Sleep and sleep disordered breathing in the first year of life: a Canadian birth cohort study

by

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Abstract

Inadequate childhood sleep may adversely affect neurodevelopment, behaviour, and metabolic function. Few population-based studies have examined sleep duration and sleep disordered breathing (SDB) within the first year of life.

Families in the Edmonton site of the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort study completed sleep questionnaires (Pediatric Sleep Questionnaires (PSQ) and Brief Infant Sleep Questionnaire (BISQ)), and questionnaires related to child health, environmental/household exposures, and parental health, stress, and sleep when their child was 3, 6, 9, and 12 months of age.

The association between self-soothing and sleep duration (i.e. total amount of sleep during day and night as reported on the BISQ) was analyzed longitudinally with multivariate linear regression using generalized estimating equations (GEE) methods with exchangeable correlation matrix and robust errors. Infant sleep was also analyzed cross-sectionally when the child was 3, 6, 9, 12 months of age using multivariable linear regression.

The association between BMI Z-Scores and SDB (i.e. answering positively to more than 1/3 of the PSQ questions or a PSQ score of 0.33 or greater) was analyzed with cox proportional hazard modeling. The earliest PSQ score of 0.33 or greater was used to define time to SDB. Follow-up started at birth and data was censored at 12 months of age if the infant did not have SDB or at the child's age if and when loss to follow up occurred. In an additional analysis, PSQ questions relating to rhinitis were excluded and added in the multivariate model to investigate the association between rhinitis and SDB.

Of the 845 Edmonton CHILD participants, 765 had sleep duration data. Sleep duration was inversely associated with age. On average, infants slept 14.08 hours at 3 months, 13.66 hours at 6 months, 13.41 hours at 9 months, and 13.51 hours at 12 months of age. Non self-

soothing was consistently associated with shorter sleep duration in longitudinal and cross-sectional analyses. A multivariate longitudinal analysis stratified by birth order was performed. Self-soothing infants (-0.31 hours; 95% Confidence Interval (95%CI) -0.51, -0.11; p<0.001 for first-born; -0.57 hours; 95%CI -0.76, -0.37; p<0.001 for subsequent-born), sleep times after 21:00 (-0.67 hours; 95%CI -0.86, -0.45; p<0.001 for first-born; -0.61 hours; 95%CI -0.81, -0.42; p<0.001 for subsequent-born), and a parent who perceived their child's sleep as a small problem (-0.62 hours; 95%CI -0.84, -0.40; p<0.001 for first-born; -0.86 hours; 95%CI -1.08, -0.65; p<0.001 for subsequent-born) and very serious problem (-2.19 hours; 95%CI -3.00, -1.38; p<0.001 for first-born; -1.91 hours; 95%CI -2.52, -1.31; p<0.001 for subsequent-born) were significantly associated with shorter sleep duration in first-born and subsequent-born infants. A child's age was significantly associated with shorter sleep duration in subsequent-born infants but not first-born infants. In subsequent-born infants, infants that were fed only solid foods slept 0.87 hours less (95%CI -1.33, -0.41) and infants that were mixed-fed slept 0.74 hours less (95%CI -1.03, -0.50) than breastfeed infants (p<0.001 for both.) Feeding type was not significantly associated with sleep duration in first-born infants.

Of the 845 Edmonton CHILD participants, 763 had SDB data. By 12 months of age, 13% (101/763) of infants had SDB. BMI Z-scores were not significantly associated with SDB risk (Hazard Ratio(HR) 1.06 per standard deviation, 95%CI 0.80, 1.41; p=0.68). In multiple variable Cox regression adjusted for gender, factors that increased SDB risk included late prematurity (HR 2.09; 95%CI 1.05, 4.15; p=0.05), maternal symptoms for SDB (HR 1.80; 95%CI 1.12, 2.90; p=0.02), and otitis media (OM) (HR 2.09 per OM event, 95%CI 1.36, 3.31; p=0.00). Sleep duration decreased SDB risk (HR 0.82 per hour; 95%CI 0.70, 0.96; p=0.02). In

the multivariate model excluding PSQ questions regarding rhinitis, symptoms for rhinitis became the strongest risk factor for SDB (HR 3.08, 95%CI 2.05, 4.67; $p<0.001$).

Problematic infant sleep may be modifiable. First-born and subsequent-born infants have fundamentally different parent-infant interactions. Regardless of birth order, parent-infant interactions may be the most direct link in affecting infant sleep-wake regulation. Behavioural interventions that focus on parent-child interactions may be utilized to achieve optimal sleep in childhood. To mitigate SDB risk, treating or monitoring rhinitis in early childhood may reduce adverse consequences. Screening susceptible infants (late prematurity, males, infant with mother with SDB symptoms, infants with OM and rhinitis) may be a valid long-term strategy for SDB prevention and treatment.

Preface

This thesis is an original work by Amanda A. Lau. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Canadian Healthy Infant Longitudinal Development (CHILD) Study, Study ID: Pro00002099, July 2009 (Appendix 1).

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Started from the bottom, now we're here.

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List of Abbreviations

3HC	Trans-3'-hydroxycotinine
95%CI	95% Confidence interval
AAP	American Academy of Pediatrics
AHI	Apnea-hypopnea index
AllerGEN NCE	Allergy, Genes, and Environment Network of Centers of Excellence
ALSPAC	Avon Longitudinal Study of Parents and Children
BIC	Behavioural insomnia of childhood
BISQ	Brief Infant Sleep Questionnaire
BMI	Body mass index
BNSM	Benign neonatal sleep myoclonus
BSID-III	Bayley's Scale of Infant Development – Version III
CES-D	Centre of Epidemiological Studies-Depression
CHAT	Childhood Adenotonsillectomy Trial
CHILD	Canadian Healthy Infant Longitudinal Development
CIHR	Canadian Institutes of Health Research
DOHaD	Development origins of health and disease
EDS	Excessive daytime sleepiness
EEG	Electoencephalography
FTT	Failure to thrive
GA	Gestational age
GEE	Generalized estimating equation
GERD	Gastroesophageal reflux disease
GSAQ	Global Sleep Assessment Questionnaire
HR	Hazard ratio

LTFU	Loss to follow up
LUR	Land use regression
MAR	Missing at random
MCAR	Missing completely at random
MNAR	Missing not at random
NADPH	Nicotinamide adenine dinucleotide phosphate
NCC	National coordinating centre
NEPSY	Development Neuropsychological Assessment
NGF	Nerve growth factor
NICU	Neonatal intensive care unit
NK1	Neurokinin 1
NSF	National Sleep Foundation
OM	Otitis media
OSAS	Obstructive sleep apnea syndrome
P-CDI	Parent-child dysfunctional interaction
ppb	Parts per billion
PSG	Polysomnography
PSQ	Pediatric Sleep Questionnaire
PSS	Perceived Stress Scale
PLMD	Periodic limb movement disorder
PLMS	Periodic limb movement in sleep
REM	Rapid eye movement
RFA	Request for application
RLS	Restless leg syndrome
RMD	Rhythmic movement disorder
RSV	Respiratory syncytial virus

SDB	Sleep disordered breathing
SES	Socioeconomic status
SEM	Structural equation modeling
SIDS	Sudden infant death syndrome
SLEEP-E	Sleep, Learning, Education, and Environment Project - Edmonton
SPT	Skin prick allergy testing
T&A	Adenotonsillectomy
TNF-α	Tumor necrosis factor alpha
TRAP	Traffic related air pollution
trkA	Tyrosine kinase A receptor
UARS	Upper airway resistance syndrome
URTI	Upper respiratory tract infection
WHO	World Health Organization

Chapter 1: Introduction

1.1 Background

Humans spend approximately one third of their life sleeping[1]. A typical three-year-old child spends more time sleeping than in time awake[2]. Optimal sleep in childhood is important for neurodevelopment as it is an ideal time for the consolidation and integration of new memories[3]. As a result, high-quality childhood sleep sets the stage for future learning and development[4,5]. Despite the importance of sleep, numerous studies have suggested a decline in average sleep duration over the past few decades[6]. Increasing use of technology[7] and "modern lifestyles" (i.e. shift from an industrial economy rather than agrarian economy[8]) have been identified as possible contributors to the decline in sleep. This decline has been coupled with compromises in sleep quality[9] such as less time spent in deep sleep and less consolidated sleep[3]. The Centres for Disease Control and Prevention have identified insufficient sleep as an unrecognized public health concern[6].

There are few community-based studies focusing on young children and sleep[10]. This thesis uses data from the Edmonton site of the Canadian Healthy Infant Longitudinal Development (CHILD) Study and examines sleep during the first year of infant life. The purpose of this thesis is to: 1) investigate the factors that influence sleep duration with a focus on an infant's ability to self-sooth and 2) investigate the risk factors for a sleep disordered breathing (SDB) with a focus on the infant's BMI Z-score.

1.2 Literature Review

Sleep is a reversible state of decreased responsiveness and interaction with the environment[2,3] that results from diminished energy and waking[11]. Sleep is an actively regulated process with high levels of neurological and physiological activity[2]. Sleep is also pivotal for restoring physical and mental health[12] although the exact mechanism is not known. Sleep deprivation studies[3] have found that sleep is essential for growth[2], neurodevelopment[2,3], emotional health[13], immune function[2,3], metabolism[3], and hormonal regulation[3,14]. Developing brains need to spend considerable amounts of each day in sleep[1,9], therefore, optimal sleep in childhood is crucial and cannot be eliminated without deleterious consequences[3].

1.2.1 Sleep Regulation and Development. Sleep-wake regulation and sleep states develops most rapidly during the first year of life[15] with more moderate changes across childhood[16]. Two independent processes regulate timing and duration of sleep and wakefulness include: 1) the homeostatic process and 2) the sleep-wake cycle. During the homeostatic process, a requirement for sleep builds as periods of wakefulness increase[2]. The homeostatic process eventually mounts a strong enough sleep pressure so that sleep will occur regardless of the presence of stimulation[3]. Sleep pressures dissipate once sleep is achieved. The homeostatic process undergoes developmental changes referred to as sleep pressure tolerance [17] where sleep pressures accumulate more slowly with increasing age. Homeostatic sleep pressures accumulate slower during wake and dissipate slower during sleep in adults compared to infants[17]. Consequently, sleep patterns change since the ability to stay awake for consolidated periods during the day builds[18].

The sleep-wake cycle, which consists of several stages collectively referred to as sleep architecture, is controlled by ultradian and circadian rhythms. The ultradian rhythm is a biological rhythm with periodicity of less than 24 hours, while the circadian rhythm is a biological rhythm with periodicity of approximately 24 hours. Strong signals called zeitgeber (i.e. time givers or entrainment cues) are required to synchronize, or entrain, the sleep-wake cycle[19]. Environmental and social cues are the primary zeitgebers that dictate periods of inactivity (sleep) and activity (wake) for the sleep-wake cycle[1,2,20]. Environmental cues include light exposure and dark, while social cues include bedtime routines, timing of feeding or mealtimes, and noise[2].

A newborn's (<2 months) sleep-wake cycle is different than any other stage of life since they do not have fully established circadian rhythms[21]. A newborn's ultradian rhythm is approximately 50-minutes and cycles from wake to equal portions of quiet and active sleep[1,22]. Characteristics of quiet sleep include rhythmic, even breathing, minimal activity, and no eye movement[2,22]. Characteristics of active sleep include irregular, uneven breathing, muscle atonia, twitching, sucking motions, smiling, and eye movement[2,22]. Newborns have fragmented sleep since their homeostatic pressures accumulate more quickly and lead to less consolidated sleep[17]. Infant sleep-wake cycles are also strongly influenced by hunger and satiety rather than light and dark cues[23]. Shorter sleep periods coincide with early needs to be fed, changed, and nurtured[1].

Thus, newborns have irregular sleep schedules [1,2], sleep more frequently for shorter periods of time (longest period of sleep will last for 3 to 4 hours[23,24]), and have fragmented sleep that is distributed equally throughout the day and night[1,22].

Sleep and wake become more organized in infants (between 2 to 12 months of age) [2,15]. The circadian rhythm develops[2,15], which causes the ultradian rhythm to length. An infant's ultradian rhythm is approximately 90-minutes[25] and cycles several times from wake to non-REM (non rapid eye movement) to REM (rapid eye movement) before an individual wakes[26]. There are distinct levels of brain activity, autonomic response, and muscle tone associated with non-REM and REM sleep[2]. Non-REM sleep has four stages, each of which represents gradual depths of sleep and difficulties in arousal[2]. Characteristics of non-REM sleep include slow waves in electroencephalography (EEG), decreased muscle tone, and decreased eye movement[2,27]. Characteristics of REM sleep include intense EEG activity, muscle atonia, and bursts of rapid eye movement[2,26]. The differences between non-REM and REM sleep suggest that they perform different functions[3]. Non-REM sleep is important for visuo-motor and perceptual skills development[27], while REM sleep is important for memory function and processing emotional information[25,26].

Infants have more regular sleep schedules, decreased total sleep requirements[2], and more consolidated sleep (i.e. longer sleep times[2,15]) compared to newborns. The majority of infant sleep is nocturnal with longer periods of wakefulness during the day[15]. Infants typically sleep throughout the night by 6 months of age[23,28] and have diurnal sleep that is organized into shorter discrete naps[2] that account for 2 to 4 additional hours of recommended sleep[23]. Night awakenings and the need for parental intervention to reinitiate sleep may increase at in the second half of the first year of life of age[29,30] due to developmental changes related to socio-emotional, cognitive, and gross motor domains[29]. By 12 months, the longest nocturnal sleep period lasts approximately 10 to 12 hours[23,28].

1.2.2 Sleep Requirements. Sleep needs are age dependent and have a high level of inter-individual variability. A recent review found wide variations in sleep recommendations[31] (Table 1). The National Sleep Foundation (NSF) guideline, like many sleep guidelines, fail to include sleep references or explain how sleep recommendations were derived[31] despite being one of the most commonly cited age-dependent sleep guidelines[1,31].

Table 1: Sleep requirements by age group, adapted from Matricciani et al.[31]		
Reference	**Age**	**Sleep needs**
National Sleep Foundation[32]	Newborns (0 to 2 months)	12 to 18 hours
	Infants (3 to 11 months)	14 to 15 hours
	Toddlers (1 to 3 years)	12 to 14 hours
	Preschool-aged children (3 to 5 years)	11 to 13 hours
	School-aged children (5 to 10 years)	10 to 11 hour
	Teens (10 to 17 years)	8.5 to 9.5 hours
	Adults	7 to 9 hours
National Heart, Lung and Blood Institute[33]	Newborns	16 to 18 hours
	Preschool-aged children	11 to 12 hours
	School-aged children	At least 10 hours
	Teens	9 to 10 hours
	Adults (including the elderly)	7 to 8 hours
Alberta Health Services[34]	Infants and babies	14 to 15 hours
	School-age children	10 to 11 hours
	Adolescents	9 to 10 hours
	Adults	7.5 to 8.5 hours
Mayo Clinic[35]	Infants	12 to 13 hours
	Toddlers	11 to 13 hours
	School-age children	9 to 11 hours
	Adults	7 to 8 hours

Wide variations in sleep guidelines suggest that optimal and adequate sleep may not be definable in absolute terms[5] since sleep needs vary amongst individuals[2]. A major source of sleep variation (50%) is due to genetics[36] in conjunction with an individual's lifestyle and health[32]. Sleep recommendations are based two theories: sleep debt and sleep need. The homeostatic process creates a sleep debt[2], a sleep drive or pressure that increases as hours of wakefulness accumulate[2]. This sleep debt is at its peak when inadequate sleep occurs over multiple days[37]. Sleep debts dissipate as sleep is achieved and sleep needs are met. Sleep needs

are individually determined amounts of sleep that a body regularly requires for optimal performance[1]. Davis et al., 2004, suggest that an individual has optimal sleep (i.e. their sleep needs are met and their sleep debt is appropriately managed) if: 1) an individual can fall asleep easily at night (>20 minutes); 2) wake easily at their normal wake time; and 3) do not require daytime naps (except when developmentally appropriate) [13].

1.2.3 Objective Measures of Sleep. Polysomnography (PSG), also known as an overnight sleep study, objectively records sleep stages (awake, REM, and non-REM), as well as cardiovascular (e.g. heart rate), neuromuscular (e.g. limb movements), and respiratory changes (e.g. airflow, respiratory effort, oxygen saturation) [2,38,39]. PSG can qualitatively and quantitatively record abnormalities in sleep and wake, sleep architecture, sleep transitions, and the physiological function of organs systems that are affected by sleep[39]. As a result, PSG is the gold standard for studying sleep and for the diagnosis of sleep disorders such as SDB[40].

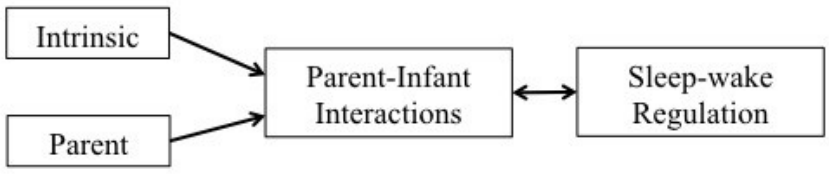
PSG can be performed in a clinical setting or at home. In-clinic PSG is actively monitored by a trained sleep technologist and as a result provides high quality data. In-clinic PSG, however, are cost prohibitive, labor-intensive, and inconvenient especially for young children[40]. Pediatric sleep laboratories with sufficient clinic capacity are also scarce, which has resulted in increased wait periods between referral and PSG testing[41]. Home PSG may be an alternative to in-clinic PSG as they are technically reliable with no significant difference in measurement outcomes (i.e. airflow, oxygen saturation, etc.) in highly selected adult populations [39,42]. Sleep duration and quality are significantly improved with home PSG due to the familiarity of sleep surroundings and unrestricted sleep times[42]. However, there is a greater potential for loss of data and poor data quality[42] with home PSG due to equipment difficulties, such as the removal of the nasal cannula during sleep or misplacement of probes[42]. Home PSG also lack standardized rules[39] for assessing sleep disruptions and have not been critically tested in a pediatric populations[41].

Actigraphs are wristwatch-like devices can also be used to objectively measure sleep-wake patterns based on activity monitoring[43] (i.e. body movements[44]). Raw activity scores captured by actigraphy can be translated into sleep-wake scores using a computerized scoring algorithm[43]. Actigraphy is invaluable for monitoring pediatric populations due to its non-invasive nature[45] and its ability to objectively measure activity and sleep in home settings for

extended periods of time[44]. Actigraphy and PSG demonstrate correlations typically above 0.80 for normal adult populations[46]. Meltzer et al., 2010, suggested that the validity of actigraphy in a pediatric population can be based on its sensitivity (i.e. the ability to accurate identify individuals with a disorder or event) and specificity (i.e. the ability to accurate identify individual without a disorder or event) in identifying periods of sleep when compared to PSG[45]. Actigraphy demonstrates high sensitivity, ranging from 83.4% to 99.3%, and lower specificity, ranging from 17.0% to 97.8% in a literature review of actigraphy validation studies[45]. Actigraphy is commonly used in pediatric sleep research; however, actigraphy data across studies is difficult to compare due to difference in scoring and reporting[45]. As a result, standardized methods of actigraphy scoring and reporting need to be developed in order to establish normative values for pediatric populations[45].

1.2.4 Factors that Affect Sleep Duration. Factors that affect sleep duration in childhood are multidimensional and include intrinsic factors (ethnicity, gender, age), parental factors (education level, socioeconomic characteristics) and extrinsic factors (routine, and environment) [47-49]. Infant sleep has been described in terms of a transactional model[50,51]. Sleep development is largely influenced by the dyadic relationship between intrinsic and parental factors: parent-infant interactions[52]. The transactional model emphasizes the dynamic, bi-directional association between parent-child interactions and sleep-wake regulation[52] and whether or not this regulation manifests as problematic sleep.

Figure 1: Transactional model of infant sleep, adapted from Sadeh[52]



1.2.4.1 Intrinsic Factors

a) Age: Age has a significance inverse relationship with sleep duration and describes about 50% of sleep variation[53]. The first six months of life has the fastest rate of sleep decline, with sleep declining about 2 hours within this age range [15]. From 6 to 12 months of age, sleep duration decreases from an average of 14.3 hours to 13.5 hours[54]. Sleep changes more moderately after the first year of life, with sleep declining 6 minutes for each year of age[55]. This decline is due to circadian rhythm maturation leading to greater organization of the sleep-wake cycle and a reduction in sleep requirements.

b) Gestational Age (GA): The association between GA and infant sleep is unclear. Very low birth weight, premature infants (born before 37 weeks GA) have 20 minutes less sleep than full-term infants[56]. In contrast, preterm infants sleep ranged an average of 5 minutes longer than full-term infants over multiple assessment points in the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort (n=11,478) [49]. GA may affect sleep duration through environmental differences in early development[57]. Light and dark cycles in neonatal intensive care units (NICU) may delay sleep architecture maturation and cause sleep-wake cycle immaturity[56,57]. Parents of preterm infants may also respond more readily to their child's arousals during sleep[38], preventing their child from learning self-soothing techniques important for sleep maintenance.

c) *Birth Order:* First-born children sleep less than subsequent-born children[29,58]. Scher et al., 2008, found that parents tend to perceive their first-born's sleep as more problematic than their subsequent-born infant[29]. Similar to parents of preterm infants, first time parents may have different parent-child interactions and respond more readily to sleep arousals when compared to parent-child interactions with their subsequent-born children[58]. Parental anxiety and unrealistic expectations of first time parents may also lead to the perception of greater sleep difficulties and shorter sleep durations[59]. This perception may account for parental report of first-born infants sleeping 1 hour and 19 minutes less than subsequent-born infants within a 24-hour period in a correlational design study of 74 mother-infant dyads[58].

d) Ethnicity: Genetic and cultural differences may lead to varying sleep durations. African American, Hispanic, Asian children (i.e. Non-Caucasians) slept 15 minutes less than their Caucasian peers between 6 months to 11 years of age in the ALSPAC birth cohort[49]. Many studies have noted similar trends, with sleep differences varying up to one hour in favor of

Caucasian children[9,47,60]. Genetic differences in African Americans may lead to differences in sleep architecture such as longer sleep onset, different depths of sleep, and different REM sleep stages compared to Caucasians[9]. Cultural practices also influence sleep routine enforcement, location of sleep, and parental levels of concern and perception of a child's sleep[49,60]. For example, non-Caucasian parents are more likely to co-sleep with their child than Caucasian parents[22,48], a practice that has been associated with shorter sleep duration[61].

e) Gender: Evidence for gender-specific sleep durations in young children is inconclusive[49]. Mong et al., 2011, proposed that sleep duration differ by sex because circadian rhythms are hormonally modulated[62]. Females tend to go to bed early, thus sleep longer than males[62], a difference that starts from adolescence and ends during menopause. Females slept 5 to 10 minutes longer than males until 11 years of age amongst participants of the ALSPAC birth cohort [49]. These findings are consistent with trends seen in older populations[47,49] suggesting there is a biological basis for gender-specific difference in sleep by age[49].

f) Obesity: A literature review found a consistent association between obesity and sleep duration; however, whether short sleep duration was a cause or consequence of obesity remains inconclusive[63]. Obese individuals may tend to be less active and require less sleep since they need less time to recover[64]. Tikotzy et al., 2010, found a significant Pearson's correlation of -0.47 between weight to length ratio and nocturnal sleep duration (excluding all periods of nighttime wakeful) amongst 6 month old girls in a four day follow-up study (n=94) [16]. Obese children are also two times more likely to have shorter, more disrupted sleep compare to normal weight children[65]. The association between obesity and reduced sleep may also be causal relationship in the opposite direction[63]. Several longitudinal studies support the notion that shorter sleep leads to obesity, with only one longitudinal supporting the opposite causal relationship[63].

1.2.4.2 Parental Factors

a) Parental-Infant Bonding and Self-Soothing: An infant's ability to self-sooth is crucial to sleep-wake pattern development and sleep duration[66]. A key element in an infant's ability to self-sooth is parent-infant bonding[66] due to an infant's high level of dependency on their mother[67]. Less securely attached infants (i.e. infants with insecure-attachment) have more sleep problems and greater difficulties falling back asleep compared to securely attached infants[1,30].

High parental involvement during bedtime is associated with decreased infant self-soothing techniques[61,66] due to decreased infant autonomy. Sleep difficulties were five times greater for infants who had parental presence until asleep compared to infants who fell asleep on their own[30,61].

b) Socioeconomic Status (SES): SES may be a proxy measure for unobserved clinical and environmental characteristics[68,69]. Lower SES infants may have shorter sleep duration because of household crowding, neighborhood disadvantages, increased chronic stress due to resource scarcity, poorer diets, and restricted access to high quality medical care[9,70]. Low maternal education and greater household sizes are associated with decreased use of bedtime routines[9,71,72] that result in shorter sleep durations. Children with mothers who did not attend post-secondary had 15 to 30 minutes less sleep than children with mothers who did attend post-secondary[60]. Children in families with incomes less than $40,000/year had 17 minutes less sleep than families with income greater than $70,000/year[72]. Household smoke exposure, which is associated with short sleep duration[60] and altered sleep architecture[73], may be explained by parental SES[60].

c) Marital Status: Parent-child interactions in two-parent and single-parent households may differ. Families with strong marital bonds may have higher levels of support and lower levels of stress[50]. As a result, children may have a greater sense of calmness and security, thus facilitating a healthy sleep environments[50]. Single-parent households use fewer bedtime routines[71], which may result in the child sleeping 40 minutes less than children of two-parent households[60]. Fathers in two-parent households may have an easier time implementing clinical suggestions (i.e. resist soothing techniques such as rocking, feeding, etc.) that promote infant autonomy and result in longer sleep durations than mothers[50].

d) Parental Mental Health: Prenatal and postnatal parental stress and depression can negatively impact infant sleep duration. Stress and depressive states in pregnant women result in higher levels of glucocorticoid which may disrupt their fetus' sleep-wake cycle's circadian rhythm[60]. Infants of mothers depressed during pregnancy slept 20 minutes less at one and two years of age compared to infants with mothers not depressed during pregnancy[60]. Post-natally, depressed parent may inadvertently foster an insecure attachment with their infants[59]. Infants with depressed mothers sleep 40 minute slept less than infants with non-depressed mothers[60]. Parents with mental distress may also have decreased competency in monitoring their child's sleep and bedtime habits[59] leading to decreased use of sleep routines and shorter sleep duration.

1.2.4.3 Extrinsic Factors

a) Sleep Routine: Consistent sleep routines, with enforced sleep and wake times, result in longer sleep durations. Routines provide a predictive, less stressful environment for young children[74]. Parents that use household routines may have lower parental mental distress[74]. These parents foster closer parent-infant bonds[74], which have been associated with longer sleep duration. Consistent sleep routines reinforce circadian cycles and homeostatic processes since children may associate these consistent bedtime cues with sleep[2,71]. Children that do have irregular bedtimes do not compensate for reduced sleep through napping or delayed wake-up times[47,75] resulting in lower total sleep durations. Sleep times before 21:00 (early sleepers) coincide with optimal environmental light and dark cue that aid in entraining the circadian rhythm[5,76]. Early sleepers had one hour more sleep than late sleepers (sleep times after 21:00) in a cross-sectional analysis of 18 to 36 month old infants (n=777) [77].

b) *Sleep Environment:* The ideal sleep environment is dark, free of environmental irritants, and has minimal noise[2]. Season can affect the sleep environment since longer light exposures in the summer can accelerate awaking or delay sleeping[2]. Child sleep durations during winter were 37.8 minutes longer than summer sleep durations in a longitudinal study of 7 year old children (n=519) [10]. Proximity to road traffic, transport related noise, and air pollution in more urbanized neighbourhoods have been associated with shorter sleep durations[72].

c) Sleeping Arrangement: Co-sleeping (i.e. bed sharing or room sharing with a parent)[78]is associated with shorter sleep duration due to frequent nighttime arousals, greater difficulty falling asleep, and less time spent in deep stages of non-REM sleep[2,30]. Co-sleepers may also become dependent on parental intervention and comforting for sleep maintenance[79]. Co-sleeping infants were two times more likely to be poor sleepers (i.e. sleeping less than six consecutive hours per night) at five months of age[61]. There are several potential confounders that may explain the association between co-sleeping and sleep duration such as breastfeeding and SES. Co-sleeping is more prevalent amongst low-income families and younger mothers[22].

d) Sleep Position: The American Academy of Pediatrics (AAP) launched the "Back to Sleep" campaign to facilitate a safe sleeping environment[2] in response to the high prevalence of sudden infants death syndrome (SIDS). However, prone sleepers (infants that sleep on their belly) have a 16% increase in hours spent in sleep and less frequent, shorter arousals[80] compared

to supine sleepers (infants that sleep on their back). Prone sleepers are able to create more ideal sleep environments by resting their face on a firm, warm surface[80] and reducing their exposure to sleep disturbances such as light and sound[80]. Ethnicity and SES may confound the association between sleep position and sleep duration . African-Americans and low-income mother are more likely to place their children in prone sleep position[2].

e) Breastfeeding: The World Health Organization (WHO) recommends exclusive breastfeeding up to 6 months of age and complementary foods with continued breastfeeding up to two years of age[81]. Breastfeeding is associated with shorter nocturnal sleep duration as breastfed infants have more fragmented sleep and greater night awakenings compared to bottle-fed infants[60,79]. Breastfed infants have shorter sleep for two reasons: 1) breast milk is digested faster than formula feeds or solid foods resulting in shorter periods of satiety and shorter intervals between feedings[28,30,79] and 2) mothers that breastfeed before bedtime may condition their infants to associate breastfeeding with sleep onset[30,79,82]. As a result, these infants are unable to self-soothe, which leads to shorter sleep durations.

f) Solid Foods: Early solid food introduction (i.e. before 6 months of age) is associated with shorter sleep durations[6]. 20 to 30% of mothers introduce solid foods to their infants before 4 months of age despite AAP recommendations[83]. These infants slept 25 minutes less at one year of age and 15 minutes less at two years of age compared to infants that were fed solid foods after 4 months[6]. Timing of solid food introduction may be a surrogate for SES and lifestyle factors[84]. Mothers that introduced solid food earlier tended to be younger, are unmarried, smoke, have lower education level, and lower income[83].

g) *Media Use:* Media use (i.e. television watching and computer use) increases an individual's arousal state impairing sleep initiation leading to poor sleep routines. As a result, media use is associated with shorter sleep[47]. Children as young as 6 months of age have significant media consumption despite AAP recommendations of no television viewing in infancy[60]. Every one hour increase in television watching (i.e. infant in an area for which a television could be viewed) was an associated with a 3 minute decrease in sleep duration per day at 6 months of age[85] and a 6 minute decrease in sleep duration per day at one year of age[60]. Older children with lenient bedtime rules may spend more time using media[55] thus leading to disruptions to regular sleep schedules[47,60].

