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MAIJA KATILA

Snoring in Early Childhood

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The future belongs to those who believe in the beauty of their dreams.

-Eleanor Roosevelt

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ABSTRACT

Background: Sleep disordered breathing (SDB) includes snoring and obstructive sleep apnea (OSA) and is common in children, with reported prevalence rates varying widely. Snoring, though less severe than OSA, can have detrimental effects on children's health. Left untreated. it can lead to elevated blood pressure, neurocognitive and behavioral problems, and adverse impacts on metabolic profiles. Research on infants' and toddlers' SDB is limited compared to data on snoring in school-aged children.

Objectives: This prospective study examined the prevalence of snoring during early childhood and the prenatal and postnatal risk factors for this condition. A further aim was to evaluate the prevalence and persistence of snoring during the first two years of life in two Finnish birth cohorts. Additionally, the association between snoring and growth during early childhood and the risk factors for cardiovascular and metabolic disorders, as measured by blood samples at age two, was examined.

Methods: The first study population consisted of 1388 infants who were recruited from the CHILD SLEEP (CS) birth cohort in the Pirkanmaa Hospital District, Finland between 2011 and 2013. Parents completed questionnaires on sleep and background factors prenatally, as well as when the infants were three and eight months old.

The second study included 947 children from the CS and 1393 children from the FinnBrain (FB) birth cohorts. At 24 months of age, both parents were given questionnaires that included sections on the child's sleep and environmental factors.

The third sample consisted of 78 children from the CS cohort who underwent full-night polysomnography (PSG) and whose parents completed a questionnaire on sleep and environmental factors at 24 months. Growth charts were obtained from well-baby clinics, and metabolic blood samples were taken from 31 children.

Results: According to the study, the prevalence of habitual snoring in infants was 3.2% at three months and 3.0% at eight months. Infants who snored at these ages experienced more sleeping difficulties. At three months, snoring infants had shorter sleep duration and more restless sleep than other infants. The risk factors for infants' snoring were maternal smoking and parental snoring. Additionally, formula

feeding, and pacifier use added to the risk of an infant's snoring at the age of three months.

The combined prevalence of habitual snoring in two birth cohorts at the age of 24 months was found to be 2.3%, which is significantly lower than that reported in previous studies. Children who experienced recurrent infections or asthma were found to be more likely to snore habitually. Moreover, the risk of a child snoring habitually increased when both parents snored every night. A child's likelihood of habitual snoring was found to be associated with a mother with lower level of education and a lower monthly income.

During the first two years of life, there were no significant differences in growth parameters between the children who snored and the control group. However, children whose total sleep snoring time recorded by PSG was in the highest quartile had lower levels of high-density lipoprotein (HDL) compared to those in the lowest quartile. Linear regression models revealed that snoring time significantly predicted lower HDL and apolipoprotein A1 (ApoA1) levels and higher levels of high-sensitivity C-reactive protein (hs-CRP).

Conclusions: In conclusion, the prevalence of habitual snoring in the Finnish birth cohort was lower than previously reported. Parental snoring, maternal smoking, and socioeconomic factors were linked to infant snoring. Snoring infants were reported to face more sleep difficulties, and independent risk factors included parental snoring, low maternal income, and low maternal education levels. In Finnish children, snoring was associated with adverse effects on the serum metabolic profile. These findings suggest that snoring during early childhood may increase the risk of cardiovascular disease in adulthood.

TIIVISTELMÄ

Taustaa: Unenaikaiset hengityshäiriöt, jotka käsittävät sekä kuorsauksen että obstruktiivisen uniapnean, ovat lapsilla varsin yleisiä, joskin raportoidut esiintyvyydet vaihtelevat suuresti. Vaikka kuorsaus on obstruktiivista uniapneaa lievempi unenaikainen hengityshäiriö, myös siihen on osoitettu liittyvän lisääntynyt riski kohonneeseen verenpaineeseen, neurokognitiivisiin ja käyttäytymisongelmiin sekä haitallisiin muutoksiin lasten aineenvaihdunnan mittareissa. Imeväisten ja taaperoiden unenaikaisia hengityshäiriöitä koskeva tutkimustieto on rajallista verrattuna kouluikäisiin lapsiin.

Tavoitteet: Tässä etenevässä tutkimuksessa tarkasteltiin kuorsauksen esiintyvyyttä imeväisiässä, sekä kuorsaukseen liittyviä riskitekijöitä ennen ja jälkeen syntymän. Lisäksi tavoitteena oli arvioida kuorsauksen esiintyvyyttä ja pysyvyyttä kahden ensimmäisen elinvuoden aikana kahdessa suomalaisessa syntymäkohortissa. Tutkimuksessa tarkasteltiin myös varhaislapsuuden kuorsauksen ja kasvun välistä yhteyttä sekä sydän- ja verisuonisairauksien ja aineenvaihduntahäiriöiden riskitekijöitä verinäytteiden avulla.

Menetelmät: Ensimmäinen tutkimusväestö koostui 1388 imeväisestä, jotka rekrytoitiin CHILD SLEEP (CS) -syntymäkohortista Pirkanmaan sairaanhoitopiirissä vuosina 2011–2013. Vanhemmille osoitetut kyselyt täytettiin ennen lapsen syntymää sekä lapsen ollessa kolmen ja kahdeksan kuukauden ikäinen.

Toinen tutkimusaineisto sisälsi 947 lasta CS-kohortista sekä 1393 lasta FinnBrain (FB) -syntymäkohortista. Molemmat vanhemmat täyttivät kyselylomakkeet lapsen ollessa 24 kuukauden ikäinen, jotka sisälsivät osiot lapsen unesta sekä ympäristötekijöistä.

Kolmas tutkimusjoukko koostui 78 lapsesta CS-kohortista, joille tehtiin yhden yön polysomnografiatutkimus (PSG), ja joiden vanhemmat olivat täyttäneet uni- ja ympäristötekijöitä koskevan kyselylomakkeen 24 kuukauden kohdalla. Kasvutiedot kerättiin neuvoloista, ja aineenvaihduntaverinäytteet otetiin 31 lapselta.

Tulokset: Tutkimuksen mukaan vauvojen kuorsauksen esiintyvyys oli 3,2 % kolmen kuukauden iässä ja 3,0 % kahdeksan kuukauden iässä. Imeväisiällä kuorsaavilla lapsilla oli enemmän univaikeuksia. Lisäksi kolmen kuukauden iässä kuorsaavien vauvojen uni oli levottomampaa ja kestoltaan lyhyempää kuin muilla

lapsilla. Vauvojen kuorsauksen riskitekijöitä olivat äidin tupakointi sekä vanhempien kuorsaus. Lisäksi korvikeruokinta ja tutinkäyttö lisäsivät vauvan kuorsauksen riskiä kolmen kuukauden iässä.

Kuorsauksen yhdistetty esiintyvyys kahdessa syntymäkohortissa 24 kuukauden iässä havaittiin olevan 2,3 %, joka on merkittävästi vähäisempi kuin aiemmissa tutkimuksissa on raportoitu. Lasten, joilla oli toistuvia infektioita tai diagnosoitu astma, kuorsasivat muita todennäköisemmin säännöllisesti. Lisäksi riski lapsen kuorsaamisesta kasvoi tavallisesti, jos molemmat vanhemmat kuorsasivat joka yö. Lapsen kuorsauksen havaittiin liittyvän myös äidin alhaisempaan koulutustasoon ja alhaisempiin kuukausituloihin.

Kahden ensimmäisen elinvuoden aikana kuorsanneiden lasten ja kontrolliryhmän kasvussa ei havaittu merkittäviä eroja. Kuitenkin lapsien, joiden PSG:n rekisteröimä kuorsausaika oli jakauman ylimmässä neljänneksessä, HDL-arvot olivat alhaisemmat verrattuna lapsiin, joiden kuorsausaika oli alimmassa neljännessä. Lineaariset regressiomallit paljastivat, että kuorsausaika ennusti merkittävästi alhaisempia HDL- ja ApoA1-tasoja sekä korkeampia hs-CRP-tasoja.

Johtopäätökset: Yhteenvetona voidaan todeta, että säännöllisen kuorsauksen esiintyvyys suomalaisissa syntymäkohorteissa oli aiemmin raportoitua pienempi. Tässä tutkimuksessa havaittiin, että vanhempien kuorsaus ja äitien tupakointi olivat kuorsauksen riskitekijöitä vauvaiässä, ja kuorsaavilla vauvoilla oli myös enemmän univaikeuksia. Riskitekijöitä kuorsaukselle kaksivuotiaana olivat vanhempien kuorsaus, äidin alhaiset tulot sekä alhainen koulutustaso. Suomalaisilla lapsilla PSG-tutkimuksessa rekisteröity kuorsausaika liittyi negatiivisiin muutoksiin seerumin metabolisissa merkkiainetasoissa. Nämä havainnot viittaavat siihen, että kuorsaus varhaislapsuudessa voi lisätä sydän- ja verisuonisairauksien riskiä aikuisiässä.

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ABBREVIATIONS

AASM	American Academy of Sleep Medicines
apoA1	apolipoprotein A1
apoB	apolipoprotein B
BISQ	Brief Infant Sleep Questionnaire
BMI	body mass index
BNSQ	Basic Nordic Sleep Questionnaire
CHAT	Childhood Adenotonsillectomy Trial
CS	CHILD-SLEEP
ERS	the European Respiratory Society
FB	FinnBrain
HDL	high density-lipoprotein
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
HPA	hypothalamic-pituitary-adrenocortical
hs-CRP	high-sensitivity C-reactive protein
IL-6	interleukin-6
ISQ	Infant Sleep Questionnaire
LDL	low density-lipoprotein
NMD	neuromuscular diseases
OSA	obstructive sleep apnea
PSG	polysomnography
PTT	pulse transit time
SDB	sleep disordered breathing
SES	socioeconomic status
SDSC	Sleep Disturbance Scale for Children
TNF-α	tumor necrosis factor-alpha
UARS	upper airway resistance syndrome

ORIGINAL PUBLICATIONS

This thesis is based on the following publications, which are referred to in the text by Roman numerals I-III

I Katila, M., Saarenpaa-Heikkila, O., Saha, M. T., Vuorela, N., & Paavonen, E. J. (2019). Parental reports showed that snoring in infants at three and eight months associated with snoring parents and smoking mothers. *Acta Paediatrica*, 108(9), 1686–1694.

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III Katila, M., Satomaa A. L., Himanen, S. L., Saha, M. T., Vuorela, N., Paunio, T., Paavonen, E. J., & Saarenpaa-Heikkila, O. (2023) The association of snoring, growth, and metabolic risk factors at the age of two years. Submitted to *Sleep and Breathing*

AUTHOR'S CONTRIBUTION

The inception of this thesis was inspired by the insights of Dr. Outi Saarenpää-Heikkilä (OSH), Dr. Juulia Paavonen (JP), and Dr. Marja-Terttu Saha (MTS). The conceptualization of studies I–III was a collaborative effort between the author of this thesis and OSH, JP, MTS, and Dr. Nina Vuorela (NV). The collection of questionnaire data for studies I–III was conducted within the CHILD-SLEEP birth cohort study and was designed by JP and OSH. In study II, the questionnaire data from the FinnBrain birth cohort were developed by Dr. Linnea Karlsson (LK) and Prof. Hasse Karlsson (HK). In study III, the clinical data was gathered by the author of this thesis and OSH.

The primary responsibility for drafting and revising the manuscripts for studies I–III lay with the author of this thesis. The manuscript for study I underwent collaborative revisions with co-authors OSH, JP, MTS, and NV. Similarly, the manuscript for study II was also revised by M.Sc. Heini Huhtala, LK, HK, Dr. Laura Korhonen, Dr. Minna Lukkarinen, and Dr. Jetro Tuulari, in addition to OSH, JP, MTS, and NV. The manuscript for study III underwent revisions from OSH, JP, MTS, NV, Prof. Tiina Paunio, Prof. Sari-Leena Himanen, and Dr. Anna-Liisa Satomaa.

The planning and execution of statistical analyses were collaborative efforts involving the author of this thesis and JP, in conjunction with HH. The interpretation of the results was a joint endeavor involving the author, HH, JP, OSH, MTS, and NV.

1 INTRODUCTION

Sleep disordered breathing (SDB) refers to a range of beathing problems that occur during sleep, including snoring and obstructive sleep apnea (OSA). In children, habitual snoring is defined as snoring at least three nights per week. The reported prevalence of habitual snoring among young children varies widely. During infancy, habitual snoring is estimated to affect between 5.0–6.6% of children under one year of age (Gislason & Benediktsdottir, 1995; Kelmanson, 2000; Montgomery-Downs & Gozal, 2006), and in some studies, the rate to between 9% and 14% (Bonuck et al., 2011; Piteo et al., 2011). Furthermore, population-based studies suggest that it affects around 10–20% of children aged 18–48 months (Bonuck et al., 2011; Byars et al., 2012; Gill et al., 2012). However, some studies have reported lower prevalence rates, which may be due to differences in how snoring is defined or to variations in the risk factors for snoring across different populations. It is widely recognized that there is a connection between SDB and lower socioeconomic status (SES). Ethnicity can also play a role in the prevalence of snoring. While there is more data available on snoring among school-aged children, research on infants' and toddlers' SDB is limited and in some areas, outdated.

The most common cause of snoring and OSA in children is enlarged adenoids or tonsils, while obesity becomes a more significant risk factor during adolescence (Arens & Marcus, 2004). It is important to determine whether obesity contributes to SDB in younger children, as well, as the prevalence of being overweight is on the rise. In Finland, approximately 24% of boys and 14% of girls between the ages of 2 and 6 years are estimated to be overweight (Mäki et al., 2018). Therefore, it is crucial to investigate the potential link between obesity and SDB in early childhood to prevent the adverse effects of SDB.

It is important to note that even though snoring is considered a milder form of SDB, it can have harmful effects on a child's health, such as causing elevated blood pressure and neurocognitive and behavioral disturbances (Biggs et al., 2014; Brockmann et al., 2012; Gill et al., 2012; A. M. Li et al., 2009; Vlahandonis et al., 2014). Longitudinal studies have also shown that more than a third of school-aged children progress to OSA over time (A. M. Li et al., 2013). Therefore, healthcare

providers should routinely ask parents if their children snore and screen for SDB, even in mild cases.

While studies have shown a link between SDB and poor metabolic health in adults, research on the relationship between SDB and serum high-sensitivity C-reactive protein (hs-CRP) and lipids in children is relatively limited. Furthermore, research on the negative impact of SDB on metabolic health has focused primarily on children with OSA and not on those who simply snore.

This study provides prevalence data on SDB in young children from two large birth cohorts, along with longitudinal data on the development of snoring and the protective and risk factors associated with SDB. Additionally, we investigated the relationship between the amount of time spent snoring, as recorded by polysomnography (PSG), and the presence of an adverse metabolic profile.

2 REVIEW OF THE LITERATURE

2.1 Definitions

2.1.1 Sleep disordered breathing

Increased upper airway resistance and pharyngeal collapsibility cause elevated respiratory effort and snoring (Kaditis et al., 2016) This obstruction while sleeping in the upper airway refers to sleep disordered breathing (SDB), which is represented by abnormal respiratory patterns and inadequate ventilation. SDB covers a wide range of breathing problems during sleep and represents a spectrum of obstructive entities ranging from primary snoring to obstructive sleep apnea (OSA).

2.1.1.1 Primary and habitual snoring

Primary snoring refers to snoring with no evidence of apnea, hypopneas, gas exchange abnormalities, or frequent arousals from sleep (Kaditis et al., 2016). The snoring sound is generated in the upper airway during sleep, and snoring typically occurs at the time of inspiration. Occasional snoring is remarkably prevalent, and almost all children snore on occasion, especially during respiratory infections. Loud snoring is the most common sign of OSA; however, not all OSA patient snore. Specifically, infants and children with neuromuscular diseases may meet the diagnostic criteria for OSA without snoring (*International Classification of Sleep Disorders,* 3rd ed., 2014).

Although primary snoring is considered a less severe form of SDB, involving occasional and partial blockage of air passages, it should not be underestimated as a harmless issue. Apart from OSA, research indicates that primary snoring is linked to increased blood pressure and disruptions in neurological and behavioral functions (Biggs et al., 2014; Brockmann et al., 2012; Gill et al., 2012; A. M. Li et al., 2009).

In epidemiological studies that frequently rely on questionnaires, habitual snoring is a widely employed definition. In the context of children, habitual snoring is defined as the occurrence of snoring three or more nights per week.

2.1.1.2 Obstructive sleep apnea

The European Respiratory Society (ERS) Taskforce for the Diagnosis and Management of Obstructive SDB in childhood defines OSA as "a syndrome of upper airway dysfunction during sleep, characterized by snoring and/or increased respiratory effort secondary to increased upper airway resistance and pharyngeal collapsibility" (Kaditis et al., 2016). Pediatric OSA indicates intermittent partial (hypopnea), complete obstruction (apnea), or continued partial obstruction in the upper airways. These obstructions may disrupt normal ventilation and sleep patterns (*International Classification of Sleep Disorders,* 3rd ed., 2014).

2.1.1.3 Upper airway resistance syndrome

Upper airway resistance syndrome (UARS) is included on the spectrum of SDB and is caused by the narrowing of the airway and blockage of air in the nasal passages. In UARS, airflow is limited as a result of increased respiratory effort. This results in arousals from sleep, but not in significant desaturations or apneas (*International Classification of Sleep Disorders,* 3rd ed., 2014).

2.2 Epidemiology of sleep-disordered breathing in childhood

The prevalence of SDB in children has been extensively researched, but the reported rates of snoring show considerable variation. Most of the studies cover OSA, and the research on milder conditions on the SDB spectrum is more sporadic. In addition, there are frequent studies concerning SDB in school-aged children, while studies on SDB during infancy and toddlerhood are scarce.

2.2.1 Epidemiology in international studies

The prevalence of habitual snoring exhibits variations across different age groups. During infancy, the occurrence of habitual snoring is relatively low compared to that of older children and adults. The prevalence of habitual snoring in children under one year of age is between 5.0 and 6.6% (Gislason & Benediktsdottir, 1995; Kelmanson, 2000; Montgomery-Downs & Gozal, 2006), although in some studies the percentage rises to between 9% and 14% (Bonuck et al., 2011; Piteo et al., 2011).

This lack of consistency could be clarified by considering the diverse nature of the studies, differences in how habitual snoring is defined, and the influence of factors such as colds.

In toddlers, habitual snoring is distinctly more prevalent than snoring in infancy. Based on previous population-based reports, habitual snoring affects approximately 10–20% of children aged 18–24 months (Bonuck et al., 2011; Byars et al., 2012; Gill et al., 2012). As children progress into the school-aged population, snoring is reported to affect 6–12% of children (Brockmann et al., 2012; S. Li et al., 2010; Sakamoto et al., 2017).

Pediatric OSA is markedly less prevalent than snoring. It has been reported to affect approximately 1–5% of children (Bixler et al., 2009; A. M. Li, So et al., 2010; O'Brien et al., 2003). OSA takes place during infancy, but between the ages of 2 and 8 years, it is reported to occur most frequently (Tan et al., 2013). Similar to the pattern observed in snoring prevalence, this is generally the time period when tonsillar tissue is at its largest compared to the diameter of the upper airways. Another peak of prevalence occurs later in adolescence, resulting from obesity.

2.2.2 Epidemiology in Finland

Previous Finnish epidemiological studies of SDB among children are limited. Approximately 10 years ago, Liukkonen et al. reported a moderately low habitual snoring prevalence of 6% among 1471 Finnish preschool-aged children in a questionnaire survey (Liukkonen et al., 2008). The frequency of snoring was evaluated on a five-point scale, and habitual snoring was defined as snoring often or always. No difference between genders was detected. Histories of adenotonsillectomy, allergic rhinitis, recurrent respiratory infections, and otitis media were significantly associated with habitual snoring. Furthermore, parental snoring and smoking were more common among habitual snorers compared to children who did not snore or snored occasionally.

The PANIC study, done in Kuopio, is another Finnish population-based study reporting the prevalence of SDB symptoms (Ikävalko et al., 2018). Snoring prevalence was evaluated based on the validated Basic Nordic Sleep Questionnaire (BNSQ). In a sample of 466 children, 10% were reported to have frequent or loud snoring, nocturnal mouth breathing, or apneas observed by the parents. There was no statistically significant difference in the prevalence of parent-reported SDB

symptoms between boys and girls. Regular snoring was remarkably low, as the prevalence was only 2%.

2.3 Pathophysiology of snoring and obstructive sleep apnea during childhood

The anatomy and proportions of the upper airway change during growth. The level of obstruction during infancy and childhood is nasopharyngeal and retropalatal. A new-born's uvula and epiglottis are in close proximity and create a secure airway during suckling. In particular, craniofacial anomalies and prematurity are risk factors for primary snoring and OSA in this age group. By the time the larynx descends, and during toddlerhood and among school-aged children, enlarged adenoids and tonsils are more common as a physical cause of snoring and OSA (Arens & Marcus, 2004). In adolescence, primary snoring and OSA are associated with being overweight more often than during infancy and early childhood, and the clinical picture corresponds to the adult type of OSA (Hakim et al., 2015). Considering the increasing rates worldwide of overweight children in early childhood, obesity is a becoming more prevalent cause for OSA among younger children as well.

2.3.1 Adenotonsillar hypertrophy

The pharynx is a funnel-shaped structure that connects the nasal cavities to the larynx and esophagus. It consists of three divisions: the nasopharynx, the oropharynx, and the hypopharynx (Arens & Marcus, 2004). Pharyngeal tonsils, also called adenoids, are located in the nasopharynx. The oropharynx includes the palatine tonsils and the lingual tonsils.

In otherwise healthy children, adenoid and/or tonsil hypertrophy are the most frequent causes of upper airway obstruction during sleep. The lymphoid tissue in the pharyngeal lymphatic ring is at its largest when a child is between ages 3 and 7 years, according to the peak incidence of OSA. Adenotonsillar hypertrophy contributes to the narrowing of the retro-palatal area thereby predisposing obstruction (Arens & Marcus, 2004; Gulotta et al., 2019).

