2.6)	116 (3.3)	35 (4.4)	174 (3.1)
Anemia[†]	1686 (10.6)	3041 (10.2)	1440 (10.5)	348 (9.9)	85 (10.7)	607 (10.9)
Threatened abortion[†]	1855 (11.6)	3248 (10.9)	1482 (10.8)	360 (10.2)	86 (10.8)	608 (11.0)
Child's sex, girl	7832 (47.7)	14 707 (48.3)	7070 (50.3)	1879 (52.0)	416 (51.5)	2867 (50.2)
First-born child[†]	6056 (39.8)	12 710 (45.5)	6755 (53.3)	2100 (65.2)	550 (78.4)	3203 (62.1)
Birth weight, g,[†] mean (SD)	3000.2 (413.8)	3005.6 (407.2)	3005.0 (414.4)	2982.6 (416.1)	2995.6 (435.9)	2996.3 (410.9)
Oral hygiene						
No of teeth at 9 mo,[†] mean (SD)	2.0 (0.9)	2.0 (0.9)	2.1 (0.9)	2.1 (0.9)	2.2 (0.9)	2.1 (0.8)
Treated by fluoride varnish at 18 mo[†]	14 009 (99.4)	26 637 (99.4)	12 212 (99.3)	3168 (99.3)	702 (98.7)	4914 (99.4)
Tooth brushing by own self at 18 mo	13 651 (83.2)	24 273 (79.7)	10 775 (76.7)	2669 (73.8)	581 (71.9)	4032 (70.6)
Tooth brushing by parents before sleep at 18 mo	12 910 (78.7)	22 688 (74.5)	9917 (70.5)	2421 (67.0)	561 (69.4)	3614 (63.3)
Tooth brushing by own self at 3 y	14 891 (90.7)	26 795 (88.0)	11 996 (85.3)	2996 (82.9)	628 (77.7)	4632 (81.2)
Tooth brushing by parents before sleep at 3 y	14 860 (90.5)	26 664 (88.0)	11 864 (84.4)	2966 (82.1)	645 (79.8)	4606 (80.7)
Plaque present at 18 mo	3261 (20.0)	6552 (21.6)	3098 (22.1)	823 (22.9)	195 (24.1)	1316 (23.1)
Plaque present at 3 y[†]	2431 (14.9)	5294 (17.5)	2708 (19.4)	668 (18.6)	170 (21.4)	1107 (19.6)
Lifestyle factors						
Exposure to tobacco smoke at 4 m						
Not exposed to second-hand smoke	8920 (54.3)	14 900 (48.9)	5778 (41.1)	1318 (36.5)	258 (31.9)	2161 (37.9)
Exposed to only household smoking	6674 (40.7)	13 742 (45.1)	7174 (51.0)	1984 (54.9)	470 (58.2)	3072 (53.8)
Exposed to tobacco smoke	823 (5.0)	1816 (6.0)	1109 (7.9)	314 (8.7)	80 (9.9)	476 (8.3)
Feeding practices:						
Age at start of baby food, mo,[†] mean (SD)	5.6 (0.8)	5.5 (0.8)	5.5 (0.8)	5.4 (0.9)	5.4 (0.9)	5.5 (0.9)
Bottle at 9 mo[†]	5590 (34.6)	11 507 (38.5)	5815 (42.4)	1602 (45.7)	390 (49.4)	2443 (44.0)
Baby food at 9 mo[†]	15 019 (93.0)	27 611 (92.4)	12 502 (91.1)	3121 (89.0)	697 (88.3)	5011 (90.2)
Bottle at 18 mo	2177 (13.3)	4689 (15.4)	2944 (20.9)	1049 (29.0)	302 (37.4)	1789 (31.3)
Breastfeeding at 18 mo	3624 (22.1)	6943 (22.8)	3281 (23.3)	860 (23.8)	168 (20.8)	1546 (27.1)
Frequency of eating sweets at 18 mo, times/d[†]						
1	8102 (51.4)	14 244 (48.6)	6610 (49.1)	1735 (51.0)	398 (52.8)	2579 (47.8)
2	7118 (45.1)	13 466 (45.9)	5943 (44.1)	1416 (41.6)	278 (36.9)	2327 (43.1)
≥3	547 (3.5)	1618 (5.5)	918 (6.8)	251 (7.4)	78 (10.3)	488 (9.1)
Frequency of eating sweets at 3 y, times/d [†]						
1	9194 (57.9)	15 399 (52.3)	6907 (50.9)	1738 (50.3)	361 (46.9)	2645 (48.5)
2	6225 (39.2)	12 667 (43.0)	5910 (43.5)	1494 (43.2)	354 (46.0)	2398 (44.0)
≥3	449 (2.8)	1400 (4.8)	758 (5.6)	224 (6.5)	55 (7.1)	406 (7.5)
Eating sweets irregularly at 18 mo[†]	3460 (21.4)	7796 (26.0)	5190 (37.5)	1915 (53.9)	519 (66.0)	3461 (61.5)
Eating sweets irregularly at 3 y[†]	2777 (17.2)	6444 (21.6)	4074 (29.5)	1476 (41.7)	406 (51.3)	2579 (46.1)
Daily juice consumption at 18 mo	5492 (33.5)	11 908 (39.0)	6843 (48.7)	1976 (54.7)	467 (57.8)	2931 (51.3)
Daily juice consumption at 3 y	5957 (36.3)	13 380 (43.9)	7351 (52.3)	2139 (59.2)	524 (64.9)	3185 (55.8)
Use of babysitter or nursery at 4 mo[†]	253 (1.6)	602 (2.0)	301 (2.2)	65 (1.9)	11 (1.4)	66 (1.2)
Use of babysitter or nursery at 18 mo	3804 (23.2)	9297 (30.6)	3539 (25.2)	486 (13.5)	54 (6.7)	856 (15.0)
Use of babysitter or nursery at 3 y	6916 (42.2)	14 980 (49.3)	6439 (45.9)	1338 (37.1)	276 (34.2)	2272 (39.9)
Mental status of the mother at 18 mo, mean (SD)	1.6 (0.7)	1.6 (0.7)	1.7 (0.8)	1.7 (0.8)	1.9 (1.0)	1.8 (0.8)
Support by family, friends, and neighbors at 18 mo	1418 (8.6)	2524 (8.3)	1233 (8.8)	371 (10.3)	89 (11.0)	544 (9.5)
Common comorbidities at 18 mo[†]						
Atopic dermatitis	475 (3.0)	907 (3.1)	387 (2.8)	116 (3.3)	34 (4.3)	156 (2.8)
Asthma	360 (2.3)	713 (2.4)	322 (2.4)	71 (2.0)	14 (1.8)	120 (2.2)
Asthmatic bronchitis	1113 (6.7)	2173 (7.3)	889 (6.5)	183 (5.2)	30 (3.8)	301 (5.4)
Food allergy	619 (3.9)	1182 (4.0)	496 (3.7)	130 (3.7)	35 (4.5)	231 (4.2)
Family members with allergenic disease	7628 (46.7)	14 525 (47.9)	6445 (46.1)	1590 (44.3)	335 (41.9)	2671 (47.2)
Varicella	2169 (13.2)	4233 (13.9)	1629 (11.6)	291 (8.1)	47 (5.8)	539 (9.4)
Pneumonia	879 (5.4)	1630 (5.4)	737 (5.2)	162 (4.5)	22 (2.7)	256 (4.5)
Severe diarrhea	887 (5.4)	1881 (6.2)	856 (6.1)	231 (6.4)	57 (7.1)	392 (6.9)

Values are numbers (percentages) unless stated otherwise.
*Data were missing for 31% of children.
†In total, 1%-13% of infants had missing data on each item.