1.2.5 Consequences of Insufficient Sleep. Sleep deficiencies negatively impact cognitive and neurodevelopment, behaviour, and metabolic function. The most immediate effect of insufficient sleep are impaired cognition[3], poor attention, poor concentration, and performance deficiencies[14]. Inadequate sleep in adults has been associated with compromised cognitive processing with sleep-deprived individuals performing motor skills two standard deviations lower than a control group that received adequate sleep[9]. Sleep deprivation in adults account for 15-20% of motor vehicle collisions[86] and sleep deprived children have an increased risk of non-intentional injury[15,76]. Insufficient sleep has also been associated with problems in memory consolidation which may impact learning and academic performance[10,15,87].

The relationship between sleep and behaviour problems is bi-directional[87]. Insufficient sleep is linked to internalizing and externalizing behavioural problems in children[10,71] with some children presenting with symptoms similar to attention deficient hyperactivity disorder[87]. Sleep problems are part of the key diagnostic criteria for affective disorders, posttraumatic stress disorder, depression, and anxiety disorders among adults [87]. Emotional and behavioural disorders may also lead to disrupted sleep[87].

Inadequate sleep been linked to metabolic disorders such as obesity[65,72,88] and type II diabetes[14]. Sleep loss mediates changes in the hormones responsible for appetite regulation[14,65] with increased levels of ghrelin, a hormone that signals hunger to the brain, and reduced levels of leptin, a hormone that signals satiety to the brain[14]. Sleep deprived individuals also have more waking hours to eat and will also have an increased appetite[14,65]. Sleep loss is associated with higher levels of glucose and reduced glucose metabolism, which in turn leads to insulin resistance[89].

1.2.6 Sleep Disorders. Sleep disorders are any conditions that interfere with the recovery process associated with sleep**[13].** Sleep disorders affect 25-40% of children between the ages of 1 to 5 **[5,90].** Few studies have examined the prevalence and impact of sleep problems in infants under one year of age**[91]**. Sleep disorders are classified into parasomnias and dyssomnias.

1.2.6.1 Parasomnias. Parasomnias are undesirable physiological or behavioural events that occur during sleep onset, between sleep stage transitions, or during arousals from sleep[13,92]. Parasomnias are more common in childhood and are reflective of central nervous system

immaturity, thus they are usually benign and outgrown in adulthood[13,93]. Parasomnias are classified into three categories: non-REM, REM, and other parasomnias.

Non-REM parasomnias occur during arousals from slow wave (non-REM) sleep[92] and may involve simple behaviours such as confusion (i.e. confusional arousals), agitation (i.e. night terrors) [13,94] or complex behaviours such as sitting up in bed or walking[13]. Most non-REM parasomnias are associated with mental confusion and amnesia concerning the event [92]. REM parasomnias, which occur while dreaming[94], include nightmares[94]; REM behaviour disorder (harmful dream-enacting behaviours) [1]; and recurrent isolated sleep head and limbs paralysis [94]. REM parasomnias are more prevalent in adults, but onset can occur in infants as early as 11 months of age[94]. Other parasomnias, which are sleep stage independent, include somniloquy (i.e. sleep talking), sleep related eating disorder, circadian rhythm sleep disorders, narcolepsy, and sleep enuresis (i.e. involuntary bladder voiding). Sleep enuresis is normal in children under 5 years old [92,94] but is also commonly associated with SDB (a dyssomnia).

1.2.6.2 Dyssomnias. Dyssomnias, disorders related to sleep initiation, maintenance, or consolidation[5,13,92], can affect the quality, duration, or timing of sleep[5,13]. Dyssomnias include behavioural insomnia of childhood (BIC), sleep-related movement disorders, and SDB.

BIC are difficulties with sleep onset (i.e. bedtime resistance or refusal) or sleep maintenance (i.e. prolonged night-time awakenings) [13,95] and are classified into three categories: sleep onset association type, limit-setting type, and combined type. Sleep onset association type BIC is associated with troubles initiating or re-initiating sleep independently and an inability to self soothe since sleep becomes associated with certain environments or settings (e.g. parental presence, being rocked, or being feed) [13,92,95]. Children with limit-setting type BIC have a delay in sleep onset[13] because they make excessive bedtime requests or refusals as the parent has difficulty setting sleep limits[13,92,95]. Combined type BIC is a combination of sleep onset association type and limit-setting type.

Sleep related movement disorders are simple stereotyped movements that disturb sleep[96]. Sleep related movement disorders include: benign neonatal sleep myoclonus (BNSM), rhythmic movement disorder (RMD), periodic limb movement in sleep (PLMS)/periodic limb movement disorder (PLMD), and restless legs syndrome (RLS).

BNSM prevalence is unknown but assumed to be common[97,98]. Myoclonus are brief, sudden, shock-like involuntary movements[97]. BNSM are sleep-related repetitive, rhythmic myoclonic movements of the body, trunk or limbs [92,97,98]. Abnormalities in the peripheral nervous system and CNS may cause BNSM, but the precise etiology is unknown[99]. BNSM spontaneously resolves typically by 3 months of age[97,98] and requires no further treatment[92].

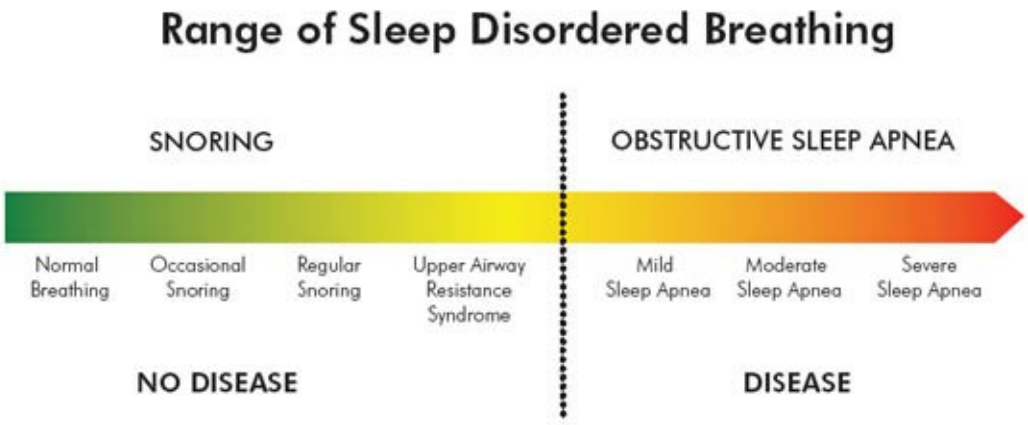
RMD incidence is 66% in 9 month olds and declines with age, affecting 6% of 5 year olds[100]. RMD are repetitive, stereotyped, and rhythmic movements of large muscle groups such as the head, trunk and limbs that occur during sleep[92,101]. Studies have suggested that RMD is a learned self-soothing behaviour that aids in the transition from wakefulness to sleep[100]. The rhythmic movements may also serve as a vestibular form of self-stimulation[100]. Symptoms of RMD include daytime impairment and self-inflicted bodily injuries[92]. RMD often spontaneously resolves by 5 years of age[101]; however, severe cases of RMD can be treated with benzodiazepines such as clonazepam[92].

PLMS affects between 12%[102] to 17%[103] of children. PLMS are brief movements lasting 0.5 to 5.0 seconds in 20 to 40 seconds intervals[92,102] that usually occur in the lower extremities[92] such as the legs, feet, and toes[102]. PLMD is defined as ≥5 PLMS per hour of sleep with symptoms of sleep disturbances[102]. Underactive dopamine function in the central nervous may cause PLMD[102]. Symptoms of pediatric PLMD include growing pains, restless sleep, and hyperactivity[103]. PLMD treatment includes iron supplementation and dopaminergic medications[103].

RLS is a neurological disorder that affects 1.9% of children [102]. RLS is characterized by uncomfortable, unpleasant sensations in the legs accompanied with an urge to move the leg[104,105]. These sensations occur at rest but are the worst at night and may be transiently relieved by leg movements[102,104,105]. Symptoms of pediatric RLS include difficulties falling asleep, bedtime resistance, and negative mood and behaviours that are similar to attention-deficit/hyperactivity disorder[104]. RLS may be caused by dopamine dysfunction[104,105], genetics[104,105], and iron deficiency[104,105]. Similar to PLMD, RLS treatment includes iron supplementations[102] since iron is integral for the biosynthesis of dopamine[105] and pharmacological treatment with clonazepam, clonidine and dopaminergics[102].

1.2.6.3 Sleep Disordered Breathing (SDB). SDB is a spectrum of diseases associated with abnormal breathing and/or gas exchange during sleep[106]. The least severe disorder in this spectrum is snoring progressing to upper airway resistance syndrome (UARS) and then obstructive sleep apnea syndrome (OSAS), the most severe form of SDB (Figure 2) [68,107,108]. There is limited data on SDB in young infants[107,109] as most epidemiology studies focus on older children. The prevalence of clinically observed SDB ranged from 0.1% to 13.0%[110] depending on the methodologies used to diagnose SDB[109]. Challenges in SDB diagnosis include variations in symptom definitions (e.g. snoring) [110], different symptom screening methods[110], and the heterogeneity in the objective diagnostic criteria for SDB[110]. Many studies focus on OSAS, the most clinically significant form of SDB [108,111]. OSAS affects approximately 1% to 4% of children[68,109]. Pediatric OSAS prevalence peaks in children 2 to 8 years of age, which coincides with the developmental peak of adeno-tonsillar hyperplasia[112,113].

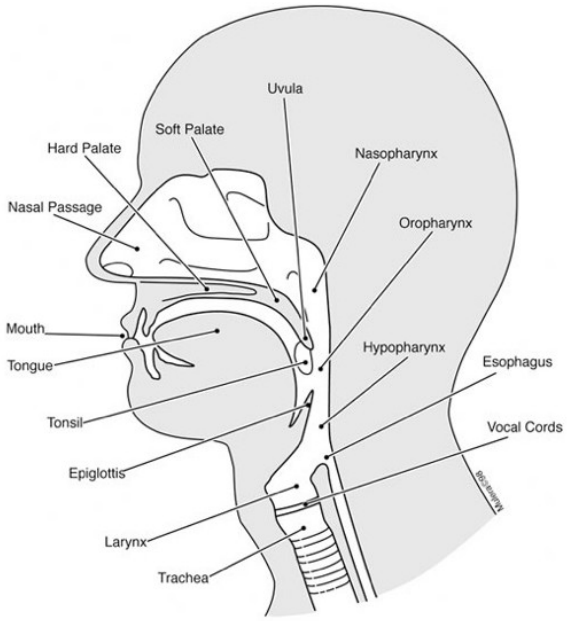
Figure 2: Spectrum of SDB[114]



1.2.6.3.1 Pathophysiology. Risk factors for the development of SDB include a combination of factors associated with upper airway dysfunction or collapse during sleep[108]. The upper airway, a passage responsible for moving air from the nose into the lungs, is divided into four anatomical sub-segments: nasopharynx (between the nares and hard palate), velopharynx (between the hard palate and soft palate), oropharynx (from the soft palate to the epiglottis) and hypoharynx (from the base of the tongue to the larynx) [115] (Figure 3). The upper airway's cross-sectional area changes due to the activity of primary and accessory respiratory

muscles in response to airway pressures to control airflow[109]. Anatomical structure, neuromotor tone, and inflammation affect the upper airway's ability to intake air. These same factors are important contributors to the pathophysiology of SDB[68,111].

Figure 3: Anatomy of the upper airway[116]



Children with SDB have structurally narrower upper airways and increased nasal resistance asleep and during wakefulness[109,111]. These anatomic differences may be due to any abnormalities that occur between the nose and trachea[108]. Nasal polyps, craniofacial dysmorphology, micrognathia (undersized jaw), retrognathia (overbite), high-arched palate, macroglossia (large tongue), and adenotonsillar hypertrophy are common anatomic abnormalities that contribute to SDB[92,108,109]. Anatomical abnormalities in the upper airway and SDB have a bi-directional association[109]. Chronic mouth breathing can lead to adenoid facies (long face syndrome), a high arched palate, and poor maxillary growth resulting in a narrower nasal passage and changes in facial growth that further increase the risk of SDB[111,112].

Abnormalities with neuromotor tone can also contribute to SDB pathophysiology[115]. Neuromotor tone contributes to the baseline size and stiffness of the upper airway[117]. Muscles that surround the upper airway actively constrict and dilate the upper airway lumen[115] in

response to hypoxemia, hypercapnia, and upper airway sub-atomspheric pressure[118]. Upper airway collapsibility is inversely related to the activity of the upper airway dilator muscles[119]. An increase in upper airway neuromotor tone and upper airway muscle activation may compensate for increased upper airway narrowing and collapse[119,120]. Upper airway tone is decrease in non-REM sleep. Upper airway tone is inhibited in REM sleep which lead to the airway narrowing and increase resistance to airflow[117]. Factors that reduce neuromotor tone can contribute to the pathogenesis of SDB by increase the propensity for airway collapse and obstruction[117]. Allergies or infections can cause nasal or pharyngeal inflammation that may restrict upper airway dimension[119] and lead to increased upper airway resistance[112]. Sleep fragmentation and hypoxemia can also lead to cellular inflammation altering the airway's function[108].

1.2.6.3.2 Clinical Symptoms. The nocturnal and diurnal presentations of SDB are different for adults and children[118]. The presentation of SDB in children has greater inter-individual variability than in adults since symptoms change with age. The increased symptom variation in children makes SDB more difficult to diagnose [40,107,111]. Clinical presentation of SDB may not accurately reflect the severity of the disease[112]. Snoring, for example, presents in both primary snoring (i.e. least severe form of SDB) and OSAS (i.e. most severe form of SDB) [112].

Snoring is a harsh noise that occurs during sleep when respiration causes the soft palate to vibrate[110,121]. Snoring may be due to increased upper airway resistance[107] which lead to imbalances between intrathoracic pressure and oropharyngeal dilator muscles[111]. Snoring is typically benign (i.e. primary snoring), but it may result from upper airway abnormalities and is considered one of the first signs of more severe forms of SDB[110]. Snoring is the main symptom for the most severe form of SDB, OSAS[91,122]; however, snoring alone is not indicative of SDB or pathological breathing patterns[112]. Approximately 20% of children snore intermittently[112] and 27% of children snore habitually[107]. The majority of children with OSAS snore loudly[112],

UARS occurs when there are increasingly negative inspiratory pressures[110] that occur concomitantly with decreased oronasal airflow[123]. As a result, UARS presents as nighttime choking and snorting[109,112] resulting in sleep arousals and fragmentation. UARS, however, is not associated with significant decreases in airflow or oxygen saturation [110,112].

OSAS is characterized as prolonged partial (hypopneas) or complete (apneas) upper airway obstruction that disrupts normal ventilation and sleep patterns[13,110,124]. These obstructions are associated with increased respiratory efforts and leads to mouth breathing[112], night sweating[111], and enuresis[111]. OSAS affects bladder functioning due to pressure changes in the intrathoracic space and abdomen that may directly lead to abdominal compression that results in enuresis[94].

Fragmented and disrupted sleep, a consequence nocturnal SDB symptoms[109], explain the diurnal symptoms associated with SDB. Excessive daytime sleepiness (EDS) is the most prominent daytime symptom in adult SDB, although EDS rarely presents in children[112]. Diurnal symptoms amongst children with SDB include bedtime resistance, difficulties arousing from sleep, napping, inattention, hyperactivity, aggression, and depression[40,109,112,124]. Diagnosing SDB in childhood based on these symptoms is difficult due to their subjective nature while symptoms such as napping and bedtime resistance may be part of normal development[112].

1.2.6.3.3 Diagnosis. Pediatric SDB often remains unrecognized and untreated because there is no standardized method or criteria for identifying patients[91,109]. Diagnostic difficulties are due to the wide variation in clinical presentation due to individual[109] and seasonal factors[124], as well as the failure to account for an individual's susceptibility to develop diurnal symptoms associated with SDB[109]. Questionnaires, clinical histories, physical examination, imaging, and polysomnography (PSG) are the main methods used to diagnosis SDB.

Questionnaires and clinical histories are the main methods used to identify symptoms of SDB[108]. There is no universally accepted definition of snoring[110] despite this symptom being the major focus of these methods. Questionnaires and histories are subjective and cannot conclusively determine which individuals need immediate clinical intervention[107,108].

Physical examinations and imaging can identify anatomical characteristics associated with SDB. Physical examination can identify adenotonsillar hypertrophy or craniofacial morphologies (e.g. positioning of the palate, maxilla, and mandible) that predispose an individual to SDB[108]. Orocraniofacial clinical scoring system can be used in conjunction with tonsil size scoring to help predict the probability of SDB[112]. Imaging can identify upper airway characteristics such as smaller cross-sectional areas or smaller airway volumes that contribute to SDB pathophysiology[108].

PSG can be used to diagnose SDB and assess SDB severity[111,122] by identifying apneas, hypopneas and arousals during sleep. PSG interpretations will vary by developmental group because of the differences in pediatric and adult SDB[112]. Apneas are complete airway collapses that result in cessation of breathing (100% airflow reduction) and are associated with hypoxemia and hypercapnia[92,125]. Apneas in children are respiratory pauses that occur for at least 6 seconds (1½ to 2 breaths) [112] and are accompanied by oxygen desaturations under 92%[126]. Apneas in adults are respiratory pauses that occur for at least 10 seconds and are accompanied by oxygen desaturation under 85%[126]. Hypopneas are defined as a partial airway collapse that causes shallow breathing (reduced airflow by 50% or greater) for at least 10 seconds in adults[101] and for 2 respiratory cycles in children[127], accompanied with a drop in blood oxygen saturation[125]. Apneas and hypopneas measured on PSG are used to calculate sleep efficiency, arousal indexes, and apnea-hypopnea index (AHI). AHI is calculated by totaling the number of apneas and hypopneas and dividing this number by the total sleep time in hours. An AHI greater than 1 in children and greater than 5 in adults is considered severe SDB[126].

1.2.6.3.4 Risk Factors for SDB. SDB risk is altered by genetics, environmental exposures, and gene-environment interactions[128]. The greatest risk factor for SDB in adults is obesity, while the greatest risk factor for SDB in children is adenotonsillar hypertrophy.

a) Adenotonsillar Hypertrophy: Adenotonsillar hypertrophy, which is at its developmental peak between 2-8 years[112,113] is one of the strongest risk factors for pediatric SDB [68,92,129]. Adenotonsillar hypertrophy leads to airway size narrowing resulting in increased upper airway resistance[109,113]. Adenotonsillectomy (T&A), the recommended treatment for pediatric SDB[122], alleviates SDB symptoms in 83% of patients[92]. SDB symptoms, however, may persist even after T&A due to the presence of additional SDB risk factors such as craniofacial abnormalities (e.g. Trisomy 21) or obesity[92].

b) Obesity: Obesity increases SDB risk because greater parapharyngeal fat deposits may alter chest wall mechanics and ventilatory control, leading to reduced upper airway dimensions [108,109,128]. Obesity is seen in half of the cases of SDB[109]. Obese children with SDB also have an increased risk of adenotonsillar hypertrophy[109] as a result of altered endocrine mediate somatic growth associated with obesity[130]. Obesity is the strongest risk factor for SDB in adults[110], but methodological challenges such as non-age or sex-specific BMI measurements have lead to

greater difficulties in interpreting the association between obesity and pediatric SDB[110] across studies. Redline et al., 1999, found that obese children (body mass index (BMI) >28) between 2 to 18 year old were four times more likely to have SDB than non-obese children[131]. There is a dose-dependent relationship between BMI and SDB [110,113]. OSAS risk, in particular, increases by 12% with every 1kg/m^2 increase in BMI above the average BMI within a pediatric population[109].

c) Sex: A recent literature review reported no difference by sex in the prevalence of pediatric SDB in most studies[110]. Males have an increased incidence of SDB starting from puberty and have SDB prevalence that are more commonly see in adults[109,110]. Sex hormones[110,111] may influence respiratory controls and body fat distribution[131,132]potentially explaining the increased incidence of SDB for males during puberty.

d) Family History of SDB: Family history of SDB, a marker of genetic risk[129], is associated with at least a two times greater risk of pediatric SDB[131]. Children may inherit craniofacial structures, ventilator control, neuromuscular compensation, and body fat distributions that increase their susceptibility to SDB if their parent has SDB[109,133]. Up to 40% of the variance in AHI among children with PSG diagnosed SDB could be explained by familial factors[134]. Twin studies have shown the concordance of snoring was higher in monozygotic twins than in dizygotic twins suggesting that specific gene(s) may be associated with the SDB[133,134]. There is limited literature on the association between specific genetic polymorphisms and SDB-associated morbidities[135]. Genes responsible for apolipoprotein E, tumor necrosis factor alpha (TNF-α), and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase have been implicated in contributing to SDB consequences[135]. Further research is needed to clarify the contribution of these genetic markers and possibly additional markers to SDB risk.

e) Ethnicity: Craniofacial differences between ethnic groups can result in increased airway resistance and subsequently increase SDB risk. Non-Caucasians are at a higher risk for SDB compared to Caucasians [70,110]. Asians have smaller maxilla and mandibles[136] and African Americans have increased upper airway soft tissue[109,134] resulting in upper airways that are more prone to collapse compared to Caucasians. Consequently, Asians and African Americans have average higher AHI values[133,137] and are more likely to have SDB than Caucasians[70,137]. SES may confound the association between ethnicity and SDB. Neighborhood level variables related to SES (i.e. different environmental exposures) explain 50% of the association between SDB and

ethnicity[133]. Cultural practices that influence sleeping environments and parental behaviours could further influence a child's risk of SDB[131].

f) GA: Premature infants have up to a threefold greater risk of SDB compared to full term infants[138]. Prematurity may predispose individuals to adverse craniofacial growth[109,138], abnormal development of respiratory control and ventilator control[109,139], and neurological impairment[109]. These abnormalities cause altered airway sizes[139] and increased airflow obstruction that results in a greater propensity for airway collapse. OSAS risk, in particular, decreases as GA increases (Hazard Ratio (HR): 1.30 for infants born 33-35 weeks, HR: 1.15 for infants born 36-38, and HR: 0.97 for infants born 38 weeks) [138]. Premature infants may also be at a higher risk for SDB due to differing in their perinatal exposures[139].

g) Chronic diseases and respiratory illnesses: Atopic diseases (asthma, allergies, eczema) and upper airway disease (e.g. sinus problems, rhinitis, sinusitis) are associated with increased SDB risk[131]. Allergic rhinitis leads to upper airway inflammation resulting in airway[122]. Sinus problems and allergies increase upper airway resistance promoting airway collapse[131]. Asthma may exacerbate SDB[122] due to common risk factors that promote airway inflammation and disrupt neuromuscular controls involved in breathing[131]. Children with a history of asthma are four times more likely to report SDB symptoms[131]. Upper respiratory tract infections (URTI) increase upper airway resistance leading to upper airway collapse, which promotes hypopneas or apneas[131]. Children with cold symptoms like coughs are nine times more likely to report SDB symptoms [131]. Pediatric SDB prevalence varies seasonally and may be due to seasonal variations of allergies, asthma, and wheezing [122]. Moderate to severe OSAS was significantly worse in in the winter (November to March) than in the summer (June to September) among patients with PSG confirmed SDB[122].

h) Craniofacial syndrome and Neuromuscular weakness: Children with craniofacial abnormalities such as Down's syndrome, Prader-Willi, and Crouzon syndrome are at increased risk of SDB[92]. Facial abnormalities such as midfacial and mandibular hypoplasia, macroglossia, shortened palate, and narrowed nasopharynx all contribute to upper airway narrowing[140]. Neuromuscular disorders such as cerebral palsy, congenital or acquired myopathies and muscular dystrophies affect upper airway control and respiratory muscle function increasing the risk of SDB [124,128].

i) Viral exposures: Viral exposures can increase the risk of adenotonsillar hypertrophy, leading to upper airway obstruction and SDB[68,82,141]. 100% of children are infected with respiratory syncytial virus (RSV) during the first year of life[142]. RSV leads to neuroimmunomodulatory changes such as increased expression of nerve growth factor (NGF), tyrosine kinase A receptor (trkA), neurokinin 1 (NK1) receptors, and substance P in the respiratory tract[143]. These changes enhance inflammatory processes in the adenotonsillar tissue to accelerate proliferative responses and promote adenotonsillar hypertrophy[142].

j) Breastfeeding: Breast milk provides immunologic protection against early viral respiratory exposures and has been associated with decreased SDB risk [91,141]. Breastfeeding is associated with healthy jaw formation and oral cavity development[141]. Conversely, bottle-feeding has been associated with altered swallowing pattern that increase the risk of collapse and narrowing in the upper airway[91]. Children who were not breastfed had a 1.47 increased odds of SDB compared to children that were breastfed in the ALSPAC study[68]. The duration of breastfeeding is inversely associated with SDB severity. Breastfeeding durations longer than 4 months were associated with a significantly lower AHI (AHI of 2 compare to an AHI of 6) compared to infants who were breastfed for less than 4 months in a cross-sectional study of 7 year old children[141].

k) SES: Individual in lower SES households may have a higher exposure to indoor and outdoor irritants (i.e. greater proportion of parental smoking), as well as allergens[109,144] leading to a greater risk of upper airway inflammation and collapse[133]. Low-income families had a higher proportion of infants (42.5% vs. 5.8%) with adenotonsillar hypertrophy compared to high-income families[129]. Parents with lower educational levels and manual labor jobs had children with at least a 20% increased risk of SDB in a longitudinal birth cohort [68].

l) Smoking: Smoking, a chronic irritant that causes upper airway inflammation[133], leads to upper airway narrowing and resistance[91,145]. Smoking and smoke exposure may also affect neurotransmitter levels that are involved in ventilatory control[133]. Having at least one household member smoke results in a 75% increased risk of childhood SDB [136]. Every 1ng/mL increase in serum cotinine, a metabolite of nicotine used to quantify environmental tobacco smoke, lead to a 1.29 increased odds of SDB symptoms in asthmatic children[73]. However, the amount of smoke exposure needed before SDB symptoms present remains unknown[91].

1.2.6.3.5 Consequences of SDB. Children with untreated SDB have an estimated 226% increased health care cost[146] due to higher hospitalization rate, emergency room visits, and medication use[108]. SDB is associated with cardiovascular morbidity, metabolic syndrome, and neurodevelopmental morbidity. It is unclear whether the consequences of SDB are a result of fragmented/disrupted sleep or hypoxemia[108].

Pediatric SDB is associated with cardiovascular morbidity which may have implications for long-term cardiovascular mortality[108]. SDB can alter autonomic function and cause systematic hypertension, alterations in blood pressure regulation, and increased heart rate[108,128,147]. There is a significant dose dependent relationship between SDB severity [108,128]. Pulmonary hypertension[147] associated with SDB may change ventricular geometry[128] and increase the risk of structural heart disease. SDB has been linked to left and right ventricular hypertrophy, cor pulmonale (right-side heart failure), and decreased left ventricular function[40,109].