2.3.2 Obesity

SDB is also associated with obesity in childhood (Anuntaseree et al., 2014; K. Bonuck et al., 2015; Gozal & Kheirandish-Gozal, 2012; Ikävalko et al., 2018). During the past decades, the mean BMI in children has increased globally, and also in Finland (Jääskeläinen et al., 2021; Ng et al., 2014). Most children who are obese between the ages of 2 and 6 are also obese in adolescence (Geserick et al., 2018). In obese children, adenotonsillar hypertrophy is not always the main cause of snoring and OSA, since the deposition of adipose tissue in the upper airway may increase airway resistance.

The links between SDB and obesity are multifactorial. The fat deposition within the muscles and tissues surrounding the airway diminishes the diameter of the pharyngeal lumen and increases upper airway collapse (Arens et al., 2011). The increased presence of fat in the thoracic and abdominal walls reduces respiratory function in obese children (Gulotta et al., 2019). Furthermore, OSA induces systemic inflammation which can lead to the same kind of morbidity as that caused by obesity (Bhattacharjee et al., 2011). This problem is discussed in detail in Chapter 2.7.2.2.

2.3.3 Craniofacial abnormalities

Variance in the size or shape of the face and mandible can accompany obstruction in the upper airway and lead to symptoms of SDB. On one hand, a convex facial profile, increased lower facial height, and mandibular retrusion have been reported to be associated with SDB in childhood (Ikävalko et al., 2018). Moreover, when compared to healthy children, children diagnosed with OSA often have narrower upper dental arches, crossbites and shortened lower dental arches (Pirila-Parkkinen et al., 2009). On the other hand, as a result of the release of nocturnal growth hormones in children with OSA (Nieminen et al., 2002), mandibular growth is hypothesized to decrease (Peltomäki, 2007), which further complicate the existing SDB symptoms in childhood.

Children with craniofacial anomalies usually present with SDB during infancy. Syndromes with craniofacial synostosis, such as Crouzon, Apert, and Pfeiffer syndromes, and those with mandibulofacial dysostoses such as Pierre Robin sequence and Treacher–Collins syndrome, narrow the airway, predisposing to obstruction. Furthermore, decreased neuromotor tone related to these syndromes may increase upper airway collapse during sleep (Arens & Marcus, 2004).

One of the most common genetic diseases that accompanies craniofacial abnormalities is Down syndrome. Children with Down syndrome are characterized by midfacial and mandibular hypoplasia, adenotonsillar hyperplasia, glossoptosis, and laryngotracheal anomalies, all of which expose them to obstruction during sleep. As with other syndromes with craniofacial anomalies, Down syndrome is accompanied by a decreased neuromuscular tone (Gulotta et al., 2019). Over half of children with Down syndrome are estimated to be diagnosed with OSA (Williamson et al., 2022).

2.3.4 Neuromuscular diseases

Neuromuscular diseases (NMD) are disorders that affect nerves and muscles in any part of the body. Motor neuron diseases, such as spinal muscular atrophy, peripheral neuropathies including Charcot-Marie-Tooth disease, and diseases directly involving muscles, such as Duchenne muscular dystrophy and Becker muscular dystrophy, are all examples of NMDs. In all of these disorders, muscle strength progressively deteriorates. Muscle weakness in the respiratory system may lead to respiratory failure, and children with NMD have a notably high risk of SDB (Albdewi et al., 2018; Kaditis et al., 2016).

2.4 Factors associated with snoring

Habitual snoring is influenced by a combination of genetic and environmental factors. Previous research has shown that SDB prevalence in infants and preschoolers is linked to being male, having a lower socioeconomic status, having African American ethnicity, and experiencing chronic rhinitis, regurgitation, and exposure to tobacco smoke. Snoring is also connected to restless sleep, parental asthma, and maternal concerns about the child's breathing. Breastfeeding has been found to lower the risk of habitual snoring and reduce the severity of SDB, while exclusive formula feeding is notably associated with habitual snoring. Additionally, a strong connection exists between a child's snoring and a family history of snoring—whether from the mother, father, or siblings—indicating a combination of inherited and environmental factors contributing to sleep-related breathing issues.

2.4.1 Breastfeeding

Breastfeeding has previously been shown to be protective against SDB in frequent studies (Beebe et al., 2012; Bonuck et al., 2011; Brew et al., 2014; Galbally et al., 2013; Montgomery-Downs et al., 2007). Furthermore, in 2019, a meta-analysis of 11 studies concluded that breastfeeding is associated with a reduced risk of habitual snoring in children (K. Sun et al., 2019).

The underlying mechanism of breastfeeding's protective effect on SDB in childhood remains unclear. Nonetheless, obstruction of the upper airway in an infant's sleep primarily arises from reduced muscle tone in the upper airway, elevated nasal resistance, and a flexible chest wall. The act of suckling engages the oral muscles, and breastfeeding significantly impacts the development of the mandible (Westover et al., 1989). When breastfeeding, the movement of the tongue molds the palate by gently curving and leveling it. Breastfeeding coordinates nose breathing and prevents adeno-tonsil hypertrophy (Storari et al., 2021). During bottle feeding and pacifier use, the tongue cannot reach the palate (Palmer, 2006). Exclusive formula feeding has been reported to significantly increase the risk of habitual snoring (Piteo et al., 2011). Early nonnutritive sucking habits, including pacifier and digit sucking, may cause disturbances in normal occlusal development, and a short duration of breastfeeding has been associated with malocclusion (Karjalainen et al., 1999).

2.4.2 Tobacco smoke exposure

The World Health Organization estimates that, globally, approximately 40%—and in many low-income countries, even a larger proportion—of children are exposed to tobacco smoke. Maternal smoking has been shown to add to a child's risk for snoring in several studies (Kuehni et al., 2008a; Liukkonen et al., 2008; Mitchell & Thompson, 2003; Paavonen et al., 2007). A meta-analysis of 24 studies including nearly 88,000 children indicates that tobacco smoke exposure increases the risk of habitual snoring, and the effects are stronger if children are exposed to prenatal tobacco smoke exposure (K. Sun et al., 2018). Additionally, the risk of habitual snoring increased for every daily cigarette smoked by people living with children.

The exact mechanisms through which tobacco smoke exposure triggers snoring remain unclear. One suggested theory is that persistent exposure to irritating substances could lead to inflammation in the upper airway, possibly accounting for this connection. Furthermore, tobacco smoke exposure may influence neurotransmitter levels connected to ventilatory control (Weinstock et al., 2014).

2.4.3 Socioeconomic factors

Sleep health disparities are impacted by various factors, such as socioeconomic status (SES), geography, neighborhood segregation, racism, and access to healthcare. These multiple factors interact with one another, exerting a cumulative influence on children's health and sleep (Figure 1).

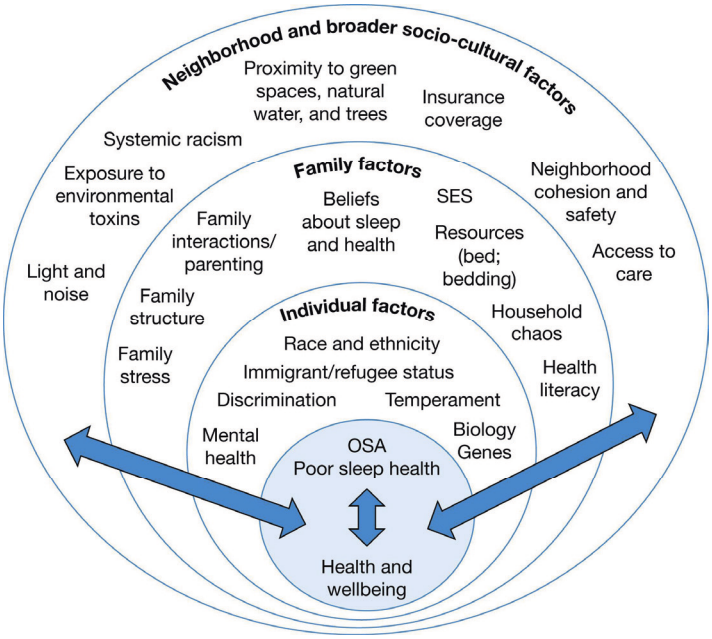

Figure 1. Social-ecological factors contributing to sleep disparities at multiple levels (adapted with permission of Billings et al, 2021). OSA; obstructive sleep apnea, SES; socioeconomic status.

The association between snoring and OSA and lower SES has been well established. In a Swedish study, a low level of familial income and parental education almost doubled the child's risk of SDB (Friberg et al., 2015). In addition, parental occupations characterized by low salary and low educational level increased the risk of SDB in offspring. In the Childhood Adenotonsillectomy Trial (CHAT), family income was linked to the severity of OSA, but after adjusting for African American race and tobacco smoke exposure, this association was no longer significant (Weinstock et al., 2014). Residing in economically disadvantaged areas in New

Zealand and Canada increased the likelihood of regular snoring in children who had not yet reached school age (Brouillette et al., 2011; Gill et al., 2012).

Racial and ethnic disparities in pediatric SDB are well documented. African American children have been reported to have more OSA symptoms more likely compared to Caucasian children (Montgomery-Downs & Gozal, 2006; Rosen et al., 2003). In addition, the African race has been associated with an increase in OSA severity (Weinstock et al., 2014). These findings suggest that there may be genetic factors that influence vulnerability to SDB, explained by influences on body fat distribution or craniofacial structure. In addition, increased exposure to air pollution and second-hand smoke experienced by African-American children living in disadvantaged neighborhoods may expose them to increased upper airway inflammation, higher rates of atopy, and asthma, leading to increased snoring and sleep disturbances (Boss et al., 2011). Furthermore, some studies have found racial differences in practice patterns regarding the diagnosis and treatment of SDB (Williamson et al., 2022). In the CHAT trial, black children had lower rates of normalization of polysomnographic findings than did children of other races after surgical treatment for OSA (Marcus et al., 2013).

2.4.4 Genetic factors

Previously, there have been reports of a connection between a parental history of snoring and a child's SDB (Kaditis et al., 2004; A. M. Li, Au et al., 2010; Liukkonen et al., 2008; Lundkvist et al., 2012; O'Brien et al., 2003). Furthermore, sibling history of SDB or parental history of adenotonsillar hypertrophy have been shown to be significant predictors of obstructive SDB during childhood (Alexopoulos et al., 2014; Friberg et al., 2009). However, the genetic and environmental factors in SDB are complex; they interact with each other, and the ultimate mechanism of the association with snoring and family aggregation is unknown. Additionally, the genetics of SDB are presumably multifactorial. One possible reason could be the passing down of facial structure traits, which has been observed to impact the likelihood of snoring (Arens & Marcus, 2004). Furthermore, adenotonsillar hypertrophy and obesity, which are important risk factors for snoring and OSA, may be inherited.

Male gender predominates in snoring among the general population (Chan et al., 2012). Some studies among young children have reported a higher incidence of snoring in boys compared to girls (Kaditis et al., 2004; Kukwa et al., 2018), but the

literature is inconsistent. The difference in the risk of snoring between genders can be explained by the differences in upper airway anatomy and the effect of sex hormones. According to the literature, the male predominance in snoring seems to be greater among adults compared to children (Chan et al., 2012). Most of these hormonal and anatomical changes occur during puberty, and this could be one explanation for why gender differences in snoring are predominantly observed in studies involving adolescents and adults, and the results among younger children are more variable.

2.4.5 Other factors

The presence of habitual snoring in childhood has been associated with excess regurgitation during infancy (Kuehni et al., 2008a). Additionally, gastroesophageal reflux disease has been reported to significantly predict habitual snoring in children with asthma (Teodorescu et al., 2009). The high frequency of upper respiratory infections is a risk factor for snoring (Kuehni et al., 2008a; Kukwa et al., 2018). Children who have been diagnosed with asthma or have a history of wheezing are more likely to snore or have an elevated apnea–hypopnea index. Additionally, this relationship appears to be bidirectional, meaning that the presence of SDB may also increase the likelihood of asthma or wheezing in children (Malakasioti et al., 2011). Furthermore, studies have shown that there is a notable connection between snoring and allergic rhinitis in pre-school and school-aged children (D'Elia et al., 2022). It is also noteworthy that having an allergic disease can increase the likelihood of adenotonsillar regrowth in children who have undergone adenotonsillectomy (D'Elia et al., 2022). Prematurity associated with a very low birth weight has also been reported to be associated with the risk of SDB (Paavonen et al., 2007).

2.5 Diagnosis of primary snoring and obstructive sleep apnea

In practical work, diagnosis and treatment are frequently accomplished based on medical history and findings in physical examinations. The observations and reports provided by parents play a crucial role. However, it has been shown that a single symptom or finding is not particularly good as a measure for diagnosing OSA in children. Various structured surveys combining symptoms and findings have been developed to evaluate the risk of OSA. Nevertheless, the gold standard for the

diagnosis of primary snoring and OSA is extensive PSG, where breathing, gas exchange, and sleep stages can be registered.

The diagnostic criteria for OSA are defined by the American Academy of Sleep Medicine (AASM) as "the presence of one or more of the following: snoring, labored, paradoxical, or obstructed breathing, and one or more obstructive events per hour of sleep" or "hypoventilation together with one or more of the following: snoring, flattening of the inspiratory nasal airway pressure waveform, or paradoxical thoracoabdominal movement" (*International Classification of Sleep Disorders,* 3rd ed., 2014). The European Respiratory Society (ERS) defines pediatric OSA as follows: "SBD symptoms in combination with obstructive apnea-hypopnea index (OAHI) ≥2 episodes/h or obstructive apnea index (OAI) ≥1 episode/h" or "SDB symptoms and AHI ≥1 episode/h (including central events)" (Kaditis et al., 2016). Several studies use AHI to classify OSA severity in categories as mild (AHI 1–4.9), moderate (AHI 5–9.9), or severe (AHI > 10) (Bitners & Arens, 2020).

2.5.1 Medical history

Snoring is the most common symptom of OSA: The majority of children with OSA snore, but it is difficult to evaluate the severity of respiratory distress on the basis of a single symptom. For example, infants and children with muscle diseases may be diagnosed with sleep apnea without snorin. Nonetheless, it has been observed that the duration of snoring during total sleep time, as measured by PSG, appears to be longer in children diagnosed with OSA than in children who snore but do not exhibit OSA (Markkanen et al., 2021).

In addition to snoring, a child with OSA can demonstrate heavy breathing or shortness of breath during sleep. Sleep may be restless, and awakenings may occur. Witnessed apneas are associated with the presence of SDB. The child may sweat profusely while sleeping. Mouth breathing is common, and the head can be bent back to allow the airways to stay as open as possible (Kaditis et al., 2016; Tan et al., 2013).

SDB has been reported to also increase bedwetting and perceptual parasomnias, such as sleepwalking, sleep drunkenness, and sleep terrors (Barone et al., 2009; Kotagal, 2009). Daytime fatigue is a common symptom, and it can be manifested as morning fatigue when it is difficult to wake up the child. Other children demonstrate fatigue as cognitive and behavioral symptoms such as difficulty concentrating, hyperactivity, and restlessness. Cognitive symptoms can also induce learning

difficulties (Biggs et al., 2014). Additionally, headaches can be a daytime symptom of OSA (Gulotta et al., 2019).

When exploring medical history, familial factors should also be considered. The records of parental snoring are shown to be significant predictors of obstructive SDB. Additionally, the presence of a sibling or parental history of adenotonsillectomy has been reported to have rather high specificity in detecting SDB (Kalampouka et al., 2014).

2.5.1.1 Sleep questionnaires

In Finland, extensive PSG for children is conducted exclusively at university hospitals, and its interpretation requires special expertise from a clinical neurophysiologist. Furthermore, PSG is expensive. Thus, screening questionnaires may offer an accessible alternative to PSG to identify children at high risk of SDB. In a population-based study conducted in Arizona, snoring among children aged 6–11 years had good accuracy (specificity 89.5%) but poor sensitivity (29.5%) in predicting apneas in PSG due to obstruction of upper airways (Goodwin et al., 2005). Furthermore, parental reports of frequent snoring have been reported to be highly sensitive and specific for assessing SDB in children compared to snoring in PSG (Montgomery-Downs et al., 2004).

The Sleep Disturbance Scale for Children (SDSC) is a tool designed to assess sleep disorders in children (Bruni et al., 1996). This survey comprises six sections that cover issues such as difficulties in starting and maintaining sleep, disrupted breathing during sleep, disturbed awakenings or nightmares, challenges in transitioning between sleep and wakefulness, excessive sleepiness, and excessive sweating during sleep. It was validated in a population of 1304 school-aged children, and it appears to be a useful tool for the evaluation of sleep disturbances during childhood in both clinical and non-clinical populations. Subsequently, it has also been validated in pre-school aged children (Romeo et al., 2013), infants, and toddlers (Romeo et al., 2021).

The BEARS is a screening tool developed to assist clinicians by posing an initial screening question to parents about potential sleep problems (Owens & Dalzell, 2005). It targets prevalent sleep issues in young children, including toddlers, preschoolers, and school-aged children. This tool comprises five fundamental sleep domains: bedtime problems, excessive daytime sleepiness, awakenings during the night, regularity of sleep/wake cycles, and snoring. These domains are deemed to

represent the most common sleep concerns in children. If parents answer in the affirmative, they are requested to explain the issue in detail.

A recent review evaluated seven questionnaires in terms of sensitivity, accuracy, feasibility in SDB diagnostics and speed (Burghard et al., 2019). Four questionnaires were found to be useful in the diagnosis of obstructive SDB in children: the Pediatric Sleep Questionnaire (PSQ), the Sleep Clinical Record (SCR), the I'm Sleepy Questionnaire (I'M SLEEPY), and the Sleeping Sleepless Sleepy Disturbed Rest Questionnaire (SSSDR).

Another current systematic review recognized two additional screening questionnaires with adequate statistical characteristics (Incerti Parenti et al., 2021): the Sleep-Related Breathing Disorder Scale of the Pediatric Sleep Questionnaire (SRBD-PSQ) and OSA-18. Of these, SRBD-PSQ showed the highest sensitivity for screening pediatric SDB. These tools are promising but nonetheless not able to replace PSG as the current reference standard for the diagnosis of SDB in children.

2.5.2 Physical examination

A careful physical examination may reveal different markers of SDB in children. Children with SDB commonly present with enlarged tonsils and adenoids. Mouth breathing is frequent in children with SDB and can generally be detected when children are awake, not only during sleep. Retrognathia, micrognathia, and a high-arched palate may reduce the space in the oropharynx obstructing nasal airflow. Furthermore, malocclusion may have the same impact and cut down the space in the mouth. When assessing occlusion and oral cavities, signs of other craniofacial anomalies should also be detected. Moreover, other reasons for obstruction of the upper airways, such as allergic rhinitis or nasal polyps, should be examined (Gipson et al., 2019).

Due to the pathophysiology of SDB and the risk factors for snoring and OSA, other physical conditions should also be determined. Growth assessment and blood pressure screening are essential considering the potential link of SDB to growth failure and hypertension, which will be discussed in detail in sections 2.7.2 and 2.7.3.1. Additionally, obesity is closely associated with SDB, and an evaluation of whether children are overweight should be included in the physical examination. Any signs of neuromuscular disease, such as muscle weakness or spasms, should be detected (Kaditis et al., 2016).

2.5.3 Diagnostic tests

The comprehensive application of PSG in children necessitates resources for its implementation and often hospital facilities. Moreover, the analysis of the recorded data is time-intensive, with a significant portion of the registrations being scored by a clinical neurophysiologist. The limited availability and high cost of PSG have raised the need to search for other methods for screening SDB. However, thus far PSG is considered to be the gold standard for the measurement of sleep and assessment of suspected SDB.

2.5.3.1 Polysomnography

PSG is a specific testing method for the diagnosis of OSA. It determines obstructive and mixed apneas, hypopneas, and periods of obstructive breathing and accompanying hypoventilation during sleep. In general, the monitored parameters in PSG include electroencephalogram derivations, eye movements, skeletal muscle activation, electrocardiogram tracing, oxygen saturation, end-tidal carbon dioxide, body position and chest movement, respiratory airflow, snoring sounds, and video images. Careful sleep stage scoring and evaluation of respiratory events by experienced clinical neurophysiologists is essential to distinguishing the etiology of a possible sleep disorder (Bitners & Arens, 2020). Contemporary pediatric guidelines are used in the visual sleep staging and scoring of respiratory events and arousals (Troester et al., 2023).

The indications for PSG are somewhat controversial. Many guidelines, including AASM and ERS, recommend PSG for all children with symptoms and signs of SDB after clinical examination. On the contrary, the American Academy of Otolaryngology Head and Neck Surgery suggests limited use of PSG only for children with a high risk of OSA, if the need for surgery is unclear, or if there is a discrepancy between the results of a physical examination regarding tonsillar size and the child's history of SDB (Bitners & Arens, 2020).

2.5.3.2 Other methods

Ambulatory PSG refers to an unattended sleep study performed at home that has been used as an alternative to in-hospital PSG. This method monitors fewer variables than full PSG, and often video and end-tidal carbon dioxide measurements are often

omitted for technical reasons. Its benefits have been considered to be lower cost, implementation with fewer resources, and minimal disruption to family life. The sensitivity of ambulatory PSG for the diagnosis of OSA has been estimated to be around 90%.

Nocturnal pulse oximetry has also been studied as a screening tool for pediatric SDB, especially when PSG is unavailable. Recurrent oxygen desaturation during sleep is extremely suggestive of OSA, but the presence of SDB cannot be verified based on nocturnal hypoxemia. Hornero et al discovered that an automatic analysis algorithm for nocturnal oximetry accurately diagnosed children with AHI levels of 1 or higher at a rate of 75.2% and those with AHI levels of 5 or higher at a rate of 81.7% (Hornero et al., 2017). These findings indicate the potential of overnight oximetry as a valuable diagnostic tool for pediatric OSA, especially in regions where PSG is less accessible. However, further research is needed to determine the optimal role of nocturnal oximetry in diagnosing SDB in children (Bitners & Arens, 2020; Kaditis et al., 2016).