Table V. Associations between bedtime at age 18 months and risk of caries at age 3 years among 71 069 children in the Kobe Offspring Study

Variables	Categories of bedtime at 18 months						P for trend*
	Before 21:00	21:00	22:00	23:00	0:00	Irregular	
Incidence of any caries, %	1948 (11.9)	4602 (15.1)	2598 (18.5)	779 (21.5)	181 (22.4)	1235 (21.6)	<.001
Unadjusted OR (95% CI)	Reference	1.32 (1.25-1.40)	1.68 (1.58-1.79)	2.04 (1.86-2.24)	2.14 (1.81-2.55)	2.05 (1.89-2.22)	
Multivariable aOR (95% CI)†	Reference	1.26 (1.19-1.33)	1.48 (1.38-1.58)	1.74 (1.58-1.92)	1.90 (1.58-2.29)	1.66 (1.53-1.81)	
Sensitivity analysis‡	Reference	1.21 (1.14-1.29)	1.40 (1.31-1.50)	1.64 (1.48-1.81)	1.71 (1.42-2.06)	1.56 (1.43-1.70)	
Sensitivity analysis§	Reference	1.13 (1.06-1.20)	1.22 (1.13-1.32)	1.36 (1.22-1.51)	1.42 (1.16-1.72)	1.36 (1.24-1.50)	
Incidence of caries in maxillary anterior teeth, %	1174 (7.2)	2857 (9.4)	1649 (11.7)	501 (13.9)	117 (14.5)	816 (14.3)	<.001
Unadjusted OR (95% CI)	Reference	1.34 (1.25-1.44)	1.72 (1.59-1.87)	2.09 (1.87-2.33)	2.20 (1.79-2.70)	2.17 (1.97-2.38)	
Multivariable aOR (95% CI)†	Reference	1.28 (1.19-1.38)	1.51 (1.39-1.64)	1.75 (1.55-1.97)	1.92 (1.55-2.39)	1.72 (1.55-1.90)	
Sensitivity analysis‡	Reference	1.23 (1.14-1.33)	1.42 (1.30-1.54)	1.64 (1.45-1.85)	1.70 (1.37-2.13)	1.60 (1.44-1.78)	
Sensitivity analysis§	Reference	1.14 (1.06-1.24)	1.24 (1.13-1.36)	1.37 (1.20-1.56)	1.43 (1.13-1.80)	1.41 (1.26-1.58)	
Incidence of caries in maxillary molars, %	568 (3.5)	1338 (4.4)	834 (5.9)	261 (7.2)	63 (7.8)	383 (6.7)	<.001
Unadjusted OR (95% CI)	Reference	1.28 (1.16-1.42)	1.76 (1.58-1.96)	2.17 (1.87-2.53)	2.36 (1.80-3.09)	2.01 (1.76-2.29)	
Multivariable aOR (95% CI)†	Reference	1.19 (1.08-1.32)	1.47 (1.31-1.64)	1.70 (1.45-2.00)	1.88 (1.42-2.49)	1.50 (1.30-1.74)	
Sensitivity analysis‡	Reference	1.14 (1.03-1.27)	1.37 (1.23-1.54)	1.58 (1.35-1.86)	1.65 (1.24-2.20)	1.39 (1.20-1.60)	
Sensitivity analysis§	Reference	1.08 (0.96-1.20)	1.23 (1.08-1.39)	1.35 (1.13-1.61)	1.37 (1.01-1.85)	1.22 (1.05-1.43)	
Incidence of caries in mandibular anterior teeth, %	98 (0.6)	272 (0.9)	166 (1.2)	61 (1.7)	17 (2.1)	78 (1.4)	<.001
Unadjusted OR (95% CI)	Reference	1.50 (1.19-1.89)	1.99 (1.55-2.56)	2.86 (2.07-3.94)	3.58 (2.13-6.02)	2.31 (1.71-3.11)	
Multivariable aOR (95% CI)†	Reference	1.44 (1.14-1.82)	1.70 (1.32-2.20)	2.22 (1.59-3.10)	2.75 (1.61-4.72)	1.75 (1.28-2.40)	
Sensitivity analysis‡	Reference	1.37 (1.08-1.73)	1.59 (1.23-2.06)	2.07 (1.48-2.90)	2.36 (1.37-4.06)	1.60 (1.16-2.20)	
Sensitivity analysis§	Reference	1.27 (0.99-1.64)	1.34 (1.01-1.79)	1.57 (1.08-2.28)	1.71 (0.96-3.04)	1.29 (0.91-1.83)	
Incidence of caries in mandibular molars, %	932 (5.7)	2322 (7.6)	1374 (9.8)	448 (12.4)	106 (13.1)	673 (11.8)	<.001
Unadjusted OR (95% CI)	Reference	1.37 (1.27-1.48)	1.80 (1.65-1.96)	2.35 (2.09-2.65)	2.51 (2.02-3.11)	2.22 (2.00-2.46)	
Multivariable aOR (95% CI)†	Reference	1.29 (1.19-1.39)	1.52 (1.39-1.66)	1.90 (1.67-2.15)	2.05 (1.63-2.57)	1.73 (1.55-1.94)	
Sensitivity analysis‡	Reference	1.23 (1.14-1.34)	1.43 (1.30-1.56)	1.76 (1.55-2.00)	1.80 (1.43-2.27)	1.60 (1.43-1.79)	
Sensitivity analysis§	Reference	1.15 (1.05-1.26)	1.26 (1.14-1.39)	1.47 (1.27-1.69)	1.48 (1.16-1.88)	1.41 (1.25-1.60)	

*The P value was calculated by the Cochran–Armitage test for trend for bedtime categories from before 21:00 to 0:00 and later only.
†Multivariable adjusted for child's sex, maternal age at delivery, gestational weeks, maternal alcohol consumption during pregnancy, maternal smoking during pregnancy, pre-eclampsia, anemia, threatened abortion, cesarean delivery, vacuum extraction, nuchal cord, asphyxia, jaundice and transfusion, convulsion, incubator, oxygen inhalation, girl, first-born child, birth weight and height, weight at 18 months, exposure to tobacco smoke at 4 months, number of teeth at 9 months, treated by fluoride varnish at 18 months, tooth brushing by own self tooth brushing at 18 months, tooth brushing by parents before sleep at 18 months, plaque present at 18 months, bottle to feeding at 9 months, age at start of baby food (months), baby food at 9 months, bottle to feeding at 18 months, breastfeeding at 18 months, eating sweets irregularly, frequency of eating sweets (1, 2, ≥3 times per day), daily juice consumption at 18 months, use of babysitter or nursery at 4 months/18 months, mental status of the mother at 18 months, support by family, friends, and neighbors at 18 months; and common comorbidities at 18 months (atopic dermatitis, asthma, asthmatic bronchitis, food allergy, varicella, pneumonia, severe diarrhea) and whether family members with allergenic disease.
‡Further adjusted for the following lifestyle patterns at age 3 years: tooth brushing by own self, tooth brushing by parents before sleep, presence or absence of plaque, eating sweets irregularly, frequency of eating sweets (1, 2, ≥3 times per day), daily juice consumption, and use of babysitter or nursery.
§Further adjusted for bedtime at age 3 years.

bottle-feeding at 18 months ($P = .001$ and $P = .004$ for interaction for bedtime and sleep duration, respectively).