Children with SDB have a six-fold increased risk of having metabolic syndromes[108,128] including obesity, insulin resistance, and dyslipidemia[108,128]. EDS associated with SDB can lead to reduced physical activity promoting weight gain[132]. Elevated levels of leptin, a hormone that regulates metabolism, and hunger, can also increased appetite[109]. SDB increases sympathetic nervous system activity and potentially alters inflammatory cytokines responsible for oxidative stress. These changes contribute to insulin resistance and impaired glucose tolerance[132]. Failure to thrive (FTT), due to increased respiratory efforts during sleep and a reduction in insulin growth factor[109] is also observed in children with SDB.

SDB, especially in the first year of life, may affect short and long-term neurodevelopment [91,110]. It has been suggested that chronic SDB leads to prefrontal cortical dysfunction that results in impaired executive functioning and behavioural difficulties[92]. Preschool aged children with a history of loud and frequent had lower academic performances during middle school in a longitudinal study[109]. However, early treatment of SDB with T&A did not lead to significant changes in attention or executive functioning scores as measured by the Development Neuropsychological Assessment (NESPY) compared to watchful waiting (7.1 change in score for T&A versus 5.1 change for watchful waiting) in the Childhood Adenotonsillectomy Trial (CHAT) Study[148]. Fragmented sleep and hypoxia, associated with severe SDB, may be responsible for neurotransmitter dysfunction and neuronal cell loss, leading to impaired cognitive

functioning[9,128]. SDB has been associated with hyperactivity, depression, anxiety, and low performance on cognition measures such as attention, memory, and executive functioning[109,112,145].

1.3 Canadian Healthy Infant Longitudinal Development (CHILD) Study

The CHILD Study is an ongoing national general population based birth-cohort study with base funding from the Canadian Institutes of Health Research (CIHR) and the Allergy, Genes, and Environment Network of Centers of Excellence (AllerGEN NCE). The developmental origins of health and disease (DOHaD) hypothesis suggests that prenatal and early childhood exposures can influence an individual's health and disease in adulthood[149]. In 2005, the CIHR announced a Request for Application (RFA) entitled "Indoor air exposures, genes, and gene-environment interactions in the etiology of asthma and allergy in early childhood" [150]. The CHILD Study was developed, in response to this RFA and based on the DOHaD hypothesis, to study the origin, development, and natural history of childhood asthma and allergies[151]. CHILD infants and their families are assessed prenatally and then annually until the child is 5 years of age using multiple methods including questionnaires, home inspections, biological sample collection, as well as in-clinic and at home testing. The study's primary objective is to determine the role of environmental factors and their interactions with genetic and immunological determinant in the development of allergies and asthma in childhood[150]. Secondary outcomes of the study include innate immunity, nutrition and intestinal microbiome, sleep and neurodevelopment, infant lung function and infection, and psychosocial outcomes[150].

Sleep, Learning, Education, and Environment Project- Edmonton (SLEEP-E) is a sub-study implemented within the Edmonton site of the CHILD Study. CHILD SLEEP-E infants and parents complete additional questionnaires, as well as in-clinic and at home testing related to infant neurodevelopment and sleep (Appendix 2). The purpose of CHILD SLEEP-E is to 1) Identify individual characteristics and environmental exposures that increase SDB risk within children and 2) To examine neurobehavioural consequences of SDB[152].

1.4 Summary

Sleep is one of the earliest examples of biobehavioural organization and adaptation[87]. As a result, sleep, especially in the first year of life, is a vulnerable process due to the rapid development of sleep-wake cycles, sleep patterns, and sleep behaviours[60]. Longitudinal birth cohorts, like the CHILD SLEEP-E, are invaluable in studying the natural development of sleep and elucidating the reasons for individual variability and causes for sleep disorders, such as SDB. Complex interactions between intrinsic, extrinsic, and parental factors shape sleep and whether or not this sleep manifests as sleep disorders. The strength of this thesis is its use of longitudinal data and analysing the critical first year of sleep development within a research field that consists primarily of cross-sectional studies. Identifying factors that affect sleep duration and lead to SDB is beneficial since optimal childhood sleep is critical in shaping future development and health[4,5].

1.5. Objectives

Primary Objective: To investigate the effect that parental-infant interactions and other modifiable sleep factors (i.e. sleep routine and sleep environment) have on total sleep duration for infants within the first year of life.

Secondary Objective: To investigate the relationship between BMI and additional risk factors (i.e. duration of breastfeeding, chronic illness, and GA) on the risk of developing SDB among infants within the first year of life.

1.6 Hypotheses

Primary Hypothesis: Infants that are self-soother (i.e. do not need soothing/parental intervention to fall asleep) sleep longer in the first year of infant life than infants that are non self-soother.

Secondary Hypothesis: Infants with a higher BMI Z-score within the first year of infant life have a greater risk of SDB than infant with a lower BMI Z-score.

Chapter 2: Materials and Methods

2.1 Overview

This thesis examines SLEEP-E CHILD Study infants and families (n=843) prenatally until the first year of infant life. Child, family and environmental variables were compared between participants to investigate their effects on two aspects of infant sleep: sleep duration and SDB.

Study variables include a child's ability to self-soothe (primary exposure variable), sleep duration (primary outcome variable), infant's BMI Z-score (secondary exposure variable), SDB (secondary outcome variable), and other variables and possible confounders related to sleep duration and SDB. Other variables/confounders include child characteristics (i.e. GA, sex, birth order, general health), family characteristics (i.e. SES, parental stress, family history of sleep problems/SDB), and environmental characteristics (i.e. proximity to pollutants, smoke exposure).

2.2 Study Population

The CHILD Study recruited 3629 eligible pregnant women (Table 2) from Edmonton, Vancouver, Toronto, and Winnipeg. Recruitment occurred at high volume maternity clinics, smaller volume clinics, community locations (i.e. tradeshows, maternity stores), and through advertisements in local media (i.e. printed ads, radio) from August 2008 to April 2012. Final enrolment was confirmed post-partum since gestational age was part of the inclusion criteria. Father participation in the study was optional and fathers (n=2600) were given a separate consent from mothers. The CHILD Study consists of two cohorts: a Vanguard cohort (i.e. pilot cohort) and a general cohort. The Vanguard cohort consists of approximately the first 5% of the participants enrolled at each site and was utilized to refine methodology as well as assess the acceptability and feasibility[153] of the study. This cohort runs in parallel with the general cohort, which consists of all other CHILD participants. The study was approved independently by each of the recruitment centre's respective Health Research Ethics Board.

CHILD SLEEP-E subjects (n=843 mothers/infants and n=735 fathers), CHILD participants from the Edmonton site, completed additional sleep questionnaires and testing (i.e. in-home PSG, neurodevelopment). Subjects could verbally opt out of questionnaires completion and in-clinic or at home testing at any point in the study. CHILD SLEEP-E infants (n=589) completed in-home PSG at 12 months of age.

Table 2: Eligibility criteria for the CHILD Study	
Inclusion criteria	**Exclusion Criteria**
Pregnant women that: • were 18 years of age or older (19 years of age or older in Vancouver) • lived within in reasonable proximity to one of the recruitment centres • are able to read and speak English • planned on giving birth at one of the recruitment centre's affiliated hospitals • had a valid number and address • were willing to give informed consent Infants that: • were born at 35 weeks gestational age or greater	Pregnant women that: • planned on moving away from their recruitment centre within 1 year Infants that: • resulted from in vitro fertilization • were born with major congenital abnormalities • were one of multiple births • did not spend at least 80% of nights in the participants home

2.3 Study Design

CHILD Study mothers completed questionnaires (www.canadianchildstudy.ca/questionnaires.html) during pregnancy and when their child was 3, 6, and 12 months of age (Table 3). Fathers completed questionnaires at time of their consent. Questionnaires were related to child characteristics (i.e. health, nutrition, medication), family characteristics (i.e. SES, parental health, maternal mental health (Perceived Stress Scale (PSS) [154] and Centre of Epidemiological Studies-Depression (CES-D) [155]), parent-infant interaction (Parent-Child Dysfunctional Interaction (P-CDI) subscale[156]) and environmental characteristics (i.e. pet ownership, proximity to pollutants). The infant's hospital birth chart was used to collection information on gestational age, date of birth, height and weight at birth. A home assessment was completed when the child was 3 months of age and included a home inspection (i.e. examining age, size, condition of house, number of cleaning products, etc.), environmental sampling (i.e. dust), outdoor pollutant exposure assessment (i.e. traffic related air pollution (TRAP)), biological sampling (i.e. infant's urine, stool, and nasal swab), and child's height and weight measurements. An in-clinic assessment, which was completed when the child was 12

months of age, included skin prick allergy testing (SPT) for the mother and infant, maternal spirometry, and child's height and weight measurements. Fathers completed SPT, spirometry, and questionnaires relating to their health during time of their consent, which could occur at any point during the study.

CHILD SLEEP-E families completed assessments relating to sleep and neurodevelopment in additional to CHILD assessments. Questionnaires related to child sleep habits (Brief Infant Sleep Questionnaire (BISQ) [157] (Appendix 3)) and SDB (Pediatric Sleep Questionnaire (PSQ) [40,158] (Appendix 4)) were completed every 3 months starting from when the child was 3 months of age. Mothers completed the Global Sleep Assessment Questionnaire (GSAQ) [159] (Appendix 5) when the child was 12 months of age. Father completed the GSAQ at the time of their consent. Infant neurodevelopment was assessed in-clinic when the child was 12 months of age using Bayley's Scale of Infant Development - Version III (BSID-III). Infant sleep was evaluated for one night at 12 months of age using a portable level 3, at-home PSG device (the NOX-T3 portable sleep monitor) that has 7 channels measuring blood oxygen saturation, abdominal and thorax respiratory inductive plethysmography, airflow pressure and temperature, snoring, and sleep/wake states[160].

Table 3: CHILD SLEEP-E data collection in the first year of life						
Questionnaires/Sample Collection	During pregnancy	Birth	Infant's age (months)			
			3	6	9	12
Mother						
Health	x					x
Mental health						
PSS	x			x		x
CES-D	x			x		x
SES	x					x
Parenting questionnaire						x
SPT						x
Spirometry						x
GSAQ						x
Home environment						
Residential history	x					
Home environment questionnaire	x		x	x		x
Home assessment			x			
Infant bedroom dust sample			x			
Outdoor pollutant exposure (TRAP)			x			
Child						
Hospital birth chart		x				
Medication		x	x	x		x
Health			x	x		x
SPT						x
Child samples						
Urine			x			x
Health and weight measurements		x	x			x
BISQ			x	x	x	x
PSQ			x	x	x	x
At-home PSG						x
BSID-III						x
Father (if applicable)						
Health	x					
SPT	x					
Spirometry	x					
GSAQ	x					

2.4 Study Variables

2.4.1 Exposure and Outcome Variables (Table 4a)

a) Infant's ability to self-soothe (Primary exposure variable): The BISQ is a 13-item, parent response questionnaire that assesses average sleep patterns for infants 0-29 months of age[38]. The BISQ reflects the parent's perception of their infant's sleep [157] with questions addressing sleep-related behaviours such as sleep time onset, number of night awakenings, sleep location, sleep position, and method of falling asleep. Parents were asked how their child fell asleep most of the time (while feeding, being rocked, being held, in bed alone, or in bed near a parent) to identify the child's ability to self-sooth. Children were self-soothers if they fell asleep independently (in bed alone or in bed near a parent). Children were not self-soothers if they fell asleep with parental intervention (while feeding, being rocked, or being held). Children were assessed at 3, 6, 9, and 12 months of age.

Self-soothing is an ideal surrogate variable to assess parent-infant bedtime interactions (a latent, unmeasured variable within our study). Self-soothing captures the relationship between intrinsic qualities (i.e. a child's temperament, age, gender) and parental qualities (i.e. attachment style, parenting competence) [161]- two variables that may be difficult to measure (i.e. child temperament), and in some cases were not measured (i.e. attachment style) within our study.

b) Sleep duration (Primary outcome variable): BISQ total nocturnal sleep duration measurements have demonstrated significant Pearson's between-measure correlation of 0.23with actigraphy[157] and a correlation of 0.27 with daily sleep logs[157]. Parents reported the amount of time (in hours and minutes) that their infant spent in sleep during the day and during the night. Daytime and night time sleep was totalled to obtain total sleep duration in hours. Sleep duration was reported when the child was 3, 6, 9, and 12 months of age.

c) Infant's BMI Z-Score (Secondary exposure variable): A child's length and weight were measured at 3 and 12 months of age. Recumbent length, in meters, was obtained using an infant length board. Weight, in kilograms, was obtained using an electronic infant scale. Age and sex-specific BMI Z-scores were determined using a Z-score calculator[162] based on 2006 WHO growth standards.

d) SDB (Secondary outcome variable): The SDB subscale of the Pediatric Sleep Questionnaire (PSQ), a 22-item, parental response questionnaire, screens for SDB in children aged 2 to 18[108]. Items address three prominent SDB symptom-complexes: snoring, excessive

daytime sleepiness, and inattentive/hyperactive behaviour [40]. Items are answered as yes (1 point), no (0 points) and "I don't know" (missing). A PSQ score, which ranges from 0 to 1, is calculated by taking the mean of the responses for non-missing items[158]. A score of 0.33 or greater has been associated with pediatric SDB, and more specifically OSAS[158]. The PSQ has been validated in numerous clinical setting and with PSG confirmed SDB[38,158]. A 3-fold increase risk of PSG diagnosed SDB is associated with every one standard deviation increase score above 0.33 on the PSQ [108,158]. The PSQ is an effective pediatric SDB screening tool for high and low risk groups with a sensitivity of 0.78 and specificity of 0.72[158,163]. PSQs were completed when the child was 3, 6, 9, and 12 months of age. Child with PSQ scores of 0.33 or greater were identified as having SDB.

Table 4a: Exposure and outcome variables used in analysis and time of variable extraction

Variable	During Pregnancy	Birth	Infant's Age (months)			
			3	6	9	12
Primary Hypothesis						
Exposure: Child's ability to self soothe (self-soother/non self-soother)			x	x	x	x
Outcome: Sleep duration (hours)			x	x	x	x
Secondary Hypothesis						
Exposure: Age and sex-specific BMI Z-Score			x			x
Outcome: SDB (yes/no)			x	x	x	x

2.4.2 Other Variables

2.4.2.1 Child Characteristics (Table 4b)

a) *Child's date of birth:* Child's date of birth was extracted from the hospital birth chart.

b) *Birth Term:* GA, in weeks, was extracted from the hospital birth chart. Infants were considered preterm if they were born before 37 weeks of GA or full term if they were born on or after 37 weeks of GA.

c) *Birth weight for GA Z-score:* Birth weight in kilograms was extracted from the hospital birth chart. Sex-specific birth weight for GA Z-scores were determined using a 2006 WHO growth standards Z-score calculator[164].

d) *Sex:* Infants were identified as male or female based on their hospital birth chart record.

e) *Infants' ethnicity:* Mothers identified the ethnic/cultural group with which they and the child's biological father belonged to on the mother's health questionnaire, which was completed prenatally. Choices included: a) Caucasian b) Black c) Filipino d) Chinese (Hong Kong/Taiwan/Mainland China) e) First Nations f) Hispanic g) South Asian (Indian continent) h) Indo-Canadian i) Japanese j) Middle Eastern k) South East Asian (Cambodia/Vietnam/Laos/Malaysia/Thai) l) Unknown m) If none of these groups, specify. Mothers were asked to check all applicable choices. Infants were categorized as Caucasian if both biological parents were identified as Caucasian. Infants were categorized as non-Caucasian if one or both parent(s) identified themselves as an ethnic/cultural group other than Caucasian.

f) *Birth Order:* A mother's number of viable, living offspring (excluding the CHILD index participant) was extracted from the hospital birth chart. Infants were categorized as first-born if their mother had no other living children or subsequent-born if their mother had at least one other living child prior to the CHILD index participant.

g) *Breastfeeding:* Mothers were asked if their child was breastfeeding, formula feeding, or eating solid food in three separate questions when the child was 3, 6, and 12 months of age. At each time point, the infant's diet was categorized as breastfed only, formula fed only, solid foods only, or mix-fed (any combination of breastfeeding, formula feeding, or solid food).

h) *Sleep time:* Parents reported, on the BISQ, the time their child usually fell asleep for the night using a 24-hour clock at 3, 6, 9, and 12 months of age. Sleep times were categorized as before 21:00 or after 21:00.

i) *Co-sleeping:* Parents were asked, on the BISQ, about their infant's usual sleeping arrangement (infant's crib in a separate room, infant crib in parent's room, in parent's bed, infant crib in room with sibling, or other) when the child was 3, 6, 9, and 12 months of age. Infants were categorized as no (to co-sleeping), room-sharing, and bed-sharing. Infants did not co-sleep if they slept in a separate room or other. Infant room-shared if they slept in an infant crib in the parent's room, or in a room with a sibling. Infants bed-shared if they shared a bed with their parents.

j) Sleeping Position: Parents report, on the BISQ, their infant's predominant sleeping position (on belly, on side, or on back) when the child was 3, 6, 9, and 12 months of age.

2.4.2.1.1 Child's General Health

a) Rhinitis: Infants were classified as having rhinitis at 3, 6, 9, and 12 months of age if parents reported yes to at least one of the following PSQ questions about their infant: 1) tends to breathe through the mouth during the day 2) have a dry mouth on waking up in the morning 3) have a stuffy nose is congested at night or 4) mouth breathes most of the time.

b) Gastroesophageal reflux disease (GERD): Infants were classified as having GERD if they were treated with any of the following medications: Prevacid, Rantiadire, Omperazole, Losec, Prilosec, Lansoprazole, or Pantoprazole at 3, 6, and 12 months of age on the child's medication questionnaire.

c) Upper respiratory tract infection (URTI): Parents reported whether their child had URTI at 3, 6, and 12 months of age. Parents were then asked to indicate the total number of URTI at each assessment point their child did have URTI.

d) Otitis media (OM): Parents reported whether their child had OM at 3, 6, and 12 months of age. Parents were then asked to indicate the total number of OM events at each assessment point if their child did have OM.

e) Wheeze: Wheeze was defined as a whistling sound coming from the chest. Parents reported whether their child had wheeze at 3, 6, and 12 months of age. Parents were then asked to indicate the total number of wheezing episodes (i.e. an episode is defined as wheeze for more than 12 minutes at a time separated by at least 7 days or more than 20 minutes if separated by less than 7 days) at each assessment point if their child did wheeze.

f) Infant atopy: Infant atopy was determined using skin prick allergy test (SPT) at 12 months of age. A positive SPT test was defined as an average wheal size >2mm than the negative control. An infant was classified as atopic if they had at least one positive test result. Allergens tested were *Alternaria alternata*, cat hair, dog epithelium*, Dermatophagoides pteronyssinus, Dermatophagoides farinae*, cockroach, peanuts, cow's milk, egg white, and soybeans.

Table 4b: Child characteristics used in analysis and time of variable extraction						
Variable	During Pregnancy	Birth	Infant's Age (months)			
			3	6	9	12
Date of birth		x				
Birth term (preterm/full-term)		x				
Birth weight for GA Z-score		x				
Sex (male/female)		x				
Ethnicity (Caucasian/non-Caucasian)	x					
Birth order (first-born/subsequent-born)		x				
Breastfeeding (breastfed only/formula fed only/solid food only/mixed-fed)			x	x		x
Sleep time (before 21:00/after 21:00)			x	x	x	x
Sleep arrangement						
Co-sleeping (no/room-sharing/bed-sharing)			x	x	x	x
Bed-sharing (yes/no)			x	x	x	x
Sleeping position (on belly/on side/on back)			x	x	x	x
General health						
Rhinitis (yes/no)			x	x		x
GERD (yes/no)			x	x		x
URTI (yes/no and number)			x	x		x
OM (yes/no and number)			x	x		x
Wheeze (yes/no and number of episodes)			x	x		x
Infant atopy (yes/no)						x

2.4.2.2 Family Characteristics (Table 4c)

a) Family Income: Mothers reported their family's total income before taxes and deductions in the past 12 month income as either: a) $0 - $19,999 b) $20,000 - $39,999 c) $40,000 - $59,999 d) $60,000 - $79,999 e) $80,000 - $99,999 f) $100,000 - $149,999 g) $150,000 or over h) "Prefer not to say" during pregnancy and when their child was 12 months of age. Family incomes were categorized, using the highest reported annual family income, as below $60,000, equal or above $60,000, or prefer not to say. The Government of Canada (Employment and Social

Development Canada) reports that $68,000 is the median after-tax income for the Canada and as a result, $60,000 was chosen as a cut-off for this analysis.

b) Marital Status: Mothers reported their marital status as a) Married or Common Law b) Divorced or Separated c) Single (never been married) d) Widowed during pregnancy. Marital status was categorized as married/common law, divorced/single, or widowed.

c) Maternal Education: Mothers reported their highest education level achieved during pregnancy and when their child was 12 months of age as either a) less than high school b) some high school c) completed high school d) some college or university e) completed college or university f) some postgraduate g) completed postgraduate or h) other. Maternal education was categorized into either: 1) did not attend post-secondary, 2) attended post-secondary, or 3) "other" based on the highest reported education level.

d) Maternal age at time of child's birth: Mothers reported their date of birth during pregnancy and the child's date of birth was extracted from the hospital birth chart. Maternal age was calculated by subtracting the child's date of birth from the mother's date of birth.

e) Maternal stress: Maternal stress was measured using Cohen, Karmarck and Mermelstein's abbreviated 10-item version of the Perceived Stress Scale (PSS) [154] questionnaire when their child was 3, 6, and 12 months of age. The PSS has a maximum score of 40 with higher scores indicating higher levels of maternal stress.

f) Maternal depression: Maternal depression was measured using Radloff's 20-item Center for Epidemiological Studies –Depression (CES-D) [155] self-administered questionnaire when their child was 3, 6, and 12 months of age. The CES-D has a maximum score of 60 with higher scores indicating greater depressive symptoms. A cut-off score of 16 or greater identifies individuals at risk for clinical depression[165].

g) Parental SDB (Maternal and Paternal): The GSAQ, an 11-item ordinal scale questionnaire, is a self-administered screening tool used to diagnosis sleep related disorders in adults[159]. Father completed the GSAQ at time of consent and mothers completed the GSAQ when their child was 12 months of age. Parents were categorized as having SDB, if they reported sometimes, usually, or always to any of the following questions a) Do you hold your breath, have breathing pauses, or stop breathing in your sleep? b) Do you snore loudly? c) Did you fall asleep unintentionally or have to fight to stay awake during the day? Maternal and paternal SDB were analyzed independently.

h) Parental sleep problems (Maternal and Paternal): Fathers at time of consent and mothers when their child was 12 months of age were categorized as having sleep problems if they answered sometimes, usually, or always to either 1) difficulty falling asleep, 2) difficulty staying asleep, or 3) feeling poorly rested in the morning on the GSAQ. Parents were categorized as not having sleep problems if they answered never to the previously mentioned question. Maternal and paternal sleep problems were analyzed independently.

i) Parent's Cognition about child's sleep: Parents were asked, on the BISQ, to rate their child's sleep problems when their child was 3, 6, 9, and 12 months of age as either 1) not a problem, 2) a small problem, or 3) a very serious problem.

j) Parental-Infant Bonding: Parent-Infant bonding was measured using the Abidin's parent-answered12-item Parent-Child Dysfunctional Interaction (P-CDI) subscale[156] when the child was 12 months of age. Items were statements such as: "My child rarely does things for me that make me feel good" and "My child doesn't seem to learn as quickly as most children". Items are rated from 1 (strongly disagree) to 5 (strongly agree), with total scores ranging from 12 to 60. Higher scores indicate that parents perceive that their child does not meet expectation and that interactions with the child are not reinforcing[166].

k) Parental Atopy (Maternal and Paternal): Maternal and paternal atopy was determined using SPT when their child was 12 months of age and time of consent respectively. Allergens tested were: *A.alternata,* Cladosporium, Penicillium, *Aspergillus fumigatus*, cat hair, dog epithelium, *D. pteronyssinus, D. farinae*, cockroach, trees, grass, weeds, ragweed, and peanuts. A positive SPT test was defined as an average wheal size >2mm than the negative control. Parents were classified as atopic if they had at least one positive test result. Maternal and paternal atopy were analyzed independently.

Table 4c: Family characteristics used in analysis and time of variable extraction						
Variable	During Pregnancy	Birth	Infant's Age (months)			
			3	6	9	12
Family income (<$60,000/ ≥$60,000)	x					x
Marital status (married or common law/divorced or single/widowed)	x					
Maternal education (did not attend post secondary/attended post secondary/other)	x					x
Maternal age at child's birth (years)	x					
Maternal mental health						
Maternal stress (continuous variable)			x	x		x
Maternal depression (continuous variable)			x	x		x
Parental sleep						
Maternal symptoms for SDB (yes/no)						x
Maternal sleep problems (yes/no)						x
Paternal symptoms for SDB (yes/no)	x					
Paternal sleep problems (yes/no)	x					
Parental cognition about child's sleep (not a problem/a small problem/a very serious problem)			x	x	x	x
Parental-infant bonding (continuous variable)						x
Parental atopy						
Maternal atopy (yes/no)						x
Paternal atopy (yes/no)	x					

2.4.2.3 Household/Environmental Characteristics (Table 4d)

a) *Proximity to pollutant source:* Parents reported yes or no to whether their house was within 100 meters of: a) a major highway/artery b) factory c) gas station d) parking lot e) major/prolonged construction activity (e.g. building of houses or other buildings, road work, typically involving heavy machinery and/or generation of noticeable amounts of dust in the air) at 3, 6, 12 months. Proximity to each pollutant source was analyzed independently as a binary variable.

b) *Average traffic-related air pollution (TRAP) exposure:* Parents reported their home address during pregnancy and when their child was 12 months of age on the residential history and home environment questionnaires. NO_2 exposure (parts per billion (ppb)), based on these addresses, was determined using Land Use Regression (LUR) model estimates of exposure. Addresses were crosschecked to determine if the family moved within the first year of the child's life. Temporally adjusted LUR estimates were calculated for a) the home address during their child's birth and b) residential mobility during the first year of the child's life[167]. TRAP exposure accounting for residential mobility during the first year of the child's life was used in this analysis and analyzed as a continuous variable.

c) *Indoor Allergen (Fine dust):* A standardized consumer model vacuum cleaner fitted with dust collection device was used to collect a dust sample from the infant's bed and a $2m^2$ area from the infant's bedroom floor at 3 months of age. The sample was sieved (<300μm size fraction) to extract fine dust and the sieved sample was then weighed[150]. Fine dust was measured in mg and analyzed as a continuous variable.

d) *Prenatal Maternal Smoking:* Mothers reported how often they smoked during pregnancy. Mothers that responded "daily or occasionally" were categorized as having smoke prenatally; mothers that responded "not at all" were categorized as not smoking prenatally.

e) *Smoke exposure:* Parents indicated yes or no to whether anyone smoked in the child's home when their child was 3, 6, and 12 months of age. If an individual did smoke in the child's home, parents identified yes or no if smoking occurred a) inside the baby's home b) inside baby's home near an open window or in the attached garage c) outside but near the baby's home. Location of smoking was analyzed separately as binary variables.

f) Cotinine (measure of smoke exposure): Children urine samples were collected at 3 months of age and analyzed for biomarkers of nicotine (cotinine and trans-3'-hydroxycotinine (3HC)) at the Centers of Disease Control and Prevention's Tobacco Laboratory in Atlanta, GA[168]. Samples were hydrolyzed with β-glucuronidase to de-conjugate and extract glucoronidated cotinine and 3HC molecules and then analyzed by liquid chromatography-atmospheric pressure chemical ionization tandem mass spectrometry[168]. Cotinine and 3HC concentrations were calculated using least-squares linear regression of the peak area ratios of native to internal standards[168]. The possibility of urine dilution was corrected for in the

biomarker concentration by using specific gravity measurements[168]. Cotinine levels adjusted for urine dilution, measured in ng/mL, were analyzed as a continuous variable.

g) *Household size:* Parents reported the total number of adults and children (including the CHILD index participant) living in the household at when the child was 3, 6, and 12 months of age.

h) Pets (Cats and Dogs): Parents reported yes or no to owning a) dog(s) and b) cat(s) when the child was 3, 6, and 12 months of age. Cat and dog ownership were analyzed independently as binary variables.

i) Season: Season of birth and season of sleep duration reporting was determined using the month of the child's date of birth, extracted from the child's hospital birth chart, and from the month of BISQ completion when the child was 3, 6, 9, and 12 months of age respectively. Seasons were categorized as summer (June, July, August), fall (September, October, November), winter (December, January, February), or spring (March, April, May).

j) Hours of daylight: Hours of daylight on the child's date of birth and hours of daylight for the date of BISQ completion (which was completed when the child was 3, 6, 9, and 12 months of age) was calculated using the following formula[169]:

$$\theta = 0.2163108 + 2\tan^{-1}[0.9671396 \tan[0.00860 \times (J - 186)]]$$

Where

θ = Revolution angle of Earth from the sun

J = Day of the year for child's birthday

$$\phi = \sin^{-1}[0.39795 \cos\theta]$$

Where

ϕ = Is the sun's predicted declination angle, or the angular distance at solar noon between the Sun and the equator, from the earth orbit revolution angle

$$D = 24 - (24 / \pi) \cos\text{-}1 [[(\sin(0.8333\,\pi)/180)) + (\sin(L\,\pi)/180)\sin\phi)] / [(\cos(L\,\pi)/180)\cos\phi)]]$$

Where

D = Length of daylight (plus twilight)

L = Latitude

Table 4d: Household/Environmental characteristics used for analysis and time of variable extraction						
Variable	During pregnancy	Birth	Infant's Age (months)			
			3	6	9	12
Proximity to pollutant source: highway/artery, factory, gas station, parking lot, major/prolonged construction activity (yes/no)			x	x		x
Average TRAP exposure – NO_2 (ppb)						x
Indoor allergens – Fine dust in child's bedroom (mg)			x			
Smoke exposure						
Prenatal maternal smoking (yes/no)	x					
Smoking in child's household (yes/no)			x	x		x
Location: Inside baby's home (yes/no)			x	x		x
Inside baby's home near an open window or attached garage (yes/no)			x	x		x
Outside but near the baby's home (yes/no)			x	x		x
Cotinine levels in child's urine (ng/mL)			x			
Household size (total number of adults and children)			x	x		x
Pet Ownership						
Dogs (yes/no)			x	x		x
Cats (yes/no)			x	x		x
Seasonality						
Season during child's birthday (fall/winter/spring/summer)		x				
Amount of daylight on child's birthday (hours)		x				
Season when sleep duration was reported (fall/winter/spring/summer)			x	x	x	x
Amount of daylight when sleep duration was reported (hours)			x	x	x	x

2.5 Statistical Analyses

2.5.1 Data Collection and Cleaning. Participants completed approximately 60 questionnaires which consisted of approximately 1500 questions, two neurodevelopmental tests, one in home-PSG, a home inspection, and provided six biological samples within the first year of

SLEEP-E CHILD participation. Questionnaire data was collected online or by paper. Quality assurance was complete at each study site, and then questionnaires were scanned and uploaded to HealthDiary, a password-protected web based electronic data capture system used for data collection and management for the CHILD study[150]. CHILD's National Coordinating Centre (NCC), in Hamilton, Ontario, has access to scanned data from all CHILD sites and is responsible for data entry and, again, quality assurance. Questionnaires and forms requiring corrections or clarifications were sent by the NCC to study sites and then entered by the NCC once resolved by the study site.