Pulse transit time (PTT) is increasingly used to measure inspiratory effort in adults with SDB. It represents the amount of time it takes for a pulse to travel through the circulatory system, providing a quick and noninvasive measure. The awakenings caused by airway blockages result in a chest pressure drop and a sharp decrease in blood pressure during inhalation. This alteration prolongs PTT, and upon awakening due to airflow obstruction, there's a brief but notable increase in blood pressure, leading to a shorter PTT. There is some evidence that measuring PTT can be a useful tool for detecting SDB in children (Bradley et al., 2012; Foo, 2007; Kaditis et al., 2016). Using the PTT arousal index could be a helpful method for identifying respiratory events. Although PTT does not offer as much detailed information as PSG studies, it could effectively supplement current screening methods for SDB in a convenient and accommodating manner.

2.6 Treatment of snoring and obstructive sleep apnea

Treatment of OSA has been shown to be beneficial, and an AHI >5 episodes/h is regularly used as an indication for therapeutic intervention. Additionally, if there is a presence of cardiovascular or central nervous system morbidity, enuresis, growth failure, decreased quality of life, or risk factors for persistence of SDB, AHI 1-5 episodes/h are considered to justify treatment.

In addition to OSA, primary snoring is accompanied by neurocognitive disturbances, behavioral disorders, and elevated blood pressure. However, studies demonstrating the efficacy of therapeutic intervention for primary snoring are lacking (Kaditis et al., 2016). Considering that overweight children who snore are at special risk of developing OSA, follow-up and regular reconsideration of treatment are essential.

2.6.1 Watchful waiting and active follow-up

Watchful waiting for approximately six months is a management option for children with mild OSA and no complex comorbidities. The CHAT study compared adenotonsillectomy with watchful waiting in 464 under-school-aged children with OSA (Marcus et al., 2013). The children had mild to moderate disease. Nearly half of the patients in the watchful waiting group had normalized PSG findings compared with 79% in the surgical treatment group. Regarding this finding, active follow-up and reassessment after a period of watchful waiting serve as valid options for treating children with SDB.

Furthermore, based on findings in a recent randomized clinical trial among children between 2 and 4 years old, the authors suggested that children with moderate OSA should be considered for early adenotonsillectomy (Fehrm et al., 2020). In turn, children with mild disease with only moderate effects on quality of life could benefit from watchful waiting for six months.

2.6.2 Surgery

The first-line treatment for SDB in children older than two years and with adenotonsillar hypertrophy is adenotonsillectomy. If severe obesity is not a contraindication to surgical intervention, adenotonsillectomy may also be deemed appropriate for obese pediatric patients. The CHAT study found that, after surgical treatment, significant improvement was detected in quality of life, behavior, and findings in PSG when compared to watchful waiting (Marcus et al., 2013). In "cold" adenotonsillectomy, the tonsillar capsule is dissected off the pharyngeal constrictor muscles. Alternatively, the surgical procedure may be carried out using mono- or bipolar electrosurgery and plasma-mediated ablation (Bitners & Arens, 2020).

Partial tonsillectomy or tonsillotomy is a modified procedure in which the tonsillar capsule is left in place. Complication rates are shown to be lower compared

to tonsillectomy. A Finnish prospective study including 101 children found that children who underwent tonsillotomy recovered faster and suffered from less pain than those who underwent tonsillectomy (Sakki et al., 2021). Furthermore, in a retrospective analysis of over 3000 children, the risk of resurgery after tonsillotomy was low (Sakki et al., 2022). Nonetheless, more prospective trials are needed to examine the therapeutic effect and generalizability of partial tonsillectomy (Parikh et al., 2019).

2.6.3 Orthodontic treatments

Rapid maxillary expansion (RME) is an orthodontic technique that aims to enlarge the maxillary dental arch and palate and, in that way, expand the airway. It involves the use of a dental device secured over the maxillary teeth with an expansion screw. Sporadic studies have shown improvement in PSG parameters and symptoms after using RME in children with maxillary restriction and malocclusion (Bitners & Arens, 2020).

Custom-made orthodontic appliances, such as tongue devices and mandibular advancement devices, can be used as supplementary treatment in OSA patients with malocclusion or retrognathia (Carvalho et al., 2016).

2.6.4 Myofunctional therapy

Myofunctional therapy is composed of exercises for facial muscles, the tongue, lips, soft palate, and the lateral pharyngeal wall. These exercises typically include isotonic and isometric training, which involves different muscles used in functions such as speaking, breathing, and swallowing. One study, albeit with a small sample size, reported a 58% reduction in AHI when children with OSA and adenotonsillectomy as a first-line treatment performed oropharyngeal exercises, while in the control group, the reduction was 7% (Villa et al., 2015). Myofunctional therapy is considered a potential adjunct to other SDB treatment options (Camacho et al., 2015).

2.6.5 Medication

Nasal corticosteroids and montelukast have been shown to decrease the severity of OSA, especially among children under 6 years of age (Kaditis et al., 2016). Intranasal

corticosteroids have been shown to decrease the severity of SDB and improve quality of life (Bitners & Arens, 2020). The effect of anti-inflammatory corticosteroids is presumably due to the reduction in adenoidal size. Nonetheless, previous studies included only children diagnosed with SDB through PSG. The objective of a recent multicenter, randomized, placebo-controlled trial, the MIST, was to assess the safety and effectiveness of intranasal mometasone in treating symptoms associated with SDB in children (Baker et al., 2023). There was no significant disparity between intranasal mometasone and saline. Furthermore, this study revealed high rates of symptom resolution in both treatment groups. Based on these findings, it is conceivable that a significant number of children with SDB symptoms could be effectively treated by their primary care providers using intranasal saline as the initial treatment. The efficacy of saline treatment may be attributed to its ability to clear nasal passages, which is a similar mechanism observed in its use for treating allergic rhinitis in children.

Montelukast is a leukotriene receptor antagonist, and it is most often used as an adjunctive therapy in asthma. A recent meta-analysis reviewed four randomized controlled trials covering the efficacy and safety of montelukast in the treatment of pediatric OSA (Ji et al., 2021). Oral montelukast significantly improved parameters characteristic of SDB in PSG and symptoms such as snoring and mouth breathing. Considering that montelukast controls the inflammatory response, it is believed to reduce the size of adenotonsillar tissue and, in that way, lessen the obstruction in upper airways. Montelukast is well tolerated and can be used to treat children with mild to moderate OSA alone or combined with nasal corticosteroids.

2.6.6 Positive airway pressure therapy

If surgical treatment is not an option, or if the child's tonsils and/or adenoids are not enlarged, positive airway pressure (PAP) therapy should be considered for the treatment of OSA. Additionally, severe residual OSA after adenotonsillectomy is an indication of PAP therapy. When OSA is related to obesity, craniofacial abnormalities, or neuromuscular disorders, PAP treatment is commonly initiated (Kaditis et al., 2016).

Continuous PAP (CPAP) is used most frequently, but bilevel PAP (BiPAP) is equally effective. With PAP therapy, the objective is to keep the airways open during sleep by creating a pneumatic splint for the upper airway tissues (Bitners & Arens, 2020). PAP treatment has been shown to improve gas exchange, neurobehavioral

disturbances, school performance, and quality of life (Beebe & Byars, 2011; Marcus, Radcliffe, et al., 2012). Nasal congestion, eye irritation from air leaks, and skin problems related to mask wearing are typical complications of CPAP or BiPAP. Midface retrusion is linked to long-term CPAP or BiPAP use (Kaditis et al., 2016). Conducting pediatric home ventilatory therapy requires special expertise and is generally centralized in tertiary referral centers. Treatment and monitoring are demanding and compel a multidisciplinary team, including several specialists from different fields of pediatrics.

2.6.7 Other treatments

For adolescents with obesity, extensive weight loss is effective for the treatment of OSA. However, evidence on the efficacy of weight loss in overweight or obese younger children is lacking (Kaditis et al., 2016). Craniofacial surgery is indicated in children with complex craniofacial anomalies and in cases when PAP therapy is not an option. Occasionally, no other method of therapy is suitable, especially for children with severe craniofacial abnormalities, and in these instances, tracheostomy is a definitive surgical treatment for OSA (Bitners & Arens, 2020).

2.7 Long-term influences of snoring and obstructive sleep apnea

The association between SDB and cognitive problems, growth, obesity, and cardiovascular diseases has been recognized by both clinicians and researchers. These negative long-term influences seem to correlate with SDB severity in a dose-dependent manner, but it is noteworthy that negative consequences of SDB have also been associated with the milder forms of obstructive sleep problems such as snoring. As most of these negative health consequences might be prevented with timely therapy, early recognition and treatment is essential.

2.7.1 Neurocognitive and behavioral problems

According to previous reports, children with SDB generally demonstrate worse cognitive functioning when compared to controls without SDB (Garagozzo & Hunter, 2022). Importantly, besides OSA, these differences have also been observed among the milder entities in the spectrum of SDB, including primary snoring.

Children with habitual snoring have been reported to a have lower intelligence quotient (R. Bourke et al., 2011; O'Brien et al., 2004) compared to children who have never snored. Additionally, habitually snoring children's academic function and school performance have been shown to be poorer (R. Bourke et al., 2011; Brockmann et al., 2012) compared to children not having SDB. In their study on the long-term impact of SDB on learning, Gozal et al. discovered that children who experienced snoring during their early childhood or required adenotonsillectomy for snoring were likelier to exhibit lower academic performance than those who did not have those symptoms (Gozal & Pope, 2001). These results were based on questionnaires sent to seventh and eighth graders, and those who reported ongoing snoring were excluded. The results might indicate that children who had SDB during crucial times for brain development and learning may have their academic potential reduced permanently, even if the symptoms had been previously resolved or SDB had been treated with surgery. However, reports imply that the overall level of children´s intellectual abilities remain within the normal range (da Silva Gusmão Cardoso et al., 2018).

In addition to neurocognition, SDB is also associated with behavioral problems. Habitually snoring children have been reported to present more hyperactive and inattentive behaviors (Brockmann et al., 2012; Gill et al., 2012; Rosen et al., 2004). Children with SDB might also display more irritability and externalizing behaviors, such as aggression (Gill et al., 2012; Rosen et al., 2004).

Studies suggest that episodic hypopneas and apneas, interruption of sleep, and disrupted sleep architecture induce neurocognitive and behavioral disorders among children with SDB. Furthermore, systemic inflammation accompanying SDB has also been associated with decreased cognitive capacity in childhood. (Garagozzo & Hunter, 2022) Early treatment of SDB is associated with improvement in some aspects of neurocognition (Biggs et al., 2014; Marcus et al., 2013).

2.7.2 Growth

The influence of snoring and sleep disorders on childhood growth is two-sided. On one hand, growth failure was reported in the 1980s and 1990s among children with OSA. Failure to thrive is illustrated by insufficient weight gain or a lack of appropriate physical growth during early childhood, and pediatric OSA has been associated with this for more than a century. On the other hand, SDB is strongly associated with obesity in childhood. Considering that obesity is becoming more and

more common and occurs at earlier ages than previously, it is also a major risk factor for developing SDB. Furthermore, it has been suggested that there is a reciprocal relationship between obesity and OSA. Children with OSA are at greater risk of developing obesity due to hormonal changes triggered during sleep to increase hunger and energy intake (Keefe et al., 2019).

2.7.2.1 Growth failure

Growth retardation has been previously reported mainly among children with markedly high OAI values, meaning they have a severe disease (Guilleminault et al., 1981; Nieminen et al., 2002). Abnormal nocturnal secretion of growth hormones is the most examined theory for growth retardation among children with sleep apnea (Chennaoui et al., 2020). A large proportion of growth hormones are secreted during slow-wave sleep, and interruptions caused by airway obstruction may disturb hormone secretion (K. Bonuck et al., 2006). Consistently, the concentrations of insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP-3), which are more stable in the serum than growth hormone levels and therefore more suitable as screening methods (Chinoy & Murray, 2016), have been reported to be lower in children with OSA (Bar et al., 1999; Nieminen et al., 2002).

In addition, OSA is associated with increased energy expenditure during sleep, nocturnal hypoxemia, and metabolic alkalosis, all of which may affect growth. Several feeding problems, such as feeding fatigue due to adenotonsillar hypertrophy and upper airway obstruction, may result in inadequate energy supply and, consequently, insufficient weight gain (K. Bonuck et al., 2006).

2.7.2.2 Obesity

The prevalence of obesity has increased worldwide in recent decades (Ng et al., 2014). Previously, in the Finnish population, a trend of increasing body-mass index (BMI) was reported in school-aged children and teens, but not among toddlers (Vuorela et al., 2011). A fairly recent study found that 23.7% of Finnish boys aged 2–6 years and 13.9% of girls in the same age group were overweight based on the age and sex adjusted body mass index (ISO-BMI) (Mäki et al., 2018). However, this trend in overweight toddlers seems to be changing in Finland. In the latest report of the Finnish Institute for Health and Welfare, the proportion of overweight children

aged 2–6 years had increased to 27% among boys and 16% among girls (Jääskeläinen et al., 2021).

Obesity and SDB seem to have a mutual influence on the initiation and progression of both problems. OSA induces systemic inflammation, which can lead to the same type of morbidity caused by obesity (Bhattacharjee et al., 2011). Children with SDB, even at normal weight, appear to have higher levels of C-reactive protein (CRP) and interleukin-6 (IL-6) than healthy children (Gozal, Sans Capdevila et al., 2008; Tauman et al., 2004, 2007). Reciprocally, the levels of anti-inflammatory interleukin-10 are reported to be lower among children diagnosed with OSA (Gozal, Serpero, et al., 2008). It has been shown that CRP and IL-6 levels return to normal when OSA is treated with adenotonsillectomy (Gozal, Serpero, et al., 2008; Kheirandish-Gozal et al., 2006).

Ghrelin is a hormone released from the stomach and gastrointestinal tract (Wiedmer et al., 2007). Ghrelin has different functions, such as controlling energy balance and glucose homeostasis. This appetite-stimulating hormone plays an important role in energy intake and expenditure. Obese children diagnosed with OSA have been reported to have higher ghrelin levels compared to non-obese children with OSA and obese children without OSA (Spruyt et al., 2010). Moreover, Spruyt et al reported that obese children with OSA had unhealthy dietary and physical activity habits than non-obese children with OSA or obese children without OSA. Taking this into account, the combination of obesity and SDB predisposes children to an increased risk of unhealthy dietary habits and reduction of physical activity.

2.7.3 Cardiovascular problems

SDB has been linked to various heart-related issues, including high blood pressure, coronary artery disease, and pulmonary hypertension in adults (Yeghiazarians et al., 2021) and in children, especially those with complex disorders such as Down syndrome or neuromuscular disease (Kaditis et al., 2016). As a result of today's somewhat earlier diagnoses of OSA compared to the past, children with severe clinical presentations, including pulmonary hypertension and cardiac dysfunction, are not routinely seen in clinical practice today. However, it is essential to recognize the conditions that increase the risk of cardiovascular morbidity in children with SDB and to offer treatment options as early as possible.

2.7.3.1 Hypertension

Elevated blood pressure during childhood has been reported to predict hypertension and metabolic syndrome in adulthood (S. S. Sun et al., 2007). Studies among children have suggested a positive association between OSA and elevated systemic blood pressure (Enright et al., 2003; Leung et al., 2006) and that children with OSA might have higher blood pressure levels or higher blood pressure variability, from which the latter is shown to be a strong predictor of cardiovascular morbidity compared to children with primary snoring (Kang et al., 2021; Marcus, Greene, et al., 1998; Weber et al., 2012). However, there is also evidence that snoring alone is associated with hypertension during childhood, and it is suggested that blood pressure levels increase across the severity range of SDB (Au et al., 2021; A. M. Li et al., 2009).

Furthermore, treatment, or active follow-up for the spontaneous resolution of SDB is essential, as improvement in obstructive sleep problems has been reported to be associated with better control of blood pressure levels (Vlahandonis et al., 2014).

2.7.3.2 Endothelial dysfunction

Endothelial dysfunction is a pathological state of the endothelium and is characterized by the imbalance of vasodilatation and vasoconstriction. It is considered an early marker of atherosclerosis, and it predicts plaque formation and thickening of the arterial wall. Among patients with OSA, systemic inflammation, which will be discussed in detail in section 2.8.1, might induce functional disruption of the endothelium (Kheirandish-Gozal et al., 2010).

The endothelial function of children with OSA is reported to be significantly impaired (K. C. C. Chan et al., 2015; Kheirandish-Gozal et al., 2010). Endothelial dysfunction becomes more frequent when the severity of OSA increases. However, primary snoring has also been reported to be associated with less optimal cardiovascular outcomes, such as reduced endothelial function and increased thickness of carotid intima-media (Au et al., 2021). Since endothelial dysfunction seems to be reversible with the treatment of SDB (Chan et al., 2015), it is essential that children with obstructive sleep problems are recognized as early as possible.

2.7.3.3 Pulmonary hypertension

One of the most serious complications of SDB is pulmonary hypertension, and without treatment, it can lead to failure of the right side of the heart. Pulmonary hypertension is a chronic disorder associated with a wide variety of respiratory diseases. It is defined by a mean pulmonary arterial pressure > 20 mmHg at rest (Humbert et al., 2022).

Studies covering the prevalence of pulmonary hypertension in children with SDB are scarce, and estimates of the prevalence vary widely, ranging from 0% to 85%. Correspondingly, studies among children with pulmonary hypertension have reported an SDB prevalence of between 6 and 24% (Ingram et al., 2017).

Regardless of the limited literature covering pulmonary hypertension in children with SDB, case series demonstrate improvement or complete resolution of pulmonary hypertension after OSA treatment. In light of this finding, screening for SDB with PSG might be appropriate to recommend to all children with newly diagnosed pulmonary hypertension. Furthermore, children with an increased risk of pulmonary hypertension, such as those with Down syndrome or neuromuscular disease, should obtain an echocardiogram to evaluate for pulmonary hypertension (Ingram et al., 2017).

2.8 Metabolic disease and snoring

Exposure to various environmental risk factors for cardiometabolic health during early childhood can increase the possibility of metabolic disease in adulthood (Berenson, 2002). Cardiovascular and metabolic risk in young children consists of components such as elevated glucose and blood pressure, obesity, and dyslipidemia (Kamel et al., 2018). The metabolic syndrome definition consists of the presence of at least three of the following measures: excess body fat around the waist, elevated plasma triglycerides, elevated fasting blood glucose, high blood pressure, and decreased high-density lipoprotein (HDL) cholesterol (Grundy et al., 2005). Definitions of metabolic syndrome with cut-points are defined for children aged 10 years and older (Zimmet et al., 2007), but not for younger children.

2.8.1 Systemic inflammation

SDB may lead to the recruitment of inflammatory mechanisms similar to those activated in obesity. In OSA, individuals experience recurring episodes of hypopneas or apneas during sleep, which lead to sleep interruptions, frequent arousals and sleep fragmentation. Possible mechanisms for the triggering of inflammatory processes have been suggested to be the activation of proinflammatory pathways among OSA patients (Arnardóttir 2009). The augmented sympathetic response as a result of nocturnal hypoxia and episodes of arousals associated with SDB could also offer an explanation fot the presence of systemic inflammation among OSA patients (Unnikrishnan et al., 2015), see Figure 2. However, it is not clear whether the triggered inflammatory mechanisms are a component or a cause of SDB (Goldbart & Tal, 2008). Furthermore, the data are often complicated by the presence of comorbid obesity, resulting in confounding effects. Changes in the levels of biomarkers studied in OSA are also observed in many of the comorbidities associated with the condition. (Arnardóttir 2009).

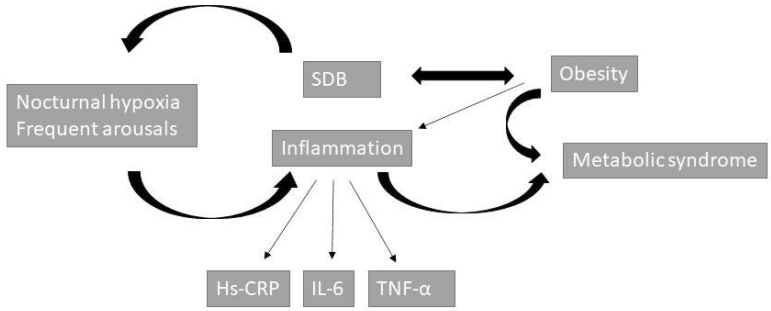

Figure 2. Multidirectional interactions with SDB, obesity, and inflammation (M. Katila). Hs-CRP; high-sensitivity C-reactive protein, IL-6; interleukin-6, SDB; sleep disordered breathing, TNF-α; tumor necrosis factor-alpha.

Systemic inflammation has been documented in adult patients with OSA. It is measured by different inflammatory markers; however, studies on pediatric SDB and inflammation are limited (Unnikrishnan et al., 2015). High-sensitivity C-reactive protein (hs-CRP) is an important marker of inflammation and cardiovascular risk. A recent meta-analysis of 13 pediatric studies on the blood levels of CRP in OSA patients reported that the levels of plasma hs-CRP were higher among children with OSA (Moslem Imani et al., 2021). Additionally, higher levels of CRP appeared to be associated with more severe diseases in adults.

In addition to hs-CRP, other markers of inflammation have also been studied. IL-6 is a pro-inflammatory cytokine released by adipose tissue. The levels of IL-6 in children with moderate or severe SDB have been reported to be significantly higher than in children without obstructive disorders during sleep (Tauman et al., 2007). Furthermore, among obese children, even mild SDB seems to be associated with higher levels of hs-CRP and IL-6 (Tsaoussoglou et al., 2010). Tumor necrosis factor-alpha (TNF-α) is a cytokine involved in sleep regulation, and its levels are elevated after sleep deprivation. The elevated TNF-α levels have been well established among adults with OSA, and there is evidence that moderate and severe OSA is associated with higher levels of TNF-α in children as well when compared to children with habitual snoring only (Gozal et al., 2010). Moreover, the levels of TNF-α were significantly reduced after OSA treatment by adenotonsillectomy.