Discussion

In this population-based cohort study of 71 069 Japanese children, having late (21:00 or later) and irregular bedtimes was positively associated with incidence of caries in deciduous teeth. This relationship also was seen with having short (≤10 hours) and irregular nighttime sleep durations but with a less pronounced effect. Other markers of the family milieu that we know are important risk factors for caries, such as lack of tooth brushing, prolonged breastfeeding, bottle-feeding, and irregular and frequent consumption of sweets, are all strongly associated with late or irregular bedtime and short nighttime sleep duration. The relationship between insufficient sleep and dental caries is present when controlling for these factors, and we confirmed our findings through sensitivity analysis using

information about behavior patterns during the ages of 18 months to 3 years.

Previous studies have examined the effects of insufficient sleep on biomarkers of caries, including reduced salivary flow rate and high levels of *Streptococcus mutans* colony counts.[8,10] A decrease in the amount or quality of saliva can significantly increase the risk of caries.[23] Saliva displays a circadian rhythmicity,[24] and previous evidence has shown that mistimed and disrupted sleep can lead to disruption of the circadian rhythms.[5] This provides a possible link between insufficient sleep and risk of caries. We also show that risk of caries in deciduous teeth is increased if with short nighttime sleep duration at age 18 month, which may be a critical period when the teeth are most susceptible to dental caries soon after they erupt. These data, in general, also suggest a dose–response relationship between child's sleep duration and the likelihood of having caries in deciduous teeth.

An increase in risk of dental caries has been recorded in 2 studies of children with late or irregular bedtimes: in the first,

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Table VII. Associations between sleep duration at age 18 months and risk of caries at age 3 years among 71 069 children in the Kobe Offspring Study

| Variables | Categories of nighttime sleep duration at 18 months, hours | | | | | P for trend* |
	≤8	9	10	≥11	Irregular	
Incidence of any caries (%)	455 (19.3)	2668 (16.6)	4595 (15.3)	2197 (13.9)	1428 (20.8)	<.001
Unadjusted OR (95% CI)	1.48 (1.32-1.66)	1.23 (1.16-1.31)	1.12 (1.06-1.18)	Reference	1.63 (1.51-1.75)	
Multivariable OR (95% CI)[†]	1.30 (1.15-1.47)	1.16 (1.09-1.24)	1.11 (1.05-1.18)	Reference	1.35 (1.25-1.46)	
Sensitivity analysis[‡]	1.24 (1.10-1.40)	1.13 (1.06-1.21)	1.09 (1.03-1.16)	Reference	1.29 (1.19-1.40)	
Sensitivity analysis[§]	1.20 (1.06-1.36)	1.11 (1.03-1.19)	1.08 (1.02-1.14)	Reference	1.26 (1.16-1.37)	
Incidence of caries in maxillary anterior teeth (%)	289 (12.3)	1661 (10.4)	2887 (9.6)	1347 (8.5)	930 (13.6)	<.001
Unadjusted OR (95% CI)	1.50 (1.31-1.72)	1.24 (1.15-1.33)	1.14 (1.06-1.22)	Reference	1.68 (1.54-1.84)	
Multivariable aOR (95%CI)[†]	1.34 (1.16-1.54)	1.20 (1.10-1.30)	1.14 (1.07-1.23)	Reference	1.38 (1.26-1.52)	
Sensitivity analysis[‡]	1.28 (1.11-1.48)	1.17 (1.07-1.27)	1.13 (1.05-1.21)	Reference	1.32 (1.20-1.46)	
Sensitivity analysis[§]	1.25 (1.08-1.45)	1.15 (1.06-1.25)	1.11 (1.04-1.20)	Reference	1.29 (1.17-1.43)	
Incidence of caries in maxillary molars (%)	132 (5.6)	826 (5.2)	1362 (4.5)	673 (4.3)	454 (6.6)	<.001
Unadjusted OR (95% CI)	1.33 (1.10-1.62)	1.22 (1.10-1.35)	1.07 (0.97-1.17)	Reference	1.59 (1.41-1.80)	
Multivariable aOR (95% CI)[†]	1.15 (0.94-1.40)	1.15 (1.03-1.29)	1.06 (0.96-1.17)	Reference	1.26 (1.11-1.44)	
Sensitivity analysis[‡]	1.09 (0.89-1.33)	1.12 (1.00-1.25)	1.03 (0.94-1.14)	Reference	1.20 (1.05-1.36)	
Sensitivity analysis[§]	1.05 (0.85-1.29)	1.09 (0.97-1.22)	1.01 (0.92-1.12)	Reference	1.15 (1.01-1.32)	
Incidence of caries in mandibular anterior teeth (%)	24 (1.0)	166 (1.0)	272 (0.9)	140 (0.9)	90 (1.3)	.160
Unadjusted OR (95% CI)	1.15 (0.74-1.78)	1.17 (0.93-1.46)	1.02 (0.83-1.25)	Reference	1.49 (1.14-1.94)	
Multivariable aOR (95% CI)[†]	1.06 (0.68-1.66)	1.18 (0.93-1.49)	1.04 (0.85-1.28)	Reference	1.17 (0.89-1.55)	
Sensitivity analysis[‡]	1.02 (0.65-1.59)	1.14 (0.90-1.44)	1.02 (0.83-1.25)	Reference	1.11 (0.84-1.46)	
Sensitivity analysis[§]	1.01 (0.64-1.59)	1.12 (0.88-1.43)	0.99 (0.8-1.22)	Reference	1.03 (0.78-1.38)	
Incidence of caries in mandibular molars (%)	257 (10.9)	1359 (8.5)	2340 (7.8)	1111 (7.0)	788 (11.5)	<.001
Unadjusted OR (95% CI)	1.62 (1.40-1.87)	1.22 (1.12-1.33)	1.11 (1.04-1.20)	Reference	1.71 (1.56-1.89)	
Multivariable aOR (95% CI)[†]	1.40 (1.21-1.63)	1.14 (1.04-1.24)	1.10 (1.02-1.19)	Reference	1.39 (1.25-1.54)	
Sensitivity analysis[‡]	1.33 (1.15-1.55)	1.10 (1.01-1.20)	1.08 (1.00-1.17)	Reference	1.32 (1.19-1.46)	
Sensitivity analysis[§]	1.30 (1.11-1.52)	1.08 (0.99-1.18)	1.07 (0.99-1.16)	Reference	1.30 (1.17-1.44)	

*The P value was calculated by the Cochran–Armitage test for trend for sleep duration categories from ≤8 hours to ≥11 hours only.
†Multivariable-adjusted for child's sex, maternal age at delivery, gestational weeks, maternal alcohol consumption during pregnancy, maternal smoking during pregnancy, pre-eclampsia, anemia, threatened abortion, cesarean delivery, vacuum extraction, nuchal cord, asphyxia, jaundice and transfusion, convulsion, incubator, oxygen inhalation, girl, first-born child, birth weight and height, weight at 18 months, exposure to tobacco smoke at 4 months, number of teeth at 9 months, treated by fluoride varnish at 18 months, tooth brushing by own self tooth brushing at 18 months, tooth brushing by parents before sleep at 18 months, plaque present at 18 months, bottle to feeding at 9 months, age at start of baby food (months), baby food at 9 months, bottle to feeding at 18 months, breastfeeding at 18 months, eating sweets irregularly, frequency of eating sweets (1, 2, ≥3 times per day), daily juice consumption at 18 months, use of babysitter or nursery at 4 months/18 months, mental status of the mother at 18 months, support by family, friends, and neighbors at 18 months; and common comorbidities at 18 months (atopic dermatitis, asthma, asthmatic bronchitis, food allergy, varicella, pneumonia, severe diarrhea) and whether family members with allergic disease.
‡Further adjusted for the following lifestyle patterns at age 3 years: tooth brushing by own self, tooth brushing by parents before sleep, presence or absence of plaque, eating sweets irregularly, frequency of eating sweets (1, 2, ≥3 times per day), daily juice consumption, and use of babysitter or nursery.
§Further adjusted for sleep duration at age 3 years.