Over 40 completed CHILD SLEEP-E questionnaires were exported from HealthDiary as a Microsoft Excel file for this analysis. Data was imported into Stata (Version 12, StataCorp, College Station, Texas) for data cleaning and analysis. Data cleaning involved merging responses between:

1. Similar but not identical questionnaires from the Vanguard and general cohort: each questionnaire had at least two versions, one for the vanguard cohort and another for the general cohort. In some instances a questionnaire in the Vanguard study was split into several different questionnaires for the general cohort. Amongst these questionnaires, questions and multiple-choice responses may have been modified. These variations were documented and corrected for to ensure comparability and consistency amongst participants during data extraction and analysis. For example, the child health questionnaire completed when the child was 3 months of age had four different versions. Response options also differed in some instances. A participant was asked "How long did [the baby's first cold] last for?". One version of the questionnaire's responses were "a) <1 day b) 1-7 days c) >7 days" while another version of the questionnaire's responses were "a) <1 day b) 1-3 days c) 4-7 days d) > 7 days". These responses were re-categorized during data cleaning and analysis.
2. Same/similar questionnaires across different time points: Questionnaires repeated up to four times. For example, the BISQ was completed when the child was 3, 6, 9, and 12 months of age.

Summary tables and scatterplots were used to identify outliers for continuous variables. Paper versions of the questionnaires (where available) were checked to ensure correct online data entry if responses were considered to be outliers. Patients were contacted to verify their response

for outliers where online data entry and paper responses matched. Consistency of responses for categorical variables was checked across time points (i.e. mothers were asked if they were breastfeeding when their child was 3, 6, and 12 month of age on the child health questionnaire. The mother's 12 month questionnaire response was checked to ensure they responded no to breastfeeding if they indicated they stopped breastfeeding on the 6 month child health questionnaire).

2.5.2 Statistical methods.

2.5.2.1 Primary hypothesis - Sleep duration. Subjects had a maximum of four reported outcome measurements since sleep duration was reported when the child was 3, 6, 9, and 12 months of age. Longitudinal and cross-sectional analyses were used to investigate the association between self-soothing (independent variable) and sleep duration (outcome variable) controlling for other modifiable sleep characteristics such as sleep position and sleep location. Longitudinal analysis was performed with linear regression modeling using the generalized estimating equation (GEE) method to account for clustering for each infant and to examine sleep duration over the first year of life. Cross-sectional analyses were performed when the child was 3, 6, 9, and 12 months of age using linear regression modeling. Both longitudinal and cross-sectional analyses were performed to ensure that sleep in the first year of life was modeled appropriately. Longitudinal modeling assumes factors associated with sleep duration are consistent across time. However, the factors associated with sleep duration may be time-specific due to the rapid maturation of sleep within the child's first year of life, thus cross-sectional analyses at each time point were also performed.

Subjects were excluded from longitudinal analysis if they did not have a sleep duration outcome reported at least one assessment point. Longitudinal analysis (i.e. multivariate linear regression using GEE methods) assumed gaussian family, identity link, and exchangeable correlation structure with robust errors. Exchangeable correlation structure was assumed to maximize power during analysis. Linear regression using GEE methods assumes missing data is missing completely at random (MCAR). Exploratory data analysis was performed using Pearson' chi-square test (for categorical variables) and student t-tests (for continuous variables) to compare baseline differences between those included and excluded from the longitudinal

analysis. Univariate longitudinal analysis was performed to determine regression co-efficients between individual sleep variables and sleep duration. Purposeful selection of variables (significance level of 0.05 or below) was used for the multivariate longitudinal analysis based on findings from the univariate analyses. Variables that had significance at or below 0.05 were retained in the multivariate longitudinal model. Another longitudinal analysis was performed with multivariate linear regression modeling using GEE methods that assumed gaussian family, identity link, and first-order autoregressive correlation structure with robust errors. First-order auto regression correlation structure was specified to reflect the assumption that sleep durations reported sequentially (i.e. at 3 months and 6 months of age) are more similar than sleep durations reported non-sequentially (i.e. at 3 months and 12 months of age).

Subjects were excluded from time-specific cross-sectional analyses if they did not have sleep duration reported at that specified assessment point (i.e. if the subject did not have a sleep duration reported at 3 months of age, they were excluded from the 3 month linear regression). Exploratory data analysis was performed using Pearson' chi-square test (for categorical variables) and student t-tests (for continuous variables) to compare baseline differences between those included and excluded from cross-sectional analyses. Univariate linear regressions were performed to determine regression co-efficients between individual sleep variables and sleep duration at each assessment point. Purposeful selection of variables (significance level of 0.05 or below) was used for the multivariable cross-sectional analyses based on findings from the univariate analyses. Variables that had significance at or below 0.05 were retained in the multivariate models.

2.5.2.2 Secondary hypothesis – SDB. Cox proportional hazard regression was used to investigate the association between age and sex-specific BMI Z-scores (independent variable) and SDB (outcome variable) while controlling for putative risk factors associated with SDB (i.e. sex, prematurity, environmental exposures). Infants were defined as having SDB if they had a PSQ score of 0.33 or above. Infant follow up started at birth (0 months of age) and ended at 12 months of age. The earliest PSQ score of 0.33 or above was used to define time to SDB. Data was right censored (i.e. information of SDB is incomplete since infant did not have SDB during period of analysis) at 12 months of age if the infant did not have SDB at any assessment point (3, 6, 9, 12 months of age). If the subject was loss to follow up (LTFU), the subject was censored at

the time at which LTFU occurred (i.e. if the subject withdrew from study at 6 months of age, they were censored at 6 months time point). Infants that did not complete a PSQ for at least one assessment point were excluded from the analysis.

Exploratory data analysis was performed using Pearson's chi squared tests (categorical variables) and student t-tests (continuous variables) to compare the baseline characteristics of subjects included and excluded from analysis. Univariate Cox proportional hazard regression was used to determine hazard rates between individual risk factors and SDB. Contingency tables with chi-square tests were used in the univariate analysis to determine the frequency of SDB for each risk factor and to test if there was a statistically significant difference of SDB between the groups (i.e. females and males) within each risk factor (i.e. gender). Purposeful selection of variables (significance level of 0.05 or below) was used for the multivariate Cox proportion hazard regression based on findings from the univariate analysis. Multivariate Cox proportion hazard regression models were adjusted for infant's gender and infant sleep duration. Variables that had significance at or below 0.05 were retained in the multivariate model. Interaction terms, which were based on current literature, were tested in multivariate analysis and were retained if they had significance at or below 0.05 and if they provided unbiased regression co-efficients (i.e. sufficient number of events per covariate entered). Generalized linear regression with scale Schoenfeld residuals as a function of time was used to test the proportional hazard assumption for all multivariate models.

Two additional analyses were performed to test the robustness of the multivariate Cox proportional hazard model. To assess the contribution of rhinitis to SDB risk, the PSQ was redefined to exclude questions relating to rhinitis. Subsequently, symptoms for rhinitis were entered as a covariate into the model. The PSQ was redefined to exclude the rhinitis questions to ensure model stability as inclusion of both PSQ questions relating to rhinitis and rhinitis as a covariate within a model would lead to unstable model estimates due to collinearity. An additional analysis was also performed using only PSQ questions relating to symptoms that were strongly associated (odds ratio 9 or greater) with SDB diagnosis according to a validation study[40]. These symptoms are easier to objectivity deteremine and include snoring, apnea, and mouth breathing. A PSQ of 0.33 or above was used to defined SDB in both of the previously mentioned models. Variables that had significance at or below 0.05 were retained in the multivariate models.

2.5.2.3 Missing data. Nominal variables and dummy variable adjustment (i.e. single imputation plus missing data indicator) were utilized to account for missing data. Missing values for categorical variables were treated as a separate category and included in analysis. Missing values for continuous variables were replaced by the variable's mean and a dummy variable was created to indicate whether the original data was missing or available. The variable, in addition to its corresponding dummy variable were included in the analysis. Theoretically, the missing category (nominal approach) and dummy variable (dummy variable adjustment approach) should not be significant or contribute to the variation in the outcome. Significance ($p<0.05$) of the missing category or dummy variable indicates missing values are dependent on the observed variable[170] (i.e. a systematic difference exists between participants with and without that variable). As a result, model estimates may be biased (i.e. overestimated or underestimated) and the degree and direction of this bias is dependent on the distribution of the missing value[170].

Chapter 3: Results

3.1 Participants' characteristics

Most mothers in SLEEP-E CHILD were older with higher SES. Mean age for mothers was 31.30 years of age (range: 18.32 – 43.13), which is older than Canada's average (mean: 21.6) [171]. 74% of mother had higher SES (626/845 subjects with average incomes greater or equal to $60,000). 58% of CHILD SLEEP-E children were Caucasian (491/845 infants with mothers and fathers who were both identified as Caucasian.)

Mean GA was 39.46 weeks (range: 34.29 – 42). Two infants born earlier than 35 weeks GA participated in the study despite the exclusion criteria of 35 weeks GA. Infants' mean birth weight was 3.42kg (range: 1.87 – 5.49).

3.2 Sleep duration over the first year of life

On average, infants slept 14.08 hours at 3 months of age, 13.66 hours at 6 months of age, 13.41 hours at 9 months of age, and 13.51 hours at 12 months of age (Figure 4). Sleep duration had a few outliers with total hours of sleep ranging from 2 to 22 hours (Figure 5).

Figure 4: Average sleep duration in the first year of life for CHILD SLEEP-E participants

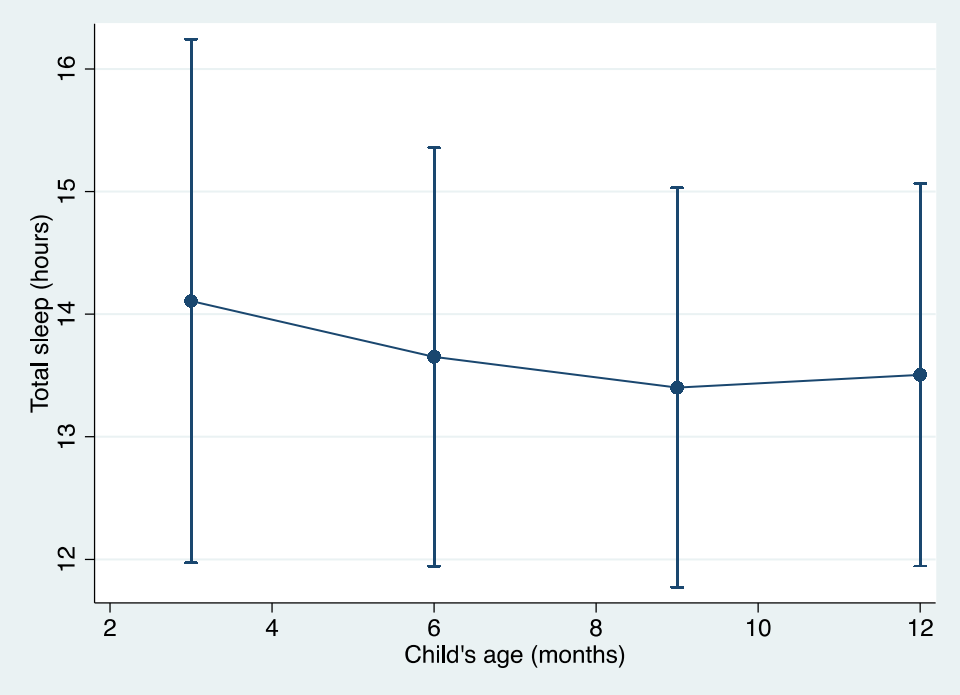
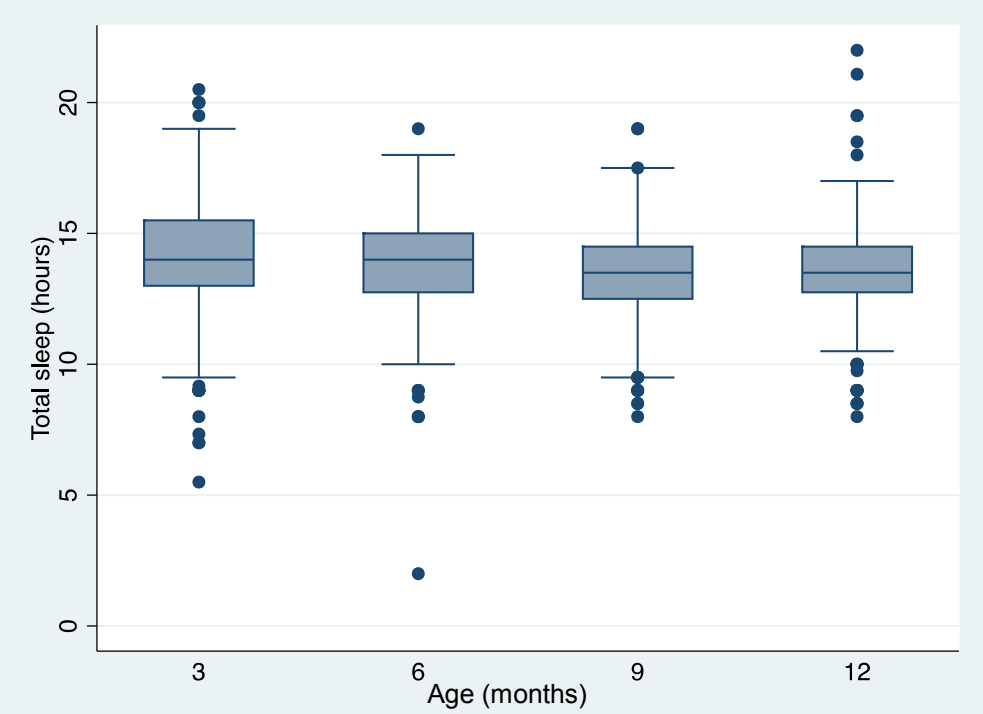


Figure 4: Variability of sleep duration by age over the first year of life



3.2.1 Follow up characteristics. Of the 845 Edmonton CHILD participants, 765 (90.4%) infants had sleep duration outcomes for at least one time point (3, 6, 9, 12 months of age) and were included in the longitudinal analysis (Table 5).

Table 5: Data completeness for subjects included in longitudinal analysis

Number of outcome measurements	Number of subjects	Percentage (%)
1	46	5.44
2	89	10.53
3	196	23.30
4	434	51.36
Total	765	90.4

3.2.2 Baseline characteristics. Infants with sleep duration data were more likely to be in higher income families (85.67%) compared to those families without data (72.34%; p=0.04; Appendix 6 Table 1b), have mothers that were more likely to be married or common (94.66%

with data vs. 88.73% without data; p=0.04) and have mother who had attended post-secondary school (91.64% with data vs. 79.59% without data; p=0.01).

There were similar proportions of males among those with data (50.46%) and without (60.71% p=0.14) and Caucasians (68.88% with data vs. 58.33% without data; p=0.09; Appendix 6 Table 1a) with and without sleep data. Levels of maternal stress and depression were not significantly different between infants with and without sleep duration data. Parent-child interactions, as measured by the P-CDI with higher scores indicating greater dysfunction between parent and child, did not vary significantly between infants with sleep data (15.33; 95% Confidence Interval (95%CI) 14.96, 15.69; Appendix 6 Table 1b) and among families without sleep data (14.50; 95%CI -17.27, 46.27; p=0.79).

3.2.3 Results for univariate longitudinal analysis for sleep duration. Self-soothing infants slept 36 minutes longer than non-self soothing infants (14.0 hours; 95%CI 13.9, 14.1 vs. 13.4 hours; 95%CI 13.3, 13.5; p<0.001; Appendix 6 Table 2a) in unadjusted longitudinal analysis. Compared to infants whose sleep was not considered a problem infants whose sleep was considered a very serious problem slept significantly less (13.9 hours; 95% CI 13.8, 14.0 vs. 11.8 hours; 95% CI 11.1,12.4; p<0.001; Appendix Table 2b), while infants whose sleep was consider a small problem slept 13.0 hours (95%CI 12.9, 13.2; p<0.001). Infants with sleep times before 21:00 slept significantly longer compared to infants with sleep times after 21:00 (14.0 hours; 95%CI 13.9, 14.0 vs. 13.3 hours, 95%CI 13.2,13.4; p<0.001; Appendix Table 2a). 30.72% (235/765) of infants slept before 21:00 at 3 months of ages, 43.57% (332/762) of infants slept before 21:00 at 6 months of age, 62.05% (461/743) of infants slept before 21:00 at 9 months of age, and 58.82% (450/765) of infants slept before 21:00 at 12 months of age. No infants included in the analysis consistently slept before 21:00 for all assessment points.

Males and females had similar sleep durations (13.7 hours, 95%CI 13.6, 13.8 for males compared to 13.7 hours, 95%CI 13.6, 13.8 for females; p=0.89). Household income was not significantly associated with sleep duration (13.6 hours; 95%CI 13.4, 13.8 for incomes under $60,000 compared to 13.7 hours; 95%CI 13.7, 13.8 for incomes $60,000 and over; p=0.47; Appendix 6 Table 2b). Neither infant symptoms for rhinitis, GERD, URTI, wheeze, nor OM significantly affected sleep duration (Appendix 6 Table 2a). Sleep duration did not significantly

vary by ethnicity. Hours of daylight were not significantly associated with sleep duration (0.01 hours of sleep per hour of daylight; 95%CI -0.01, -0.04; p=0.15).

3.2.4 Results from multivariate longitudinal analysis for sleep duration. Self-soothing infants slept 28.8 minutes longer than non-self-soothing infants (0.48 hours self-soother compared to non self-soother 95%CI 0.34, 0.62; p<0.001; Table 6) in multivariate longitudinal analysis adjusted for gender. Infants with sleep times after 21:00 slept less than infants with sleep times before 21:00 (-0.66 hours; 95%CI -0.80, -0.51; p<0.001). Parents that considered their infant's sleep a very serious problem had 1 hour and 57.6 minutes less sleep (-1.96 hours; 95%CI -2.44, -0.48; p<0.001), while infants whose sleep was considered small problem had 45.6 minutes less sleep (-0.76 hours; 95%CI -0.96, -0.60; p<0.001) when compared to infant's whose sleep was not considered a problem (reference).

Age had a significant linear association with sleep duration. Infants at 3 months (reference) slept the most (14.1 hours; 95%CI 13.9, 14.3) followed by 6 months of age (-0.41 hours compared to reference; 95%CI -0.59, -0.23; p<0.001), 9 months of age (-0.56 hours compared to reference; 95%CI -0.86, -0.27; p<0.001), and 12 months of age (-0.83 hours compared to reference; 95%CI -1.05, -0.63; p<0.001). Subsequent-born infants slept 19.2 minutes more than their first-born peers (0.32 hours, 95%CI 0.15, 0.50; p<0.001). Compare to infants with diets of exclusively breast milk (reference), infants that had diets of formula feed only (-0.43 hours; 95%CI -0.95, 0.08; p=0.02), solid food only (-0.49 hours; 95%CI -0.83, -0.14; p=0.01), or mixed-feed (-0.39 hours; 95%CI -0.61, -0.18, p<0.001) slept significantly less.

Table 6 – Multivariate longitudinal analysis for sleep duration		
Variable	**Co-efficient (hours) (95% CI)**	**p-value**
Needs to be soothed	-0.48 (-0.62, -0.34)	<0.001
Sleep time after 21:00	-0.66 (-0.80, -0.51)	<0.001
Sleep Problem (not a problem at all ref.)		
A small problem	-0.76 (-0.91, -0.60)	<0.001
A very serious problem	-1.96 (-2.44, -1.48)	<0.001
Subsequent-born	0.32 (0.15, 0.50)	<0.001
Age (3 months as ref)		
6	-0.41 (-0.59, -0.23)	<0.001
9	-0.56 (-0.86, -0.27)	<0.001
12	-0.83 (-1.05, -0.63)	<0.001
Feed (breastfeeding only as ref.)		
Formula feed only	-0.43 (-0.95, 0.08)	0.02
Only Solids	-0.49 (-0.83, -0.14)	0.01
Mixed-fed	-0.39 (-0.61, -0.18)	<0.001
Paternal symptoms for SDB	-0.33 (-0.59, -0.06)	0.02
Female	-0.08 (-0.25, 0.09)	0.37
Intercept	15.44 (15.11, 15.77)	<0.001

A longitudinal analysis using multivariate linear regression using GEE methods assuming a first-order autoregressive correlation matrix (n=566; Appendix 6 Table 3) confirmed results from the multivariate linear regression using GEE methods assuming an exchangeable correlation matrix.

Interaction terms were incorporated into the multivariate analysis based on a-priori hypotheses and statistical significance. Interaction terms were retained in the model if: 1) they provided stable estimates 2) had a significance of 0.05 or below or 3) their addition lead to a change of 10% or greater in the estimates of another variable. Variables that were significant in the multivariate longitudinal analysis model using GEE methods (i.e. self-soothing, sleep times, parent's perception of their child's sleep, birth order, feeding method, paternal symptom for SDB) were interacted with the child's age to reflect the changes the in sleep development within the first year of life. Self-soothing by age interactions were not significantly different when compared to self-soothers at 3 months of age (-0.04 hours; 95%CI -0.38, 0.01; p=0.82 if non-self soother at 6 months of age; -0.06 hours; 95%CI -0.44, 0.32; p=0.76 if non-self soother at 9 months of age; 0.18 hours; 95%CI -0.22, 0.60; p=0.38 if non-self soother at 12 months of age). Interaction terms such as age by sleep time, and age by parental perceptions of sleep also were not statistically significant. Compared to children that breastfeed only at 3 months of age, children that were mixed fed at 12 months of age had significantly shorter sleep duration (-0.77 hours; 95%CI -1.43, -0.10; p=0.02). However, this interaction term was not retained in the model because many of the feeding by age interaction estimates were unstable due to small sample sizes.

Birth order by age interaction terms were significant. Their inclusion in the multivariate model caused infant's age to be insignificantly associated with sleep duration. A stratified analysis by birth order (first born versus subsequent born) was performed to further investigate the association of birth term and sleep duration,. Non self-soothers and sleep times after 21:00 remained significantly associated with shorter sleep duration amongst first-born and subsequent-born children (Table 7). However, age and feeding methods were only significant among subsequent-born children but not first-born children. Among subsequent-born children, infants that were solid fed and mixed fed infants had shorter sleep durations compared to those breastfeed only (-0.46 hours; 95%CI -0.96, 0.04; p= 0.001 for solid fed; -0.74 hours; 95%CI -1.03, -0.50; p<0.001 for mixed-fed. Among first-born infants, solid fed and mixed fed infant did not have significantly shorter sleep durations compared to those breastfeed (-0.02 hours; 95%CI -0.52, 0.50; p=0.95 for solid fed; -0.02 hours; 95%CI -0.34, 0.30; p=0.91 for mixed fed). Breastfeeding compared to formula feeding in both first-born and subsequent-born infants were

not significantly associated with shorter sleep durations (-0.34 hours; 95%CI -0.84, 0.15; p=0.17 for first-born; -0.46 hours, 95%CI -0.96, 0.04; p=0.07).

Table 7 – Multivariate longitudinal analysis for sleep duration stratified by birth order

	First-born		*Subsequent-born*	
Variable	**Co-efficient (hours) (95% CI)**	**p-value**	**Co-efficient (hours) (95% CI)**	**p-value**
Non self-soothing	-0.31 (-0.51, -0.11)	<0.001	-0.57 (-0.76, -0.37)	<0.001
Sleep time after 21:00	-0.67 (-0.86, -0.45)	<0.001	-0.61 (-0.81, -0.42)	<0.001
Sleep Problem (not a problem at all ref.)				
A small problem	-0.62 (-0.84, -0.40)	<0.001	-0.86 (-1.08, -0.65)	<0.001
A very serious problem	-2.19 (-3.00, -1.38)	<0.001	-1.91 (-2.52, -1.31)	<0.001
Age (3 months as ref)				
6	-0.27 (-0.53, -0.01)	0.05	-0.47 (-0.96, 0.04)	<0.001
9	-0.17 (-0.61, 0.27)	0.46	-0.79 (-1.17, -0.41)	<0.001
12	-0.68 (-0.99, -0.36)	<0.001	-0.87 (-1.16, -0.59)	<0.001
Feed (breastfeeding only as ref.)				
Formula feed only	-0.34 (-0.84, 0.15)	0.17	-0.46 (-0.96, 0.04)	0.07
Only Solids	-0.02 (-0.53, 0.50)	0.95	-0.87 (-1.33, -0.41)	<0.001
Mixed-fed	-0.02 (-0.34, 0.30)	0.91	-0.74 (-1.03, -0.50)	<0.001
Paternal symptoms for SDB	-0.39 (-0.74, -0.04)	0.03	-0.26 (-0.68, 0.15)	0.21
Female	-0.09 (-0.35, 0.16)	0.46	-0.08 (-0.30, 0.15)	0.52
Intercept	14.94 (14.50, 15.37)	<0.001	16.07 (15.62, 16.53)	<0.001

3.3 Cross-sectional analyses of sleep duration at 3, 6, 9, and 12 months of age

3.3.1 Common factors associated with sleep duration across the 4 assessment times (3 months, 6 months, 9 months, and 12 months) in multivariate cross-sectional analysis.

Self-soothing infants slept longer than non-self-soothing infants at all-time points in cross-

sectional analysis (Table 8, 9, 10, 11). Infants with bedtime after 21:00 slept less than infants with bedtimes before 21:00 at all-time points in cross-sectional analyses. At all time points in cross-sectional analysis, infants whose sleep was considered a very serious problem slept less than infants whose sleep was not considered a problem. Similarly, infants whose sleep was considered a small problem also slept less than infants whose sleep was not considered a problem.