2.8.2 Changes in lipid profiles

Previous reports covering SDB and unfavorable effects on the metabolic profile have focused on children with OSA but not on snoring alone. However, in addition to OSA, primary snoring has been associated with dyslipidemia among obese adults (Zhang et al., 2017).

Elevated blood total cholesterol and low-density lipoprotein (LDL) levels add to the risk of cardiovascular diseases. The National Cholesterol Education Program (NCEP) Expert Panel has defined the cut-off values for pediatric lipid concentrations (de Jesus, 2011). An acceptable concentration of HDL is defined as 1.2 mmol/l or more and the borderline level is 1.0–1.2 mmol/l. Levels below 1.0 mmol/l are considered abnormal values. Apolipoproteins B (ApoB) are important agents in atherogenic lipoprotein particles, i.e., LDL (Ference et al., 2018). Apolipoprotein A-I (ApoA1) is the major apolipoprotein in HDL and has a protective effect against coronary disease.

In children, only a few studies have evaluated the association between sleep quality and disadvantageous lipid profiles regarding cardiovascular health. Limited evidence suggests that higher sleep disturbance scores and irregular sleep patterns are associated with unfavorable blood lipid profiles (Quist et al., 2016). Koren et al. (2016) reported that children with OSA had an accompanying significant increase in their HDL levels after adenoidectomy. Furthermore, non-obese children with OSA and children with adenoid or tonsillar hypertrophy have been reported to have lower HDL levels (Alexopoulos et al., 2011; Zong et al., 2013).

2.8.3 Glucose and insulin

Insulin resistance is a condition in which either the insulin produced within the body or the insulin taken from outside is less effective in increasing the uptake and utilization of glucose in an individual compared to the general population (Lebovitz, 2001). To measure insulin resistance, the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) formula is used, which includes fasting plasma glucose and serum insulin levels. It is computed using the formula as follows: fasting plasma glucose (mmol/l) times fasting serum insulin (mU/l) divided by 22.5.

OSA in adults has been linked to insulin resistance, regardless of whether the individual is obese or not. Studies have also shown that children with OSA and obesity have higher levels of triglycerides and HOMA-IR than those with obesity alone (Flint et al., 2007). Adolescents with SDB are likelier to develop metabolic syndrome (Redline et al., 2007), but obesity may be a stronger contributing factor to insulin resistance than the severity of SDB (Tauman et al., 2005).

2.8.4 Cortisol

The hypothalamic-pituitary-adrenocortical (HPA) axis and the sympathetic adrenomedullary system work together to regulate our response to stress. The HPA axis triggers the release of cortisol from the adrenal glands, which is an important marker of our body's stress levels. Cortisol levels can be measured in multiple ways, including through blood, urine, hair, and saliva. Saliva sampling is a convenient and non-invasive way to measure cortisol levels without causing additional stress and allows for multiple measurements.

Abnormal and fragmented sleep among SDB patients can activate the stress response system, but there is inconsistency in the literature. Räikkönen et al. (2010) found that children with short sleep duration demonstrated a higher cortisol awakening response and nadir compared to children with average sleep duration. Additionally, children with low sleep efficiency displayed higher cortisol levels across the entire day, and their response to standardized stress testing was greater in comparison to the children having average or high sleep efficiency. Another study including children with SDB discovered that the ratio of cortisol measurements before and after PSG was negatively associated with OSA severity, possibly indicating a chronically stressed HPA axis (Park et al., 2013). Increased salivary cortisol diurnal production including significantly elevated morning cortisol levels, both in the groups of mild and moderate/severe OSA, was detected by Patacchioli

et al. (2014), whereas another study reported that children with moderate or severe OSA and tonsillar hypertrophy had reduced morning serum cortisol levels (Malakasioti et al., 2013). Further studies are needed to clarify the interactions between SDB and HPA axis functioning among children.

2.8.5 Microbiota

Initial exposures that disrupt the natural formation of gut bacteria have been linked to the emergence of conditions such as obesity and allergies. These same disorders are frequently seen as outcomes of child snoring. There is evidence that children who snore have a distinct collection of microorganisms in their bodies compared to healthy children (Collado et al., 2019). Snoring children showed a reduced variety of microbes and a greater presence of bacteria that promote inflammation. Furthermore, children with OSA displayed a reduced range of microorganisms in comparison to healthy individuals (Valentini et al., 2020). It is necessary to carry out additional research to fully comprehend the involvement of gut microorganisms in the development of OSA and related health issues in children.

To sum up, the relationship between the risk factors and consequences of SDB, growth, obesity, and metabolic syndrome is intricate and interlinked. There is a notable overlap in biomarkers and health outcomes between obesity and SDB. Investigating these phenomena in early childhood is of paramount importance to gain a better understanding of the origins of these disorders and to comprehend the cause-and-effect relationships more thoroughly.

3 AIMS OF THE STUDY

1. To study the prevalence of snoring at the ages of 3 months and 8 months, as well as the prenatal and postnatal parental-reported factors associated with this condition. (I)

2. To study the prevalence and persistence of snoring during the first two years of life and associated factors. (II)

3. To study the association between snoring and growth and whether the unfavorable effect of SDB on children's metabolic profiles based on blood samples can already be seen in early childhood. (III)

4 MATERIALS AND METHODS

4.1 Study design

These recent studies were based on the CHILD-SLEEP (CS) project. It is a longitudinal birth cohort study with several measurement points, undertaken in collaboration with Pirkanmaa Hospital District, the Finnish Institute for Health and Welfare, Tampere University, the University of Eastern Finland, and the University of Helsinki. The CS protocol included several subsamples, such as clinical snoring studies and PSG (Paavonen et al., 2017).

The cohort was recruited prenatally at 32 weeks of pregnancy in Pirkanmaa Hospital District, Finland. Pirkanmaa is an area situated in southern Finland. It comprises 23 municipalities and almost 530,000 residents. The population in the area is mainly Finnish. Tampere is the main city of Pirkanmaa, with a population of 244,000. The infants were born between April 2011 and February 2013. During that period, there were two maternity hospitals in Pirkanmaa Hospital District, but only the children born in Tampere University Hospital were considered eligible for the study. During the recruitment period, there were approximately 5,100–5,500 deliveries per year at Tampere University Hospital.

The health centers recruited parents for the study during follow-up pregnancy visits. A total of 63 maternity clinics took part in the recruitment process. Only Finnish-speaking families were considered eligible for the study. The families who decided to take part in the study were asked to sign consent forms for participation and were given the first questionnaire. Follow-up visits to take measurements of the children took place at birth, and at three, eight, 18, and 24 months.

Study II was conducted in two population-based birth cohort studies: the CS and the FinnBrain (FB). The FB study is described in detail in section 4.2.2.

4.1.1 Questionnaires

The sleep questionnaires in the CS protocol included questions from three screening tools for children, the Brief Infant Sleep Questionnaire (BISQ), the the Infant Sleep

Questionnaire (ISQ), the SDSC, and one for adults, the BNSQ (Bruni et al., 1996; Morrell, 1999; Sadeh, 2004).

The BISQ is a validated tool for screening sleep problems among infants and young children. Items from the BISQ were included in the set of CS questionnaires to evaluate children's sleep. Sleep arrangements and sleep positions were investigated. Furthermore, questions covering the time taken for a child to settle off to sleep were included. In addition to the BISQ, we used questions from the ISQ. The test is a parental self-report questionnaire designed to evaluate sleeping behavior in 12–18-month-old children. It shows high levels of sensitivity and specificity in assessing sleeping problems in young children and asks parents, among other things, how frequently they have trouble getting their children to sleep. Additionally, questions about the frequency of night awakenings and the time taken for a child to resettle off to sleep after awakening were included in the questionnaires. We also included the question of whether parents think their children have sleep difficulties.

The BNSQ is a standardized questionnaire developed in 1988 by the Scandinavian Sleep Research Society Taskforce (Partinen & Gislason, 1995). It includes 21 questions concentrating on different sleep disorders. The task group chose a five-point scale for the frequency of sleep problems as follows: never or less than once per month, less than once per week, 1–2 nights per week, 3–5 nights per week, or every night. The response alternatives for evaluating sleep quality were as follows: well, quite well, not well/not poorly, quite poorly, and poorly. Several later questionnaires used the same scaling regarding the frequency of sleep disorders. Questions from the BNSQ were utilized in the present studies to assess parental sleep habits and quality.

To assess SDB in children, we used questions from the SDB subscale in the SDSC, which is discussed in detail in section 2.5.1.1. On this scale, the response alternatives were "never," "occasionally" (indicating once or twice per month), "sometimes" (meaning once or twice per week), "often" (suggesting three to five times per week), and "always" (indicating daily). In the analyses, we combined the frequency of snoring into a dichotomy as follows: habitual snorers, meaning snoring at least three nights per week, versus the others.

In addition to sleep-related questions, the CS questionnaire consisted of sections concerning environmental factors that may affect sleep. We asked about the child's medical history, including surgeries such as adenotonsillectomy, and the frequency of respiratory infection. We also asked whether the child was breastfed or had only formula during the first months of life. We also gathered background factors, such

as parents' BMI, smoking history, and snoring history. To evaluate socioeconomic factors, we asked about parental level of education and parents' monthly income.

4.2 Study population

4.2.1 CHILD-SLEEP cohort (I, II)

In the CS project, a total of 2244 parents were approved to receive prenatal questionnaires during their visits to maternity clinics, from which 1673 (74%) families returned the baseline questionnaires. Questionnaires were provided by mail or in electronic form by email to both mother and father. The infant questionnaire was completed jointly by the parents. The response rate was 85% at the age of three months and 78% at the age of eight months. The families who did not answer the question concerning snoring were excluded, leaving 1388 infants at the age of three months and 1216 infants at the age of eight months (I). At the age of 24 months, 950 families out of 1673 originally recruited families responded to the 24-month questionnaire concerning their child's health and sleep patterns, yielding a response rate of 56.8%. In 3 (0.3%) cases, the family did not answer the question about snoring. These cases were excluded from further analysis, leaving 947 (56.4%) families (II).

4.2.2 FinnBrain cohort (II)

Study II was conducted within two population-based birth cohort studies: CS and FB. FB cohort was a population-based sample comprising 3808 families gathered in Southwest Finland. A more detailed description of the characteristics of the sample and the recruitment process has been described previously (Korja et al., 2018). The sample was recruited between December 2011 and April 2015 at maternal welfare clinics in a geographically defined area comprising all women eventually referred to give birth at Turku University Hospital in the Southwest Finland Hospital District and the Åland Islands in Finland. The recruitment took place after the pregnancy ultrasound scan at gestational week 12. The study inclusion criteria were sufficient knowledge of Finnish or Swedish and a normal ultrasound screening result.

Initially, a total of 3808 mothers and 2623 fathers participated. At the child age of 24 months, 1454 families out of 3808 initially recruited families responded to the

24-month questionnaire, yielding a response rate of 38.2%. There were 61 (4.2%) responses missing information on the child's snoring status, leaving 1393 (36.6%) children in the final sample.

4.2.3 Clinical sample (III)

In addition to the questionnaires, the CS study comprised several subsamples. Two subsamples of the CS study underwent PSG at the age of 24 months: 1) the home PSG group (Satomaa et al., 2016) and 2) the clinical PSG group comprising snoring children and their non-snoring controls, whose PSGs were recorded at the sleep laboratory (Markkanen et al., 2021).

Inclusion in study III required participating in the PSG subsamples of CS at 24 months of age and responding to the study questionnaire regarding snoring at 24 months. According to these criteria, study III comprised 78 children.

For the home PSG group, all eligible families with healthy and full-term newborns were asked personally to participate during their postnatal stay at the hospital. More specific inclusion and exclusion criteria of the home PSG group have been published previously (Satomaa et al., 2016). At 24 months of age, 65 children had stayed in the home PSG group.

For the clinical PSG group, a question about snoring frequency from the SDB subscale of the SDSC was used to select participants. The habitually snoring children were recruited as snorers, and the non-regularly snoring children as controls. In practice, based on the questionnaire, the families were contacted by telephone to confirm the occurrence of snoring or the lack thereof, and they were asked to participate in the clinical PSG group. The children recruited in the clinical PSG group previously (at the age of 8 months; N = 35) were asked to continue in the clinical group at the age of 24 months. At 24 months of age, 31 additional children were recruited. A total of 52 children took part in the clinical PSG group at 24 months.

There were 12 children in the clinical PSG study and 27 children in the home PSG study recruited previously whose 24-month questionnaire was not available, leaving 78 children in the final sample (see Figure 3).

Regardless of the children's questionnaire-based status as a snorer or a non-snoring control, or whether the child was a participant in the home PSG group, we divided the children into two groups based on their snoring time in their PSG recordings. We analyzed the distribution and the quartiles of snoring time as percentages of total sleep time (TST) and found that the 75th percentile cut point

was 12.10% of the TST. The children snoring at least 12.10% of the TST were denoted as PSG snorers (N = 19), whereas the children snoring less than 12.10% of TST were denoted as PSG non-snorers (N = 59). Over half (N = 38) of the PSG non-snorers were snoring less than 1% of the TST. Considering that the study population scored low on the obstructive apnea-hypopnea index (OAHI), we applied the amount of snoring in PSG to assess the consequences of SDB on metabolic parameters. The amount of snoring in PSG was used as a substitute for OAHI because results from the previous study in the CS cohort indicated that snoring time percentage is associated with the likelihood of OSA (Markkanen et al., 2021).

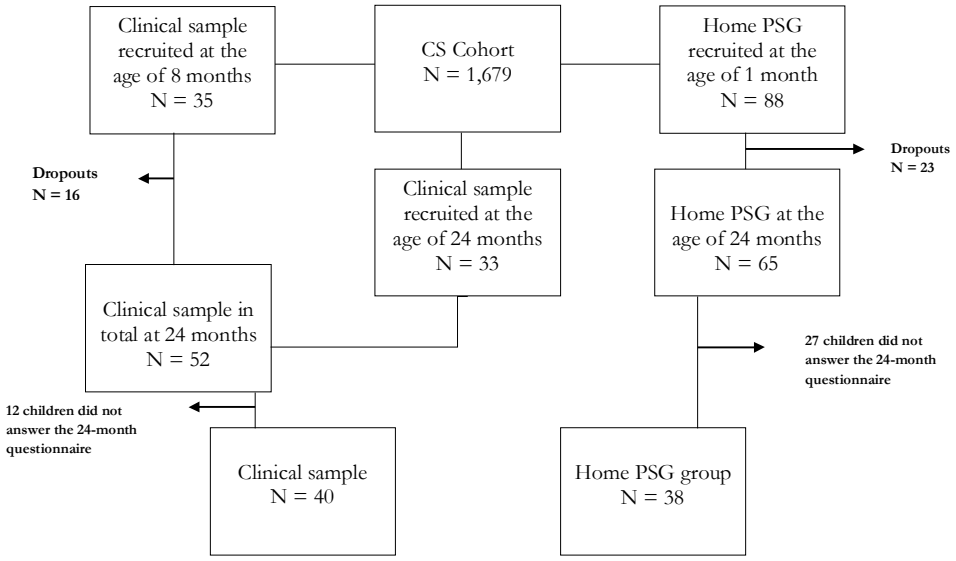

Figure 3. Study population in study III (M. Katila).

4.3 Main outcomes

4.3.1 Prevalence and evolution of snoring (I, II)

Prevalence rates were reported for the CS and FB cohorts separately and jointly (I, II). We also longitudinally analyzed the prevalence of persistent snoring. There were 856 children in the CS cohort with complete data on snoring from all three measurement points at three, eight, and 24 months (II). The positive and negative

predictive values were calculated to evaluate the probability of snoring at 8 and 24 months based on the child's snoring status at the age of three months (II).

4.3.2 Associated factors (I, II)

Based on the parents' answers to the SDSC question about snoring, we combined the frequency of snoring into a dichotomy as follows: habitual snorers, meaning snoring at least three nights per week, versus the others in the analyses (I, II).

The total sleep time was calculated from the answers to the following questions: "How much time does your child spend in sleep during the night (between 7 in the evening and 7 in the morning)?" and "How much time does your child spend in sleep during the day (between 7 in the morning and 7 in the evening)?" The question "Has your child had recurrent infections?" was applied as a method to determine which children suffered from recurrent infections because no absolute consensus exists on the number of infections per year that would define recurrent infections (Nokso-Koivisto et al., 2002). The frequency of the parents' snoring was gathered from the questions of the BNSQ at the end of the pregnancy.

There were some differences in the questionnaires for the CS and FB cohorts (II). Information on whether the child was being breastfed or having only formula was available from the first three months of life in the CS cohort and from the first four months in the FB cohort. In the CS cohort, we compared those parents who answered smoking today or less than six months ago in the 24-month questionnaire to those who had last smoked more than six months ago or had never smoked. In the FB cohort, we had information on whether the parent was smoking when the child was one year old. This information on smoking was gathered only from a subsample comprising 275 mothers and 168 fathers. In the CS cohort, we inquired as to parental monthly income at the end of the pregnancy, whereas in the FB cohort, we gathered information at the beginning of the pregnancy. Information on the parents' BMI was available from the 24-month questionnaire in the CS cohort and the 12-month questionnaire in the FB cohort.

4.3.3 Growth (III)

The growth charts were collected from well-baby clinics. There was some variation in the number of growth measurement points between the children. To evaluate the association between snoring and growth, we chose the measurement points at three,

eight, 18, and 24 months corresponding to the follow-up questionnaire points. Growth values for these specific follow-up points were obtained by interpolating, or if not available, by extrapolating the anthropometric measurements for the four fixed time points using the two nearest available measurements and assuming linear growth based on these values. These interpolated or extrapolated values were then used in the analyses (Tuohino et al., 2019).

The body mass index standard deviation score (BMI-SDS) at the child's age of 2 years was calculated based on the Finnish growth reference (Saari et al., 2011). We used standardized Finnish classifications of overweight and obese based on BMI-SDS information and combined classes into the dichotomy as follows: children who were obese or overweight versus normal-weight or underweight children.

4.3.4 Polysomnography (III)

The home PSGs were recorded with an Embla Titanium device and consisted of six electroencephalography channels, two channels of electro-oculography, submental electromyography, oxygen saturation by pulse oximeter, thoracoabdominal inductance plethysmography, diaphragmatic, and abdominal electromyography, Emfit mattress sensor, electrocardiography, airflow by oronasal thermistor, and snore sensor. The nasal pressure transducer was omitted from the protocol to minimize the sleep-disturbing effects of the recording equipment (Goodwin et al., 2001).

The in-laboratory PSGs of the snoring children and their controls were recorded with an Embla N7000 device, and comprised, in addition to the signals recorded in the home PSGs, the recordings of the frontopolar electroencephalography channels, nasal pressure transducer signal, oxygen saturation by two pulse oximeters, end-tidal partial pressure of carbon dioxide, sleeping position, and video.

Contemporary pediatric guidelines (Berry et al., 2012) have been used in the visual sleep staging and scoring of respiratory events and arousals. All recordings were manually analyzed by a clinical neurophysiologist. Snoring was quantified using a PSG piezo channel. The piezo sampling rate was set at 256 Hz. In the Somnologica software, automated snoring detection utilized a 10 uV threshold. Visual scoring of snoring involved the use of a low-cut filter of 5 Hz and a notch filter of 50 Hz. The piezo sensor was positioned on the top of the thyroid cartilage. The piezo snoring signal was automatically analyzed using REMlogic software. Subsequently, the detections underwent manual evaluation, during which all clear artifacts were

meticulously eliminated. The snoring signal had to manifest as well-formed snoring periods, either continuous or intermittent, distinctly separate from the background noise, without strict amplitude criteria. These snoring periods needed to be synchronized with breathing, occurring specifically during sleep and lasting for at least three respiratory cycles. Verification of snoring events was conducted through listening, whenever possible, especially in laboratory recordings. In laboratory recordings, cannula snoring could serve as an additional signal, but the piezo signal remained the primary indicator for snoring.

The percentage of time with snoring, referred to as total sleep time, was calculated for each child.

4.3.5 Metabolic blood samples (III)

The families were offered the option to join the study without any invasive research methods. Consequently, the majority of the families refused blood samples. In the end, metabolic blood samples were drawn from 31 children from the polysomnography studies (PSG non-snorers N = 22, PSG snorers N = 9). The blood samples were collected in the morning after awakening. Children refrained from eating breakfast prior to the blood sample collection. The samples were drawn in Tampere, then promptly frozen and transported to Helsinki under proper storage conditions. To analyze the children's metabolic profiles further, we also compared the lipid levels of children at the lowest 25th percentile cut point (N = 10) to the lipid levels of PSG snorers. The blood analysis was provided by the laboratory of the Finnish Institute for Health and Welfare using enzymatic assays for measuring total cholesterol, triglycerides, and glucose; the homogenous method for direct measurement of HDL cholesterol; the ultrasensitive immunoturbidimetric assay for hs-CRP; and a chemiluminescent microparticle immunoassay (CMIA) for insulin. LDL cholesterol was calculated using the Friedewald formula. Lipid and lipoprotein traits were also measured using nuclear magnetic resonance (Ala-Korpela, 2008). This metabolic profile was available for 24 children (PSG non-snorers N = 18, PSG snorers N = 6).