children with bedtimes after 23:00 at age 18 months had an OR of 1.85 (95% CI 1.61-2.12) for dental caries in deciduous teeth at age 3 years; in the second, children with bedtimes after 21:00 at age 7 years had an OR of 1.90 (1.10-3.10) for dental caries in permanent teeth at age 10 years.[13,14] Our findings of a dose–response relationship between bedtime and risk of dental caries builds on these previous reports, with the additional strengths of a larger sample size that enabled analyses across various subgroups and adjustment for more potential confounders. Notably, we noted an increase in odds of caries in maxillary anterior teeth among children with late and irregular bedtimes, which are less likely to be affected by inappropriate feeding practices,[25,26] which may suggest a specific effect of sleep on dental caries. In contrast, this association was not seen for sleep duration. Although we included information for more than 70 000 children, risk of caries in this site is low. Low statistical power might be the reason why we failed to find associations for sleep duration categories.

The principal concern with interpreting this study is the possibility that insufficient sleep is simply a marker for some unmeasured true cause of caries formation. For example, socioeconomic status is likely to influence the risk of dental caries,[3] and it also may be an important modifier of sleep behaviors in children.[27] In addition, because children's sleep habits are largely determined by their parents, it could be that parents who set the bedtime late or irregular for their children also practice other unhealthy behaviors before bedtime that would put their children at risk for caries, for example, not using fluoride toothpaste, nocturnal bottle-feeding or breastfeeding, and intake of sugary foods or drinks before going to bed.[28-30] Because the Kobe Offspring Study does not include data on socioeconomic status, our findings must be considered exploratory. Georeferenced information indicated that the study children were mostly from working households and that their parents had completed at least a high school education. Furthermore, we attempted to assess the degree of potential confounding by socioeconomic status by adjusting for parental smoking, which was reported to be strongly associated with parental education and household income.[31] We found that exposure to household smoking at age 4 months was associated with a 1.6-fold greater odds of dental caries, a result consistent with previous findings.[15] The fluoridation of water in the community has been carried out in Japan since 1972, and more than 99% of children received fluoride varnish at 18 months (Table III). This may in part attenuate the effect of socioeconomic status on risk of caries in young children.[32]

We attempted to control for prolonged breastfeeding for 18 months, which may be associated with nocturnal breastfeeding on demand.[33,34] About one-fifth of children were still breastfed at 18 months, and this was associated with a 2-fold increase in odds of caries. Bottle-feeding at 18 months also was associated slightly with increased odds of caries. In contrast, parents' cleaning their children's teeth before going to bed was found in more than 70% of children and was associated with a 24% reduction in odds of caries. Fluoride toothpaste can reduce tooth demineralization, but this depends on sugar consumption.[35] Although we lacked data on toothpaste use, the effect of insufficient sleep on dental caries was not confounded by dietary factors. In our subgroup analyses, the associations between insufficient sleep and caries also were found among children without bottle-feeding or breastfeeding, with a lower frequency of eating sweets, without daily juice consumption, and with tooth brushing by parents before going to bed. These findings, together with the association found for caries in maxillary anterior teeth, argue against insufficient sleep being merely a marker for dietary and nocturnal feeding practices. Intriguingly, we found that the associations between insufficient sleep and caries were stronger in children who did not than who did have bottle-feeding. We speculate that the family routine of the children who were bottle-fed might be more flexible, which in turn affects the child's risk of caries.

In addition to the need for more comprehensive information on risk factors for caries, especially socioeconomic status, other limitations of our study include the fact that parent-reported sleep behaviors may be subject to recall bias; a lack of data on daytime naps that still represent a certain proportion of total sleep in young children; and oral conditions that were not necessarily assessed by pediatric dentistry. It is impossible to establish causality based on our findings owing to the observational study design. Also, given the substantial variability in the prevalence of caries, sleep patterns and lifestyle across countries,[36] our results may not be generally applicable to populations with different environmental and lifestyle factors.

Our findings might potentially have important public health implications. More than 60% of children had bedtimes after 21:00, and 8% had irregular bedtimes. This would increase odds of caries by 1.2- to 1.9-fold. Risk of caries also would increase by 1.1- to1.3-fold among children with sleep durations of 10 hours or less. Our estimate of 16.0% children with caries is slightly lower than the average estimates in Japan.[37] Provided that the distributions of sleep variables are similar to those nationally reported,[38] the estimates of associations we observed, if anything, could represent an underestimation of the effect of unfavorable sleep hygiene on odds of caries. Indeed, exposure to having late bedtime is common among Asian children,[36] and decreasing sleep duration among young children has already triggered growing concern over the century.[39] The associations between insufficient sleep and risk of caries would thus support the expansion of public health strategies to provide appropriate sleep conditions in which young children can flourish.

Having late bedtime and short nighttime sleep duration, which are experienced by more than one-half of all children in Kobe City, Japan, are consistently associated with increased odds of dental caries in deciduous teeth. It is unclear whether insufficient sleep is simply associated with caries or whether it is a cause. Due to the lack of data on socioeconomic status, our findings must be considered exploratory. Further studies are warranted to examine the effect of insufficient sleep on caries in mid-childhood and adolescents and to determine whether better sleep hygiene impacts favorably on caries and other health outcomes. ■

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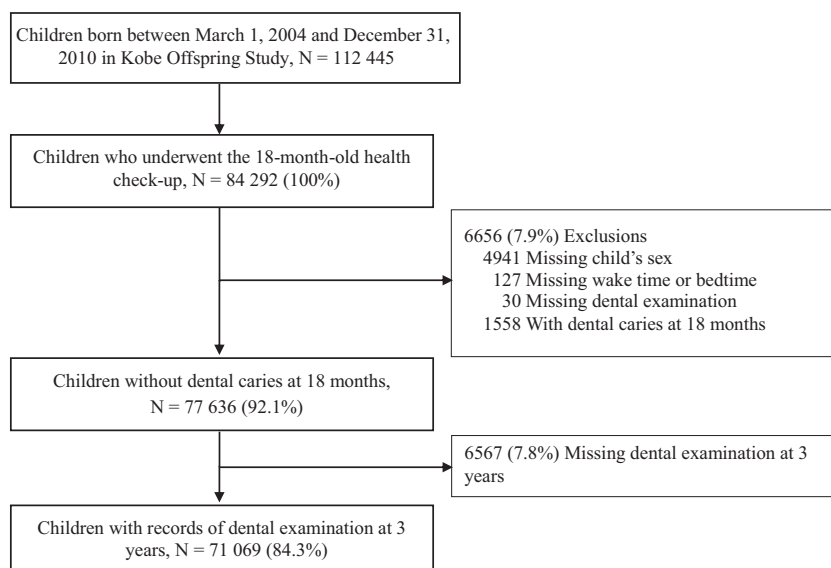
Figure. Flowchart of subject selection.