3.3.2 Unique factors associated with sleep duration at 3-months in multivariate cross-sectional analysis. Of the 845 subjects in SLEEP-E CHILD, 678 (80.2%) subjects had sleep durations reported at 3 months and were included in the 3-month cross-sectional analysis. Subsequent-born infants had greater sleep durations than their first-born peers (0.75 hours; 95%CI 0.43, 1.03; $p<0.001$; Table 8). Only infants that were mixed-fed slept significantly less (-0.35 hours; 95%CI -0.69, -0.01; p 0.05) than children that were breastfed only. No infants were solid-fed only at 3 months of age and formula feed only infants' sleep durations did not differ significantly from breastfed only infants. Infants born in the summer had 30.6 minutes less sleep (-0.51 hours; 95%CI -0.95, -0.06; p 0.03), while infants born in the fall had 27.6 minutes less sleep (-0.46 hour; 95%CI -0.89, -0.03; p 0.04) compared to infants born in the winter.

Table 8- Multivariate cross-sectional analysis for sleep duration at 3 months of age		
Variable	**Co-efficient (hours) (95% CI)**	**p-value**
Common factors		
Needs to be soothed	-0.62 (-0.96, -0.28)	<0.001
Sleeps after 21:00	-0.75 (-1.07, -0.42)	<0.001
Sleep Problem (not a problem at all ref.)		
A small problem	-0.64 (-1.03, 0.25)	0.00
A very serious problem	-2.73 (-3.93, 1.52)	<0.001
Unique factors		
Subsequent-born	0.72 (0.41, 1.03)	<0.001
Feed (breastfeeding only as ref.)		
Formula feed only	-0.43 (-0.95, 0.08)	0.10
Mixed-fed	-0.35 (-0.69, -0.01)	0.05
Season of birth (Winter as ref.)		
Spring	-0.24 (-0.66, 0.18)	0.26
Summer	-0.51 (-0.95, -0.06)	0.03
Fall	-0.46 (-0.89, -0.03)	0.04
Intercept	15.36 (14.81, 15.90)	<0.001

3.3.3 Unique factors associated with sleep duration 6-months in multivariate cross-sectional analysis. Of the 845 subjects, 618 (73.1%) subjects had sleep durations reported at 6 months. and were included in the 6 month cross-sectional analysis. Subsequent-born infants had 18 minute more sleep than their first-born peers (0.30 hours if subsequent-born; 95%CI 0.05, 0.56; p 0.02; Table 9). Co-sleeping (i.e. room sharing and bed sharing) was significantly associated with reduced sleep duration compared to infants that did not co-sleep. Infant of fathers

with SDB symptoms had shorter sleep durations (-0.37 hours; 95%CI -0.76, 0.02; p=0.06) compared to infants with fathers that did not have symptoms for SDB.

Table 9 - Multivariate cross-sectional analysis for sleep duration at 6 months of age

Variable	Co-efficient (hours) (95% CI)	p-value
Common factors		
Needs to be soothed	-0.66 (-0.92, -0.39)	<0.001
Sleeps after 21:00	-0.51 (-0.77, -0.25)	<0.001
Sleep Problem (not a problem at all ref.)		
A small problem	-0.52 (-0.80, -0.25)	<0.001
A very serious problem	-2.58 (-3.39, -1.78)	<0.001
Unique factors		
Subsequent-born	0.30 (0.05, 0.56)	0.02
Co-sleeping (no as ref.)		
Room sharing	-0.32 (-0.63, 0.00)	0.05
Bed sharing	-0.37 (-0.74, 0.01)	0.05
Paternal symptoms for SDB	-0.37 (-0.76, 0.02)	0.06
Intercept	14.77 (14.39, 15.16)	<0.001

3.3.4 Unique factors associated with sleep duration at 9-months in multivariate cross-sectional analysis. Of the 845 subjects, 637 (75.4%) subjects had sleep durations reported at 9 months and were included in the 9 month cross-sectional analysis. Females slept less significantly less than males. Infants with mothers that attended post secondary had a significantly shorter sleep duration (-0.57 hours; 95%CI -1.05, -0.09; p 0.02; Table 10) compared to infants with mother that did not attend post secondary.

Table 10- Multivariate cross-sectional analysis for sleep duration at 9 months of age		
Variable	**Co-efficient (hours) (95% CI)**	**p-value**
Common factors		
Needs to be soothed	-0.58 (-0.81, -0.35)	<0.001
Sleeps after 21:00	-1.12 (-1.37, -0.87)	<0.001
Sleep Problem (not a problem at all ref.)		
A small problem	-0.85 (-1.13, -0.57)	<0.001
A very serious problem	-1.80 (-2.70, -0.90)	<0.001
Unique factors		
Female	-0.25 (-0.48, -0.03)	0.03
Maternal Education (did not attend post secondary ref.)		
Completed Post Secondary	-0.57 (-1.05, -0.09)	0.02
Other	-0.71 (-2.18, 0.77)	0.45
Intercept	14.85 (14.37, 15.34)	<0.001

3.3.5 Unique factors associated with sleep duration at 12-months in multivariate cross-sectional analysis. Of the 845 subjects, 615 (74.0%) subjects had sleep durations reported at 12 months and were included in the 12 month cross-sectional analysis. Infants with mothers that smoked prenatally slept longer (0.71 hours; 95%CI 0.08, 1.34; p=0.03, Table 11) than infants with mothers that did not smoke prenatally.

Table 11- Multivariate cross-sectional analysis for sleep duration at 12 months of age		
Variable	**Co-efficient (hours) (95% CI)**	**p-value**
Common factors		
Needs to be soothed	-0.40 (-0.65, -0.14)	0.00
Sleeps after 21:00	-0.91 (-1.17, -0.64)	<0.001
Sleep Problem (not a problem at all ref.)		
A small problem	-0.77 (-1.05, -0.48)	<0.001
A very serious problem	-0.62 (-1.57, 0.33)	<0.001
Unique factors		
Pre-natal maternal smoke	0.71 (0.08, 1.34)	0.03
Intercept	14.04 (13.89, 14.20)	<0.001

3.4 Risk factors for SDB

3.4.1 Follow up characteristics. Of the 845 Edmonton CHILD participants, 763 (90.4%; Table 12) infants had PSQ scores for at least one time point (3, 6, 9, or 12 months of age) and were included in the survival analysis.

Table 12: Data completeness for subjects included in survival analysis		
Number of outcome measurements	**Number of subjects**	**Percentage (%)**
1	47	5.57
2	106	12.56
3	189	22.39
4	421	49.88
Total	763	90.4

3.4.2 Baseline characteristics. There was greater proportion of female infants with data than female infants without data with SDB data (49.80% vs. 36.21%, p=0.05; Appendix 6 Table 9a). Infants with SDB data were more likely to be in higher income families compared to those without SDB data (85.78% vs. 71.42%; p=0.01). Infants with SDB data were more likely to have mothers that attended post-secondary compared to infants without SDB data (91.02% vs. 80.77%; p=0.01).

There was no significant difference in Birth weight for GA Z-Scores among infants with SDB data compared to infants without SDB data (-0.01; 95%CI -0.07, 0.05 vs. 0.03; 95%CI -0.25, 0.31; p=0.77; Appendix 6 Table 9a) or BMI Z-scores at 12 months of age among infants with SDB data compared to those without SDB data (0.27; 95%CI 0.18, 0.37 vs. 0.10; 95%CI -0.95, 1.14; p=0.73). Parental history of atopy and SDB were not significantly different for infants with and without SDB data (Appendix 6 Table 9b). Infant urine cotinine levels at 3 months were not significantly different among infants with SDB compared to infants without SDB data (2.39 ng/mL, 95%CI 0.82, 3.96 vs. 0.27ng/mL; 95%CI -0.18, 0.72; p=0.76; Appendix 6 Table 9a). Rhinitis, GERD, URTI, OM, and wheezing episodes did not significant differ amongst infants with and without SDB data.

3.4.3 Univariate analysis for SDB. Among the 763 infants analyzed, 101 (13%) infants had SDB for at least one assessment point (31 infants had SDB at 3 months, 20 infants had SDB first reported at 6 months, 34 infants at 9 months, and 16 infants first reported SDB symptoms at 12 months). Infants' BMI Z-scores did not significantly increase the risk of having SDB within the first year of life (HR 1.06; 95%CI 0.80, 0.41; p=0.68; Appendix 6 Table 10a). Similarly, Birth weight for GA Z-Scores did not significantly affect SDB risk (HR 1.10; 95%CI 0.88, 1.37; p=0.43). Preterm infants were 2.08 times more likely have SDB compared to full term infants (95%CI 1.05,4.06; p=0.04). Females were 35% less likely to have SDB compared to males (HR 0.65; 95%CI 0.44, 0.97; p=0.03). Symptoms for rhinitis (HR 8.29; 95%CI 5.17, 13.26; p<0.001), URTI (HR 1.23 per URTI; 95%CI 1.03, 1.48; p=0.03), OM (HR 2.30 per OM; 95%CI 1.48, 3.59; p=0.01), and wheezing symptoms (HR 1.22 per wheeze episode; 95%CI 1.05, 1.43; p 0.01) all increased the risk of SDB. An infant's risk of SDB was 1.84 greater if their mother had symptoms for SDB (95%CI 1.14, 2.95; p=0.01).

Paternal symptoms for SDB did not increase the infant's risk of SDB (HR 1.39; 95%CI 0.74, 2.61; p=0.31; Appendix 6 Table 10b). There was no difference in SES and ethnicity between

subjects with and without SDB. Environmental irritants such as TRAP (HR 0.88 per every 1 ppb of NO_2; 95%CI 0.98, 1.10; p=0.22; Appendix 6 Table 10c) and amount of fine dust vacuumed in the infant's bedroom (HR 1.00 per every 1 mg; 95%CI 1.00, 1.00; p=0.96) were not significantly associated with SDB risk. Parental reports of infant smoke exposure (prenatal and post partum) were not significantly associated with SDB. Urine cotinine levels at 3 months were also did not significantly affect SDB risk (HR 0.99 per every 1 ng/mL; 95%CI 0.96, 1.04; p=0.87; Appendix 6 Table 10a).

3.4.4 Multivariate analyses for SDB. Risk factors associated with an increased risk of SDB in multivariate Cox regression, adjusted for gender (Table 13), included OM (HR 2.09 per OM; 95%CI 1.36, 3.21; p< 0.001), prematurity as defined as GA less than 37 weeks but greater than 34 weeks (HR 2.09 per GA week; 95%CI 1.05, 4.15; p=0.05), and maternal symptoms for SDB (HR: 1.80, 95%CI1.12, 2.90; p=0.02). The analyses were adjusted for sleep duration. SDB risk decreased by 17% for every one hour increase in average sleep duration (HR 0.83 per hour; 95%CI 0.73,0.95; p=0.01). SES, birth weight for GA Z-Scores, and BMI Z-scores were not associated with SDB in multivariate analysis.

Table 13: Survival analysis for SDB risk factors

	Model 1: PSQ with rhinitis questions included		*Model 2: PSQ with rhinitis questions excluded*	
Factor	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Female	0.67 (0.45, 1.01)	0.06	0.76 (0.51 - 1.13)	0.18
Preterm	2.09 (1.05, 4.15)	0.05	1.24 (0.54 - 2.83)	0.61
Maternal symptoms for SDB	1.80 (1.12, 2.90)	0.02	1.37 (0.85, 2.22)	0.19
Average sleep in first year of life (hours)	0.82 (0.70, 0.96)	0.02	0.80 (0.68, 0.94)	0.01
Total number of OM events	2.09 (1.36, 3.21)	<0.001	1.55 (0.99, 2.44)	0.06
Child has symptoms for rhinitis	NA	NA	3.08 (2.05, 4.67)	<0.001

Infant symptoms for rhinitis were associated with a 3.08 increase risk of SDB (95%CI 2.05, 4.67; p<0.001) in the model where the PSQ questions related to rhinitis were excluded and symptoms for rhinitis were entered as a covariate in the model. OM and sleep duration remained significantly associated with SDB risk in this model. Prematurity (HR 1.24; 95%CI 0.54, 2.83; p=0.61) and maternal symptoms for SDB (HR 1.37; 95%CI .85, 2.22; p=0.19) were not significantly associated with SDB in the redefined model that included PSQ rhinitis questions as a SDB risk factor.

An additional analysis was also completed where only PSQ questions relating to symptoms that were strongly associated with SDB risk with an odds ratio 9 or greater[40] were used to define SDB. Similar to the prior analyses, every additional OM event was associated with a 2.32 increase risk of SDB (95%CI 1.55, 3.47; p<0.001; Table 14). Maternal symptoms for SDB were associated with a 1.70 increase risk for infant SDB (95%CI 1.05, 2.74; p=0.03). Female sex was not associated with an increased risk of SDB in the additional analysis (HR 0.73; 95%CI 0.49, 1.09; p=0.12). When PSQ rhinitis questions were excluded from the PSQ, child symptoms for rhinitis had the strongest association with SDB risk (HR 9.12, 95%CI 5.42, 15.38; p<0.001) and OM remained a risk factor for SDB (HR 1.83 per OM; 95%CI 1.22, 2.75; p<0.001). Maternal symptoms for SDB were not significantly associated with SDB risk in this model.

Table 14: Survival analysis using only symptoms strongly associated with SDB*				
	Model 1: PSQ with rhinitis questions included		*Model 2: PSQ with rhinitis questions excluded*	
Factor	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Female	0.73 (0.49, 1.09)	0.12	0.80 (0.53, 1.20)	0.28
Preterm	1.51 (0.70, 3.27)	0.29	1.53 (0.70, 3.27)	0.29
Maternal symptoms for SDB	1.70 (1.05, 2.74)	0.03	1.40 (0.87, 2.27)	0.17
Average sleep in first year of life (hours)	0.83 (0.71, 0.98)	0.02	0.87 (0.73, 1.02)	0.09
Total number of OM events	2.32 (1.55, 3.47)	<0.001	1.83 (1.22, 2.75)	<0.001
Child has symptoms for rhinitis	NA	NA	9.12 (5.42, 15.38)	<0.001

* PSQ questions were related to symptoms associated with SDB with an odds ratio of 9 or more according to a validation study[40]. Symptoms included: snoring, apnea, and mouth breathing.

Chapter 4: Discussion and Conclusions

This study expands on our knowledge that the factors that influence infant sleep duration are multidimensional. Sleep, however, is strongly influenced by social cues such as parental behaviours[66]. Self-soothing, breastfeeding, sleep times before 21:00, and independent sleeping were significantly associated with longer sleep durations. These findings have implications for clinical practice and suggest that infant sleep may be modifiable[157]. Behavioural interventions that focus on parental-child interactions may be advantageous in instances in which infant sleep problems do arise[172]. Extinction (i.e. removing inappropriate parental attentions that foster problematic sleep[172]) and stimulus control (i.e. setting appropriate cues for sleep onset such as pre-bedtime routines[172]) are examples of behavioural interventions that focus on parentally set social interactions and cues that are conducive to infant sleep. These interventions have shown high rates of success[157] and may effectively treat common childhood sleep disorders[172].

Our study supports the transactional model of sleep-wake regulation. The transactional model proposes that parent-infant interactions[52] mediate the dynamic, bidirectional interaction between infant sleep and their social environmental. Parental interventions may lead to infant sleep problems and infant sleep problems may lead to parental interventions[52,173]. This bidirectional relationship is evident within our population as parent's perception of infant sleep problems was consistently associated with sleep duration. Parental perceptions may predict parental behaviours[174] and influence the type and amount of parental involvement[173] with regards to their infant's sleep. A parent that perceives that their child has problematic sleep may intervene more during sleep, which, in turn, may lead to sleep problems. Consequently, adjusting parental expectations may also be an important intervention strategy[175] since parent-child interactions may be the most direct, immediate link in affecting infant sleep[66].

Sleep times and self-soothing were consistently and strongly associated with infant sleep duration in cross-sectional and longitudinal analysis in our population. Similarly, sleep times explained 23.8% of the variation in sleep duration while self-soothing explained 3.2% of the variation seen in sleep duration in a cross-cultural study of 29,287 infants[66]. Shimada et al., 1999, suggest that infants' sleep-wake cycle (i.e. circadian and ultradian rhythms) are entrained to maternal social cues (i.e. such as bedtime interactions) which are dictated by mother's regular daily cycle[176]. Parental-infant bedtime interactions may be the most important sleep-wake

entrainment cue in early infancy since an infant's visual pathways are still developing and unable to fully utilize environmental cues such as light and dark[177]. As a result, inappropriate social cues such as excessive parental soothing and late bedtimes may lead to circadian rhythm entrainments that manifest as problematic sleep. Our study suggests that parents may want to enforce consistent sleep times before 21:00 and focus on interactions that promote self-soothing to facilitate longer sleep durations. Placing a child in their crib awake so that they do not become dependent on particular parental cues (i.e. rocking if the child often falls asleep while being rocked) and use of sleep aids (i.e. objects infused with maternal odour, pacifiers) have been associated with greater self-soothing in infants[161]. Future analyses may be needed to identify the predictors of self-soothing in infants.

Subsequent-born infants had longer sleep durations at 3 and 6 months of age in our population compared to first-born infants. This finding provides further evidence that parental interactions, especially in the few months, have a strong influence on sleep duration prior to the development of the sleep-wake cycle[58]. Our study also suggests that first-born and subsequent-born infants have may fundamentally different parent-infant interactions, as factors associated with sleep durations were different amongst the two groups (i.e. age and feeding method were significantly associated with sleep duration in subsequent-born infants but not first-born infants). Parents may feel and behave differently toward their children depending on their child rearing experiences, availability of time, and energy (i.e. a mother with multiple children may, by necessity, spend less time with subsequent-born in the child's first year of life compared to a first-born child. This mother, therefore, may intervene less during their subsequent-born child's sleep. As a result, their child may be more likely to learn self-soothing techniques and have longer sleep durations) [178]. First time parents may also have greater anxiety and respond more readily to their infant's needs, and inadvertently prevents their child from learning self-soothing techniques in early infancy[58]. Excessive parental soothing may lead to sleep disorders such as sleep-onset association type BIC and result in shorter sleep durations, especially if a parent attempts to change parent soothing interactions after 9 months of age[52]. The association between birth order and sleep duration suggests that parent-child bedtime interactions in infancy are the best predictors of sleep and sleep problems in early childhood[82]. Future studies may want to examine parent-child interactions and sleep duration in more depth. Other variables such as infant-parent attachment may be a more direct measure of parent-infant interactions. Attachment

describes the relationship between parent and infant in situations in which the infant requires security, safety, and protection[179]. The type of attachment a parent has to their child may predict parental actions during child sleep and sleep disruptions, and thus parent-child bedtime interactions.

Season of birth was one of the few environmental characteristic significantly associated with sleep duration in our population. Light and dark cues are critical in sleep-wake cycle entrainment[2] particularly when circadian and ultradian rhythms are establishing. This importance may explain the early influence (i.e. at 3 months of age) of birth season on sleep duration. Summer has longer periods of daylight or photoperiods, which has been associated with phase delays in the circadian rhythm[180] that lead to longer sleep latency[181] (i.e. time from bedtime to sleep onset), and shorter sleep durations[181]. Circadian typology, an individual's preference for sleep timing, is also affected by photoperiods associated with season of birth[182,183]. Individuals born in summer and spring tend to be evening-types, while individuals born in the winter in the fall tend to be morning-types[182]. Cohen et al., 2012, suggested contextual-family variables such family routines along with photic factors influence sleep timing[180]. Birth seasons and sleep time were not significantly associated in our study. This association may have been confounded through omission of family routines since they were not measured within our study. Sleep-wake schedule in infancy are also greatly influenced by parental choice[183] and an infants needs (i.e. feeding) [180] rather than endogenous schedules[183]. Thus, circadian typology, although seen in pre-school aged children[184], may not be fully apparent until adolescence and adulthood, when individuals are able to set their own sleep schedules.

Breastfeeding was associated with longer sleep durations at 3 months of age in cross-sectional analysis and in longitudinal analysis in our study. Numerous studies have associated breastfeeding with greater night awakenings[60,61,79] and less consolidated nocturnal sleep[82] due to the quick digestibility of breast milk compared to formula and solid foods[58]. Our study focused on total sleep duration (i.e. nocturnal and diurnal sleep) rather than only nocturnal sleep duration, which may account for the discrepancy in our findings compared to other studies. Ramamurthy et al., 2012, found that breastfed infants under 6 months of age compensated for shorter nocturnal sleep duration through increased daytime sleep, which resulted in longer overall sleep durations in a cross-sectional analysis of 0-11 month old infants (n=10,321) [82]. Maternal melatonin found in breast milk may also lead to earlier establishment of infant circadian

rhythms, thus promoting longer sleep durations especially for newborns[185]. Future analysis may want to focus on nocturnal or diurnal sleep independently and specifically from 6 to 12 months of ages, a period at which nocturnal sleep consolidation is achieved.

A substantial portion of the variation in the risk for developing SDB (35-40%) can be attributed to factors with a genetic basis (e.g. craniofacial morphology and central control of ventilation[186]) and gene-environment interactions[186] rather than the social cues that affect infant sleep duration. BMI Z-scores were not associated with SDB risk in our population. However, having a mother with SDB symptoms, male sex, prematurity, OM, and rhinitis increased SDB risk in our population. These risk factors are similar to those seen in older children[147]. The AAP has excluded infants under one year of age in their most recent guidelines for the diagnosis and management of childhood SDB[187]. Characterizing SDB risk factors and understanding the trajectory of pediatric SDB may be helpful in identifying and monitoring genetically susceptible individuals in infant populations[68,131] where guidelines are not available. The findings of this study suggest that screening and treating infants at risk for SDB[68] may be the best strategy in SDB prevention.

Genetic factors such as maternal history of SDB and male sex increased an infant's risk of SDB in our study, a finding that is consist with current literature[129,131]. Infants with a family history of SDB may be genetically predisposed to inherit airway sizes and functions that have a greater propensity for upper airway collapse[129]. Males also had increased SDB risk potentially because of longer upper airways that are more prone collapse compared to females[147]. Perinatal environments experienced by premature infants[139] and environmental factors (i.e. viruses or air pollution) [135] that lead to rhinitis and OM may increase SDB risk in genetically susceptible individuals. Rhinitis was the strongest risk factor for SBD in our population when included in the analysis, causing all other risk factors to be insignificant. Parental reports of habitual snoring and allergic rhinitis were significantly associated with an odds ratio of 5.27 in a cross-sectional study of pre-school children (n=85) with a mean age of 7.25 year olds [136], which supports the association between rhinitis and SDB within our population. Nasal congestion associated with rhinitis exacerbates SDB risk due to increased upper airway resistance[188]. Our study suggests that, since rhinitis is a modifiable risk factor[188], rhinitis monitoring or treatment in infancy may be advantageous in mitigating SDB risk and severity. Our results should be interpreted with caution. To investigate the association between rhinitis and SDB, questions from the validated

PSQ were removed to prevent collinearity. This removal leads to the invalidation of the PSQ. Future analysis using objective measures will be necessary to elucidate the association between rhinitis and SDB.

SDB presents as a heterogeneous disorder: early SDB symptoms such as snoring, apneas, and mouth breathing and lead to later SDB symptoms such as hyperactivity and inattention[189]. OM and rhinitis were strong SDB risk factors when focusing only on snoring, apneas, and mouth breathing symptoms. These risk factors may contribute more readily to disrupted breathing characteristic of SDB because they lead to reduced airway dimensions[190]. Prematurity, maternal symptoms for SDB, and gender became additional SDB risk factors when attention deficit disorder and hyperactivity were included as SDB symptoms. Cognitive impairment (i.e. hyperactivity and attention deficient disorder) and SDB have been found to be more strongly associated in preterm compared to full-term infants[191]. Furthermore, prematurity[192] and male sex[193] may predispose an infant to attention deficit disorder and hyperactivity outside of SDB since not all children with SDB manifest cognitive morbidities[128]. Objective measures, such as PSG, will be needed in future analysis to determine if infants that present with behavioural SDB consequences do so as a result of SDB (i.e. as measured by AHI) or risk factors independent of SDB. Children's whose SDB risk is not associated with prematurity, maternal symptoms for SDB, and gender in early infancy may also need to be followed up in later childhood to determine if they present with "later" SDB symptoms such as attention deficit disorder and hyperactivity.

This study has several strengths. Birth cohort studies are ideal for ascertaining outcome incidence[194]. Temporal sequence between exposures and outcomes may be easier to ascribe in longitudinal studies since all subjects are free of the outcome at study onset[194]. Timing of exposures, which may be as important as exposure itself, during critical periods of development (i.e. in utero, infancy, and childhood) may also be examined in birth cohorts[195]. Prospective collection of broad amounts of information may allow for greater efficiency when identifying risk factors and provides added value for studying outcomes when compared to more narrowly defined cross-sectional studies[195]. Biological sampling prior to outcome onset may provide direct objective evidence for exposure (i.e. smoke, TRAP) and outcome associations, which is an important step in inferring causality[195].

Few studies have examined sleep during early infancy[60]. CHILD SLEEP-E is capable of studying long-term influence of a broad range of genetic and environmental factors on sleep. This study is also able to track the natural history and prevalence of SDB and inadequate sleep within a Canadian population, since currently available literature primarily focuses on American population. Edmonton, the site of the CHILD SLEEP-E project, provides a unique location to investigate the effects of environmental pollutants that are a by-product of oil refineries such as sulphur oxides[196], nitrogen oxides[196], and volatile organic compounds[196] on childhood sleep.

This study has certain limitations. BMI Z-scores were not associated with SDB because our study may have had limited power to detect an association. Obesity (i.e. BMI>28 or BMI Z-score>3 standard deviations[130]) has been strongly associated with SDB[131]; however, only a small proportion of our population was obese (4% at 3 months and 7% at 12 months of age). Our finding is consistent with Redline et al., 1999, who suggested SDB and obesity associations may be less apparent in children than in adults due to relatively lower levels of obesity observed in child[131]. Studies that report a significant association between obesity and SDB also tend to have a high percentage of ethnically diverse populations (i.e. higher proportions of African Americans and Asians) [197]. Ethnicity may independently modulate the relationship between obesity and SDB since certain ethnicities are at greater risk of being obese[197]. A majority of CHILD SLEEP-E participants are Caucasian (58%), further limiting our power to detect an association between obesity and SDB. Obesity and SDB have been significantly associated in older children (>8 years old) rather than in younger children (<8 year olds) potentially because younger children have greater neuromotor tones and stronger ventilator drives that can compensate for upper airway collapse associated with SDB[197]. Studies also suggest that obesity is less apparent in children than adults since children have brisker upper airway reflexes that can serve as a "protective" factor from SDB because they promote greater upper airway stability [131,147].

Environmental irritants were not associated with SDB because our study may have had limited power to detect an association. Exposure to environmental irritants, such as nicotine and TRAP, also demonstrated small variability within our population. Urine cotinine levels of 50ng/ml have been used to distinguish second hand smoke exposures between smokers and non-smokers[198]. Only 2% of our study population had urine cotinine levels above 50ng/ml even though 17% of parents reporting smoking in the infant's household. Non-smoking mothers tend to report higher smoke exposure for their infant than expected based on their infant's observed

urine cotinine levels[199]. A majority of CHILD SLEEP-E mothers (95.6%) were non-smoker, which may explain discrepancies between infant smoke exposure reports and infant urine cotinine measurements.

Our study had a non-representative sample, which may be a result of selection bias. Selection bias occurs when there is a substantial difference in association measurements between participants and non-participants because of some underlying factor[200]. Many of our participants had higher SES, higher levels of education, and were Caucasian. This bias may have been introduced due to recruitment methods[201] since a majority of our successfully recruited participant visited prenatal clinics in more affluent areas. Participants of the ALSPAC study, a pregnancy cohort of 13,761 families spanning two generations, also had higher SES than the general population and were predominantly Caucasian[202]. Individuals with higher SES and higher levels of education may be more likely to participate in studies due to greater trust in scientific research and higher levels of volunteerism in these groups compared to individuals of lower SES and education levels[203]. As a result, selection bias limits generalizability and our study findings may not be applicable to non-Caucasian ethnicities, lower SES, and lower educated groups[202].