4.4 Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (IBM Corp). Frequency analyses were performed first. The prevalence and persistence of snoring were assessed (I, II). Dichotomized background factor variables were compared with parent reported (I, II) and PSG snoring (III). The comparisons were based on t-tests or the chi-square test, depending on the type of variable to be analyzed. Ordinal logistic regression models were constructed to study which of the risk factors were significantly related to snoring at the ages of three and eight months when the infant's age, sex, allergies, and number of infections, plus the parents' education and income, were controlled for (I). A multivariable logistic regression model was constructed in order to study which of the risk factors were significantly related to snoring when controlling for the children's age, sex, prevalence of asthma, and recurrent cycle of infections at the age of 24 months (II). The second model included the first model plus maternal smoking status. The evaluation of associations between snoring and growth variables at each time point was performed by t-tests and multivariate ANCOVA (III). The comparisons between PSG snoring and other sleep parameters and metabolic blood samples were carried out using the Mann–Whitney U test, considering the relatively small size of the recruited population (III). All reported p-values were two-tailed with the statistical significance set at <0.05. Finally, multiple linear regression models were performed for further associations between metabolic test results and snoring time in PSG (III). In logistic regression models, the residuals (errors) of the regression line were approximately normally distributed.

4.5 Ethical considerations

The study protocol was approved by the Ethics Committee of Pirkanmaa Hospital District on March 9, 2011 (number R11032). Written consent was obtained from at least one parent after the families were personally asked to participate in the CS study. All research procedures were carried out in accordance with admissible guidelines.

5 RESULTS

5.1 Snoring prevalence in Finland during infancy (I)

Based on parental reports on three-month questionnaires, 10.6% of Finnish children snored at least once a week. The corresponding prevalence of weekly snoring at the age of eight months was 10.4%. The prevalence of habitual snoring among Finnish children was remarkably low. Only 3.2% of the infants at 3 months and 3.0% at 8 months were snoring habitually. When the longitudinal data in the CS cohort were analyzed, we found that there were 15 infants who snored habitually and 53 infants who snored weekly at both measurement points. The detailed prevalence rates for all the SDB subscales in the SDSC are shown in Figures 4 and 5.

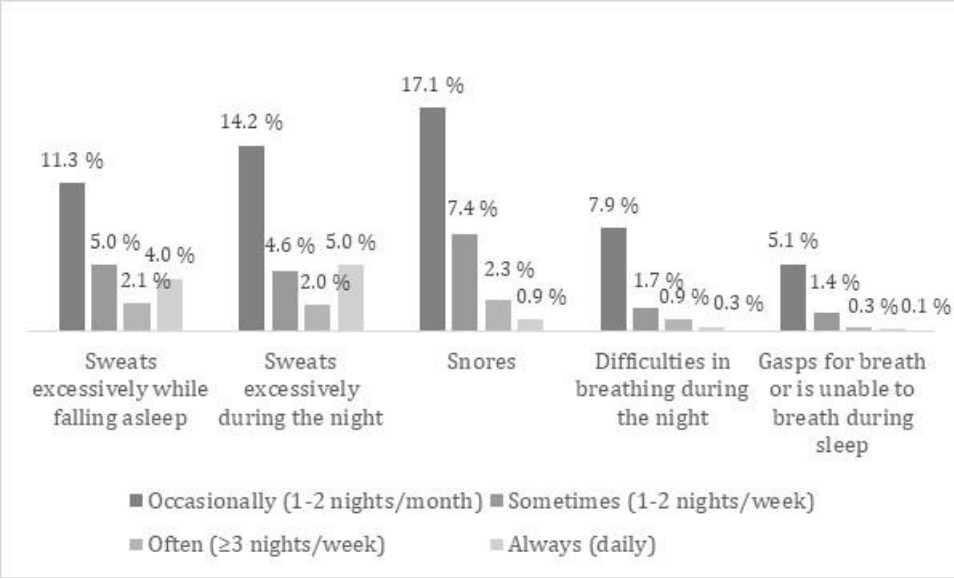

Figure 4. SDB subscales in the SDSC based on parental reports at the age of 3 months.

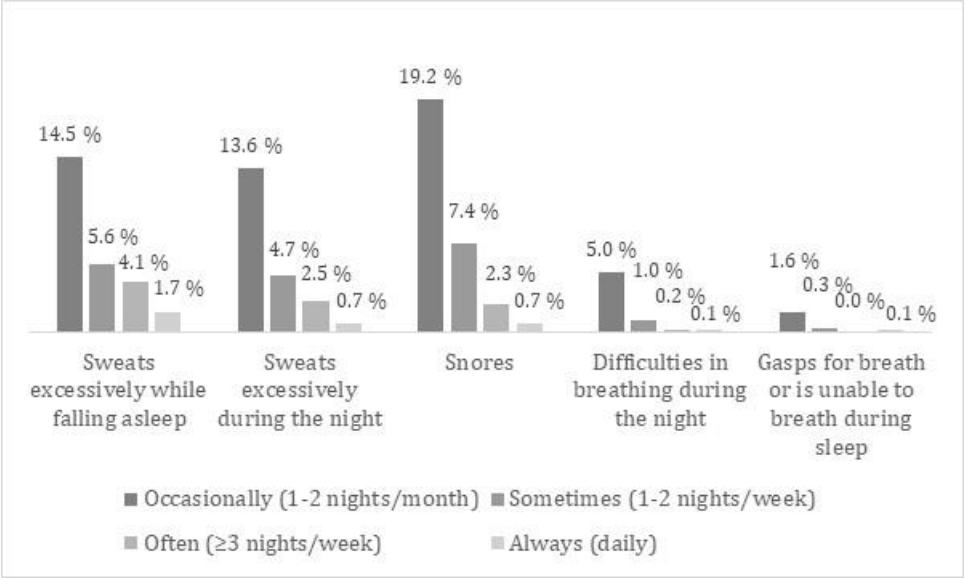

Figure 5. SDB subscales in the SDSC based on parental reports at the age of 8 months.

Within the CS cohort, a limited number of babies were delivered prematurely between 33 and 36 + 6 weeks of gestation. Two infants were identified with specific conditions: one with Crouzon syndrome and one with Down syndrome. However, all analyses were conducted with both illnesses and prematurity. Notably, these exclusions had a minimal impact on the obtained results, as they remained essentially unchanged.

5.2 Sleep of snoring infants (I)

The majority of infants shared their sleeping space with their parents, and there was no distinction in sleeping arrangements between infants who snored and those who did not. Based on parental reports, the sleep length of habitually snoring infants was more than one hour shorter than that of those who snored weekly or less at the age of three months. The statistically significant difference in the sleep lengths of habitually snoring infants and others was no longer detected at eight months. The infants' sleep was considered restless when there were several arousals and periods of wakefulness at night lasting more than 20 minutes at a time. Parents of habitually snoring infants considered the sleep of their baby to be more often restless at the age of three months compared to parents of infants snoring less. Similar to the case

with sleep length, at the age of 8 months, a statistically significant difference was no longer seen. Overall, the sleep of habitually snoring infants was more often considered problematic by parents at three months and at eight months.

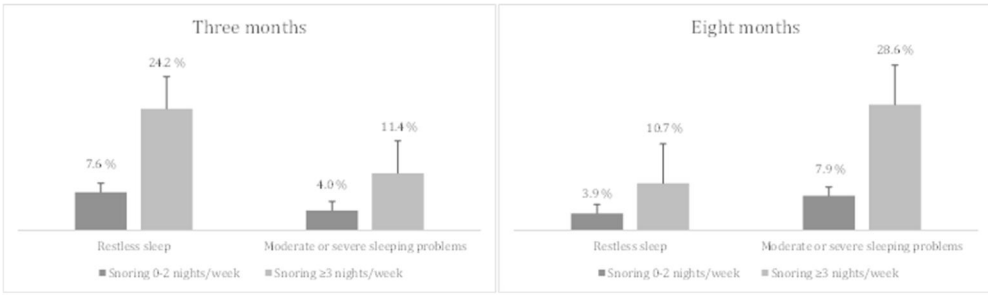

Figure 6. The prevalence of restless sleep and sleeping problems at the age of 3 months and 8 months, comparing infants snoring twice a week or less and habitual snorers.

Most of the three-month-old infants (74.3%) slept in a supine position. At the age of eight months, the majority of infants, specifically 52.5%, adopted the lateral position, while 42.7% of infants slept in the supine position. The majority of infants shared the same sleeping space as their parents, and no difference was observed in terms of sleeping arrangements between infants who snored and those who did not.

5.3 Snoring prevalence at the age of 24 months in two different birth cohorts and evolution of snoring in the CS cohort (II)

In the CS birth cohort, the prevalence of habitual snoring was 2.4%. There were five children snoring every night based on the parental reports, and 615 children not snoring at all. In the FB cohort, the snoring prevalence was as low as that in the CS cohort. There were 31 children (2.2%) snoring habitually, and only 6 snored every night. There were 905 children who did not snore at all at the age of two. The prevalence rates of parent-reported snoring prevalence are shown in Figure 7. The combined prevalence of habitual snoring in the CS and FB birth cohorts was 2.3%.

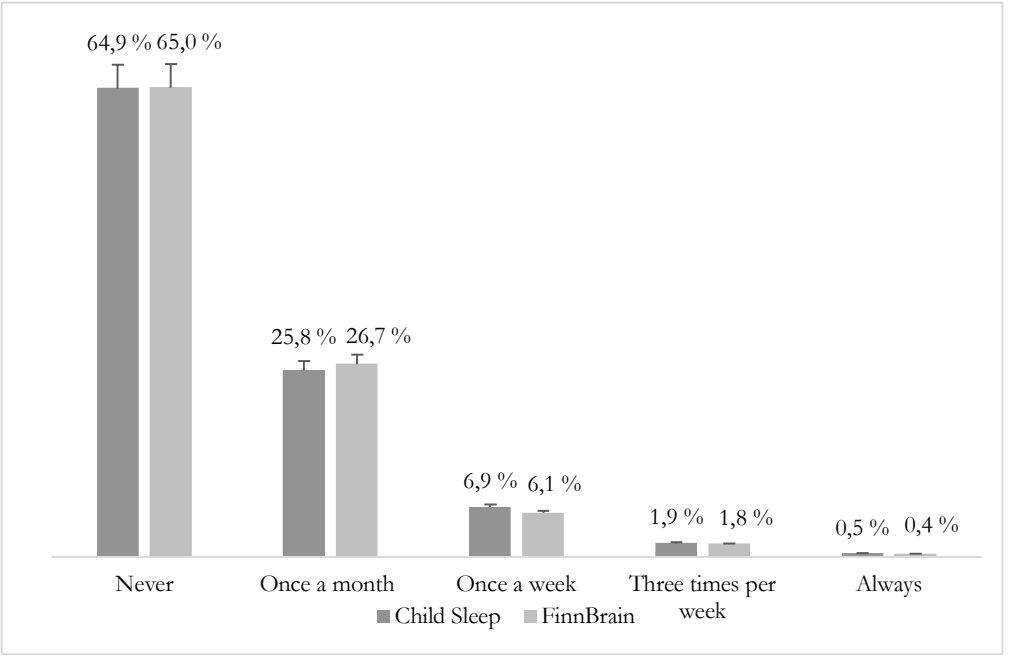

Figure 7. Parent-reported snoring prevalence for 24-month-old children in the CS and FB cohorts.

In the CS cohort, there were 856 children whose SDSC scaling was available for every measurement point (3, 8 and 24 months) providing longitudinal data to evaluate the evolution of snoring during the first two years of life (Table 1). Persistent regular snoring was extremely rare; there were only 6 children snoring habitually throughout the first 2 years of life. Some 2.5% of the children snored at least once a week at all three measurement points. Of the 23 habitually snoring children, almost all had snored previously. Only 2 children snored for the first time at 24 months. The remainder of the two-year-old habitual snorers snored at least occasionally at one or two additional measurement points. Of the 856 children, 47.0% did not snore at any measurement point.

Table 1. Evolution of parent-reported snoring during the first 2 years of life in the CS cohort.

		Snoring at 8 months			
Snoring at 24 months	**Snoring at 3 months**				**Total**
		Never	Sometimes or occasionally	Often or always	
Never	Never	402	52	4	
	Sometimes or occasionally	64	31	1	
	Often or always	1	2	1	
Sometimes or occasionally	Never	103	51	4	
	Sometimes or occasionally	42	59	6	
	Often or always	1	9	4	
Often or always	Never	2	1	1	
	Sometimes or occasionally	3	6	0	
	Often or always	0	0	6	
					856

When the infant snored at the age of 3 months, the positive, predictive values of snoring at 8 and 24 months were 84.6% and 63.6%, respectively. The children not snoring at all during infancy seemed to have a persistent low risk for habitual snoring, as the negative predictive values were 98.3% at 8 months and 98.3% at 24 months.

5.4 Risk factors for snoring (I, II)

Several factors were found to be significantly associated with habitual snoring in these studies. In infancy, the diagnosis of gastro-esophageal reflux was more prevalent in habitual snoring 3-month-old infants compared to those snoring less. Furthermore, 3-month-old infants who snored habitually had fathers with a significantly higher BMI and a lower frequency of higher education. Infants who were exclusively breastfed snored significantly less than infants who were receiving formula at the age of 3 months. At the age of 8 months, infants snoring habitually had a habitually snoring mother significantly more often. The infants of habitually snoring fathers had a greater risk of snoring at both the age of 3 months and at 8 months. Both at the age of 3 months and at the age of 8 months, a mother's smoking was significantly more prevalent among the infants who snored habitually.

At the age of 24 months, when analyzing overweight status and obesity in the FB cohort, there was a significantly higher proportion of obese children in the snorer group. In the FB but not in the CS cohort, the male gender was more prevalent

among the habitually snoring children. A recurrent cycle of infections in the CS cohort and asthma diagnosis in the FB cohort were distinctly more common in the habitual snorer group. When comparing the parents' weight status, we found that the fathers of habitually snoring children in the FB cohort had a higher BMI compared to the fathers in the control group. The parents in the CS cohort were snoring every night and smoking significantly more often in the habitual snorer group. In both birth cohorts, the educational levels of the mothers in the snorer group were more frequently lower compared to the mothers in the control group. Finally, in comparison to the control group in the FB cohort, the mothers of habitually snoring infants had a significantly lower monthly income more often.

After controlling for confounding factors (i.e., infant's sex, age, earlier respiratory infections, and allergies, plus the parents' lower level of education and lower income), exclusive formula feeding, and pacifier use were significantly associated with snoring at the age of three months. In both age groups, parental snoring and maternal smoking added to the risk of snoring. In all models, of the background factors, male sex was significantly associated with snoring.

At the age of 24 months, in the CS cohort, parents' snoring every night and mothers' lower level of education, and in the FB cohort, mothers' lower income were significantly associated with the child's habitual snoring after controlling for age, sex, prevalence of asthma, recurrent infections, and maternal smoking status.

Table 2. The adjusted risk of parent reported background factors in the CS cohort at the age of three and eight months when age, sex, earlier respiratory infections, and the infant's allergies, plus the parents' lower level of education and lower income, exclusive formula milk feeding, and dummy use were controlled for.

	Three months			Eight months		
	aOR	**95% CI**	***p*-value**	**aOR**	**95% CI**	***p*-value**
Parental snoring	**1.65**	**1.10–2.46**	**0.015**	**2.60**	**1.65–4.10**	**<0.001**
Maternal smoking	**2.21**	**1.04–4.50**	**0.014**	**2.17**	**1.01–4.69**	**0.039**

Table 3. The adjusted risk of parent reported background factors at the age of 24 months when age, sex, prevalence of asthma, recurrent infections, and maternal smoking status were controlled for.

	Child sleep N=947			FinnBrain N=1393		
	OR_a	95% CI	p	OR_a	95% CI	p
Parental snoring every night	**3.66**	**1.34–10.01**	**0.011**	1.84	0.76–4.44	0.175
Maternal lower level of education	**2.78**	**1.01–7.65**	**0.048**	2.09	0.99–4.44	0.054
Maternal monthly income < 2000 €	1.48	0.41–5.36	0.552	**2.82**	**1.27–6.23**	**0.011**

5.5 Findings in polysomnography (III)

Somewhat surprisingly, sleep stage N1 was shortened in PSG snorers as shown in Table 4. Furthermore, PSG snorers had significantly higher snoring and OAHI values compared to PSG non-snorers, which was expected. In total, seven children had OAHI greater than 1, and we determined that these children met the OSA criteria based on ERS definition. In polysomnography studies, total sleep time was approximately 8 h 45 min. There were no statistically significant differences in total sleep time between the PSG non-snorers and the PSG snorers.

Table 4. Snoring, obstructive apnea-hypopnea index (OAHI), and percentages of N1 sleep stage recorded by PSG; comparison between PSG non-snorers and PSG snorers with Mann-Whitney U-test; median and interquartile range 0.25–0.75 presented.

	PSG non-snorers N=59		**PSG snorers N=19**		***p-value***
	Median	**IQR**	**Median**	**IQR**	
Snore %	0.00	0.00–2.50	31.98	18.10–71.15	**<0.001**
N1 %	5.60	3.60–8.70	3.00	1.50–7.20	**0.043**
OAHI	0.00	0.00–0.10	0.60	0.00–1.45	**<0.001**

5.6 Growth and metabolic blood samples (III)

There were no significant differences between the growth parameters among PSG snorers and PSG non-snorers as shown in Figure 8 and 9. After adjusting for birth

weight, the weight of snoring boys was significantly lower compared to PSG non-snorers at 24 months.

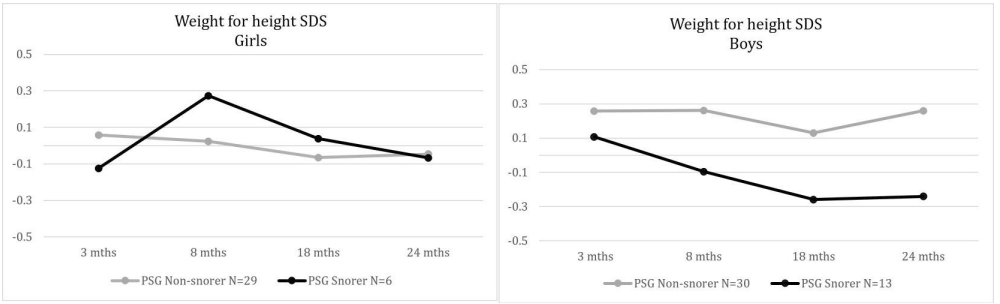

Figure 8. Weight for height SDS, comparison between PSG non-snorers (N = 29), PSG snorers (N = 6).

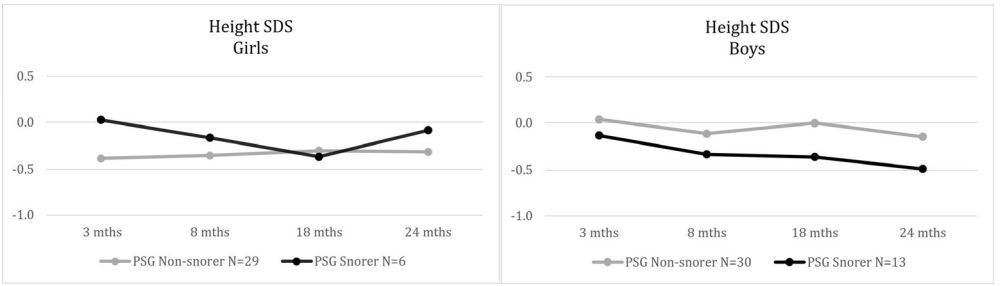

Figure 9. Height SDS, comparison between PSG non-snorers (N = 30) and PSG snorers (N = 13).

Blood samples were taken from 31 children. Of these children, 16% (N = 5) had HDL concentrations below 1.0 mmol/l, which was below the acceptable limit set by the NCEP. Three of these children were in the PSG snorer group. Additionally, 26% (N = 8) of the children had borderline HDL concentrations, with half of these being PSG snorers. HDL levels were normal in 58% (N = 18) of the children.

There were no significant differences between the PSG non-snorers and PSG snorers in the metabolic blood sample results. However, when comparing children whose snoring time was in the lowest quartile and PSG snorers, the HDL levels of PSG snorers were significantly lower compared to the levels of children with snoring time in the lowest quartile, see Figure 10.

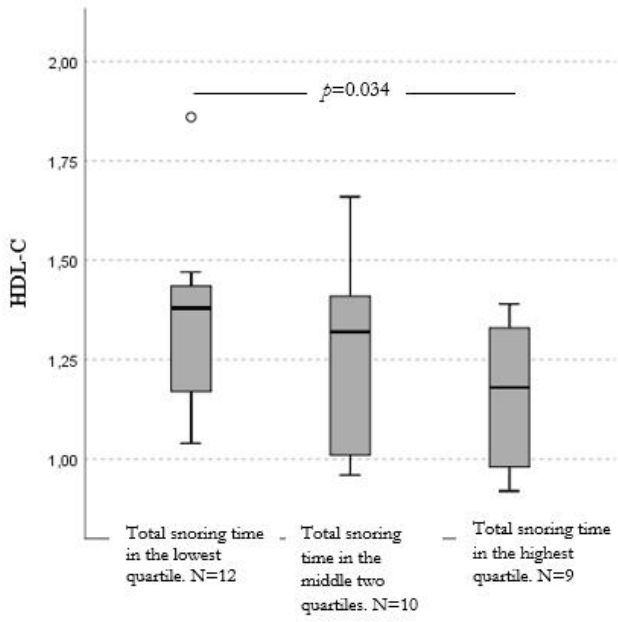

Figure 10. HDL levels of children with snoring time in the lowest and the highest quartile of the total sleep time.

The results of regression analysis are shown in Tables 5-7. In multiple linear regression models an increase in snoring time of 10% in PSG was significantly associated with lower levels of HDL and ApoA1. In addition, snoring time was associated with higher levels of hs-CRP. Furthermore, the boys' HDL levels were higher and hs-CRP levels lower than the girls' levels.

Table 5. Multiple regression analysis with serum hs-CRP level as the dependent variable.

	Unstandardized coefficients		Standardized coefficients β	t	*p-value*	95% CI	
	B	SE				Lower	Upper
Constant	-0.80	1.40		-0.57	0.58	-3.68	2.09
Age	0.81	0.65	0.20	1.25	0.22	-0.52	2.14
Gender, boy	-0.35	0.16	-0.38	-2.28	**0.03**	-0.67	-0.04
Snoring 10%	0.01	0.00	0.41	2.51	**0.02**	0.00	0.02

Table 6. Multiple regression analysis with serum HDL level as the dependent variable.