Table II. Comparison of background characteristics of children followed and not followed to age 3 years

Baseline characteristics	Followed (n = 71 069)		Not followed* (n = 74 249)		
	Mean	SD	Mean	SD	P
Maternal age at delivery, y	31.4	4.7	31.3	5.0	.004
Maternal age at delivery ≥35 y	22.6		24.1		<.001
Maternal smoking during pregnancy	16.8		16.4		.122
Maternal alcohol consumption during pregnancy	93.7		93.7		
Occasional	17.4		17.8		.155
Daily	0.6		0.7		
Girl	48.9		48.4		.056
First-born child	48.4		53.0		<.001
Pre-eclampsia	2.3		2.3		.697
Anemia	10.4		10.9		.01
Threatened abortion	11.0		12.5		<.001
Gestation, wk					
22-27	0.1		0.3		<.001
28-36	6.1		6.0		
36-43	93.7		93.7		
Birth weight, g	3003.1	411.2	3007.5	418.8	.038
Bedtime at 18 mo					<.001
Before 21:00	23.1		25.3		
21:00	42.9		42.0		
22:00	19.8		18.2		
23:00	5.1		4.9		
0:00	1.1		1.1		
Irregular	8.0		8.6		
Nighttime sleep duration at 18 mo, h					<.001
≤8	3.3		3.1		
9	22.6		22.0		
10	42.3		41.6		
≥11	22.2		23.0		
Irregular	9.7		10.4		

*Comparison within the entire dataset of 145 318 children in the health check-up program in Kobe City between 2004 and 2014. Major reasons for exclusion are provided in the **Figure**.

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Table IV. Characteristics of 71 069 children by categories of nighttime sleep duration at age 18 months

Characteristics	Categories of nighttime sleep duration at 18 months of age (hours)				
	≤8	9	10	≥11	Irregular
Number of children	2353	16 043	30 044	15 773	6856
Background characteristics					
Maternal age at delivery, y,* mean (SD)	32.2 (5.0)	32.0 (4.6)	31.6 (4.5)	30.8 (4.5)	30.5 (5.5)
Maternal age ≥35 y*	512 (30.6)	3034 (26.7)	4744 (22.5)	1902 (17.5)	1002 (21.9)
Gestational wk†					
22-27	1 (0.1)	22 (0.2)	38 (0.1)	24 (0.2)	10 (0.2)
28-36	150 (6.8)	926 (6.2)	1765 (6.3)	879 (6.0)	367 (5.7)
36-43	2064 (93.2)	14 102 (93.7)	26 415 (93.6)	13 833 (93.9)	6047 (94.1)
Maternal alcohol consumption during pregnancy*					
Occasional	299 (18.3)	2118 (19.0)	3558 (17.2)	1701 (16.0)	802 (17.9)
Daily	19 (1.2)	76 (0.7)	122 (0.6)	56 (0.5)	35 (0.8)
Maternal smoking during pregnancy*	299 (18.3)	1835 (16.4)	3266 (15.8)	1731 (16.2)	1053 (23.5)
Pre-eclampsia†	56 (2.4)	399 (2.6)	638 (2.2)	308 (2.0)	213 (3.2)
Anemia†	231 (10.0)	1552 (9.9)	3048 (10.4)	1647 (10.8)	729 (10.9)
Threatened abortion†	268 (11.6)	1736 (11.1)	3236 (11.1)	1684 (11.0)	715 (10.7)
Child's sex, girl	1157 (49.2)	7566 (47.2)	14 583 (48.5)	8037 (51.0)	3428 (50.0)
First-born child†	1100 (50.6)	6994 (47.2)	12 777 (46.5)	6606 (46.5)	3897 (62.9)
Birth weight, g,† mean (SD)	2992.8 (424.4)	3000.6 (410.3)	3004.6 (411.3)	3003.5 (409.6)	2995.0 (412.2)
Oral hygiene					
No. of teeth at 9 mo,† mean (SD)	2.1 (0.9)	2.1 (0.9)	2.1 (0.9)	2.0 (0.9)	2.1 (0.9)
Treated by fluoride varnish at 18 mo†	2061 (99.4)	14 029 (99.2)	26 105 (99.5)	13 539 (99.4)	5908 (99.4)
Tooth brushing by own self at 18 mo	1624 (69.1)	12 120 (75.6)	24 205 (80.6)	13 120 (83.2)	4912 (71.7)
Tooth brushing by parents before sleep at 18 mo	1518 (64.5)	11 153 (69.5)	22 574 (75.1)	12 418 (78.7)	4448 (64.9)
Tooth brushing by own self at 3 y	1939 (83.4)	13 725 (85.6)	26 542 (88.4)	14 151 (89.7)	5581 (81.4)
Tooth brushing by parents before sleep at 3 y	1871 (79.6)	13 532 (84.4)	26 487 (88.2)	14 134 (89.6)	5581 (81.4)
Plaque present at 18 mo	593 (25.3)	3711 (23.2)	6355 (21.2)	3015 (19.2)	1571 (23.0)
Plaque present at 3 y†	504 (21.6)	3111 (20.0)	5122 (17.2)	2399 (15.0)	1302 (19.2)
Lifestyle factors					
Exposure to tobacco smoke at 4 mo					
Not exposed to second-hand smoke	1017 (43.2)	7612 (47.5)	14 579 (48.5)	7504 (47.6)	2623 (38.3)
Exposed to only household smoking	1149 (48.8)	7298 (45.5)	13 685 (45.6)	7325 (46.4)	3659 (53.4)
Exposed to tobacco smoke	187 (8.0)	1133 (7.1)	1780 (5.9)	944 (6.0)	574 (8.4)
Feeding practices					
Age at start of baby food, mo,† mean (SD)	5.4 (0.9)	5.5 (0.8)	5.5 (0.8)	5.5 (0.8)	5.5 (0.8)
Bottle at 9 mo†	1065 (46.5)	6488 (41.5)	11 263 (38.1)	5623 (36.4)	2908 (43.6)
Baby food at 9 mo†	2085 (91.0)	14 344 (91.7)	27 265 (92.3)	14 242 (92.1)	6025 (90.3)
Bottle at 18 mo	587 (25.0)	2938 (18.3)	4776 (15.9)	2585 (16.4)	2064 (30.1)
Breastfeeding at 18 mo	552 (23.5)	3455 (21.5)	6864 (22.9)	3725 (23.6)	1826 (26.7)
Frequency of eating sweets at 18 mo, times/d†					
1	811 (36.0)	6080 (39.2)	14 701 (50.9)	8895 (59.4)	3181 (49.2)
2	1186 (52.7)	8138 (52.5)	12 878 (44.6)	5614 (37.5)	2732 (42.2)
≥3	254 (11.3)	1294 (8.3)	1316 (4.6)	478 (3.2)	558 (8.6)
Frequency of eating sweets at 3 y, times/d†					
1	946 (41.8)	7095 (45.6)	15 858 (54.5)	9131 (60.3)	3214 (49.2)
2	1115 (49.2)	7462 (48.0)	12 037 (41.4)	5588 (36.9)	2846 (43.6)
≥3	204 (9.0)	997 (6.4)	1182 (4.1)	436 (2.9)	473 (7.2)
Eating sweets irregularly at 18 mo†	703 (30.4)	4225 (26.8)	8343 (28.2)	4918 (31.6)	4152 (61.5)
Eating sweets irregularly at 3 y†	600 (26.1)	3546 (22.6)	6721 (22.8)	3794 (24.5)	3095 (46.0)
Daily juice consumption at 18 mo	1100 (46.8)	6723 (41.9)	12 010 (40.0)	6280 (39.8)	3504 (51.1)
Daily juice consumption at 3 y	1187 (50.5)	7432 (46.3)	13 309 (44.3)	6808 (43.2)	3800 (55.4)
Use of babysitter or nursery at 4 mo†	67 (2.9)	442 (2.9)	522 (1.8)	181 (1.2)	86 (1.3)
Use of babysitter or nursery at 18 mo	1123 (47.8)	6924 (43.2)	7327 (24.4)	1707 (10.8)	955 (13.9)
Use of babysitter or nursery at 3 y	1458 (62.1)	9431 (58.9)	13 462 (44.9)	5205 (33.1)	2665 (38.9)
Mental status of the mother at 18 mo, mean (SD)	1.7 (0.8)	1.7 (0.7)	1.6 (0.7)	1.6 (0.7)	1.8 (0.8)
Support by family, friends, and neighbors at 18 mo	252 (10.7)	1531 (9.5)	2496 (8.3)	1225 (7.8)	675 (9.9)
Common comorbidities at 18 mo†					
Atopic dermatitis	72 (3.2)	540 (3.5)	859 (2.9)	422 (2.7)	182 (2.7)
Asthma	71 (3.1)	433 (2.8)	661 (2.3)	291 (1.9)	144 (2.2)
Asthmatic bronchitis	193 (8.5)	1295 (8.3)	1977 (6.8)	860 (5.6)	364 (5.5)
Food allergy	83 (3.6)	628 (4.1)	1158 (4.0)	555 (3.6)	269 (4.1)
Family members with allergenic disease	1123 (47.9)	7675 (48.1)	14 001 (46.9)	7179 (45.8)	3216 (47.4)
Varicella	362 (15.4)	2384 (14.9)	3806 (12.7)	1743 (11.1)	613 (8.9)
Pneumonia	147 (6.3)	988 (6.2)	1570 (5.2)	700 (4.4)	281 (4.1)
Severe diarrhea	157 (6.7)	1081 (6.7)	1818 (6.0)	796 (5.1)	460 (6.7)