Missing data and attrition (or LTFU) may have introduced selection bias[201,204]. Data was not always missing completely at random (MCAR) within our population, and in some instances missing values may have been dependent on other variables that were included in the analysis[201] (i.e. there was a statistically significant association of infants with missing family income values and sleep duration in longitudinal analysis). Missing data and LTFU are most likely to occur in socioeconomically deprived groups[49]. Attrition was found to be greatest for mother that experienced more adversity during index pregnancy such as inadequate housing and lack of social support in the ALSPAC birth cohort[202]. This limitation is of particular importance in the longitudinal analysis of sleep duration since GEE methods assume that data is MCAR. Missing values for self-soothing were not significantly associated with sleep duration; however, the missing values for some variables (i.e. paternal symptoms for SDB and feeding type) were significantly associated with the outcome. A systematic difference is likely to exist between participants with and without missing data, as demonstrated by the significance of the missing value term. As a result, model co-efficients may be biased. The degree (i.e. magnitude) and the direction (i.e. over or underestimated) of this bias is difficult to determine since the mechanism

by which the data is missing (i.e. missing values are dependent on the variable with the missing data – Missing not at random (MNAR) or missing value is dependent on another variable-Missing at random (MAR)) is not explicitly known[170]. The results of this study, therefore, must be interpreted with caution. Furthermore, the entire trajectory for SDB occurrence and sleep duration could not be determined because some measurements were not collected at all assessment points to reduce participation burden (i.e. missing by design). Missing anthropometric measurements (i.e. weight and height) at 6 and 9 months of age may explain the null association between BMI Z-score and SDB risk[68]. Missing data, regardless of whether the data is missing selectively, randomly, or by design, is a common limitation of cohort studies[201]. As a result, missing data needs to be addressed when interpreting study associations as it reduces the external generalizability (i.e. the validity and extent to which study inferences can be applied to populations outside of source population).

Media use was not measured within the first year of life, and may be a possible unmeasured confounder in our analysis of sleep duration. Studies have reported 19% of child under the age of one have televisions in their bedroom and 30% of parents incorporate television viewing into bedtime routines[205]. Media use has been significantly associated with increased bedtime resistant, delays and difficulties with sleep onset, and shorter sleep duration[205]. SLEEP-E CHILD measures media usage in child five years of age. Future analysis may be needed to elucidate the association between sleep duration and media in young infants.

Parental reports are the main source of data for children's sleep[44] and were the primary method of data collection within our study. Parents may only be aware of sleep disturbance or problems that require parental intervention[44]. Parental fatigue may distort perceptions of their child's sleep when parents are aware of sleep problems[206]. As a result, parental reports of infant sleep are vulnerable to measurement errors, despite being validated against objective measures, because the accuracy of these measurements are dependent on the quality of the reporter's observations[108]. A comparative study of actigraphy and sleep questionnaires found that parents overestimate their children's total sleep[49] as they tend to report earlier sleep times and later wake times[207]. Increasing discrepancies in sleep quality measurements (i.e. night wakings) were also observed between parental reports and actigraphy measurements over several weeks due to decreased parental motivation and increased burden of monitoring their child's sleep[206].

Similarly, SDB outcomes in our study are vulnerable to measurement error. Pediatric SDB symptoms are subtle and may not be immediately recognized by parents[147]. In young infants, it may also be difficult to identify more subjective symptoms of SDB such as inattention and hyperactivity. Some parents may tend to rate their child high for any pathologic finding[158], thus perceptions of their child's sleep and reports about SDB symptoms may be biased by factors unrelated to actual sleep problems[206]. Biases inherent in parental reports are expected to be non-differential[55] meaning that measurements errors not dependent on the status of other variables[201] (i.e. all parents have the same amount of measurement error). Sleep duration and SDB associations found in our study, therefore, should not be distorted[49,55].

Future analyses will incorporate objective sleep measures such as PSG. SLEEP-E subjects completed in-home PSG (NOX-T3 portable sleep monitoring) for one night at 12 months of age. PSG can be used to diagnosis SDB, examine sleep duration, and also sleep quality – an outcome measure that may be of interest in future studies. In-home sleep studies, when scored by a trained sleep physician, can take up to 45 minutes to fully score (i.e. reviewing data quality, identifying hypopneas and apneas) [160]. Thus, objective measures, although available, were not incorporated in this analysis because the labour-intensive process of study scoring has not been completed. Literature on the reliability in-home pediatric PSG also remains sparse[41]. SLEEP-E is currently undertaking a validation study to determine the concordance between in-home PSG and in-clinic PSG, as well determining if automated scoring can reliably replace manual scoring of pediatric sleep studies. Scored sleep studies will be incorporated in study analysis once available.

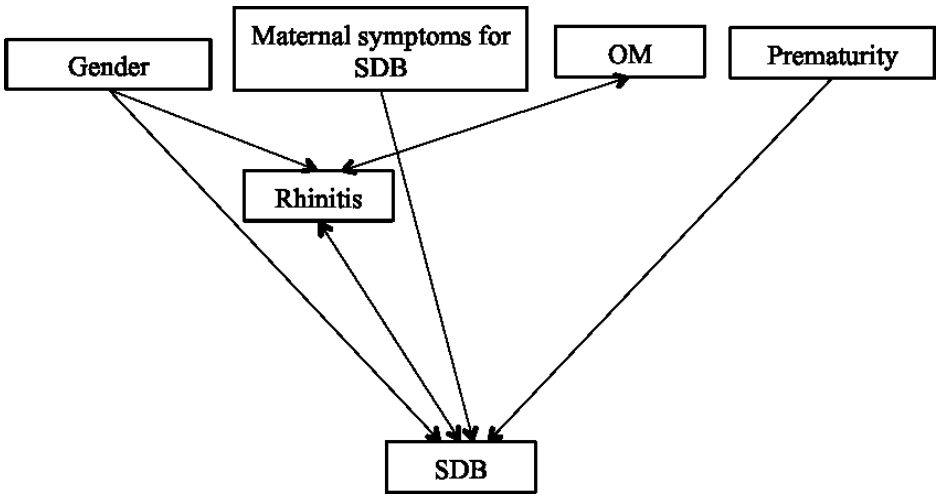
A first born child in our study had 19 minutes less sleep than a subsequent born child, while a child that slept after 21:00 had 40 minutes less a child that slept before 21:00 – two differences that were statistically significant. Future studies are also needed to assess the clinical relevance of sleep duration differences. CHILD SLEEP-E participants complete neurodevelopmental testing such as the NEPSY and BAYLEY's annually until the age of 5. Differences in neurodevelopment in later childhood may be used to evaluate the clinical significance and elucidate whether the magnitude of sleep duration differences affect the severity of adverse health outcomes previously associated with inadequate sleep.

Use of alternative modelling methods, such as growth curve modeling may be beneficial in future analyses. Growth curves use a subject-specific statistical approach[208] to estimate

between-person differences in within-person change over time[209] (i.e. models individual trajectories and the group trajectory[209]). Conversely, multivariate linear regression using GEE methods uses a population-averaged statistical approach and accounts for clustering but does not distinguish between observations of the same or different individuals[208] (i.e. models only the group trajectory[209]). Growth curve models of sleep duration may identifying the variables that lead to individual sleep differences, whereas the multivariate linear regression using GEE methods used in this thesis identifies the variables that affect the sleep duration of the sample mean. Growth modelling was not undertaken in this analysis because of the complexities in modeling infant sleep in the first year of life due to the nonlinear age-related trends of sleep in first year of life[157]. More frequent assessments may also be needed for future infant sleep studies to reflect sleep milestones and the rapid development of sleep in the first year of life[15].

Factors that affect rhinitis may be investigated in future analyses. Rhinitis was the strongest risk factor for SDB within our population; however, the causal relationship of rhinitis and SDB is unclear[210]. Rhinitis can lead to SDB-like symptoms such as snoring and daytime sleepiness through mechanisms different from SDB[210]. Structural equation modelling (SEM) may be used to determine rhinitis risk factors to elucidate its contributions to SDB. SEM can be used to examine reciprocal relationships between risk factors and outcomes, making SEM a powerful tool in longitudinal pediatric sleep research[211]. SEM uses path diagrams to examine complex, multidimensional relationships between independent variable(s) and dependent variable(s) simultaneously[212]. Path diagrams present variables within boxes that are connected by lines with arrows to indicate hypothesized relationships[212] (Figure 6). These diagrams along with sample data can be translated into a series of analyzable equations and matrices, using maximum likelihood estimation, to estimate regression coefficients and variances and covariances of independent variables in the model[212].

Figure 6: Proposed SEM for SDB



Childhood sleep should be a major public heath focus. Sleep losses, which lead to sleep problems, during childhood may be additive and persist well into adulthood if left untreated[60,72]. This study provides further support that problematic infant sleep may be modifiable[65]. Parents may employ behavioural interventions that focus on parent-child bedtime interactions such a parental soothing, co-sleeping, and bedtimes when addressing infant sleep problems[175]. Parent-child interactions (i.e. use of sleep aids, putting child asleep while they are awake) that foster a child's ability to self-soothe may be of particular importance. Sleep problems such as SDB that have a greater gene and gene-environment basis may not be as easily modified. Treatment of rhinitis, a strong risk factor for SDB, may mitigate SDB consequences. However, identifying[131] and monitoring[68] susceptible individuals may be an ideal long-term strategy for SDB prevention and treatment. Childhood may be the ideal point of entry to introduce intervention or prevention strategies to address problematic sleep[49] that lead to healthier lifestyles well into adulthood[47].

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Appendices

Appendix 1: CHILD Study University of Alberta Research Ethics Approval

Re-Approval Form

Date:	March 7, 2014
Principal Investigator:	Piushkumar Mandhane
Study ID:	Pro00002099
Study Title:	The Canadian Healthy Infant Longitudinal Development (CHILD) study
Approval Expiry Date:	March 13, 2015
Sponsor/Funding Agency:	Alberta Centre for Child, Family and Community Research CIHR - Canadian Institutes for Health Research
Sponsor/Funding Agency	AllerGen NCE Inc.

The Health Research Ethics Board - Biomedical Panel has reviewed the renewal request and file for this project and found it to be acceptable within the limitations of human experimentation.

The re-approval for the study as presented is valid for another year. It may be extended following completion of the annual renewal request. Beginning 45 days prior to expiration, you will receive notices that the study is about to expire. Once the study has expired you will have to resubmit. Any proposed changes to the study must be submitted to the HREB for approval prior to implementation.

All study-related documents should be retained so as to be available to the HREB on request. They should be kept for the duration of the project and for at least five years following study completion. In the case of clinical trials approved under Division 5 of the Food and Drug regulations of Health Canada, study records must be retained for 25 years.

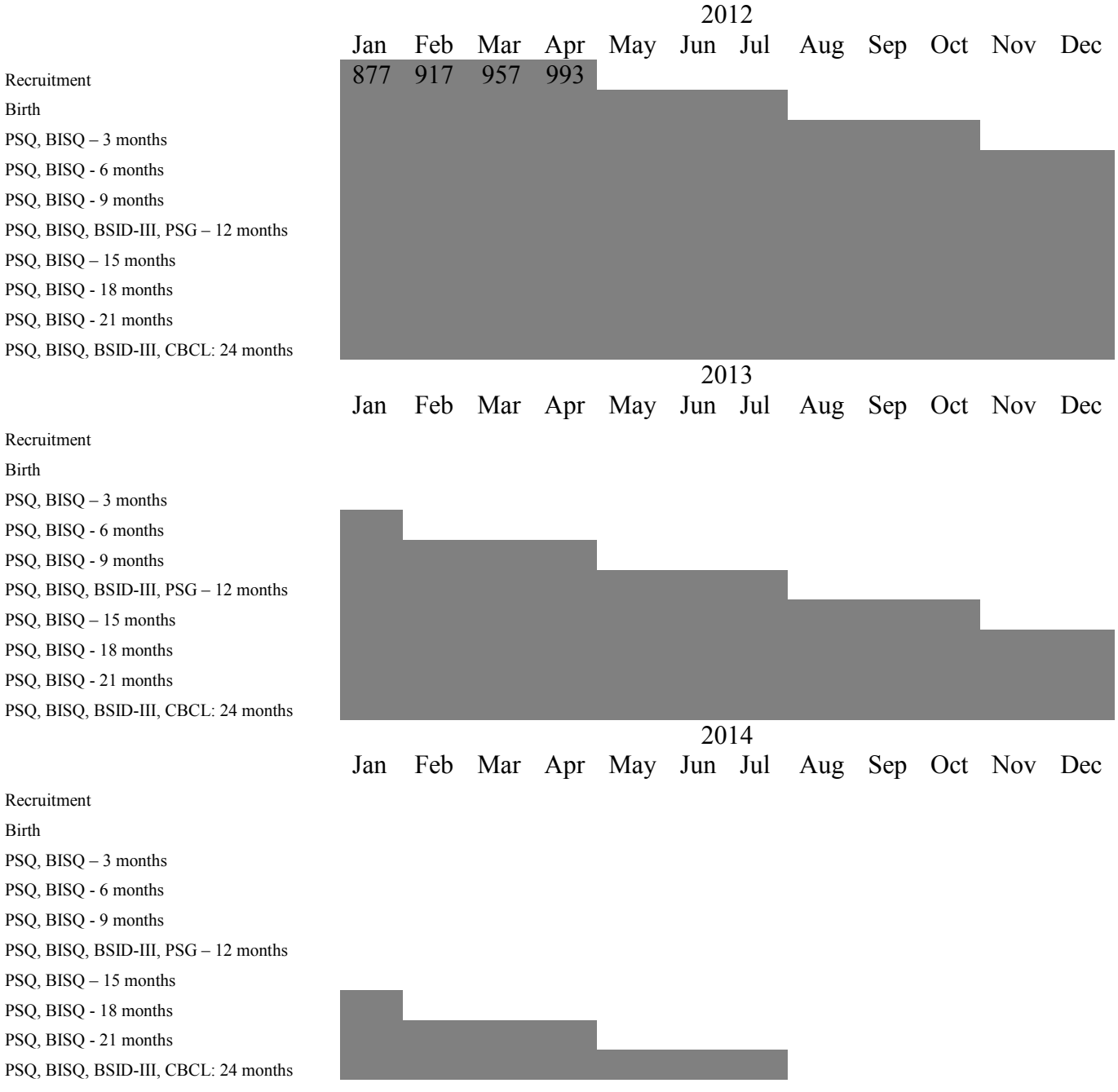
Sincerely,

Dr. Glen J. Pearson, BSc, BScPhm, PharmD, FCSHP
Associate Chair, Health Research Ethics Board – Biomedical Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Appendix 2: Study timeline for SLEEP-E Project

Grey boxes mean active study participant visits are occurring. The numbers in the boxes estimate the number of study participants who have completed that phase of the SLEEP-E project. The numbers from the top row are repeated for each subsequent row with a lag of 3 months reflecting recruitment at 28 weeks gestational age or earlier in pregnancy.



Legend:

PSQ: Pediatric Sleep Questionnaire
BISQ: Brief Infant Sleep Questionnaire
PSG: Polysomnography
BSID-III: Bayley Scale of Infant Development - Version III
CBCL: Child Behaviour Checklist

Appendix 3: Brief Infant Sleep Questionnaire (BISQ)

Role of Responder: [ ] Father [ ] Mother [ ] Grandparent [ ] Other, Specify:
Name of the child: _____
Date of Birth: Month _____ Day: _____ Year: _____
Sex: ___ Male ___ Female

Sleeping arrangement:
[ ] Infant crib in a separate room
[ ] Infant crib in parents' room
[ ] In parents' bed
[ ] Infant crib in room with sibling
[ ] Other, Specify: _____

In what position does your child sleep most of the time?
[ ] On his/her belly
[ ] On his/her side
[ ] On his/her back

How much time does your child spend in sleep during the NIGHT (between 7 in the evening and 7 in the morning)? Hours: _____ Minutes: _____

How much time does your child spend in sleep during the DAY (between 7 in the morning and 7 in the evening)? Hours: _____ Minutes: _____

Average number of night wakings per night: _____

How much time during the night does your child spend in wakefulness (from 10 in the evening to 6 in the morning)? Hours: _____ Minutes: _____

How long does it take to put your baby to sleep in the evening? Hours: _____ Minutes: _____

How does your baby fall asleep?
[ ] While feeding
[ ] Being rocked
[ ] Being held
[ ] In bed alone
[ ] In bed near parent

When does your baby usually fall asleep for the night: Hours: _____ Minutes: _____

Do you consider your child's sleep as a problem?
[ ] A very serious problem
[ ] A small problem
[ ] Not a problem at all

Appendix 4: Pediatric Sleep Questionnaire (PSQ)

Name: _____ Person completing form_____

Date that you are completing the questionnaire: ____/____/____

Instructions: Please answer the questions on the following pages regarding the behaviour of your child during sleep and wakefulness **IN THE LAST MONTH**. The questions apply to how your child acts in general, not necessarily during the past few days since these may not have been typical if your child has not been well. If you are not sure how to answer any question, please feel free to ask your husband or wife, child, or physician for help. You should circle the correct response or *print* your answers neatly in the space provided. A "Y" means "yes," "N" means "no," and "DK" means "don't know." When you see the word "usually" it means "more than half the time" or "on more than half the nights."

Please answer the following questions as they pertain to your child <u>in the past month</u>.

		YES	NO	Don't Know
1.	**While sleeping, does your child:**			
	Ever snore?	Y	N	DK
	Snore more than half the time?	Y	N	DK
	Always snore?	Y	N	DK
	Snore loudly?	Y	N	DK
	Have "heavy" or loud breathing?	Y	N	DK
	Have trouble breathing, or struggle to breath?	Y	N	DK
2.	**Have you ever seen your child stop breathing during the night**... *if so, please describe what happened:*	Y	N	DK
3.	**Does your child:**			
	Tend to breathe through the mouth during the day?	Y	N	DK
	Have a dry mouth on waking up in the morning?	Y	N	DK
	Occasionally wet the bed?	Y	N	DK
4.	**Does your child:**			
	Wake up feeling unrefreshed in the morning?	Y	N	DK
	Have a problem with sleepiness during the day?	Y	N	DK
5.	**Has a teacher or other supervisor commented that your child appears sleepy during the day?**	Y	N	DK
6.	**Is it hard to wake your child up in the morning?**	Y	N	DK
7.	**Does your child wake up with headaches in the morning?**	Y	N	DK
8.	**Did your child stop growing at a normal rate at any time since birth?**	Y	N	DK
9.	**Is your child overweight?**	Y	N	DK

		YES	NO	Don't Know
	if yes, at what age did this first develop?			
10.	**This child often:**			
	Does not seem to listen when spoken to directly.....	Y	N	DK
	Has difficulty organizing tasks and activities.....	Y	N	DK
	Is easily distracted by extraneous stimuli	Y	N	DK
	Fidgets with hands or feet, or squirms in seat	Y	N	DK
	Is "on the go" or often acts as if "driven by a motor"	Y	N	DK
	Interrupts or intrudes on others (ex. Butts into conversations or games).....	Y	N	DK
11.	**Is your child**			
	Restless during sleep?	Y	N	DK
	Sweaty during sleep so that pyjamas are wet? ……..……	Y	N	DK
12.	**Does your child**			
	Wake up during the night to pee?.....	Y	N	DK
	Have a stuffy nose or is congested at night?.....	Y	N	DK
	Have asthma that is diagnosed by a doctor?.....	Y	N	DK
	Mouth breathes most of the time?.....	Y	N	DK
	Complain of an upset stomach at night?.....	Y	N	DK
	Get a burning feeling in the throat at night?.....	Y	N	DK
	Cough before falling asleep or first thing in the morning? ……..……	Y	N	DK
	Cough during the night?.....	Y	N	DK

Appendix 5: Global Sleep Assessment Questionnaire

GLOBAL SLEEP ASSESSMENT QUESTIONNAIRE

Patient Initials: ___ ___ ___ Date: ___/___/___	Employment Status: ☐ Day shift ☐ Night shift ☐ Rotating shift
Age:_____ Sex: ☐ Male ☐ Female	☐ Retired ☐ Unemployed ☐ Employed Full-time
Height: ____ Weight: _____	☐ Employed Part-time ☐ Homemaker (Please check all that apply.)
Over the past month, have you had a major or stressful event that you feel affected your sleep? If so, please describe: _____	

INSTRUCTIONS: Please answer the questions below by writing on the line provided or by checking the box that best describes you. Please select only one answer for each question.

During the **PAST 4 WEEKS**, how often . . .

(Check one box on each line.)

1	Did you have difficulty falling asleep, staying asleep, or feeling poorly rested in the morning?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
2.	Did you fall asleep unintentionally or have to fight to stay awake during the day?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
3.	Did sleep difficulties or daytime sleepiness interfere with your daily activities?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
4.	Did work or other activities prevent you from getting enough sleep?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
5.	Did you snore loudly?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
6.	Did you hold your breath, have breathing pauses, or stop breathing in your sleep?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
7.	Did you have restless or "crawling" feelings in your legs at night that went away if you moved your legs?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
8.	Did you have repeated rhythmic leg jerks or leg twitches during your sleep?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
9.	Did you have nightmares, or did you scream, walk, punch, or kick in your sleep?	☐ Never	☐ Sometimes	☐ Usually	☐ Always
10.	Did the following things disturb your sleep:				
	a. Pain	☐ Never	☐ Sometimes	☐ Usually	☐ Always
	b. Other physical problems.....	☐ Never	☐ Sometimes	☐ Usually	☐ Always
	c. Worries.....	☐ Never	☐ Sometimes	☐ Usually	☐ Always
	d. Medications	☐ Never	☐ Sometimes	☐ Usually	☐ Always
	e. Other:	☐ Never	☐ Sometimes	☐ Usually	☐ Always
	_____ (Please specify)				
11	Did you feel sad or anxious?	☐ Never	☐ Sometimes	☐ Usually	☐ Always

Appendix 6: Additional tables

Table 1a: Child characteristics of study population with and without total sleep duration data in longitudinal analysis

Variable	Included	Excluded	p value
Categorical	**% (SDB/total)**	**% (SDB/total)**	
Non self-soother	71.13 (483/679)	NA	NA*
Preterm	4.94 (37/749)	4.55 (2/44)	0.91
Male	50.46 (386/765)	60.71 (34/56)	0.14
Caucasian	68.88 (456/662)	58.33 (35/60)	0.09
First-born	43.61 (331/759)	42.22 (19/26)	0.86
SDB	4.58 (31/677)	NA	NA*
Symptoms for rhinitis	35.31 (238/674)	NA	NA*
GER	3.54 (23/650)	0.00 (0/2)	0.79*
URTI	45.72 (299/654)	50.00 (1/2)	0.90*
Wheeze	9.34 (61/653)	0.00 (0/2)	0.65*
OM	0.92 (6/651)	0.00 (0/2)	0.89*
Atopy	15.41 (104/675)	33.33 (2/6)	0.23
Breastfed Only	49.20 (309/628)	NA	NA*
Sleeps on belly	8.26 (56/678)	NA	NA*
Bed Shares	82.89 (562/678)	NA	NA*
Sleep time after 21:00	35.02 (235/671)	NA	NA*
Born in the Winter	46.27 (180/389)	38.71 (12/31)	0.42
Continuous	**Mean (95%CI)**	**Mean (95%CI)**	
Amount of daylight on date of birth (hours)	12.46 (12.23, 12.69) n=765	12.86 (11.98, 13.74)	0.37
Birth weight for GA Z-Score	-0.01 (-0.07, 0.06) n=758	-0.02 (-0.28, 0.24) n=44	0.91
BMI Z-score	0.09 (0.00, 0.17) n=638	1.9 (NA) n=1	NA*

*measured at 3 months
** measured at 6 months

Table 1b: Family characteristics of study population with and without total sleep duration data in longitudinal analysis			
Variable	**Included**	**Excluded**	**p value**
Categorical	**% (SDB/total)**	**% (SDB/total)**	
Married/Common Law	94.68 (712/752)	88.73 (63/71)	0.04
Household income ≥$60,000	85.67 (592/691)	72.34 (34/47)	0.01
Mother attended post- secondary	91.64 (581/634)	79.59 (39/49)	0.01
Maternal symptoms for SDB	58.39 (362/620)	100.00 (3/3)	0.14
Maternal sleep problems	86.11 (533/619)	100.00 (3/3)	0.49
Paternal symptoms for SDB	75.68 (308/407)	87.50 (21/24)	0.19
Paternal sleep problems	78.38 (319/407)	87.50 (21/24)	0.29
Child's sleep is considered very serious problem	79.09 (537/679)	NA	NA*
Continuous	**Mean (95%CI)**	**Mean (95%CI)**	
Mother's Age (years)	31.37 (31.05, 31.69) n=765	30.01 (28.61, 31.40) n=56	0.03
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)	15.33 (14.96, 15.69) n=571	14.5 (-17.27, 46.27) n=2	0.79
Maternal Stress (PSS)	11.83 (11.28, 12.38) n=556	9.00 (-54.53, 72.53) n=2	0.54**
Maternal Depression (CES-D)	7.99 (7.35, 8.63) n=556	4.00 (4, 4) n=2	0.47**
Number of household members	3.95 (3.87, 4.02) n=687	3.00 (NA) n=1	NA*

*measured at 3 months

** measured at 6 months

Table 1c: Environmental/household characteristics of study population with and without total sleep duration data in longitudinal analysis			
Variable	**Included**	**Excluded**	**p-value**
Categorical	**% (SDB/total)**	**% (SDB/total)**	
Smoking			
Prenatal Smoking	4.09 (28/684)	14.75 (9/61)	<0.001
Smoking location			
At baby's home	16.89 (116/687)	100.00 (1 /1)	0.03*
Inside baby's home	5.22 (6/115)	0.00 (0/1)	0.82*
Outside baby's home	18.26 (21/115)	0.00 (0/1)	0.64*
Near baby's home	89.57 (103/115)	100.00 (1 /1)	0.73*
Proximity to:	21.80 (150/688)	0.00 (0/1)	0.60*
Highway	0.58 (4/688)	0.00 (0/1)	0.94*
Factory	12.79 (88/688)	0.00 (0/1)	0.70*
Gas station	14.51 (94/648)	0.00 (0/1)	0.68*
Parking lot	22.84 (148/ 648)	100.00 (1 /1)	0.07*
Construction	22.34 (142/635)	50.00 (7/14)	0.02
Continuous	**Mean (95%CI)**	**Mean (95%CI)**	
Amount of daylight on sleep duration reporting (hours)	NA	NA	NA
Average TRAP exposure (ppb)	11.20 (10.89, 11.51) n=581	10.33 (7.91, 12.74) n=7	0.54
Infant bedroom fine dust sample (mg)	1413.72 (1336.31, 1491.12) n=700	2420.60 (NA) n=1	NA

*measured at 3 months

Table 2a: Univariate analysis of child variables for total sleep duration in longitudinal analysis			
Variables			**p-value**
Continuous	**Categories**	**Average Sleep (hours) (95% CI)**	
Child's ability to self soothe	Self-soother	14.0 (13.9, 14.1)	Reference
	Not self-soother	13.4 (13.3, 13.5)	<0.001
Age	3	14.1 (13.9, 14.3)	Reference
	6	13.7 (13.5, 13.8)	<0.001
	9	13.4 (13.3, 13.5)	<0.001
	12	13.5 (13.4, 13.6)	<0.001
Term	Preterm	13.7 (13.4, 14.0)	Reference
	Full term	13.7 (13.6, 13.7)	0.95
Gender	Male	13.7 (13.6, 13.8)	Reference
	Female	13.7 (13.6, 13.8)	0.89
Ethnicity	Caucasian	13.7 (13.6, 13.8)	Reference
	Non-Caucasian	13.7 (13.5, 13.8)	0.79
Birth order	First-born	13.5 (13.4, 13.6)	Reference
	Subsequent-born	13.8 (13.7, 13.9)	<0.001
Symptoms for Rhinitis	No	13.7 (13.7, 13.8)	Reference
	Yes	13.6 (13.4, 13.7)	0.83
GER	No	13.8 (13.7, 13.9)	Reference
	Yes	13.4 (12.7, 14.2)	0.33
URTI	No	13.8 (13.7, 13.9)	Reference
	Yes	13.8 (13.7, 13.9)	0.40
Wheeze	No	13.8 (13.7, 13.9)	Reference
	Yes	13.6 (13.3, 14.0)	0.20
OM	No	13.8 (13.7, 13.9)	Reference
	Yes	13.5 (13.1, 13.8)	0.10
Atopy	No	13.7 (13.6, 13.8)	Reference
	Yes	13.7 (13.5, 13.9)	0.96
Breastfeeding	Breastfed Only	14.2 (14.0, 14.4)	Reference
	Formula Fed Only	13.9 (13.4, 14.4)	0.17
	Solids Only	13.7 (13.4, 13.9)	<0.001
	Mix-fed	13.7 (13.6, 13.8)	<0.001
Sleep Position	On Belly	13.6 (13.5, 13.7)	Reference
	On Side	13.5 (13.3, 13.7)	0.67
	On Back	13.8 (13.7, 13.9)	0.001
Co-sleep	No	13.8 (13.7, 13.9)	Reference
	Room sharing	13.6 (13.4, 13.8)	0.47
	Bed sharing	13.2 (13.0, 13.4)	0.01
Sleep time	Before 21:00	14.0 (13.9, 14.0)	Reference
	After 21:00	13.3 (13.2, 13.4)	<0.001
Birthday Season	Winter	13.8 (13.6, 13.9)	Reference
	Spring	13.7 (13.6, 13.9)	0.82
	Summer	13.6 (13.5, 13.3)	0.41
	Fall	13.6 (13.4, 13.7)	0.26
Continuous		**Co-efficient (hours) (95% CI)**	
Amount of daylight on date of birth (hours)		0.00 (-0.03, 0.03)	1.00
Birth weight for GA Z-Score		0.11 (0.00, 0.21)	0.05
BMI Z-Score		-0.08 (-0.18, 0.02)	0.11