	Unstandardized coefficients		Standardized coefficients β	t	*p-value*	95% CI	
	B	**SE**				**Lower**	**Upper**
Constant	1.27	0.75		1.71	0.10	-0.26	2.80
Age	-0.12	0.34	-0.06	-0.35	0.73	-0.83	0.59
Gender, boy	0.18	0.08	0.37	2.18	**0.04**	0.01	0.35
Snoring 10%	-0.01	0.00	-0.48	-2.93	**0.01**	-0.01	-0.00

Table 7. Multiple regression analysis with serum ApoA1 level as the dependent variable.

	Unstandardized coefficients		Standardized coefficients β	t	*p-value*	95% CI	
	B	**SE**				**Lower**	**Upper**
Constant	1.58	0.46		3.42	<0.01	0.61	2.55
Age	-0.1	0.22	-0.10	-9.45	0.66	-0.55	0.36
Gender, boy	0.05	006	0.17	0.78	0.45	-0.08	0.18
Snoring 10%	-0.03	0.01	-0.45	-2.11	**<0.05**	-0.06	0.00

6 DISCUSSION

6.1 Principal findings

6.1.1 Prevalence and multifactorial background of habitual snoring in early childhood

In our Finnish study population, the prevalence of habitual snoring was lower than previously reported in other countries. The reported prevalence of snoring in our study was 3.2% at the age of three months and 3.0% at the age of eight months. Furthermore, the combined prevalence of habitual snoring at the age of 24 months in the two large birth cohorts was 2.3%, and the prevalence rates were basically equal in both populations: 2.4% in the CS cohort and 2.2% in the FB cohort. Previous studies concerning infants have reported a 5–14% prevalence of habitual snoring (Bonuck et al., 2011; Gislason & Benediktsdottir, 1995; Kelmanson, 2000; Montgomery-Downs & Gozal, 2006; Piteo et al., 2011), and based on previous population-based reports among toddlers, the condition affects approximately 10–20% of children aged 18–48 months (Bonuck et al., 2011; Byars et al., 2012; Gill et al., 2012). Considering these previously published results, the remarkably low snoring prevalence in Finnish children during early childhood is somewhat surprising. Nevertheless, the notable prevalence of breastfeeding, low incidence of infections, high socioeconomic status, and low prevalence of smoking within our cohort provide some plausible explanations for this phenomenon.

Previous longitudinal studies concerning snoring during early childhood are scarce. In addition to the low snoring prevalence, the children in our studies who were not snoring at all during infancy seemed to have a persistent low risk of habitual snoring during the first two years of life. Overall, as many as half of the children in the CS cohort did not snore at any measurement point. In order to find explanations for this low snoring rate in Finnish children, we need to evaluate the multifactorial background of pediatric SDB.

Lower SES is a risk factor for childhood snoring that has been identified in previous studies (Friberg et al., 2015; Kuehni et al., 2008b). In our study population,

the parents were relatively highly educated. It can be expected that the low prevalence of snoring is connected to the fact that both cohorts were skewed toward higher socioeconomic classes. In line with this, the study population in a previous study with a higher prevalence rate of snoring (Bonuck et al., 2011) included a considerably higher proportion of mothers with lower education (62.3%) compared to our study populations (CS 20.9%, FB 27.2%). When this was considered, and our study sample was stratified according to education, the prevalence of snoring was 5.1% in the CS cohort and 4.0% in the FB cohort in families with lower maternal education. These rates are higher, but nevertheless somewhat closer, to those reported previously.

Based on previous reports, breastfeeding in the first months of life can protect children from habitual snoring by preventing risk factors for SDB (Bonuck et al., 2011; Brew et al., 2014; Galbally et al., 2013; Montgomery-Downs et al., 2007). Breastfeeding positively affects oral muscles, tongue posture, and the development of the oral cavity and jaws. Moreover, it might prevent adeno-tonsillar hypertrophy and protect against childhood obesity and becoming overweight (Storari et al., 2021). In the present studies, 65% of the 3-month-old infants were exclusively breastfed, and 22% were fed both breast milk and formula. Similarly, a study conducted by Bonuck et al. (2011) revealed a significant prevalence of habitual snoring (14%) among infants at the age of six months, with a notable proportion (25%) of these infants having never received breastfeeding. In the CS cohort, characterized by a notably lower snoring prevalence, exclusive formula feeding was observed in only 13% of the infants at 3 months of age. Conversely, Piteo et al. (2011) reported a habitual snoring prevalence of 9%, which, although still higher than in the present studies exhibited a similar proportion of exclusively formula-fed infants, with 12% relying solely on formula feeding. The high rates of breastfeeding in Finland likely contribute to the lower prevalence of snoring observed among infants and toddlers in the present studies as breastfeeding has been recognized as a protective factor against snoring. However, it is important to acknowledge that while breastfeeding plays a significant role, there may be other contributing factors influencing low snoring prevalence. Therefore, it is necessary to recognize the multifactorial nature of snoring prevalence in infants and toddlers.

The first-line therapy for OSA in childhood is adenotonsillectomy. In our study population, adenoidectomy was performed on 9 children in the CS cohort and 20 children in the FB cohort by the age of 24 months. However, this does not explain the low prevalence of habitual snoring in the present studies. If we assume that all these children with adenoidectomy would have snored without the surgical

procedure, the prevalence of habitual snoring would have risen to 3.4% in the CS cohort and 3.7% in the FB cohort. Even in this scenario, Finnish toddlers to date seem to snore markedly less than previously reported in other countries.

Tobacco smoke exposure is associated with SDB symptoms throughout early childhood in a dose-dependent manner (K. Sun et al., 2018). In the present studies, habitual snoring was significantly more prevalent in the children of smoking parents compared to children living in smoke-free families. In infancy, maternal but not paternal smoking had a significant effect on the infant's snoring, possibly due to the proximity of the mother and infant during the first months of life especially in Finland, where the duration of maternity leave is 9 months. Evaluation of the association between parental smoking status and SDB is complicated by the fact that socioeconomic status, itself a risk factor for snoring, is known to influence smoking patterns as well. However, previous results suggest that after controlling for measures of socioeconomic status, the associations between tobacco smoke exposure and snoring remain significant. These results support the importance of professional counseling and encouraging families to provide a tobacco-free environment throughout childhood.

In addition to socioeconomic status and tobacco smoke exposure, a parental history of snoring is a well-known risk factor for children's snoring (Kaditis et al., 2004; Li et al., 2010). Furthermore, some reports have suggested that children have a higher risk of SDB when having siblings with the same condition (Friberg et al., 2009). Consistent with a genetic component to SDB incidence, the outcomes in the present studies support preceding research that inherited anatomic factors that determine obesity, facial structure, and body composition might increase the tendency to snore in some families. Moreover, tonsillar hypertrophy rates are higher in children (Kalampouka et al., 2014). Thus, clinicians should ask the family members of SDB patients whether they have similar symptoms in order to identify potentially underlying diseases and provide early treatment when appropriate.

Snoring on occasion during infections is highly prevalent among children. Reciprocally, the high frequency of upper respiratory infections is a risk factor for habitual snoring (Kukwa et al., 2018), and this association was found in the present study in the CS cohort as well. However, it should be noted that the prevalence of recurrent infections was only 3.7% in the CS cohort, while previously, approximately 10% of children under two years of age have been reported to suffer from frequent infections (Toivonen et al., 2016). Regardless of the higher prevalence of recurrent infections in the FB cohort (11%), the same association with snoring and infection frequency could not be established. Despite the absence of an association between

infections and snoring, the diagnosis of asthma was associated with habitual snoring in the FB cohort. This association might reflect the association of snoring and cyclic infections in the CS cohort since the diagnosis of asthma is usually made based on a history of recurrent wheezing during respiratory infections.

Male predominance in SDB is usually observed in epidemiological studies in general populations, but not always in most childhood studies. In a systematic review of 17 studies among children, the odds ratio of snoring in males versus females was 1.45 (Chan et al., 2012). In the present studies, there were significantly more boys among the group of habitual snorers at the age of 24 months in the FB cohort, most probably reflecting the fact that boys in the FB cohort were significantly more often overweight or obese than girls. Physiological factors such as anatomical and hormonal distinctions between boys and girls may offer insights into the pathogenic mechanisms of gender differences in SDB. However, it is important to note that these changes in hormonal levels and anatomy do not manifest in early childhood.

There are different types of snoring in children, and although there are limited long-term data on toddlers' habitual snoring, it is possible to identify different patterns of SDB in childhood. These patterns are determined based on the age at which the symptoms began and how long they have been present (Freeman & Bonuck, 2012; Kamal et al., 2018). Furthermore, SDB phenotypes might overlap depending on adenotonsillar hypertrophy, craniofacial anatomy, and body composition (Kheirandish-Gozal & Gozal, 2013). Each specific phenotype may be associated with different risk factors, genetics, and environmental exposures for SDB symptoms. These various phenotypes of SDB and the different risk factors in each cluster can explain the differences in the associations with habitual snoring in the CS and FB cohorts, although the evaluation of different phenotypes in these cohorts was not possible due to the low snoring prevalence. Improving our understanding of phenotypic variability and acknowledging that SDB is not a homogenous syndrome will help us to better identify underlying risk factors and target interventions more precisely to improve patient care.

6.1.2 Snoring and disadvantageous consequences

When comparing parental reports of infants' sleep quality, differences were observed between habitually snoring children and those snoring less. Overall, the parents of snoring infants reported significantly more sleeping problems, and the sleep length of habitually snoring infants was shorter. Furthermore, parents of habitually snoring

infants considered the baby's sleep to be restless. All of the above-mentioned factors indicate that snoring has a negative effect on quality of sleep. Even though it is natural for infants to have several arousals from sleep, it is important to note that there might also be non-physiological aspects behind the baby's restless sleep.

Evidence of adverse unfavorable effects of SDB on metabolic health has been unveiled in epidemiologic studies among adults. Nevertheless, previous reports concerning the association of OSA and serum hs-CRP (Gozal, Sans Capdevila, et al., 2008; Tauman et al., 2004, 2007) and lipids (Alexopoulos et al., 2011; Quist et al., 2016; Zong et al., 2013) in childhood are somewhat scarce. Furthermore, reports covering SDB and disadvantageous effects on the metabolic profile have concentrated on children with OSA, but not on snoring alone (Alexopoulos et al., 2011; Gozal, Sans Capdevila, et al., 2008; Quist et al., 2016; Tauman et al., 2004, 2007; Zong et al., 2013).

This present study reported consistently with previous results that snoring time in PSG significantly predicted lower levels of HDL and ApoA1 among Finnish toddlers. Although there was no significant difference in HDL levels between the PSG snorers and non-snorers when comparing them directly as dichotomous groups, the results of the multiple linear analysis showed that the amount of time spent snoring during PSG was linked to lower levels of HDL and ApoA1 and higher levels of hs-CRP. In the current study, blood samples were taken from 31 children, and 13 children had HDL concentrations below the acceptable limit borderline HDL concentrations set by the NCEP, half of these being PSG snorers. Looking at the findings in the present study from this perspective, the slight changes in HDL levels among the children in our cohort, although small, should not be completely ignored.

Exposure to various environmental factors that affect cardiometabolic health during early childhood can increase the risk of developing metabolic disorders in adulthood (Berenson, 2002). In young children, cardiovascular and metabolic risk factors include high blood pressure, elevated glucose, dyslipidemia, and obesity (Kamel et al., 2018). Considering the findings in the present study, it is notable that negative changes in HDL concentrations can occur in snoring children as early as toddlerhood. This raises the question of whether addressing SDB in childhood could be an effective way to prevent metabolic disorders in adulthood.

In the present study, the majority of children had a relatively mild form of SDB, with only one child experiencing a more severe form of OSA. All of the children with any degree of OSA, meaning children with OAHI > 1, were in the group of PSG snorers. Aside from OSA, primary snoring has been linked to abnormal levels of lipids in obese adults (Zhang et al., 2017). The present study is a significant

contribution to the limited existing research on the connection between milder forms of SDB and negative changes in metabolic health markers in young children.

After examining the parameters of PSG, it was surprising to find that PSG snorers had a reduced amount of sleep in stage N1. This sleep stage is typically associated with the transition from being awake to falling asleep. Previous studies have suggested that snoring is associated with an increase in sleep stage N1 (Miano et al., 2010), but this was not observed in the current study. The reduction in N1 may be due to disrupted sleep caused by snoring, which increases sleep pressure and decreases the amount of light sleep. However, there was no significant increase in deeper sleep stages (N2 and N3), indicating that the relationship between snoring and changes in sleep architecture requires further investigation in the present cohort.

Hs-CRP indicates inflammation in the body and is also an indicator of the risk of cardiovascular disease in adults with OSA (J. Wang et al., 2015). In children with SDB, hs-CRP levels are also higher and are linked to the severity of the condition (Moslem Imani et al., 2021). Furthermore, this is still true after adjusting for the degree of obesity. In the present study, snoring time in PSG significantly predicted higher levels of hs-CRP. Despite the fact that the levels were generally low, and the observed differences were minor in magnitude, a statistically significant trend in multiple linear analysis cannot be completely disregarded. Similar to HDL and ApoA1, it is noteworthy that even minor changes that have detrimental impacts on future health can be detected in young children. Owing to the limited sample size in the present study, it is imperative to validate these findings in larger cohorts.

Previous studies have reported that growth retardation is likelier to be present in children with severe OSA (Nieminen et al., 2002). Since the children in the present study had relatively mild disease, it was not surprising to find no association between SDB and growth failure. Moreover, in the present study, the children enrolled were also notably younger compared to a previous report, wherein the mean age was 6 years. Since growth during infancy and early childhood is primarily dependent on nutrition, and growth hormone plays a more important role at a later stage (Benyi et al., 2017), any effects of abnormal nocturnal growth hormone secretion may be more evident in older children.

6.2 Strengths and limitations

These present studies are based on extensive questionnaire surveys of a significant birth cohort, CS, with a total of 1388 infants and 947 toddlers. In the second

publication, we also utilized data obtained from an additional birth cohort, FB, with 1393 participants. In the CS cohort, a long-term trend of snoring during early childhood was also reported. To our knowledge, this is the first study to identify both maternal and paternal factors associated with infant snoring. However, the proportion of habitual snorers remained small, and additional studies employing case-control study designs should enhance our comprehension of the cause-and-effect relationship in a more thorough manner.

A limitation of the present community-based survey studies is the lack of an objective snoring measurement, while PSG is considered the standard for diagnosing sleep disorders. It should be noted that parental reports may occasionally be subject to unreliability, especially when parents do not share the same sleeping space with their children. However, within the specific sample under consideration, it was found that, during infancy, a significant proportion of infants slept in close proximity to their parents, sharing the same room. Importantly, no difference in sleeping arrangements was observed between infants who snored and those who did not. This leads to the conclusion that parents were able to assess the snoring prevalence in the present cohort rather accurately. The use of standardized scales to evaluate snoring on all questionnaires further increased the reliability of the results. Moreover, the similar prevalence of snoring observed in both the CS and FB cohorts at the age of two years suggests that the findings of this study can be considered representative of the prevalence of snoring among young children in Finland.

The third of the present studies involved 78 children who were part of the CS cohort, and their snoring was assessed using PSG. One of the limitations of this study was the relatively small sample size, which is partly due to the fact that PSG is an extensive overnight procedure that is challenging to perform on a large number of individuals. Furthermore, families were given the option to participate in the study without invasive procedures, which explains the limited number of blood samples. Despite the small sample size, the present study demonstrated that snoring is linked to adverse metabolic outcomes. However, future studies with larger sample sizes are necessary to confirm these findings.

Both the piezoelectric sensor and nasal pressure transducer are objective methods employed to measure snoring. The piezo sensor gauges the vibration of pharyngeal structures, recognized as the source of snoring sound. The impact of pharyngeal vibration is contingent upon the sensor's location and the skin and subdermal tissues beneath it. On the other hand, the nasal pressure transducer measures airflow through the nose, with its waveform indirectly reflecting pharyngeal vibration. Incorrect positioning of the transducer within the nasal cavity and significant mouth

breathing can hinder snoring detection. Moreover, the nasal cannula itself may disrupt sleep (Goodwin et al., 2001) or influence nasal breathing (Kim et al., 2023).

There is currently no consensus on the objective measurement or scoring of snoring, leading to variations in scoring criteria, equipment selection, and their placement on the patient, depending on local protocols (Arnardóttir et al, 2016, Kim et al., 2023). In this study, snoring was identified using the piezo snoring sensor and validated by listening whenever possible. The piezo signal was chosen because nasal prongs were excluded from the home recording protocol to avoid potential disturbances to sleep. The scoring of snoring periods predominantly relied on the extensive clinical experience of the scorers, who were clinical neurophysiologists, given the absence of universally accepted scoring rules for children's snoring.

6.3 Future consideration and clinical implications

While in many cases snoring may be harmless, it can also be a sign of more serious health conditions, such as OSA. Therefore, it is important to consider the potential implications of snoring in small children and to explore possible strategies for addressing this issue. Given that SDB is associated with a range of negative health outcomes, including cardiovascular disease, metabolic disorders, and cognitive and behavioral impairments, it is essential that parents and healthcare providers take snoring in young children seriously and seek appropriate evaluation and treatment.

The present studies indicate that the prevalence of habitual snoring is significantly lower compared to earlier reports. Additionally, they suggest that the risk of habitual snoring remains low as children progress from infancy to toddlerhood. As such, early childhood presents an opportunity for screening and implementing preventive interventions for the risk factors associated with snoring. These measures may prove instrumental in mitigating the well-documented negative health outcomes of SDB in later life.

SDB encompasses various conditions that can result from multiple underlying factors. Common risk factors for snoring and OSA in children include adenotonsillar hypertrophy, obesity, and craniofacial abnormalities. Furthermore, a parental history of snoring, parental smoking, and lower SES add to the risk of SDB during childhood. To effectively treat children with SDB, it is essential to evaluate each individual risk factor and any related medical conditions. This allows for the appropriate planning and modification of treatment approaches, as needed, as the

effectiveness of treatment for SDB can vary depending on the severity of the disorder and the underlying causes. To ensure that the treatment is working as effectively as possible, regular follow-up is essential. SDB is a condition that can change over time, with symptoms getting better or worse. It is crucial to understand that the illness being treated also requires ongoing monitoring. For example, after surgery, a child may still have remaining symptoms that requires further treatment.

SDB is now recognized as a significant risk factor for negative health consequences, especially neurocognitive and behavioral deficits, in children. Although there is a growing amount of research in this area, many questions remain unanswered, including the underlying mechanisms of these deficits and the most effective ways to treat them. Specifically, more investigation is needed to understand the processes that lead to neurocognitive deficits in children who snore. While it is evident that intermittent hypoxia and sleep fragmentation related to SDB can harm neurocognitive function, we do not fully understand the mechanisms behind the negative effects of snoring alone. It is also crucial to broaden our understanding of the long-term implications of snoring as children transition into adulthood. Additionally, we need to explore how the early detection and treatment of SDB can affect neurocognitive outcomes in children, including determining the best timing and duration of treatment for optimal results.

Despite the onerous nature of research protocols that incorporate PSG registrations, which can be particularly burdensome for children, given that the registrations are typically conducted within a hospital setting, such research remains essential. To confirm and strengthen the conclusions drawn from previous studies, it is necessary to conduct future research within register-based or case-control settings.

7 CONCLUSIONS

1. Snoring prevalence in Finnish infants was lower than has been reported in other countries. According to parental reports, habitual snoring is associated with parental snoring and maternal smoking when infants reach three months and eight months of age. Habitually snoring infants displayed a higher frequency of sleeping difficulties compared to infants with lower levels of snoring.

2. The prevalence of habitual snoring among Finnish toddlers was also lower compared to previous findings. Infants who did not snore at all during infancy exhibited a persistent low risk of habitual snoring throughout the first two years of life. Habitual snoring among toddlers was associated with parental snoring, lower socioeconomic status of mothers, exposure to smoking, recurrent respiratory infections, and asthma.

3. There were no significant variances observed in the growth parameters among children with longer snoring durations in PSG recordings when compared to those with shorter snoring durations. The duration of snoring identified in the PSG recordings predicted lower levels of HDL and ApoA1, as well as higher levels of hs-CRP among Finnish toddlers. Accordingly, snoring during early childhood may have the potential to negatively impact the serum metabolic profile; consequently, it could contribute to the risk of cardiovascular diseases in adulthood.

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PUBLICATION I

Parental reports showed that snoring in infants at three and eight months associated with snoring parents and smoking mothers

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REGULAR ARTICLE

Parental reports showed that snoring in infants at three and eight months associated with snoring parents and smoking mothers

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ABSTRACT

Aim: This prospective study examined the prevalence of snoring during infancy and the prenatal and postnatal risk factors for this condition.

Methods: The study population comprised 1388 infants from the CHILD-SLEEP birth cohort, who were recruited in the Pirkanmaa Hospital District, Finland, between 2011 and 2013. Sleep and background factor questionnaires were filled out prenatally by parents and when the infant was three and eight months old.

Results: The prevalence of habitual snoring was 3.2% at the age of three months and 3.0% at eight months, and snoring infants had more sleeping difficulties at those ages, with odds ratios (ORs) of 3.11 and 4.63, respectively. At three months, snoring infants slept for a shorter length of time ($p = 0.001$) and their sleep was more restless ($p = 0.004$). In ordinal logistic regression models, parental snoring (adjusted OR = 1.65 and 2.60) and maternal smoking (adjusted OR = 2.21 and 2.17) were significantly associated with infant snoring at three and eight months, while formula feeding and dummy use (adjusted OR = 1.48 and 1.56) were only associated with infant snoring at three months.

Conclusion: Parental snoring and maternal smoking increased the risk of snoring. Infants who snored also seemed to suffer more from other sleep difficulties.