Values are numbers (percentages) unless stated otherwise.
*Data were missing for 31% of children.
†In total, 1%-13% of infants had missing data on each item.

Table VI. Associations between covariates at age 18 months and risk of caries at age 3 years among 71 069 children in the Kobe Offspring Study

Covariates	Unadjusted model OR (95% CI)	P	Multivariable-adjusted model for bedtime* OR (95% CI)	P	Multivariable-adjusted model for sleep duration† OR (95% CI)	P
Background characteristics						
Maternal age at delivery, y, mean (SD)	0.98 (0.98-0.99)	<.001	0.97 (0.97-0.98)	<.001	0.97 (0.97-0.98)	<.001
Gestational weeks						
22-27	Reference		Reference		Reference	
28-36	0.42 (0.19-0.90)	.026	0.46 (0.20-1.04)	.061	0.47 (0.21-1.05)	.064
36-43	0.92 (0.84-1.01)	.066	1.11 (0.99-1.24)	.062	1.11 (0.99-1.24)	.068
Maternal alcohol consumption during pregnancy						
None	Reference		Reference		Reference	
Occasional	0.93 (0.87-0.99)	.022	0.89 (0.84-0.95)	.001	0.89 (0.83-0.95)	.001
Daily	1.29 (0.97-1.72)	.076	1.18 (0.83-1.67)	.341	1.17 (0.83-1.66)	.349
Maternal smoking during pregnancy	1.33 (1.25-1.42)	<.001	1.16 (1.09-1.23)	<.001	1.17 (1.10-1.25)	<.001
Pre-eclampsia	1.07 (0.94-1.22)	.290	1.15 (1.00-1.33)	.048	1.17 (1.01-1.34)	.031
Anemia	0.99 (0.93-1.06)	.779	0.98 (0.91-1.05)	.586	0.98 (0.91-1.05)	.584
Threatened abortion	0.87 (0.82-0.93)	<.001	0.90 (0.84-0.97)	.007	0.90 (0.84-0.97)	.006
Cesarean delivery	0.94 (0.88-0.99)	.020	1.02 (0.96-1.09)	.563	1.02 (0.96-1.09)	.527
Vacuum extraction	0.88 (0.80-0.96)	.004	1.05 (0.96-1.16)	.301	1.05 (0.95-1.15)	.342
Nuchal cord	1.02 (0.91-1.15)	.694	1.04 (0.92-1.18)	.515	1.04 (0.91-1.18)	.570
Asphyxia	0.85 (0.67-1.08)	.175	0.97 (0.75-1.25)	.788	0.97 (0.75-1.25)	.797
Jaundice and transfusion	0.94 (0.88-1.00)	.058	1.03 (0.96-1.10)	.411	1.03 (0.96-1.10)	.377
Convulsion	1.04 (0.56-1.92)	.911	1.10 (0.58-2.11)	.767	1.09 (0.57-2.09)	.783
Incubator	0.91 (0.84-1.00)	.052	1.07 (0.94-1.21)	.301	1.07 (0.94-1.21)	.302
Oxygen inhalation	0.91 (0.81-1.01)	.087	0.99 (0.85-1.15)	.907	0.99 (0.86-1.15)	.915
Birth year (years)	0.94 (0.93-0.95)	<.001	0.96 (0.95-0.97)	<.001	0.96 (0.95-0.97)	<.001
Child's sex, girl	0.91 (0.87-0.95)	<.001	0.92 (0.88-0.96)	<.001	0.93 (0.89-0.97)	.001
First-born child	0.56 (0.53-0.58)	<.001	0.47 (0.45-0.50)	<.001	0.49 (0.46-0.51)	<.001
Birth weight, g, mean (SD)	1.00 (1.00-1.00)	<.001	1.00 (1.00-1.00)	<.001	1.00 (1.00-1.00)	<.001
Birth height, cm, mean (SD)	1.02 (1.01-1.03)	<.001	0.99 (0.97-1.01)	.183	0.99 (0.97-1.01)	.203
Weight at 18 mo, kg, mean (SD)	1.00 (1.00-1.00)	.071	1.00 (1.00-1.00)	.085	1.00 (1.00-1.00)	.027
Oral hygiene						
No. teeth at 9 mo, mean (SD)	1.09 (1.06-1.12)	<.001	1.08 (1.05-1.11)	<.001	1.08 (1.06-1.11)	<.001
Treated by fluoride varnish at 18 mo	0.55 (0.43-0.69)	<.001	0.67 (0.52-0.86)	.002	0.66 (0.51-0.85)	.002
Tooth brushing by own self at 18 mo	0.78 (0.74-0.82)	<.001	0.99 (0.94-1.05)	.841	0.99 (0.94-1.04)	.623
Tooth brushing by parents before sleep at 18 mo	0.59 (0.56-0.61)	<.001	0.71 (0.68-0.75)	<.001	0.71 (0.67-0.74)	<.001
Plaque present at 18 mo	1.64 (1.56-1.71)	<.001	1.47 (1.40-1.54)	<.001	1.47 (1.40-1.54)	<.001
Lifestyle factors						
Exposure to tobacco smoke at 4 mo						
Not exposed to second-hand smoke	Reference		Reference		Reference	
Exposed to only household smoking	1.50 (1.44-1.57)	<.001	1.30 (1.24-1.36)	<.001	1.32 (1.26-1.39)	<.001
Exposed to tobacco smoke	2.28 (2.12-2.45)	<.001	1.58 (1.46-1.72)	<.001	1.63 (1.50-1.77)	<.001
Feeding practices						
Age at start of baby food, mo, mean (SD)	0.92 (0.90-0.95)	<.001	0.94 (0.91-0.96)	<.001	0.94 (0.91-0.96)	<.001
Bottle at 9 mo	0.82 (0.79-0.86)	<.001	0.89 (0.84-0.93)	<.001	0.90 (0.85-0.94)	<.001
Baby food at 9 mo	0.76 (0.71-0.81)	<.001	0.91 (0.84-0.98)	.013	0.89 (0.83-0.96)	.004
Bottle at 18 mo	1.39 (1.32-1.46)	<.001	1.30 (1.23-1.37)	<.001	1.33 (1.26-1.41)	<.001
Breastfeeding at 18 mo	1.96 (1.88-2.05)	<.001	2.08 (1.98-2.19)	<.001	2.11 (2.01-2.21)	<.001
Frequency of eating sweets at 18 mo, times/d						
1	Reference		Reference		Reference	
2	1.73 (1.66-1.81)	<.001	1.63 (1.56-1.71)	<.001	1.61 (1.54-1.69)	<.001
≥3	2.37 (2.19-2.57)	<.001	2.04 (1.87-2.23)	<.001	2.04 (1.87-2.23)	<.001
Eating sweets irregularly at 18 mo	1.42 (1.36-1.48)	<.001	1.23 (1.17-1.29)	<.001	1.28 (1.22-1.35)	<.001
Daily juice consumption at 18 mo	1.72 (1.65-1.79)	<.001	1.51 (1.45-1.58)	<.001	1.55 (1.48-1.62)	<.001
Use of babysitter or nursery at 4 mo	1.17 (1.01-1.35)	.033	1.06 (0.91-1.23)	.486	1.07 (0.92-1.24)	.399
Use of babysitter or nursery at 18 mo	1.03 (0.98-1.08)	.193	0.88 (0.83-0.93)	<.001	0.86 (0.81-0.91)	<.001
Mental status of the mother at 18 mo, mean (SD)	0.93 (0.91-0.96)	<.001	0.88 (0.85-0.90)	<.001	0.88 (0.85-0.91)	<.001
Support by family, friends, and neighbors at 18 mo	0.77 (0.71-0.83)	<.001	0.90 (0.83-0.98)	.014	0.90 (0.83-0.98)	.016
Common comorbidities at 18 mo						
Atopic dermatitis	1.21 (1.08-1.35)	.001	1.13 (1.00-1.28)	.043	1.13 (1.00-1.28)	.041
Asthma	1.37 (1.21-1.55)	<.001	1.03 (0.90-1.18)	.686	1.03 (0.90-1.18)	.694
Asthmatic bronchitis	1.33 (1.23-1.43)	<.001	1.16 (1.07-1.26)	<.001	1.15 (1.06-1.25)	.001
Food allergy	1.02 (0.92-1.14)	.661	0.92 (0.85-1.01)	.069	0.98 (0.88-1.10)	.784
Family members with allergenic disease	0.98 (0.94-1.02)	.286	0.93 (0.89-0.97)	.001	0.93 (0.89-0.97)	<.001
Varicella	1.19 (1.12-1.26)	<.001	1.05 (0.99-1.12)	.112	1.04 (0.98-1.11)	.182
Pneumonia	1.26 (1.16-1.37)	<.001	1.18 (1.08-1.29)	<.001	1.18 (1.08-1.29)	<.001
Severe diarrhea	0.97 (0.89-1.05)	.416	0.97 (0.88-1.06)	.459	0.97 (0.89-1.06)	.470