Table 2b: Univariate analysis of family variables for total sleep duration in longitudinal analysis			
Variables			**p-value**
Categorical	**Categories**	**Average Sleep (hours) (95% CI)**	
Marital Status	Married/Common Law	13.7 (13.6, 13.8)	Reference
	Divorced or Separated/Single	13.3 (12.9, 13.6)	0.07
Household Income	< $60,000	13.6 (13.4, 13.8)	Reference
	≥ $60,000	13.7 (13.7, 13.8)	0.47
Maternal Education	Mother has not attended post-secondary	13.9 (13.6, 14.1)	Reference
	Mother attended post-secondary	13.6 (13.6, 13.7)	0.25
	Other	13.1 (11.9, 14.3)	0.23
Mother has symptoms for SDB	No	13.8 (13.7, 13.9)	Reference
	Yes	13.6 (13.5, 13.7)	0.14
Mother reported sleep problems	No	14.0 (13.8, 14.2)	Reference
	Yes	13.6 (13.5, 13.7)	0.01
Father has symptoms for SDB	No	14.0 (13.8, 14.1)	Reference
	Yes	13.6 (13.5, 13.7)	0.01
Father reported sleep problems	No	13.6 (13.4, 13.8)	Reference
	Yes	13.7 (13.6, 13.8)	0.61
Parent's cognition of child's sleep	Not a problem	13.9 (13.8, 14.0)	Reference
	A small problem	13.0 (12.9, 13.2)	<0.001
	A very serious problem	11.8 (11.1, 12.4)	<0.001
Continuous		**Co-efficient (hours) (95% CI)**	
Mother's Age (years)		-0.02 (-0.04, 0.01)	0.14
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)		0.00 (-0.03, 0.03)	0.87
Maternal Stress (PSS)		-0.02 (-0.04, -0.01)	0.00
Maternal Depression (CES-D)		-0.02 (-0.04, -0.01)	0.00

Table 2c: Univariate analysis of environment/household variables for total sleep duration in longitudinal analysis			
Variables			**p-value**
Categorical	**Categories**	**Average Sleep (hours) (95% CI)**	
Season when total sleep was reported	Winter	13.6 (13.5, 13.8)	Reference
	Spring	13.8 (13.6, 13.9)	0.06
	Summer	13.7 (13.6, 13.9)	0.19
	Fall	13.6 (13.4, 13.7)	0.80
Maternal prenatal smoking	No	13.7 (13.6, 13.8)	Reference
	Yes	13.9 (13.5, 14.2)	0.31
Smoking location:			
At baby's home	No	13.8 (13.7, 13.9)	Reference
	Yes	13.8 (13.6, 14.0)	0.62
Inside baby's home	No	13.8 (13.6, 14.1)	Reference
	Yes	13.4 (12.3, 14.4)	0.43
Outside baby's home	No	13.8 (13.6, 14.1)	Reference
	Yes	13.7 (12.9,14.4)	0.67
Near baby's home	No	13.2 (12.2, 14.3)	Reference
	Yes	13.9 (13.6, 14.1)	0.21
Proximity to:			
Highway	No	13.9 (12.8, 14.0)	Reference
	Yes	13.7 (13.4, 13.9)	0.50
Factory	No	13.8 (13.7, 13.9)	Reference
	Yes	12.1 (8.3, 15.9)	0.38
Gas station	No	13.9 (12.7, 14.0)	Reference
	Yes	13.7 (13.3, 14.0)	0.35
Parking lot	No	13.8 (13.7, 14.0)	Reference
	Yes	14.0 (13.6, 14.3)	0.31
Construction	No	13.9 (13.8, 14.0)	Reference
	Yes	13.8 (13.5, 14.0)	0.22
Continuous		**Co-efficient (hours) (95% CI)**	
Amount of daylight on sleep duration reporting (hours)		0.01 (-0.01, 0.04)	0.15
Average TRAP exposure (ppb)		0.01 (-0.02, 0.04)	0.39
Infant bedroom fine dust sample (mg)		NA	NA

Table 3 – Sensitivity analysis of multivariate longitudinal analysis model for sleep duration		
Variable	**Co-efficient (hours) (95% CI)**	**p-value**
Needs to be soothed	-0.44 (-0.60, -0.29)	<0.001
Sleeps after 21:00	-0.63 (-0.79, -0.46)	<0.001
Sleep Problem (not a problem at all ref.)		
A small problem	-0.74 (-0.91, -0.57)	<0.001
A very serious problem	-1.95 (-2.47, -1.44)	<0.001
Subsequent-born	0.40 (0.21, 0.59)	<0.001
Age (3 months as ref)		
6	-0.41 (-0.59, -0.23)	<0.001
9	-0.69 (-1.01, -0.37)	<0.001
12	-0.78 (-1.04, -0.52)	<0.001
Feed (breastfeeding only as ref.)		
Formula feed only	-0.49 (-0.90, 0.08)	0.02
Only Solids	-0.53 (-0.93, -0.13)	0.01
Mixed-fed	-0.40 (-0.64, -0.15)	<0.001
Paternal symptoms for SDB	-0.30 (-0.59, -0.01)	0.04
Female	-0.14 (-0.33, 0.04)	0.12
Intercept	15.37 (15.01, 15.72)	<0.001

Table 4a: Child characteristics of study population with and without total sleep duration data in cross-sectional analysis

	3 months of age			*6 months of age*			*9 months of age*			*12 months of age*		
Variable	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**
Categorical	**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**	
Non self-soother	71.24 (483/ 678)	0.00 (0/1)	0.12	60.19 (372/618)	100.00 (1/1)	0.42	44.27 (282/637)	100 (3/3)	0.05	33.77 (207/613)	NA	NA
Preterm	4.98 (33/663)	4.62 (6/130)	0.86	4.64 (28/604)	5.78 (10/173)	0.54	5.13 (32/624)	3.85 (5/130)	0.54	4.63 (28/605)	5.85 (11/188)	0.50
Male	49.71 (337/ 678)	57.75 (82/142)	0.08	50.97 (315/618)	50.85 (90/177)	0.98	49.61 (316/637)	56.06 (74/132)	0.18	50.08 (308/615)	54.37 (112/206)	0.29
Caucasian	69.05 (406/ 588)	63.85 (83/130)	0.25	72.54 (391/539)	52.41 (76/145)	<0.001	71.17 (390/548)	57.14 (64/112)	0.00	72.81 (399/548)	52.87 (92/174)	<0.001
First-born	44.28 (298/ 673)	39.69 (52/131)	0.33	46.00 (282/613)	35.63 (62/174)	0.02	43.60 (276/633)	44.62 (58/130)	0.83	44.26 (270/610)	41.24 (80/194)	0.46
SDB	4.61 (31/ 673)	0.00 (0/4)	0.66	4.96 (29/585)	0.00 (0/2)	0.75	7.56 (48/635)	0.00 (0/3)	0.62	6.13 (37/604)	25.00 (1/4)	0.12
Symptoms for rhinitis	35.07 (235/670)	75.00 (3/4)	0.10	23.58 (137/581)	0.00 (0/2)	0.43	34.65 (219/632)	33.33 (1/3)	0.96	23.13 (139/601)	50.00 (2/4)	0.21
GER	3.46 (22/ 636)	6.25 (1/16)	0.55	3.15 (17/540)	0.00 (0/5)	0.69	NA	NA	NA	1.61 (9/560)	0.00 (0/14)	0.63
URTI	45.62 (292/ 640)	50.00 (8/16)	0.73	51.52 (289/561)	75.00 (3/4)	0.35	NA	NA	NA	79.21 (461/582)	100.00 (6/6)	0.21
Wheeze	9.55 (61/ 639)	0.00 (0/16)	0.19	5.35 (30/561)	0.00 (0/4)	0.64	NA	NA	NA	10.67 (62/581)	16.67 (1/6)	0.64
OM	0.94 (6/ 637)	0.00 (0/16)	0.70	2.32 (13/560)	0.00 (0/4)	0.76	NA	NA	NA	10.50 (61/581)	16.67 (1/6)	0.63
Atopy	15.07 (91/ 604)	19.48 (15/ 77)	0.31	13.49 (75/556)	24.39 (30/123)	0.00	15.56 (91/585)	16.09 (14/87)	0.90	15.65 (92/588)	15.05 (14/93)	0.88
Breastfed Only	49.19 (302/ 614)	50.00 (7/14)	0.84	9.68 (54/558)	0.00 (0/4)	NA	NA	NA	NA	NA	NA	NA
Sleeps on belly	8.27 (56/ 677)	0.00 (0/1)	0.88	16.83 (104/618)	0.00 (0/1)	0.74	42.70 (272/637)	33.33 (1/3)	0.21	51.95 (319/614)	NA	NA
Bed Shares	17.13 (116/ 677)	0.00(0/1)	0.65	14.40 (89/618)	0.00 (0/1)	0.68	12.87 (82/637)	33.33 (1/3)	0.29	11.91 (73/613)	NA	NA
Sleep time after 21:00	64.93 (435/670)	100.00 (1/1)	0.46	45.84 (281/ 613)	0.00 (0/1)	0.36	27.60 (175/634)	33.33 (1/3)	0.83	26.59 (163/613)	NA	NA
Born in the Winter	25.07 (170/678)	15.49 (22/142)	0.16	25.24 (156/618)	16.95 (30/177)	0.08	26.37 (168/637)	11.36 (15/132)	<0.001	25.85 (159/615)	16.02 (33/206)	0.01
Continuous	**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**	
Amount of daylight on date of birth (hours)	12.21 (11.98, 12.45) n=678	13.80 (13.26, 14.33) n=142	<0.001	12.38 (12.13 - 12.63) n= 618	12.96 (12.48, 13.44) n=177	0.03	12.25 (12.00, 12.50) n=637	13.77 (13.27, 14.27) n=132	<0.001	12.40 (12.14, 12.66) n= 615	12.74 (12.32, 13.17) n=206	0.19
Birth weight for GA Z-Score	-0.01 (-0.07, 0.06) n=672	0.01 (-0.16, 0.17) n=130	0.86	-0.03 (-0.10, 0.04) n=612	0.07 (-0.06, 0.20) n=174	0.17	-0.03 (-0.09, 0.04) n=633	0.07 (-0.08 - 0.22) n=130	0.26	0.01 (-0.06, 0.08) n=610	-0.05 (-0.18, 0.08) n=192	0.46
BMI Z-score	0.09 (0.01, 0.17) n=625	0.14 (-0.45, 0.73) n =14	0.86	NA	NA	NA	NA	NA	NA	0.27 (0.17, 0.38) n=471	0.26 (- 0.02, 0.54) n=61	0.92

Table 4b: Family characteristics of study population with and without total sleep duration data in cross-sectional analysis												
	3 months of age			*6 months of age*			*9 months of age*			*12 months of age*		
Variable	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**
Categorical	**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**	
Married/Common Law	94.90 (633/667)	90.73 (137/151)	0.05	95.21 (576/605)	90.45 (161/178)	0.02	95.37 (597/626)	88.64 (117/132)	0.00	95.23 (579/608)	91.16 (196/215)	0.03
Household income ≥$60,000	86.62 (531/613)	75.61 (93/123)	0.00	86.89 (497/572)	79.29 (111/140)	0.02	87.46 (509/582)	77.68 (87/112)	0.01	88.30 (513/581)	71.97 (113/157)	<0.001
Mother attended post-secondary	91.52 (518/566)	84.03 (100/119)	0.00	92.16 (482/523)	83.21 (114/137)	0.01	92.19 (484/525)	83.93 (94/112)	0.75	92.22 (486/527)	83.75 (134/160)	<0.001
Maternal symptoms for SDB	57.87 (320/553)	64.29 (45/70)	0.30	57.20 (306/535)	66.67 (58/87)	0.10	58.72 (313/533)	60.26 (47/78)	0.80	58.02 (340/586)	67.57 (25/37)	0.25
Maternal sleep problems	86.05 (475/552)	87.14 (61/70)	0.80	85.96 (459 /534)	87.36 (76/87)	0.73	85.71 (456/532)	88.46 (69/78)	0.51	85.81 (502/585)	91.89 (34/37)	0.30
Paternal symptoms for SDB	75.41 (279/370)	81.67 (49/60)	0.29	75.75 (253/334)	80.49 (66/82)	0.36	75.57 (266/352)	80.39 (41/51)	0.45	75.00 (255/340)	81.32 (74/91)	0.21
Paternal sleep problems	78.38 (290/370)	81.67 (49/60)	0.56	79.34 (265/334)	74.39 (61/82)	0.33	79.26 (279/352)	74.51 (38/51)	0.44	77.65 (264/340)	83.52 (76/91)	0.22
Child's sleep is considered very serious problem	1.62 (11/678)	0.00 (0/1)	NA	2.43 (15/618)	0.00 (0/1)	NA	1.57 (10/636)	0.00 (0/3)	NA	1.47 (9/613)	NA	NA
Continuous	**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**	
Mother's Age (years)	31.35 (31.01, 31.68) n=678	30.97 (30.13, 31.80) n=142	0.36	31.49 (31.15, 31.84) n=618	30.64 (29.92, 31.36) n=177	0.03	31.56 (31.21, 31.91) n=637	30.40 (29.59, 31.21) n=132	0.01	31.63 (31.28, 31.97) n=615	30.24 (29.56, 30.92) n=206	<0.001
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)	15.26 (14.88, 15.64) n=512	15.85 (14.53, 17.18) n=61	0.33	15.40 (15.00, 15.80) n=500	14.65 (13.88, 15.42) n=72	0.18	15.33 (14.93, 15.72) n=494	15.14 (14.17, 16.12) n=71	0.74	15.31 (14.94, 15.68) n=562	16.00 (13.17, 18.83) n=11	0.61
Maternal Stress (PSS)	NA	NA	NA	11.83 (11.28, 12.38) n=553	10.60 (7.22, 13.98) n=5	0.68	NA	NA	NA	12.26 (11.71, 12.80) n=561	10.67 (7.65, 13.68) n=12	0.41
Maternal Depression (CES-D)	NA	NA	NA	8.01 (7.36, 8.66) n =553	4.20 (3.47, 4.93) n=5	0.28	NA	NA	NA	7.82 (7.19, 8.45) n=561	6.00 (3.85, 8.15) n=12	0.41
Number of household members	3.94 (3.87, 4.02) n=670	3.94 (3.51, 4.38) n=18	1.00	3.87 (3.78, 3.95) n=556	3.25 (2.76, 3.74) n=4	0.21	NA	NA	NA	3.94 (3.85, 4.02) n=570	4.00 (3.55, 4.45) n=23	0.77

Table 4c: Environmental/household characteristics of study population with and without total sleep duration data in cross-sectional analysis												
	3 months of age			*6 months of age*			*9 months of age*			*12 months of age*		
Variable	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**	**Included**	**Excluded**	**p value**
Categorical	**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**		**% (SDB/total)**	**% (SDB/total)**	
Smoking												
Prenatal Smoking	4.44 (27/608)	6.77 (9/133)	0.26	3.95 (22/557)	6.67 (10/150)	0.16	3.53 (20/567)	9.57 (11/115)	0.01	3.72 (21/565)	8.89 (16/180)	0.01
Smoking location												
At baby's home	16.87 (113/670)	22.22 (4/18)	0.55	11.73 (65/554)	0.00 (0/4)	0.47	NA	NA	NA	15.11 (86/569)	4.35 (1/23)	0.15
Inside baby's home	5.36 (6/112)	0.00 (0/4)	0.64	4.62 (3/65)	NA	NA	NA	NA	NA	3.49 (3/86)	0.00 (0/1)	0.85
Outside baby's home	18.75 (21/112)	0.00 (0/4)	0.34	4.62 (3/65)	NA	NA	NA	NA	NA	10.47 (9/86)	0.00 (0/1)	0.73
Near baby's home	89.29 (100/112)	100.00 (4/4)	0.49	92.31 (60/65)	NA	NA	NA	NA	NA	89.53 (77/86)	100.00 (1/1)	0.73
Proximity to:												
Highway	21.76 (146/671)	22.22 (4/18)	0.96	NA	NA	NA	NA	NA	NA	20.70 (118/570)	21.74 (5/23)	0.90
Factory	0.60 (4/671)	0.00 (0/18)	0.74	NA	NA	NA	NA	NA	NA	0.00 (0/570)	4.35 (1/23)	<0.001
Gas station	12.82 (86/671)	11.11 (2/18)	0.83	NA	NA	NA	NA	NA	NA	13.16 (75/570)	8.70 (2/23)	0.53
Parking lot	14.65 (93/635)	7.14 (1/14)	0.43	NA	NA	NA	NA	NA	NA	11.23 (64/570)	13.04 (3/23)	0.79
Construction	22.34 (142/635)	50.00 (7/14)	0.02	NA	NA	NA	NA	NA	NA	22.63 (129/570)	30.43 (7/23)	0.38
Continuous	**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**		**Mean (95%CI)**	**Mean (95%CI)**	
Amount of daylight on sleep duration reporting (hours)	12.37 (12.15, 12.59) n=677	11.05 (NA) n=1	0.66	12.25 (12.00, 12.50) n=611	8.45 (NA) n=1	0.38	11.75 (11.50, 12.00) n=573	11.83 (6.75, 16.92) n=3	0.96	12.60 (12.32, 12.88) n=518	NA	NA
Average TRAP exposure (ppb)	11.17 (10.83 , 11.50) n=529	11.41 (10.83, 11.99) n=59	0.64	11.00 (10.66, 11.36) n=480	12.11 (11.56, 12.68) n=105	0.01	11.19 (10.86, 11.53) n=504	11.39 (10.64, 12.15) n=75	0.67	11.13 (10.80, 11.47) n=503	11.52 (10.80, 12.25) n=85	0.38
Infant bedroom fine dust sample (mg)	681.02 (635.82, 726.22) n=672	641.52 (163.13, 819.92) n 25	0.74	NA	NA	NA	NA	NA	NA	NA	NA	NA

Table 5a: Univariate analysis of child variables for total sleep duration at 3 months of age

Variables				p-value
Continuous	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Child's ability to self soothe	Self-soother	28.76 (195)	14.6 (14.3, 14.9)	Reference
	Not self-soother	71.24 (483)	13.9 (13.7, 14.1)	<0.001
Term	Preterm	4.87 (33)	14.3 (13.5, 15.0)	Reference
	Full term	92.92 (630)	14.1 (13.9, 14.2)	0.65
Gender	Male	49.71 (337)	14.0 (13.8, 14.3)	Reference
	Female	50.29 (341)	14.2 (13.9, 14.4)	0.42
Ethnicity	Caucasian	59.88 (406)	14.0 (13.9, 14.2)	Reference
	Non-Caucasian	26.84 (182)	14.3 (14.0,14.7)	0.14
Birth order	First-born	43.95 (298)	13.6 (13.4, 13.9)	Reference
	Subsequent-born	55.31 (375)	14.5 (14.3, 14.7)	<0.001
Symptoms for Rhinitis	No	64.16 (435)	14.2 (14.0, 14.4)	Reference
	Yes	34.66 (235)	14.0 (13.7, 14.2)	0.13
GER	No	90.56 (614)	14.2 (14.0, 14.3)	Reference
	Yes	3.24 (22)	13.6 (12.5, 14.7)	0.20
URTI	No	51.33 (348)	14.0 (13.8, 14.3)	Reference
	Yes	43.07 (292)	14.3 (14.1, 14.6)	0.06
Wheeze	No	85.25 (578)	14.2 (14.0, 14.3)	Reference
	Yes	9.00 (61)	14.2 (13.6, 14.8)	0.94
OM	No	93.07 (631)	14.2 (14.0, 14.3)	Reference
	Yes	0.88 (6)	13.9 (11.9, 15.9)	0.77
Atopy	No	75.66 (513)	14.1 (13.9, 14.3)	Reference
	Yes	13.42 (91)	14.5 (14.1, 14.9)	0.10
Breastfeeding	Breastfed Only	44.54 (302)	14.3 (14.0, 14.5)	Reference
	Formula Fed Only	10.77 (73)	14.0 (13.4, 14.5)	0.28
	Solids Only	NA	NA	NA
	Mix-fed	35.35 (239)	14.1 (13.8, 14.4)	0.35
Sleep Position	On Belly	8.26 (56)	14.2 (13.6, 14.8)	Reference
	On Side	12.39 (84)	14.0 (13.5, 14.6)	0.63
	On Back	79.20 (537)	14.1 (13.9, 14.3)	0.68
Co-sleep	No	44.10 (299)	14.2 (13.9, 14.4)	Reference
	Room sharing	38.64 (262)	14.0 (13.7, 14.3)	0.37
	Bed sharing	17.11 (116)	14.2 (13.8 14.6)	0.83
Sleep time	Before 21:00	34.66 (235)	14.6 (14.4, 14.9)	Reference
	After 21:00	64.16 (435)	13.8 (13.6, 14.0)	<0.001
Birthday Season	Winter	25.07 (170)	14.4 (14.0, 14.7)	Reference
	Spring	28.17 (191)	14.2 (13.9, 14.5)	0.47
	Summer	21.98 (149)	14.0 (13.7, 14.3)	0.14
	Fall	24.78 (168)	13.9 (13.6, 14.2)	0.04
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on date of birth (hours)		678	-0.01 (-0.06, 0.04)	0.61
Birth weight for GA Z-Score		672	0.14 (-0.04, 0.33)	0.14
BMI Z-Score		625	-0.07 (-0.22, 0.09)	0.40

Table 5b: Univariate analysis of family variables for total sleep duration at 3 months of age				
Variables				**p-value**
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Marital Status	Married/Common Law	93.36 (633)	14.1 (14.0, 14.3)	Reference
	Divorced or Separated/Single	5.01 (34)	13.4 (12.8, 14.0)	0.04
Household Income	< $60,000	12.09 (82)	14.1 (13.6, 14.5)	Reference
	≥ $60,000	78.32 (531)	14.2 (14.0, 14.4)	0.64
Maternal Education	Mother has not attended post-secondary	6.49 (44)	13.9 (13.4, 14.4)	Reference
	Mother attended post-secondary	76.40 (518)	14.1 (13.9, 14.2)	0.57
	Other	0.59 (4)	13.1 (12.5, 13.7)	0.51
Mother has symptoms for SDB	No	34.37 (233)	14.2 (13.9, 14.5)	Reference
	Yes	47.20 (320)	14.1 (13.9, 14.4)	0.63
Mother reported sleep problems	No	11.36 (77)	14.4 (13.9, 14.9)	Reference
	Yes	70.06 (475)	14.1 (13.9, 14.3)	0.31
Father has symptoms for SDB	No	13.42 (91)	14.3 (13.8, 14.7)	Reference
	Yes	41.15 (279)	14.0 (13.8, 14.3)	0.40
Father reported sleep problems	No	11.80 (80)	14.0 (13.5, 14.5)	Reference
	Yes	42.77 (290)	14.1 (13.9, 14.4)	0.60
Parent's cognition of child's sleep	Not a problem	79.06 (536)	14.3 (14.1, 14.5)	Reference
	A small problem	19.32 (131)	13.5 (13.1, 13.9)	<0.001
	A very serious problem	1.62 (11)	11.5 (10.5, 12.4)	<0.001
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Mother's Age (years)		678	0.03 (-0.01, 0.06)	0.15
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)		512	-0.01 (-0.05, 0.04)	0.80
Maternal Stress (PSS)		NA	NA	NA
Maternal Depression (CES-D)		NA	NA	NA

Table 5c: Univariate analysis of environment/household variables for total sleep duration at 3 months of age

Variables				p-value
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Season when total sleep was reported	Winter	26.25 (178)	14.0 (13.7, 14.3)	Reference
	Spring	32.01 (217)	14.2 (13.9, 14.5)	0.25
	Summer	23.60 (160)	14.2 (13.9, 14.5)	0.32
	Fall	18.14 (123)	14.0 (13.6, 14.2)	0.91
Maternal prenatal smoking	No	85.69 (581)	14.1 (13.9, 14.3)	Reference
	Yes	3.98 (27)	13.8 (13.1, 14.5)	0.48
Smoking at baby's home	No	82.15 (557)	14.2 (14.0, 14.3)	Reference
	Yes	16.67 (113)	13.9 (13.5, 14.3)	0.31
Smoking inside baby's home	No	15.63 (106)	13.9 (13.5, 14.3)	Reference
	Yes	0.88 (6)	14.3 (13.2, 15.3)	0.04
Smoking outside baby's home	No	13.42 (91)	13.9 (13.5, 14.4)	Reference
	Yes	3.10 (21)	14.0 (12.9, 15.0)	0.91
Smoking near baby's home	No	1.77 (12)	13.7 (12.0, 15.3)	Reference
	Yes	14.75 (100)	14.0 (13.5, 14.4)	0.65
Proximity to highway	No	77.43 (525)	14.2 (14.0, 14.4)	Reference
	Yes	21.53 (146)	13.9 (13.6, 14.3)	0.21
Proximity to factory	No	98.38 (667)	14.1 (14.0, 14.3)	Reference
	Yes	0.59 (4)	12.1 (8.3, 15.9)	0.06
Proximity to gas station	No	86.28 (585)	14.1 (13.9, 14.3)	Reference
	Yes	12.68 (86)	14.1 (13.6, 14.5)	0.90
Proximity to parking lot	No	79.94 (542)	14.1 (14.0, 14.3)	Reference
	Yes	13.72 (93)	14.3 (13.9, 14.7)	0.48
Proximity to construction	No	72.71 (493)	14.2 (14.1, 14.4)	Reference
	Yes	20.94 (142)	13.9 (13.6 14.3)	0.13
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on sleep duration reporting (hours)		677	0.05 (-0.01, 0.10)	0.10
Average TRAP exposure (ppb)		529	0.05 (0.00, 0.09)	0.05
Infant bedroom fine dust sample (mg)		676	0.00 (0.00, 0.00)	0.75

Table 6a: Univariate analysis of child variables for total sleep duration at 6 months of age

Variables				p-value
Continuous	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Child's ability to self soothe	Self-soother	39.81 (246)	14.2 (14.0, 14.4)	Reference
	Not self-soother	60.19 (372)	13.3 (13.1, 13.4)	<0.001
Term	Preterm	4.53 (28)	13.6 (13.0, 14.3)	Reference
	Full term	93.20 (576)	13.7 (13.5, 13.8)	0.90
Gender	Male	50.97 (315)	13.6 (13.4, 13.8)	Reference
	Female	49.03 (303)	13.7 (13.5, 13.9)	0.87
Ethnicity	Caucasian	63.27 (391)	13.7 (13.5, 13.8)	Reference
	Non-Caucasian	23.95 (148)	13.6 (13.3, 13.9)	0.61
Birth order	First-born	45.63 (282)	13.5 (13.3, 13.7)	Reference
	Subsequent-born	53.56 (331)	13.8 (13.6, 14.0)	0.05
Symptoms for Rhinitis	No	71.84 (444)	13.8 (13.6, 13.9)	Reference
	Yes	22.17 (137)	13.3 (13.1, 13.6)	0.01
GER	No	84.63 (523)	13.7 (13.5, 13.8)	Reference
	Yes	2.75 (17)	13.1 (11.5, 14.6)	0.13
URTI	No	44.01 (272)	13.7 (13.5, 13.8)	Reference
	Yes	46.76 (289)	13.0 (12.0, 14.0)	0.72
Wheeze	No	85.92 (531)	13.7 (13.5, 13.8)	Reference
	Yes	4.85 (30)	13.0 (12.0, 14.0)	0.04
OM	No	88.51 (547)	13.6 (13.5, 13.8)	Reference
	Yes	2.10 (13)	14.0 (13.1, 14.8)	0.47
Atopy	No	77.83 (481)	13.7 (13.6, 13.9)	Reference
	Yes	12.14 (75)	13.7 (13.3, 14.1)	0.81
Breastfeeding	Breastfed Only	8.74 (54)	13.7 (13.3, 14.2)	Reference
	Formula Fed Only	2.91 (18)	13.7 (13.0, 14.5)	0.98
	Solids Only	NA	NA	NA
	Mix-fed	78.64 (486)	13.6 (13.5, 13.8)	0.75
Sleep Position	On Belly	16.83 (104)	13.8 (13.4, 14.1)	Reference
	On Side	20.39 (126)	13.4 (13.2, 13.7)	0.11
	On Back	62.78 (388)	13.7 (13.5, 13.9)	0.63
Co-sleep	No	64.72 (400)	14.0 (13.7, 14.1)	Reference
	Room sharing	20.87 (129)	13.3 (13.0, 13.6)	0.00
	Bed sharing	14.40 (89)	13.0 (12.7, 13.4)	<0.001
Sleep time	Before 21:00	53.72 (332)	14.0 (13.8, 14.2)	Reference
	After 21:00	45.47 (281)	13.3 (13.1, 13.5)	<0.001
Birthday Season	Winter	25.24 (156)	13.9 (13.6, 14.2)	Reference
	Spring	27.51 (170)	13.5 (13.2, 13.8)	0.04
	Summer	24.60 (152)	13.6 (13.4, 13.9)	0.12
	Fall	22.65 (140)	13.6 (13.4, 13.8)	0.12
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on date of birth (hours)		618	-0.02 (-0.07, 0.02)	0.25
Birth weight for GA Z-Score		612	0.09 (-0.07, 0.24)	0.27
BMI Z-Score		NA	NA	NA