INTRODUCTION

Sleep-disordered breathing represents a spectrum ranging from primary snoring to obstructive sleep apnoea. Primary snoring refers to snoring with no evidence of apnoea or gas exchange abnormalities (1). Habitual snoring is generally defined as snoring three or more nights per week.

The prevalence of sleep-disordered breathing in children has been quite well studied, but the reported prevalence rates of snoring in infants vary widely (2–6). The prevalence of habitual snoring is estimated to be about 5.0–6.6% of children under one year of age (2,3,6), and in some studies the prevalence even rises to 9–14% (4,5). This may be explained by the heterogeneity of the studies, variation in the definition of habitual snoring and the presence of colds.

The presence of snoring in infants and preschool children has been associated with male gender (7–9), lower socioeconomic status (7,10), African American race (2), chronic rhinitis (9,10), regurgitation (10) and tobacco smoke exposure (11). Snoring has also been associated with restless sleep (2,5,6), parental asthma (7,10) and maternal concern about the child's breathing (2,5). There is evidence that breastfeeding reduces the risk of habitual snoring (4,12,13) and the severity of sleep-disordered breathing (14). Exclusive formula feeding has been significantly associated with habitual snoring (5).

Familial factors also seem to play a role in the development of sleep-disordered breathing. Maternal cigarette smoking is associated with snoring in children (8,10,15). In addition, there seems to be a significant association

Abbreviations
aOR, Adjusted odds ratio; BMI, Body mass index; CI, Confidence interval; OR, Odds ratio; SD, Standard deviation.

Key notes

- This study analysed the prevalence and the risk factors of snoring during infancy. The prevalence of snoring was lower than reported earlier.
- The sleep of snoring infants was shorter and more restless than other infants. Maternal smoking and parental snoring increased the risk of snoring.
- Considering that snoring has been associated with several negative health consequences, it is essential to identify the symptoms of sleep-disordered breathing as early as possible.

between the child's snoring and a history of snoring or the snoring by the mother, father or siblings (9), suggesting that inherited and environmental factors play a role in disordered breathing during sleep.

The main objective of this study was to add to the limited knowledge on infant snoring and the factors associated with it. We examined the prevalence of snoring at the ages of three and eight months, as well as the prenatal and postnatal parental-reported factors that are associated with this condition.

METHODS

Study settings and subjects

This was a prospective study based on the CHILD-SLEEP birth cohort. The study protocol was approved by the Ethics Committee of Pirkanmaa Hospital District on March 9, 2011 (number R11032). The cohort was recruited prenatally in Pirkanmaa Hospital District, Finland. The infants were born between April 2011 and February 2013. A total of 2244 parents were approved to receive the prenatal questionnaires during their visits to maternity clinics, from which 1673 (74%) families returned the baseline questionnaires. The parents filled in the first questionnaire before the mother went into labour. Follow-up measurements took place at three and eight months postnatally. Questionnaires were provided by post to both the mother and father. The infant questionnaire was filled out by the parents together. Details of the recruitment procedure have been reported previously (16). The response rate was 85% at the age of three months and 78% at the age of eight months. The families who did not answer the question concerning snoring were excluded, leaving 1388 infants at the age of three months and 1216 infants at the age of eight months.

Data collection

The sleep questionnaire included questions from four screening tools: the Basic Nordic Sleep Questionnaire, the Brief Infant Sleep Questionnaire, the Infant Sleep Questionnaire and the Sleep Disturbance Scale for Children (17–20).

The Sleep Disturbance Scale for Children (18) is a rating scale developed for the evaluation of sleep disorders in children. To assess sleep-disordered breathing, we used questions from the sleep-disordered breathing subscale. On this scale the response alternatives were *always* indicating daily, *often* suggesting three to five times per week, *sometimes* meaning once or twice per week, *occasionally* indicating once or twice per month and *never*.

The infants' birthweight, length and gestational age were collected from the hospital records.

Statistical analysis

Frequency analyses were performed first. The prevalence and persistence of snoring was assessed. We then evaluated how snoring was related to parent-reported infant sleep quality. The comparisons were based on *t*-tests or the chi-square test depending on type of the variable to be analysed. Next, we performed bi-variable analyses between snoring and the potential risk factors using the chi-square test. In these analyses, we combined the frequency of snoring into a dichotomy as follows: the habitual snorers stood for snoring at least three times per week versus infants snoring less than three times per week. Based on the findings of previous studies among infants, the potential risk factors considered were formula feeding, parental snoring and parental smoking. Dummy use was studied because of its similarity to bottle feeding.

Finally, ordinal logistic regression models were constructed in order to study which of the risk factors previously listed were significantly related to snoring at the ages of three and eight months when the infant's age, sex, allergies and number of infections, plus the parents' education and income, were controlled for. We used three ordinal categories with the following cut-off points: snoring never or one or two times per month (n = 1241 at the age of three months and n = 1089 at the age of eight months), snoring one to two times per week (n = 103 at three months and n = 90 at eight months) and habitual snoring indicating snoring three to five times per week or always (n = 44 at three months and n = 37 at eight months).

RESULTS

There were 1388 infants (52.4% boys) in the sample at the age of three months and 1216 infants (52.0% boys) at the age of eight months. The mean gestational age was 40 weeks. A small number of the infants (1.7%) were born prematurely at 33–36 + 6 weeks of gestation. Four of them were habitual snorers.

The parents reported chronic illnesses as follows: one infant with Down syndrome, Turner syndrome and Crouzon syndrome, 10 infants with apnoeas of infancy and three infants with laryngomalacia. Only the infant with Crouzon syndrome and one infant with laryngomalacia were habitual snorers. All the analyses were carried out excluding the infants with illnesses and prematurity, and the results remained virtually the same.

Some 64.6% of the infants were exclusively breastfed during the first three months. Most of the three-month-old infants (70.8%) used a dummy and the majority (74.3%) slept in a supine position. At the age of eight months, 40.1% of the infants were receiving breast milk and no formula milk. The majority of the infants (59.9%) were using a dummy at the age of eight months. Most of the eight-month-old infants slept in a lateral position (52.5%) or supine position (42.7%).

The prevalence of snoring

In total, 10.6% of the families with a 95% confidence interval (95% CI) of 9.0–12.2% reported that their child had snored at least once a week at the age of three months. The corresponding prevalence of weekly snoring at the age of eight months was 10.4% (95% CI: 8.7–12.1%). Some 3.2% (95% CI: 2.3–4.1%) of the infants at three months and 3.0% (95% CI: 2.0–3.0%) at eight months were snoring at least

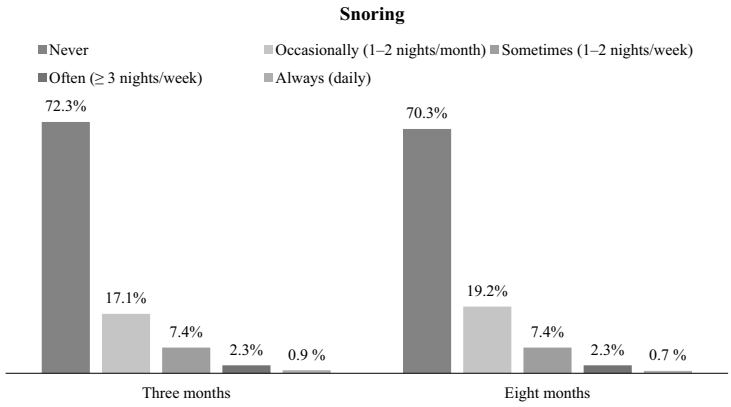

Figure 1 The prevalence (%) of snoring at the age of three and eight months.

three nights per week. The detailed prevalence rates are shown in Figure 1. There were 15 infants (1.1%, 95% CI: 0.6–1.7%) who snored habitually and 53 infants who snored weekly (3.8%, 95% CI: 2.8–4.8%) based on parental reports at both measurement points. There were six habitually snoring infants (0.4%) whose parents only answered the questionnaire at the age of three months.

Factors associated with snoring

The factors associated with habitual snoring in bi-variable models are shown in detail in Tables 1 and 2. The infants who were diagnosed with gastro-oesophageal reflux snored significantly more ($p = 0.017$) than those not suffering from reflux at the age of three months. At the age of three months, the infants who were exclusively breastfed snored significantly less than the infants who were receiving formula milk ($p = 0.024$). Birth characteristics, allergies, colic, the number of respiratory infections and dummy use did not associate with habitual snoring during infancy.

Infants who snored habitually at the age of three months had fathers with a significantly higher body mass index (BMI) (26.3 versus 27.7 kg/m^2, $p = 0.014$) and a lower frequency of higher education ($p = 0.031$). Infants whose mother snored habitually had a greater risk of snoring at the age of eight months ($p = 0.033$). The infants of habitually snoring fathers had a greater risk of snoring as well at both the age of three months ($p = 0.003$) and at eight months ($p = 0.039$). The infants of smoking mothers had a greater risk of snoring both at the age of three months ($p = 0.031$) and at the age of eight months ($p = 0.018$) (Table 3).

The sleep of snoring infants

At the age of three months the sleep length of habitually snoring infants was more than one hour shorter than those who snored weekly or less ($p < 0.001$) but this was no longer the case at eight months ($p = 0.057$) (see Fig. 2). The infants' sleep was considered to be restless when there were several arousals and periods of wakefulness at night lasting more than 20 minutes at a time. The sleep of habitually snoring infants was more restless ($p = 0.004$, OR 3.88, 95% CI: 1.70–8.86) at the age of three months. However, at the age of eight months the difference was no longer seen ($p = 0.102$, OR 2.96, 95% CI: 0.86–10.42) (see Fig. 3). In addition, the sleep of habitually snoring infants was more often considered problematic by parents at three months ($p = 0.034$, OR 3.11, 95% CI: 1.18–8.21) and at eight months ($p < 0.001$, OR 4.63, 95% CI: 2.16–9.94; Fig. 4).

There was no difference in the sleeping place between snorers and the infants who did not snore at three months ($p = 0.101$, OR 0.59, 95% CI: 0.29–1.19) nor at eight months ($p = 0.256$, OR 1.39, 95% CI: 0.65–3.01). Some 80% of the infants at the age of three months slept in the same room as their parents and 64% did so at the age of eight months.

The adjusted risk

Ordinal logistic regression analysis was used in calculating ORs adjusted for the infant's sex, age, earlier respiratory infections and the infant's allergies, plus the parents' lower level of education and lower income. We added the potential risk factors listed previously to the model. The adjusted odds ratios (aORs) are shown in Table 4.

When the confounding factors were controlled for in the adjusted models, exclusive formula milk feeding (aOR = 1.48) and dummy use (aOR = 1.56) were significantly associated with snoring at the age of three months. In both age groups, parental snoring (aOR = 1.65 and 2.60) and maternal smoking (aOR: 2.21 and 2.17) add to the risk of snoring. In all models, of the background factors, male sex was significantly associated with snoring (aOR = 1.55–2.20, $p = 0.001$–0.047).

DISCUSSION

The reported prevalence of snoring in our study was 3.2% at the age of three months and 3.0% at the age of eight months,

Table 1 The characteristics of the study population, infant factors[†]

	Three months				Eight months			
Study population	All infants (N = 1388)	Non-habitual snorers (N = 1344)	Habitual snorers (N = 44)	p*	All infants (N = 1216)	Non-habitual snorers (N = 1179)	Habitual snorers (N = 37)	p*
Boys N (%)	728 (52.4)	702 (52.2)	26 (59.1)	0.444	632 (52.0)	617 (52.3)	15 (40.5)	0.182[‡]
Age, days, Mean ± SD	97 ± 12	97 ± 14	100 ± 12	0.166	247 ± 9	246 ± 8.8	250 ± 14	0.261
Gestational age, weeks, Mean ± SD	40 ± 1.3	40 ± 1.3	40 ± 1.6	0.157	40 ± 1.3	40 ± 1.3	40 ± 1.5	0.827
Birthweight, grams, Mean ± SD	3580 ± 460	3580 ± 460	3570 ± 380	0.850	3580 ± 460	3580 ± 460	3450 ± 400	0.101
Weight, grams Mean ± SD	6320 ± 740	6190 ± 790	6400 ± 760	0.110	8750 ± 1150	8830 ± 1050	8890 ± 1400	0.754
Milk allergy, N (%)	13 (0.9)	11 (0.8)	2 (4.5)	0.061	52 (4.3)	49 (4.2)	3 (8.1)	0.208
Other allergies, N (%)	7 (0.5)	7 (0.5)	0 (0)	1.000	44 (3.6)	41 (3.5)	3 (8.1)	0.146
Gastro-oesophageal reflux, N (%)	**49 (3.5)**	**44 (3.3)**	**5 (11.4)**	**0.017**	52 (4.3)	48 (4.1)	4 (10.8)	0.069
Infantile colic, N (%)	46 (3.3)	45 (3.3)	1 (2.3)	1.000	22 (1.8)	21 (1.8)	1 (2.7)	0.496
One or more respiratory infections, N (%)	310 (22.3)	297 (22.1)	13 (29.5)	0.269	734 (60.4)	708 (60.1)	26 (70.3)	0.236
Dummy use, N (%)	983 (70.8)	948 (70.5)	35 (79.5)	0.239	728 (59.9)	705 (59.8)	23 (62.2)	0.866
Formula milk feeding, N (%)	**491 (35.4)**	**468 (34.8)**	**23 (52.3)**	**0.024**	728 (59.9)	706 (59.9)	22 (59.5)	1.000

*To compare habitually snoring infants to other infants, p-value is based on t-test or chi-square test depending on the variable type.
[†]Data shown as mean with standard deviation or proportion as appropriate. The statistically significant factors are bolded.

which is lower than reported earlier (2–6). Only 15 infants snored both at the ages of three and eight months when reported by parents. Previous studies concerning infants have reported a 5–14% prevalence of habitual snoring (2–6). In our study, 65% of the three-month-old infants were exclusively breastfed and 22% were fed both breast milk and formula milk. The protective aspect of breastfeeding may partly explain the lower prevalence of habitual snoring. Furthermore, in the present study, the cohort was skewed towards a higher educational background.

Primary snoring is not a benign condition. In previous studies snoring has been associated with neurocognitive disturbances in infants (21,22). Among older children, snoring has also been linked to cardiovascular disorders (23,24) and behavioural disorders (7,25). For these reasons, it is essential to identify the risk factors for snoring. These factors – including formula feeding, dummy use, maternal smoking and parental snoring – were largely the same as those reported in previous studies. In this study, snoring in infants was associated with male gender in ordinal logistic regression models, as has been previously reported (7–9). The explanation for this association is not clear and requires further study.

Consistent with our findings, breastfeeding has previously been shown to be protective against sleep-disordered breathing (4,12–14). Upper airway obstruction during the infant's sleep is mainly caused by decreased upper airway muscle tone, high nasal resistance and a compliant chest wall (1). The oral muscles are exercised in suckling, and breastfeeding has an important influence on the growth of the mandible (26). During breastfeeding, the tongue action shapes the palate by rounding and flattening it. During bottle feeding and dummy use, the tongue cannot reach the palate (27). A short duration of breastfeeding has been associated with malocclusion (28). There is also evidence that myofascial education can be beneficial in the treatment of obstructive sleep apnoea (29).

It seems that there are multifactorial mechanisms behind infant snoring, including several intrinsic components, environmental factors and genetic aspects. In our study, parental snoring was an independent risk factor for infant snoring. The association of a parental history of snoring and sleep-disordered breathing has been reported earlier (9,30). However, the mechanism of this association is unknown. One explanation could be the inheritance of facial anatomy, which has been reported to affect the risk of snoring (1).

Higher paternal BMI was significantly associated with infants' snoring at the age of three months in this study. It is well known that obesity is related to snoring in the adult population. The interconnection with the father's higher BMI may reflect the association of the father's and infant's snoring.

Lower socioeconomic status has been reported as a risk factor for children's snoring (7,10). In our study cohort, the infants of fathers with a higher education snored significantly less at the age of three months but not thereafter. As discussed earlier, the majority of fathers in our cohort were highly educated, which may explain the finding.

Table 2 The characteristics of the study population, familial factors*

	Three months				Eight months			
Study population	All infants (N = 1,388)	Non habitual snorers (N = 1,344)	Habitual snorers (N = 44)	p**	All infants (N = 1,216)	Non habitual snorers (N = 1,179)	Habitual snorers (N = 37)	p**
Maternal BMI, Mean±SD	28.2 ± 4.3	28.2 ± 4.3	29.4 ± 4.4	0.129	28.2 ± 4.3	28.2 ± 4.3	28.1 ± 4.4	0.942
Paternal BMI, Mean±SD	**26.3 ± 3.6**	**26.3 ± 3.5**	**27.7 ± 5.0**	**0.014**	26.3 ± 3.6	26.3 ± 3.5	26.4 ± 3.7	0.834
≥ 3 children in the family, N (%)	174 (12.5)	171 (12.7)	3 (6.8)	0.355	157 (12.9)	155 (13.1)	2 (5.4)	0.293
Firstborn, N (%)	853 (61.5)	509 (37.9)	26 (59.1)	0.755	727 (59.8)	467 (39.6)	22 (59.5)	1.000
Maternal tertiary qualification, N (%)	847 (61.0)	824 (61.3)	23 (52.3)	0.271	796 (65.5)	776 (65.8)	20 (54.1)	0.160
Paternal tertiary qualification, N (%)	**673 (48.5)**	**659 (49.0)**	**14 (31.8)**	**0.031**	640 (52.6)	557 (47.2)	19 (51.4))	0.739
Family monthly income < 2000 euros, N (%)	348 (25.1)	337 (25.1)	11 (25.0)	1.000	324 (26.6)	311 (26.4)	13 (35.1)	0.257
Maternal snoring ≥3 nights/week, N (%)	159 (11.5)	154 (11.5)	5 (11.4)	1.000	**145 (11.9)**	**136 (11.5)**	**9 (24.3)**	**0.033**
Paternal snoring ≥3 nights/week, N (%)	**381 (27.4)**	**360 (26.8)**	**21 (47.7)**	**0.003**	**335 (27.5)**	**319 (27.1)**	**16 (43.2)**	**0.039**
Maternal smoking <6 months ago, N (%)	**57 (4.1)**	**52 (3.9)**	**5 (11.4)**	**0.031**	**52 (4.3)**	**47 (4.0)**	**5 (13.5)**	**0.018**
Paternal smoking <6 months ago, N (%)	431 (31.1)	414 (30.8)	17 (38.6)	0.320	364 (29.9)	349 (29.6)	15 (40.5)	0.200

*Data shown as mean with standard deviation or proportion as appropriate. The statistically significant factors are bolded.
**To compare habitually snoring infants to other infants, p-value is based on t-test or X^2 –test depending on the variable type.

Table 3 The crude associations between risk factors and habitual snoring at three and eight months*

	Three months			Eight months		
	OR	95% CI	p	OR	95% CI	p
Infant factors						
Sex, boy	1.32	0.72–2.43	0.444	0.62	0.32–1.21	0.182
Milk allergy	5.77	1.24–26.85	0.061	2.04	0.60–6.86	0.208
Other allergies	N/A	N/A	1.000	2.45	0.72–8.30	0.146
Gastro-oesophageal reflux	**3.79**	**1.42–10.08**	**0.017**	2.85	0.97–8.36	0.069
Infantile colic	0.67	0.90–4.98	1.000	1.53	0.20–11.70	0.496
One or more respiratory infections	1.48	0.76–2.86	0.269	1.57	0.77–3.21	0.236
Dummy use	1.62	0.77–3.41	0.239	1.08	0.55–2.12	0.866
Formula milk feeding	**2.05**	**1.12–3.74**	**0.024**	0.98	0.50–1.91	1.000
Familial factors						
≥3 children in the family	0.50	0.15–1.64	0.353	0.216	0.09–1.59	0.293
Firstborn	1.11	0.60–2.04	0.755	1.01	0.52–1.98	1.000
Maternal tertiary qualification	0.69	0.38–1.26	0.271	0.61	0.32–1.18	0.160
Paternal tertiary qualification	**0.49**	**0.26–0.92**	**0.031**	0.85	0.44–1.63	0.739
Family monthly income <2000 euros	1.00	0.50–2.0	1.000	1.51	0.76–3.01	0.257
Maternal snoring ≥ nights/week	0.99	0.39–2.55	1.000	**2.47**	**1.14–5.34**	**0.033**
Paternal snoring ≥3 nights/week	**2.50**	**1.37–4.56**	**0.003**	**2.05**	**1.06–3.99**	**0.039**
Maternal smoking <6 months ago	**3.19**	**1.21–8.42**	**0.031**	**3.76**	**1.40–10.09**	**0.018**
Paternal smoking <6 months ago	1.41	0.76–2.62	0.320	1.62	0.83–3.16	0.200

N/A = Not applicable.
*The statistically significant factors are bolded.

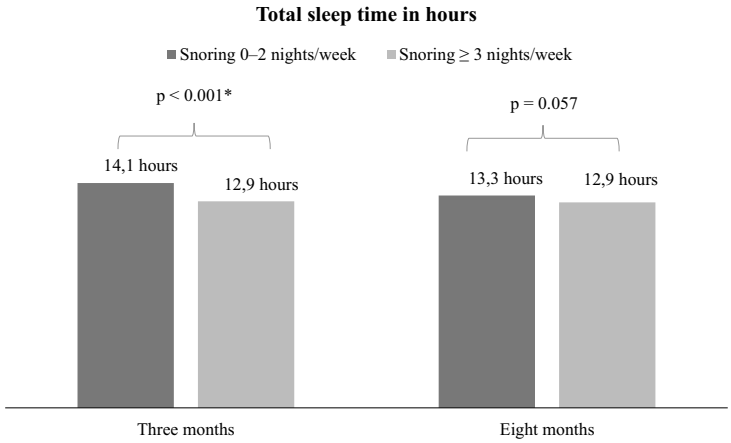

Figure 2 The total sleep time presented (in hours) at the ages of three and eight months among infants who snore two nights per week or less versus habitual snorers.