*Multivariable-adjusted for all the covariates listed in the **table** and bedtime at 18 months.
†Multivariable-adjusted for all the covariates listed in the **table** and nighttime sleep duration at 18 months.

Table VIII. Subgroup analyses of associations between bedtime at age 18 months and dental caries in any site at age 3 years among 71 069 children in the Kobe Offspring Study

Subgroups	Categories of bedtimes at 18 months						P for interaction*
	Before 21:00	21:00	22:00	23:00	0:00	Irregular	
Sex							
Boy	Reference	1.29 (1.19-1.40)	1.50 (1.36-1.64)	1.85 (1.61-2.13)	1.57 (1.19-2.06)	1.72 (1.52-1.93)	.158
Girl	Reference	1.22 (1.12-1.33)	1.45 (1.32-1.60)	1.63 (1.41-1.88)	2.24 (1.74-2.88)	1.61 (1.42-1.82)	
Birth order							
First	Reference	1.19 (1.06-1.33)	1.59 (1.41-1.79)	1.87 (1.60-2.18)	1.98 (1.56-2.52)	1.77 (1.55-2.03)	.002
Second or later	Reference	1.31 (1.21-1.40)	1.44 (1.32-1.57)	1.63 (1.40-1.89)	1.77 (1.24-2.52)	1.55 (1.37-1.74)	
Presence of plaque							
No	Reference	1.22 (1.14-1.31)	1.44 (1.33-1.56)	1.66 (1.47-1.86)	1.90 (1.53-2.37)	1.63 (1.47-1.80)	.578
Yes	Reference	1.38 (1.22-1.55)	1.60 (1.40-1.83)	1.99 (1.65-2.41)	1.92 (1.35-2.71)	1.79 (1.51-2.11)	
Tooth brushing by parents before going to bed							
No	Reference	1.11 (0.99-1.24)	1.39 (1.24-1.57)	1.59 (1.34-1.87)	1.91 (1.41-2.60)	1.56 (1.36-1.80)	.124
Yes	Reference	1.32 (1.23-1.42)	1.51 (1.39-1.64)	1.81 (1.59-2.05)	1.85 (1.47-2.33)	1.70 (1.52-1.90)	
Bottle feeding							
No	Reference	1.29 (1.21-1.38)	1.55 (1.43-1.67)	1.87 (1.67-2.10)	2.23 (1.77-2.81)	1.84 (1.66-2.04)	.001
Yes	Reference	1.11 (0.97-1.28)	1.23 (1.05-1.43)	1.34 (1.11-1.64)	1.34 (0.98-1.83)	1.24 (1.04-1.47)	
Breastfeeding							
No	Reference	1.28 (1.19-1.38)	1.47 (1.35-1.59)	1.79 (1.59-2.02)	2.02 (1.63-2.50)	1.67 (1.52-1.88)	.274
Yes	Reference	1.21 (1.09-1.34)	1.51 (1.34-1.70)	1.61 (1.34-1.92)	1.62 (1.12-2.36)	1.59 (1.37-1.85)	
Eating sweets irregularly							
No	Reference	1.30 (1.21-1.39)	1.53 (1.41-1.66)	1.96 (1.71-2.25)	1.83 (1.33-2.51)	1.62 (1.42-1.83)	.136
Yes	Reference	1.17 (1.04-1.31)	1.37 (1.21-1.54)	1.51 (1.29-1.76)	1.82 (1.43-2.30)	1.60 (1.40-1.83)	
Frequency of eating sweets, times/d							
1	Reference	1.24 (1.14-1.36)	1.38 (1.24-1.53)	1.71 (1.47-1.99)	2.09 (1.60-2.74)	1.75 (1.53-1.99)	.027
2	Reference	1.31 (1.21-1.43)	1.60 (1.46-1.76)	1.86 (1.61-2.14)	1.49 (1.10-2.01)	1.63 (1.44-1.84)	
≥3	Reference	1.01 (0.78-1.30)	1.28 (0.98-1.68)	1.32 (0.92-1.90)	2.37 (1.39-4.03)	1.33 (0.98-1.82)	
Daily juice consumption							
No	Reference	1.30 (1.20-1.40)	1.61 (1.46-1.77)	1.54 81.31-1.80)	1.82 (1.33-2.49)	1.63 (1.43-1.85)	.007
Yes	Reference	1.22 (1.11-1.33)	1.37 (1.24-1.51)	1.83 (1.60-2.08)	1.89 (1.50-2.38)	1.66 (1.48-1.87)	

Values are ORs (95% CIs) unless stated otherwise.