Table 6b: Univariate analysis of family variables for total sleep duration at 6 months of age

Variables				p-value
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Marital Status	Married/Common Law	93.20 (576)	13.7 (13.6, 13.8)	Reference
	Divorced or Separated/Single	4.69 (29)	13.3 (12.6, 13.9)	0.18
Household Income	< $60,000	12.14 (75)	13.6 (13.3, 14.0)	Reference
	≥ $60,000	80.42 (497)	13.7 (13.6, 13.9)	0.71
Maternal Education	Mother has not attended post-secondary	5.99 (37)	13.9 (13.3, 14.4)	Reference
	Mother attended post-secondary	77.99 (482)	13.7 (13.5, 13.8)	0.51
	Other	0.65 (4)	11.5 (10.5, 12.5)	0.01
Mother has symptoms for SDB	No	37.06 (229)	13.8 (13.6, 14.0)	Reference
	Yes	49.51 (306)	13.6 (13.4, 13.8)	0.13
Mother reported sleep problems	No	12.14 (75)	14.0 (13.6, 14.4)	Reference
	Yes	86.41 (459)	13.6 (13.5, 13.8)	0.10
Father has symptoms for SDB	No	13.11 (81)	14.1 (13.8, 14.4)	Reference
	Yes	40.94 (253)	13.6 (13.4, 13.5)	0.01
Father reported sleep problems	No	11.17 (69)	13.7 (13.3, 14.1)	Reference
	Yes	42.88 (265)	13.7 (13.5, 13.9)	0.93
Parent's cognition of child's sleep	Not a problem	69.26 (428)	13.9 (13.8, 14.1)	Reference
	A small problem	28.32 (175)	13.2 (13.0, 13.4)	<0.001
	A very serious problem	2.43 (15)	11.3 (9.7, 12.9)	<0.001
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Mother's Age (years)		618	-0.02 (-0.05, 0.01)	0.25
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)		500	0.00 (-0.04, 0.03)	0.76
Maternal Stress (PSS)		553	-0.03 (-0.05, 0.01)	0.01
Maternal Depression (CES-D)		553	-0.03 (-0.05, -0.01)	0.00

Table 6c: Univariate analysis of environment/household variables for total sleep duration at 6 months of age

Variables				p-value
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Season when total sleep was reported	Winter	22.65 (140)	13.7 (13.4, 14.0)	Reference
	Spring	24.11 (149)	13.5 (13.2, 13.7)	0.21
	Summer	25.08 (155)	13.8 (13.6, 14.1)	0.60
	Fall	28.16 (174)	13.6 (13.3, 13.9)	0.60
Maternal prenatal smoking	No	86.57 (535)	13.7 (13.6, 13.8)	Reference
	Yes	3.56 (22)	13.7 (13.1, 14.3)	0.96
Smoking at baby's home	No	79.13 (489)	13.7 (13.5, 13.8)	Reference
	Yes	10.52 (65)	13.8 (13.4, 14.2)	0.59
Smoking inside baby's home	No	10.03 (62)	13.9 (13.5, 14.3)	Reference
	Yes	0.49 (3)	11.8 (8.7, 15.0)	0.59
Smoking outside baby's home	No	10.03 (62)	13.9 (13.5, 14.3)	Reference
	Yes	0.49 (3)	13.5 (10.6, 16.4)	0.77
Smoking near baby's home	No	0.81 (5)	12.2 (9.9, 14.5)	Reference
	Yes	9.71 (60)	13.9 (13.5, 14.2)	0.03
Proximity to highway	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to factory	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to gas station	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to parking lot	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to construction	No	NA	NA	NA
	Yes	NA	NA	NA
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on sleep duration reporting (hours)		611	0.02 (-0.02, 0.06)	0.35
Average TRAP exposure (ppb)		480	0.00 (-0.03, 0.04)	0.84
Infant bedroom fine dust sample (mg)		NA	NA	NA

Table 7a: Univariate analysis of child variables for total sleep duration at 9 months of age				
Variables				**p-value**
Continuous	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Child's ability to self soothe	Self-soother	55.73 (355)	13.8 (13.6, 14.0)	Reference
	Not self-soother	44.27 (282)	12.9 (12.7, 13.1)	<0.001
Term	Preterm	5.02 (32)	13.5 (13.1, 14.0)	Reference
	Full term	92.04 (592)	13.4 (13.3, 13.5)	0.68
Gender	Male	49.61 (316)	13.5 (13.3, 13.6)	Reference
	Female	50.39 (321)	13.3 (13.2, 13.5)	0.29
Ethnicity	Caucasian	61.22 (390)	13.4 (13.3, 13.6)	Reference
	Non-Caucasian	24.80 (158)	13.3 (13.0, 13.6)	0.28
Birth order	First-born	43.44 (276)	13.3 (13.1, 13.5)	Reference
	Subsequent-born	56.04 (357)	13.5 (13.3, 13.6)	0.34
Symptoms for Rhinitis	No	64.84 (413)	13.4 (13.3, 13.6)	Reference
	Yes	34.38 (219)	13.3 (13.1, 13.6)	0.50
GER	No	NA	NA	NA
	Yes	NA	NA	NA
URTI	No	NA	NA	NA
	Yes	NA	NA	NA
Wheeze	No	NA	NA	NA
	Yes	NA	NA	NA
OM	No	NA	NA	NA
	Yes	NA	NA	NA
Atopy	No	77.55 (494)	13.5 (13.3, 13.6)	Reference
	Yes	14.29 (91)	13.3 (13.0, 13.6)	0.39
Breastfeeding	Breastfed Only	NA	NA	NA
	Formula Fed Only	NA	NA	NA
	Solids Only	NA	NA	NA
	Mix-fed	NA	NA	NA
Sleep Position	On Belly	42.70 (272)	13.5 (13.3, 13.7)	Reference
	On Side	24.80 (158)	13.3 (13.1, 13.6)	0.34
	On Back	32.50 (207)	13.4 (13.1, 13.8)	0.46
Co-sleep	No	73.94 (471)	13.6 (13.5, 13.7)	Reference
	Room sharing	13.19 (84)	13.1 (12.7, 13.5)	0.00
	Bed sharing	12.87 (82)	12.5 (12.2, 12.9)	<0.001
Sleep time	Before 21:00	72.06 (459)	13.8 (13.6, 13.9)	Reference
	After 21:00	27.47 (175)	12.5 (12.2, 12.7)	<0.001
Birthday Season	Winter	26.37 (168)	13.4 (13.2, 13.7)	Reference
	Spring	26.22 (167)	13.5 (13.2, 13.7)	0.83
	Summer	23.55 (150)	13.4 (13.1, 13.7)	0.87
	Fall	23.86 (152)	13.3 (13.1, 13.6)	0.50
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on date of birth (hours)		637	0.01 (-0.02, 0.05)	0.62
Birth weight for GA Z-Score		633	0.10 (-0.04, 0.25)	0.16
BMI Z-Score		NA	NA	NA

Table 7b: Univariate analysis of family variables for total sleep duration at 9 months of age				
Variables				**p-value**
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Marital Status	Married/Common Law	93.72 (597)	13.4 (13.3, 13.5)	Reference
	Divorced or Separated/Single	4.55 (29)	13.0 (12.4, 13.7)	0.20
Household Income	< $60,000	11.46 (73)	13.2 (12.8, 13.6)	Reference
	≥ $60,000	79.91 (509)	13.5 (13.3, 13.6)	0.12
Maternal Education	Mother has not attended post-secondary	5.81 (37)	14.1 (13.5, 14.6)	Reference
	Mother attended post-secondary	75.98 (484)	13.4 (13.2, 13.5)	0.01
	Other	0.63 (4)	12.8 (11.3, 14.2)	0.12
Mother has symptoms for SDB	No	34.54 (220)	13.6 (13.3, 13.8)	Reference
	Yes	49.14 (313)	13.3 (13.1, 13.5)	0.07
Mother reported sleep problems	No	11.93 (76)	13.9 (13.5, 14.2)	Reference
	Yes	71.59 (456)	13.3 (13.2, 13.5)	0.01
Father has symptoms for SDB	No	13.50 (86)	13.7 (13.3, 14.0)	Reference
	Yes	41.76 (266)	13.3 (13.1, 13.5)	0.11
Father reported sleep problems	No	11.46 (73)	13.4 (13.0, 13.8)	Reference
	Yes	43.80 (279)	13.4 (13.2, 13.6)	0.90
Parent's cognition of child's sleep	Not a problem	75.98 (484)	13.7 (13.5, 13.8)	Reference
	A small problem	22.29 (142)	12.6 (12.3, 12.9)	<0.001
	A very serious problem	1.57 (10)	11.7 (10.6, 12.9)	<0.001
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Mother's Age (years)		637	-0.05 (-0.08, -0.02)	0.00
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)		494	-0.01 (-0.04, 0.02)	0.54
Maternal Stress (PSS)		NA	NA	NA
Maternal Depression (CES-D)		NA	NA	NA

Table 7c: Univariate analysis of environment/household variables for total sleep duration at 9 months of age

Variables				p-value
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Season when total sleep was reported	Winter	29.83 (190)	13.4 (13.2, 13.6)	Reference
	Spring	23.55 (150)	13.4 (13.1, 13.7)	0.96
	Summer	18.52 (118)	13.4 (13.1, 13.8)	0.84
	Fall	28.10 (179)	13.4 (13.1, 13.6)	0.82
Maternal prenatal smoking	No	85.87 (547)	13.4 (13.2, 13.5)	Reference
	Yes	3.14 (20)	13.9 (13.3, 14.5)	0.17
Smoking at baby's home	No	NA	NA	NA
	Yes	NA	NA	NA
Smoking inside baby's home	No	NA	NA	NA
	Yes	NA	NA	NA
Smoking outside baby's home	No	NA	NA	NA
	Yes	NA	NA	NA
Smoking near baby's home	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to highway	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to factory	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to gas station	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to parking lot	No	NA	NA	NA
	Yes	NA	NA	NA
Proximity to construction	No	NA	NA	NA
	Yes	NA	NA	NA
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on sleep duration reporting (hours)		573	-0.02 (-0.07, 0.02)	0.34
Average TRAP exposure (ppb)		504	0.00 (-0.05, 0.03)	0.63
Infant bedroom fine dust sample (mg)		NA	NA	NA

Table 8a: Univariate analysis of child variables for total sleep duration at 12 months of age

Variables				p-value
Continuous	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Child's ability to self soothe	Self-soother	66.02 (406)	13.8 (13.7, 13.9)	Reference
	Not self-soother	33.66 (207)	13.0 (12.7, 13.2)	<0.001
Term	Preterm	4.55 (28)	13.3 (12.9, 13.7)	Reference
	Full term	93.82 (577)	13.5 (13.4, 13.7)	0.52
Gender	Male	50.08 (308)	13.6 (13.4, 13.8)	Reference
	Female	49.92 (307)	13.4 (13.2, 13.6)	0.17
Ethnicity	Caucasian	64.88 (399)	13.6 (13.5, 13.7)	Reference
	Non-Caucasian	24.23 (149)	13.3 (13.0, 13.6)	0.05
Birth order	First-born	43.90 (270)	13.4 (13.2, 13.6)	Reference
	Subsequent-born	55.28 (340)	13.5 (13.4, 13.6)	0.23
Symptoms for Rhinitis	No	75.12 (462)	13.5 (13.4, 13.6)	Reference
	Yes	97.72 (139)	13.5 (13.2, 13.8)	0.97
GER	No	89.59 (551)	13.5 (13.4, 13.6)	Reference
	Yes	1.46 (9)	13.7 (12.9, 14.5)	0.76
URTI	No	19.67 (121)	13.5 (13.3, 13.8)	Reference
	Yes	74.96 (461)	13.5 (13.4, 13.6)	0.87
Wheeze	No	84.39 (519)	13.5 (13.4, 13.6)	Reference
	Yes	10.08 (62)	13.4 (12.9, 14.0)	0.63
OM	No	84.55 (520)	13.5 (13.4, 13.7)	Reference
	Yes	9.92 (61)	13.3 (12.9, 13.7)	0.27
Atopy	No	80.65 (496)	13.5 (13.4, 13.7)	Reference
	Yes	14.96 (92)	13.4 (13.1, 13.7)	0.36
Breastfeeding	Breastfed Only	NA	NA	NA
	Formula Fed Only	NA	NA	NA
	Solids Only	27.80 (171)	13.7 (13.4, 13.9)	Reference
	Mix-fed	66.67 (410)	13.4 (13.3, 13.6)	0.10
Sleep Position	On Belly	51.87 (319)	13.6 (13.4, 13.7)	Reference
	On Side	22.44 (138)	13.4 (13.1, 13.7)	0.38
	On Back	25.52 (157)	13.5 (13.3, 13.7)	0.67
Co-sleep	No	79.19 (487)	13.7 (13.5, 13.8)	Reference
	Room sharing	8.62 (53)	13.2 (12.6, 13.7)	0.02
	Bed sharing	11.87 (73)	12.7 (12.4, 13.1)	<0.001
Sleep time	Before 21:00	73.17 (450)	13.8 (13.7, 13.9)	Reference
	After 21:00	26.50 (163)	12.7 (12.4, 13.0)	<0.001
Birthday Season	Winter	25.85 (159)	13.4 (13.1, 13.6)	Reference
	Spring	26.83 (165)	13.6 (13.4, 13.9)	0.16
	Summer	25.53 (157)	13.5 (13.3, 13.8)	0.39
	Fall	21.79 (134)	13.4 (13.2, 13.7)	0.78

Continuous	**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on date of birth (hours)	615	0.02 (-0.02, 0.06)	0.26
Birth weight for GA Z-Score	610	0.07 (-0.08, 0.21)	0.35
BMI Z-Score	471	-0.05 (-0.17, 0.07)	0.40

Table 8b: Univariate analysis of family variables for total sleep duration at 12 months of age				
Variables				**p-value**
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Marital Status	Married/Common Law	94.15 (579)	13.5 (13.4, 13.6)	Reference
	Divorced or Separated/Single	4.72 (29)	13.3 (12.4, 14.2)	0.52
Household Income	< $60,000	11.06 (68)	13.5 (13.0, 14.0)	Reference
	≥ $60,000	83.41 (513)	13.6 (13.4, 13.7)	0.71
Maternal Education	Mother has not attended post-secondary	6.02 (37)	13.7 (13.1, 14.3)	Reference
	Mother attended post-secondary	79.02 (486)	13.5 (13.3, 13.6)	0.36
	Other	0.65 (4)	14.9 (10.6, 19.1)	0.15
Mother has symptoms for SDB	No	40.00 (246)	13.5 (13.3, 13.7)	Reference
	Yes	55.28 (340)	13.5 (13.3, 13.7)	0.90
Mother reported sleep problems	No	13.50 (83)	13.7 (13.4, 14.0)	Reference
	Yes	81.63 (502)	13.5 (13.3, 13.6)	0.13
Father has symptoms for SDB	No	13.82 (85)	13.8 (13.5, 14.1)	Reference
	Yes	41.46 (255)	13.4 (13.2, 13.6)	0.05
Father reported sleep problems	No	12.36 (76)	13.4 (13.0, 13.7)	Reference
	Yes	42.93 (264)	13.6 (13.4, 13.8)	0.30
Parent's cognition of child's sleep	Not a problem	76.26 (469)	13.7 (13.6, 13.9)	Reference
	A small problem	21.95 (135)	12.8 (12.5, 13.0)	<0.001
	A very serious problem	1.46 (9)	12.9 (12.0, 13.8)	<0.001
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Mother's Age (years)		615	-0.02 (-0.04, 0,01)	0.28
Parent-Child Dysfunctional Interaction (PSI Subscale the P-CDI)		562	0.02 (-0.01, 0.04)	0.29
Maternal Stress (PSS)		561	-0.02 (-0.04, 0.00)	0.01
Maternal Depression (CES-D)		561	-0.03 (-0.04, 0.01)	0.00

Table 8c: Univariate analysis of environment/household variables for total sleep duration at 12 months of age				
Variables				**p-value**
Categorical	**Categories**	**% (n)**	**Average Sleep (hours) (95% CI)**	
Season when total sleep was reported	Winter	25.37 (156)	13.5 (13.3, 13.7)	Reference
	Spring	25.04 (154)	13.7 (13.5, 14.0)	0.18
	Summer	26.83 (165)	13.4 (13.2, 13.7)	0.76
	Fall	22.44 (138)	13.4 (13.1, 13.6)	0.50
Maternal prenatal smoking	No	88.46 (544)	13.5 (13.4, 13.6)	Reference
	Yes	3.41 (21)	14.1 (13.3, 15.0)	0.08
Smoking at baby's home	No	78.54 (483)	13.5 (13.3, 13.6)	Reference
	Yes	13.98 (86)	13.2 (12.0, 14.3)	0.28
Smoking inside baby's home	No	13.50 (83)	13.7 (13.3, 14.1)	Reference
	Yes	0.49 (3)	13.2 (12.0, 14.3)	0.57
Smoking outside baby's home	No	12.52 (77)	13.7 (13.4, 14.1)	Reference
	Yes	1.46 (9)	13.0 (12.2, 13.8)	0.18
Smoking near baby's home	No	1.46 (9)	13.3 (11.7, 14.9)	Reference
	Yes	12.52 (77)	13.7 (13.4, 14.1)	0.43
Proximity to highway	No	73.50 (452)	13.5 (13.4, 13.7)	Reference
	Yes	19.19 (118)	13.4 (13.1, 13.7)	0.40
Proximity to factory	No	92.68 (570)	13.5 (13.4, 13.6)	Reference
	Yes	0 (0)	NA	NA
Proximity to gas station	No	80.49 (495)	13.5 (13.4, 13.7)	Reference
	Yes	12.20 (75)	13.1 (12.8, 13.5)	0.04
Proximity to parking lot	No	82.28 (506)	13.5 (13.4, 13.6)	Reference
	Yes	10.41 (64)	13.4 (13.0, 13.9)	0.79
Proximity to construction	No	71.71 (441)	13.5 (13.3, 13.6)	Reference
	Yes	20.98 (129)	13.6 (13.3, 13.9)	0.29
Continuous		**n**	**Co-efficient (hours) (95% CI)**	
Amount of daylight on sleep duration reporting (hours)		518	0.01 (-0.03, 0.05)	0.57
Average TRAP exposure (ppb)		503	0.01 (-0.03, 0.05)	0.58
Infant bedroom fine dust sample (mg)		NA	NA	NA

Table 9a: Child characteristics of study population with and without SDB data			
Variable	**Outcome Present**	**Outcome Absent**	**p-value**
Categorical variables	% (#/total)	% (#/total)	
Female	49.80 (380/763)	36.21 (21/58)	0.05
Caucasian	68.74 (453/659)	60.32 (38/63)	0.17
First-born	43.86 (332/757)	38.30 (18/47)	0.46
Full Term	95.05 (710/747)	95.65 (44 /46)	0.85
Breastfeed ≥ 3 months	77.15 (564/731)	0.00 (0/0)	NA
Child is atopic	15.41 (104/675)	33.33 (2/6)	0.23
Symptoms for rhinitis	54.00 (412/763)	0.00 (0/0)	NA
Treated for GER	4.66 (34/730)	0.00 (0/6)	0.59
Continuous variables	Mean (95% CI)	Mean (95%CI)	
Birth weight for GA Z-Score	-0.01 (-0.07, 0.05)	0.03 (-0.25, 0.31)	0.77
BMI Z-score at 3 months	0.09 (0.00, 0.17)	1.90 (NA)	0.08
BMI Z-score at 12 months	0.27 (0.18, 0.37)	0.10 (-0.95, 1.14)	0.73
Total URTI	2.38 (2.22, 2.53)	1.50 (0.23, 2.77)	0.41
Total OM	0.14 (0.11, 0.18)	0.00 (NA)	NA
Total Wheezing Episodes	0.36 (0.27, 0.45)	0.00 (NA)	NA
Average Sleep in first year of life (hours)	13.65 (13.55, 13.74)	13.50 (12.00, 15.00)	0.85
Infant urine cotinine at 3 months (ng/mL)	2.39 (0.82, 3.96)	0.27 (-0.18, 0.72)	0.76

Table 9b: Family characteristics of study population with and without SDB data			
Variable	**Outcome Present**	**Outcome Absent**	**p-value**
Categorical variables	% (#/total)	% (#/total)	
Household income of ≥$60,000	85.78 (591/689)	71.43 (35/49)	0.01
Mother attended post-secondary	91.02 (578/635)	80.77 (42/52)	0.01
Mother is atopic	61.50 (417/678)	66.67 (4/6)	0.80
Mother has symptoms for SDB	58.39 (362/620)	100.00 (3/3)	0.14
Father is atopic	61.26 (204/333)	62.50 (15/24)	0.90
Father has symptoms for SDB	75.62 (307/406)	88.0 (22/25)	0.16

Table 9c: Environmental/household characteristics of study population with and without SDB data			
Variable	**Outcome Present**	**Outcome Absent**	**p-value**
Categorical variables	% (#/total)	% (#/total)	
Owns a dog	37.42 (281/751)	25.00 (1/4)	0.61
Owns a cat	47.94 (360/751)	25.00 (1/4)	0.36
Smoking at the house	25.69 (195/759)	35.38 (23/65)	0.09
Mother smoked prenatally	4.11 (28/681)	14.06 (9/64)	0.00
Continuous variables	Mean (95% CI)	Mean (95%CI)	
Average number of household members	3.95 (3.88, 4.02)	5.25 (3.57, 6.93)	0.02
Average TRAP exposure (ppb)	11.20 (10.89, 11.51)	10.33 (8.39, 12.27)	0.54
Infant bedroom fine dust sample at 3 months (mg)	679.61 (635.52, 723.70)	672.60 (NA)	0.99

Table 10a: Univariate analysis of child risk factors for SDB				
Variable			**HR (95% CI)**	**p-value**
Categorical variables	% (n)	% with SDB (# SDB/total)		
Gender				
Male	50.20 (383)	15.93 (61/383)	Reference	
Female	49.80 (380)	10.53 (40/380)	0.65 (0.44, 0.97)	0.03
Ethnicity				
Caucasian	59.37 (453)	12.80 (58/453)	Reference	
Non-Caucasian	27.00 (206)	12.14 (25/206)	0.93 (0.58, 1.49)	0.78
Missing	13.62 (104)	17.31 (18/104)	NA	
Birth Order				
First Child	43.51 (332)	14.46 (48/332)	Reference	
Other	55.70 (425)	12.24(52/425)	0.84 (0.57, 1.24)	0.38
Missing	0.79 (6)	16.67 (1/6)	NA	
Term of Delivery				
Full Term	93.05 (710)	12.57 (90/710)	Reference	
Preterm	4.85 (37)	24.32 (9/37)	2.08 (1.05, 4.12)	0.04
Missing	2.10 (16)	16.67(3/16)	NA	
Breastfeed for ≥3 months				
No	21.89 (167)	13.77 (23/167)	Reference	
Yes	73.92 (564)	12.94 (73/564)	0.93 (0.58 - 1.49)	0.76
Missing	4.19 (32)	15.63 (5/32)	NA	
Child is atopic				
No	74.84 (571)	12.61 (72/571)	Reference	
Yes	13.62 (104)	17.31 (18/104)	1.38 (0.83, 2.32)	0.22
Missing	11.53 (88)	12.50 (11/88)	NA	
Symptoms for rhinitis				
No	59.11 (451)	6.38 (23/451)	Reference	
Yes	22.15 (169)	44.38 (75/169)	8.29 (5.17, 13.28)	<0.001
Missing	18.74 (143)	2.10 (3/143)	NA	
Treated for GER				
No	71.17 (543)	10.50 (57/543)	Reference	
Yes	1.44 (11)	27.27 (3/11)	1.77 (0.55, 5.68)	0.33
Missing	27.39 (209)	19.62 (41/209)	NA	
Continuous variables	n			
Birth weight for GA Z-Score	756	NA	1.10 (0.88, 1.37)	0.43
BMI Z-Score	527	NA	1.06 (0.80, 1.41)	0.68
Total URTI	733	NA	1.23 (1.03, 1.48)	0.03
Total OM	732	NA	2.30 (1.48, 3.59)	<0.001
Total wheezing episodes	733	NA	1.22 (1.05, 1.43)	0.01
Average sleep in first year of life (hours)	762	NA	0.83 (0.73, 0.95)	0.01
Urine cotinine at 3 months (ng/mL)	194	NA	0.99 (0.96, 1.04)	0.87

Table 10b: Univariate analysis of family risk factors for SDB				
Variable			**HR (95% CI)**	**p-value**
Categorical variables	% (n)	% with SDB (# SDB/total)		
Household income				
< $60,000	12.84 (98)	13.27 (13/98)	Reference	
≥ $60,000	77.46 (591)	12.69 (75/591)	0.97 (0.54,1.76)	0.93
Missing	9.70 (74)	17.57 (13/74)	NA	
Mother's highest level of education				
Did not attend post-secondary	6.95 (53)	18.87 (10/53)	Reference	
Did attend post-secondary	75.75 (578)	11.76 (68/578)	0.59 (0.31,1.15)	0.12
Other	0.52 (4)	25.00 (1/4)	1.46 (0.19, 11.40)	0.7
Missing	16.78 (128)	17.19 (22/128)	NA	
Mother is atopic				
No	34.21 (261)	14.18 (37/261)	Reference	
Yes	54.65 (417)	13.43 (56/417)	0.95 (0.62, 1.43)	0.79
Missing	11.14 (85)	9.41 (8/85)	NA	
Mother has symptoms for SDB				
No	33.81 (258)	9.30 (24/258)	Reference	
Yes	47.44 (362)	16.57 (60/362)	1.84 (1.14, 2.95)	0.01
Missing	18.74 (143)	11.89 (17/143)	NA	
Father is atopic				
No	16.91 (129)	17.83 (23/129)	Reference	
Yes	26.74 (204)	13.24 (27/204)	0.74 (0.43, 1.29)	0.29
Missing	56.36 (430)	11.86 (51/430)	NA	
Father has symptoms for SDB				
No	12.98 (99)	12.12 (12/99)	Reference	
Yes	40.24 (307)	16.29 (50/307)	1.39 (0.74, 2.61)	0.31
Missing	46.79 (357)	10.92 (39/357)	NA	

Table 10c: Univariate analysis of environmental risk factors for SDB				
Variable			**HR (95% CI)**	**p-value**
Categorical variables	% (n)	% with SDB (# SDB/total)		
Has a dog				
No	61.60 (470)	12.98 (61/470)	Reference	
Yes	36.83 (281)	12.81 (36/281)	0.97 (0.65, 1.47)	0.90
Missing	1.57 (12)	33.33 (4/12)	NA	
Has a cat				
No	51.25 (391)	12.02 (47/391)	Reference	
Yes	47.18 (360)	13.89 (50/360)	1.17 (0.79, 1.75)	0.43
Missing	1.57 (12)	33.33 (4/12)	NA	
Season				
Winter	19.92 (152)	15.79 (24/152)	Reference	
Spring	21.20 (161)	16.15 (26/161)	1.07 (0.62, 1.87)	0.80
Summer	22.54 (172)	12.21 (21/172)	1.02 (0.57, 1.84)	0.94
Fall	18.87 (144)	20.83 (30/144)	1.38 (0.81, 2.37)	0.24
Missing	17.56 (134)	0.00 (0/134)	NA	
Smoke at the house				
No	73.92 (564)	13.65 (77/564)	Reference	
Yes	25.56 (195)	10.77 (21/195)	0.78 (0.45, 1.26)	0.31
Missing	0.52 (4)	75.00 (3/4)	NA	
Mother smoked prenatally				
No	85.58 (653)	12.25 (80/653)	Reference	
Yes	3.67 (28)	14.29 (2/48)	1.18 (0.43, 3.22)	0.75
Missing	10.75 (82)	20.73 (17/82)	NA	
Continuous variables	n			
Average number of household members	751	NA	0.88 (0.71, 1.09)	0.23
Average TRAP exposure (ppb)	581	NA	1.04 (0.98, 1.10)	0.22
Infant bedroom fine dust sample at 3 months (mg)	696	NA	1.00 (0.9997, 1.00)	0.96