All subgroup analyses were multivariable adjusted for child's sex, maternal age at delivery, gestational weeks, maternal alcohol consumption during pregnancy, maternal smoking during pregnancy, pre-eclampsia, anemia, threatened abortion, cesarean delivery, vacuum extraction, nuchal cord, asphyxia, jaundice and transfusion, convulsion, incubator, oxygen inhalation, girl, first-born child, birth weight and height, weight at 18 months, exposure to tobacco smoke at 4 months, number of teeth at 9 months, treated by fluoride varnish at 18 months, tooth brushing by own self tooth brushing at 18 months, tooth brushing by parents before sleep at 18 months, plaque present at 18 months, bottle to feeding at 9 months, age at start of baby food (months), baby food at 9 months, bottle to feeding at 18 months, breastfeeding at 18 months, eating sweets irregularly, frequency of eating sweets (1, 2, ≥3 times per day), daily juice consumption at 18 months, use of babysitter or nursery at 4 months/18 months, mental status of the mother at 18 months, support by family, friends, and neighbors at 18 months; and common comorbidities at 18 months (atopic dermatitis, asthma, asthmatic bronchitis, food allergy, varicella, pneumonia, severe diarrhea) and whether family members with allergenic disease.

*P values for interactions were computed by testing whether the coefficients on the interaction terms are jointly equal to zero with the use of mi test command for imputed date.

Table IX. Subgroup analyses of associations between sleep duration at age 18 months and dental caries at age 3 years among 71 069 children in the Kobe Offspring Study

Subgroups	Categories of nighttime sleep duration at 18 months, hours					P for interaction*
	≤8	9	10	≥11	Irregular	
Sex						
Boy	1.31 (1.11-1.55)	1.22 (1.11-1.34)	1.13 (1.04-1.23)	Reference	1.39 (1.24-1.55)	.471
Girl	1.29 (1.09-1.53)	1.10 (1.00-1.21)	1.09 (1.00-1.18)	Reference	1.32 (1.18-1.47)	
Birth order						
First	1.33 (1.14-1.56)	1.15 (1.05-1.25)	1.13 (1.05-1.22)	Reference	1.27 (1.13-1.43)	.134
Second or later	1.26 (1.03-1.53)	1.19 (1.06-1.34)	1.08 (0.98-1.20)	Reference	1.39 (1.23-1.57)	
Presence of plaque						
No	1.30 (1.13-1.50)	1.18 (1.09-1.27)	1.10 (1.03-1.18)	Reference	1.36 (1.24-1.49)	.719
Yes	1.30 (1.04-1.62)	1.12 (0.98-1.27)	1.12 (1.00-1.26)	Reference	1.34 (1.14-1.56)	
Tooth brushing by parents before going to bed						
No	1.35 (1.12-1.62)	1.12 (0.99-1.25)	1.04 (0.93-1.15)	Reference	1.30 (1.14-1.48)	.569
Yes	1.25 (1.07-1.46)	1.18 (1.09-1.28)	1.14 (1.06-1.22)	Reference	1.37 (1.24-1.52)	
Bottle feeding						
No	1.38 (1.20-1.58)	1.18 (1.10-1.28)	1.13 (1.06-1.21)	Reference	1.48 (1.35-1.63)	.004
Yes	1.10 (0.87-1.39)	1.09 (0.95-1.26)	1.02 (0.90-1.16)	Reference	1.07 (0.92-1.25)	
Breastfeeding						
No	1.23 (1.06-1.42)	1.17 (1.08-1.27)	1.13 (1.06-1.22)	Reference	1.35 (1.23-1.49)	.451
Yes	1.51 (1.22-1.86)	1.17 (1.04-1.31)	1.06 (0.96-1.17)	Reference	1.34 (1.17-1.54)	
Eating sweets irregularly						
No	1.33 (1.15-1.54)	1.16 (1.07-1.26)	1.08 (1.01-1.16)	Reference	1.32 (1.17-1.49)	.588
Yes	1.28 (1.05-1.57)	1.19 (1.06-1.34)	1.18 (1.07-1.30)	Reference	1.40 (1.25-1.57)	
Frequency of eating sweets, times/d						
1	1.15 (0.93-1.41)	1.22 (1.10-1.35)	1.09 (1.00-1.18)	Reference	1.38 (1.22-1.55)	.024
2	1.38 (1.18-1.63)	1.17 (1.07-1.29)	1.12 (1.03-1.21)	Reference	1.32 (1.17-1.48)	
≥3	1.40 (0.96-2.04)	0.99 (0.75-1.30)	1.22 (0.94-1.57)	Reference	1.35 (1.01-1.81)	
Daily juice consumption						
No	1.29 (1.08-1.54)	1.18 (1.07-1.30)	1.10 (1.02-1.20)	Reference	1.35 (1.20-1.52)	.96
Yes	1.31 (1.11-1.54)	1.15 (1.05-1.26)	1.12 (1.03-1.21)	Reference	1.35 (1.21-1.50)	

Values are ORs (95% CIs) unless stated otherwise.
All subgroup analyses were multivariable adjusted for child's sex, maternal age at delivery, gestational weeks, maternal alcohol consumption during pregnancy, maternal smoking during pregnancy, pre-eclampsia, anemia, threatened abortion, cesarean delivery, vacuum extraction, nuchal cord, asphyxia, jaundice and transfusion, convulsion, incubator, oxygen inhalation, girl, first-born child, birth weight and height, weight at 18 months, exposure to tobacco smoke at 4 months, number of teeth at 9 months, treated by fluoride varnish at 18 months, tooth brushing by own self tooth brushing at 18 months, tooth brushing by parents before sleep at 18 months, plaque present at 18 months, bottle to feeding at 9 months, age at start of baby food (months), baby food at 9 months, bottle to feeding at 18 months, breastfeeding at 18 months, eating sweets irregularly, frequency of eating sweets (1, 2, ≥3 times per day), daily juice consumption at 18 months, use of babysitter or nursery at 4 months/18 months, mental status of the mother at 18 months, support by family, friends, and neighbors at 18 months; and common comorbidities at 18 months (atopic dermatitis, asthma, asthmatic bronchitis, food allergy, varicella, pneumonia, severe diarrhea) and whether family members with allergenic disease.
*P values for interactions were computed by testing whether the coefficients on the interaction terms are jointly equal to zero with the use of mi test command for imputed date.