Maternal smoking increased the risk of snoring at the ages of three and eight months in ordinal logistic regression analysis. This has been shown in previous studies as well (8,10,15). However, paternal smoking had no significant effect on the infant's snoring. The explanation could be the proximity of the mother and infant during the first months of life especially in Finland, where the duration of maternity leave is nine months.

Kuehni et al. (10) found an association between gastro-oesophageal reflux during infancy and snoring among children aged 1–4 years. In our study, the presence of reflux was only significantly associated with snoring at the age of three months.

The parents of snoring infants reported significantly more sleeping problems. The sleep length of habitually snoring infants was shorter and the sleep was more restless, which

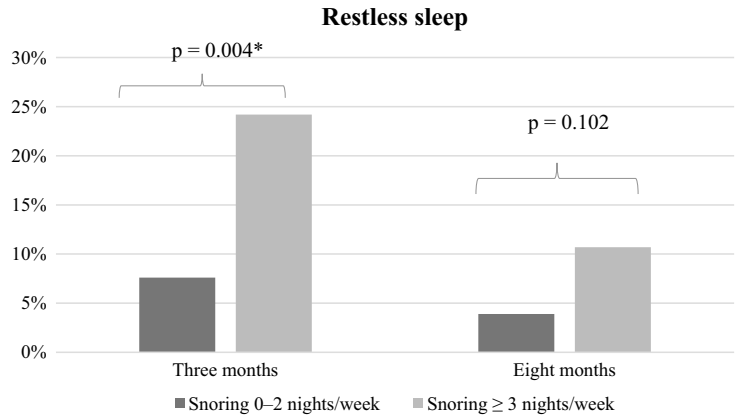

Figure 3 The prevalence of restless sleep (several arousals and periods of wakefulness at night lasting more than 20 minutes at a time) at the ages of three and eight months among infants who snore two nights per week or less versus habitual snorers.

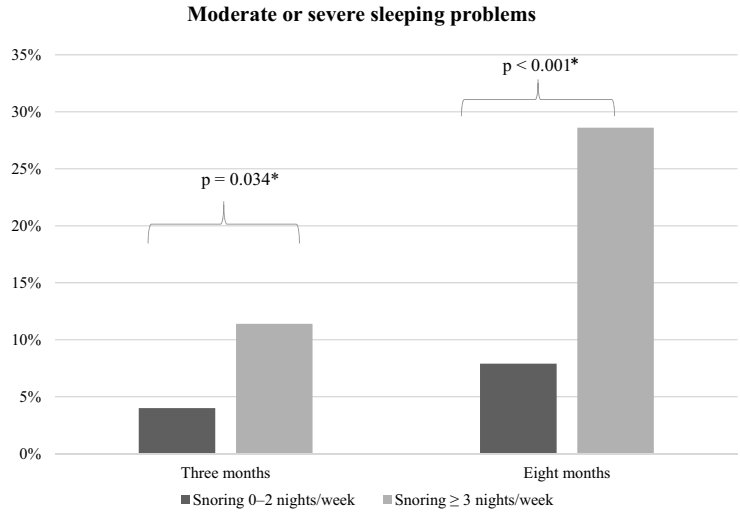

Figure 4 The prevalence of sleeping difficulties at the ages of three and eight months among infants who snore two nights per week or less versus habitual snorers.

can be a sign of the harmfulness of snoring. Even though it is natural for infants to have several arousals from sleep, it is important to note that there might be some non-physiological aspects behind the baby's restless sleep as well. It is important for physicians treating infants and their family to pay attention to parents' reports of infant sleeping problems and to ask specifying questions in order to identify any sign of a snoring disorder. While the treatment of snoring during infancy is remarkably controversial, our results support an active approach and the consideration of the intervention in snoring even in this young population.

Strengths and limitations

This longitudinal study on the prevalence of snoring in infants is based on a large and representative population-based follow-up sample comprising 1388 families. As far as we know, this is the first study to report both maternal and paternal factors associated with infant snoring. In this study, the prevalence of snoring was lower than reported previously, and thus, the number of habitual snorers remained small. In further studies, even larger samples are needed in order to confirm the findings of our study and to study factors that are related to persistent snoring.

Table 4 Ordinal logistic regression models to predict snoring*

	Three months			Eight months		
	aOR	95% CI	p-value	aOR	95% CI	p-value
Formula milk feeding	**1.48**	**1.04–2.10**	**0.028**	0.69	0.45–1.05	0.081
Dummy use	**1.56**	**1.03–2.36**	**0.037**	0.78	0.50–1.24	0.293
Parental snoring	**1.65**	**1.10–2.46**	**0.015**	**2.60**	**1.65–4.10**	**<0.001**
Maternal smoking	**2.21**	**1.04–4.50**	**0.014**	**2.17**	**1.01–4.69**	**0.039**
Paternal smoking	1.10	0.76–1.59	0.628	0.92	0.58–1.47	0.730

aOR = Adjusted odds ratio.

*Data were adjusted for the infant's sex, age, earlier respiratory infections and allergies, as well as the parents' education and income. Three ordinal categories were used with the following cut-off points: never or less-than-weekly snoring, weekly snoring (snoring 1–2 nights per week) and habitual snoring (snoring at least three nights per week). The statistically significant factors are bolded.

The snoring prevalence was based on parental reports of their infant's sleep, and polysomnography was not included in the study protocol. Parental reports of snoring may not always be accurate particularly if the parents are not sleeping in the same room as the infants. In this sample, most of the infants slept in the same room as the parents and there was no difference in the sleeping place between the snorers and non-snorers. Based on this, we assume that parents can assess the prevalence of snoring relatively accurately. Further studies should consider including polysomnography in the study protocol in order to increase the reliability of the findings.

CONCLUSION

Sleep-disordered breathing is a long-lasting condition with a significant influence on the health and well-being of children, so it is essential to identify the children with symptoms of sleep-disordered breathing as early as possible. However, the reported prevalence of snoring in our study is lower than reported earlier. We found that breastfeeding was a protective factor against snoring. This is valuable information to highlight when motivating mothers to breastfeed.

Several of the risk factors reported both in this study and previously – including formula feeding, dummy use and maternal smoking – can be modified. For this reason it is important to already identify these risk factors during infancy in order to diminish the risk of snoring. Paediatricians should also remember to consider snoring when evaluating a child's restless sleep. Furthermore, longitudinal studies are needed in order to clarify the factors behind snoring in infants and the health consequences in later life.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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Prevalence and evolution of snoring and the associated factors in two-year-old children

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Prevalence and evolution of snoring and the associated factors in two-year-old children

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ABSTRACT

Objectives: To evaluate the prevalence and persistence of snoring during the first two years of life in two Finnish birth cohorts and to assess the associated factors.
Study design: The study population comprised 947 children from the CHILD-SLEEP (CS) and 1393 children from the FinnBrain (FB) birth cohorts. Questionnaires were provided to both parents when the child was 24 months of age. The questionnaire consisted of parts concerning the child's sleep and environmental factors.
Results: The combined prevalence of habitual snoring in the two birth cohorts at the age of 24 months was 2.3% (95% CI 1.5–3.1), which is markedly lower than reported previously.
Children suffering from recurrent infections (CS odds ratio (OR) 3.9, 95% CI 1.2–12.5) or asthma (FB OR 4.3, 1.4–13.5) snored habitually more often. Both the mother's (CS OR 3.2, 1.2–9.0) and father's (CS OR 3.4, 1.4–8.0) snoring every night added to the risk of the child snoring. In the multivariate models, parental snoring (CS adjusted odds ratio (OR_a) 2.8, 1.1–6.8), the mother's lower level of education (CS OR_a 2.9, 1.2–7.5, FB OR_a 2.1, 1.0–4.5), and the mother's lower monthly income (FB OR_a 2.9, 1.3–6.3) associated with the child's habitual snoring.
Conclusions: The prevalence of habitual snoring in two Finnish birth cohorts is lower than reported previously. The independent risk factors for habitual snoring at the age of two years were the parents' snoring and the mother's low income and low education.

1. Introduction

Sleep disordered breathing (SDB) covers a range of breathing problems during sleep, from primary snoring to obstructive sleep apnea (OSA). Habitual snoring in children is generally defined as snoring three or more nights per week. The variation in the reported prevalence among young children is broad. Based on previous population-based reports, the condition affects approximately 10–20% of children aged 18–48 months [1–3]. However,

Abbreviations: OR_a, adjusted odds ratio; BNSQ, Basic Nordic Sleep Questionnaire; BMI, body mass index; BMI-SDS, body mass index standard deviation score; CI, confidence interval; CS, CHILD SLEEP; FB, FinnBrain; OR, odds ratio; OSA, obstructive sleep apnea; SES, socioeconomic status; SD, standard deviation; SDB, sleep disordered breathing; SDSC, Sleep Disturbance Scale for Children.

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approximately 10 years ago Liukkonen et al. reported a moderately lower habitual snoring prevalence of 6% among 1471 Finnish preschool-aged children in a questionnaire survey [4]. This inconsistency may partly be due to the variety in the definition of habitual snoring or the different prevalence of risk factors for snoring in the study populations. In addition, there are actual differences in study samples based on ethnicity. Reported studies on the prevalence of snoring have mostly focused on school aged children. There is clearly lesser data available concerning toddlers' SDB and most of these studies concern are relatively old or concern infants aged less than one year [1,3,5–10]. Furthermore, longitudinal studies describing the persistence and evolution of snoring during early childhood are infrequent [1,3].

The most common cause of children's snoring and OSA is large adenoids or tonsils blocking the upper airway. During adolescence, obesity has an important role in causing obstructive sleep disordered breathing [11]. Whether obesity plays a role in SDB in earlier childhood needs to be established considering that the number of overweight young children is increasing. Between the ages of 2 and 6 years, 24% of boys and 14% of girls are estimated to be overweight in Finland [12].

Snoring and OSA have been associated with a higher frequency of upper respiratory infections [13] and allergic diseases [14,15] during childhood. Children with gastroesophageal reflux disease seem to have a higher risk for snoring [16]. In addition, male sex [2,13,17,18], parental snoring [17–19], and passive smoking [17,19–21] have been reported to add to the risk of snoring among infants and toddlers.

The association between snoring and OSA and lower socioeconomic status (SES) has been well established [2,22,23]. In a Swedish study, a low level of familial income and parental education increased the risk of SDB [22]. Living in socio-economically disadvantaged neighborhoods in New Zealand and Canada added to the risk of habitual snoring among children under school age [2,23].

Even if snoring corresponds to an intermittent and partial obstruction of the airway and represents the milder end of the SDB spectrum, it is not a benign condition. Besides OSA, studies provide evidence that snoring is also associated with elevated blood pressure and neurocognitive and behavioral disturbances [2,24–27]. In addition, Li et al. found that more than one-third of snoring school-aged children progressed to OSA after a follow-up period of four years [28]. Considering the reported disadvantageous consequences of snoring already in childhood, it is essential for physicians to ask parents about snoring and routinely also screen the milder forms of SDB.

Compared to toddlers, the prevalence of habitual snoring during infancy has been estimated to be somewhat lower, ie, about 5.0–6.6% [9,29,30], although some studies report a prevalence of 9–14% [1,6]. We have previously reported that the prevalence rates of snoring at the age of three and eight months are as low as 3.2% and 3.0%, respectively [19]. However, it is not known whether Finnish children have a persistent low risk for habitual snoring, nor is it known what causes the low snoring prevalence in Finland. In addition, the reports of young children's snoring from European countries are scarce and longitudinal information not available. The objective of this study was to examine the current prevalence and persistence of snoring during the first two years of life and the associated factors. Gathering updated information is highly valuable, taking into account the well-characterized changes in the currency of risk factors for SDB as they may exert direct influences on the prevalence of snoring as well.

2. Methods

2.1. Study design and population

This study was conducted within two prospective, population-based birth cohort studies, CHILD-SLEEP (CS) [31] and FinnBrain (FB) [32]. The original sample was composed of 1679 families from the CS birth cohort and 3808 families from the FB cohort.

Recruitment of the CS cohort took place in Pirkanmaa Hospital District, Finland. The study protocol was approved by the Ethics Committee of Pirkanmaa Hospital District on March 9, 2011 (number R11032). The infants were born between April 2011 and February 2013. The baseline questionnaire was sent by mail to the parents before the babies were born, and the follow-up measurements took place at several time points. Questionnaires were provided to both mothers and fathers. The questionnaire concerning the child was filled out by the parents together. As the questionnaire was sent only to the Finnish-speaking population, the ethnic background of the participants is Finnish. The details of the recruitment procedure have been reported previously [31].

From the CS cohort, 950 families out of 1679 originally recruited families responded to the 24-month questionnaire concerning the child health and sleep, yielding a response rate of 56.8%. In 3 (0.3%) cases, the family did not answer the question about snoring. These cases were excluded from further analysis, leaving 947 (56.4%) families.

The FB cohort was a population-based sample gathered in Southwest Finland. A more detailed description of the characteristics of the sample and the recruitment process have been described previously [33]. The sample was recruited between December 2011 and April 2015 at maternal welfare clinics in a geographically defined area, comprising all women eventually referred to give birth at Turku University Hospital in the Southwest Finland Hospital District and the Åland Islands in Finland. The recruitment took place at the pregnancy ultrasound scan at gestational week 12. The study inclusion criteria were a sufficient knowledge of Finnish or Swedish and a normal ultrasound screening result. Initially, a total of 3808 mothers and 2623 fathers participated. At the child age of 24 months, 1454 families out of 3808 initially recruited families responded to the 24-months questionnaire, so the response rate was 38.2%. There were 61 (4.2%) responses missing information on the child's snoring status, leaving 1393 (36.6%) children in the final sample.

2.2. Questionnaire

In both cohorts, the parents filled in the first questionnaires before labor. In the CS cohort, the follow-up questionnaire was sent to the families when the child was three months, eight months, and 24 months old. The time points for the follow-up questionnaires in the FB cohort were six, 12, and 24 months after the child was born. The questionnaire consisted of parts concerning the child's sleep and environmental factors that may affect sleep.

The sleep questionnaires included questions from four screening tools: the Basic Nordic Sleep Questionnaire (BNSQ) [34], the Brief Infant Sleep Questionnaire [35], the Infant Sleep Questionnaire [36], and the Sleep Disturbance Scale for Children (SDSC) [37].

The SDSC [37] is a rating scale developed for the evaluation of sleep disorders in children. This questionnaire is divided into six subscales, including disorders of initiating and maintaining sleep, sleep-disordered breathing, disorders of arousal/nightmares, sleep–wake transition disorders, disorders of excessive somnolence, and sleep hyperhidrosis. In the CS cohort, the questionnaires at every measurement point included the SDSC scale. In the FB cohort, only the 24-month questionnaire comprised the questions of the SDSC scale.

To assess sleep-disordered breathing, we used questions from the SDSC scale's sleep disordered subscale. The answer options were *always* (daily), *often* (3–5 times per week), *sometimes* (once or twice per week), *occasionally* (once or twice per month or less), and *never*. In the analyses, we combined the frequency of snoring into a

dichotomy as follows: habitual snorers, meaning snoring at least three nights per week, versus the others.

The total sleep time was calculated from the answers of the following questions: “What time does your child fall asleep?” and “What time does your child wake up?” The question “Has your child had recurrent infections?” was included in the 24-month questionnaire in both cohorts. This question was applied as a method to determine the children suffering from recurrent infections, because no absolute consensus exists on the number of infections per year that would define recurrent infections [38]. The frequency of parents’ snoring was gathered from the questions of the BNSQ at the end of the pregnancy.

There were some variations in the questionnaires of the CS and FB cohorts. Information on whether the child was being breastfed or having only formula was available from the first three months of life in the CS cohort and the first four months in the FB cohort. In the CS cohort, we compared those parents who answered smoking today or less than six months ago in the 24-month questionnaire to those who had last smoked more than six months ago or had never smoked. In the FB cohort, we had information on whether the parent was smoking when the child was one year old. This information on smoking was gathered only from a subsample comprising 275 mothers and 168 fathers. In the CS cohort, the parental monthly income was inquired at the end of the pregnancy, whereas in the FB cohort, the information was gathered at the beginning of the pregnancy. Information on the parents’ BMI was available from the 24-month questionnaire in the CS cohort and the 12-month questionnaire in the FB cohort.

2.3. Growth

The growth charts were collected from well-baby clinics. The body mass index standard deviation score (BMI-SDS) at the child age of two years was calculated based on Finnish growth references [39]. We used standardized Finnish classifications of overweight and obesity based on BMI-SDS information and combined classes into the dichotomy as follows: children with obesity or severe obesity versus overweight, normal weight, or underweight children [39].

2.4. Statistical analysis

Frequency analyses were performed first separately for both birth cohorts. We reported prevalence rates with 95% confidence intervals separately for the two cohorts and jointly. We also analyzed longitudinally the prevalence of persistent snoring. There were 856 children in the CS cohort with complete data on snoring from all three measurement points at three, eight, and 24 months. The positive and negative predictive values were calculated to evaluate the probability of snoring at eight and 24 months based on the child's snoring status at the age of three months. Next, we evaluated how snoring was related to parent-reported background factors. The comparisons were based on *t*-tests or the chi-squared test depending on the type of variable to be analyzed. The first logistic regression model was constructed in order to study which of the risk factors were significantly related to snoring when controlling for the children's age, sex, prevalence of asthma, and recurrent cycle of infections. The second model included the first model plus the maternal smoking status.

3. Results

The prevalence rates of snoring at the age of two years are shown in Fig. 1.

In the CHILD-SLEEP birth cohort, the prevalence of habitual snoring was 2.4% (95% CI 1.6–3.2). There were five children snoring every night based on the parental report. Some 9.2% (7.7–10.7) of the children snored at least weekly. There were 615 (64.9%, 61.9–67.9) children not snoring at all. In the FinnBrain cohort, the snoring prevalence was as low as in the CS cohort (Fig. 1). There were 31 children (2.2%, 1.4–3.0) snoring habitually, and only six of them snored every night. The prevalence of weekly snoring in the FB cohort was 8.3% (6.9–9.8). There were 905 children (65.0%, 62.5–67.5) who did not snore at all at the age of two years.

The combined prevalence of habitual snoring in these two birth cohorts was 2.3% (1.5–3.1).

In the CS cohort, there were 856 children whose SDSC scaling was available for every measurement point (see Fig. 2).

There were only six children (0.7%) snoring habitually throughout the first two years of life, ie, at the age of three, eight, and 24 months. Some 2.5% of the children (N = 21) snored at least once a week at all three measurement points. Of the 23 habitually snoring children, almost all had snored already previously. Only two children snored for the first time at 24 months. The remainder of the two-year-old habitual snorers snored at least occasionally at one or two additional measurement points. Of the 856 children, 47.0% (N = 402) did not snore at any measurement point.

When the infant snored at the age of three months, the positive predictive value of snoring at eight and 24 months was 84.6% (56.6–95.9) and 63.6% (37.1–83.8), respectively. The children not snoring at all during infancy seemed to have a persistent low risk for habitual snoring subsequently, as the negative predictive values were 98.3% (97.2–99.0) at eight months and 98.3% (96.8–99.2) at 24 months.

The associations of selected background factors and snoring are shown in Tables 1 and 2.

The parents reported six children with chronic illnesses potentially affecting the snoring status in the CS cohort [Goldenhar syndrome, Down syndrome, cleft palate, craniosynostosis, developmental disability (N = 2)] and nine children in the FB cohort (Beckwith-Wiedemann syndrome, Kabuki syndrome, Malan syndrome, Turner syndrome, Poland syndrome, laryngomalacia, scaphocephaly, tp63 gene mutation, neurometabolic syndrome). All the analyses were carried out excluding the children with illnesses, and the results remained virtually the same.

There were no statistically significant differences in the age, weight, height, BMI-SDS, gestational age, or total sleep time based on the parental reports between the habitually snoring children and the other children in either cohort. When analyzing the dichotomies “overweight” and “obesity” in the CS cohort, there was no significant difference between the weight status of snorers and the controls. However, in the FB cohort, there was a significantly

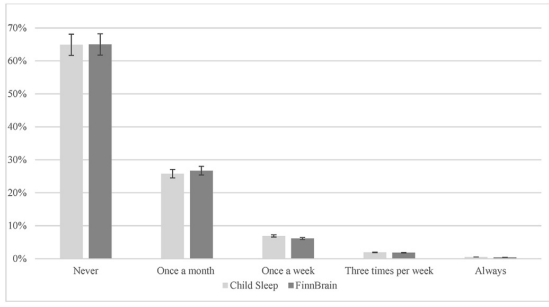

Fig. 1. Parent-reported snoring prevalence (%) for 24-month-old children. The bars display standard errors.

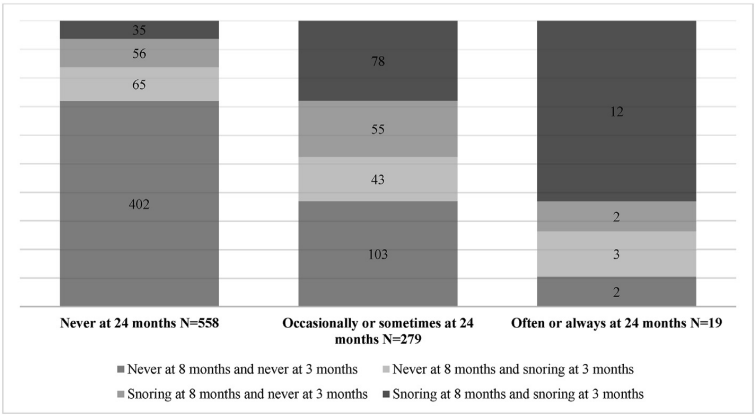

Fig. 2. Snoring at the age of 24 months (N = 856) and evolution of parent-reported snoring during the first two years of life in the CS cohort.

Table 1
The associations of parent-reported child's background factors and snoring.

	Child sleep N = 947						FinnBrain N = 1393					
	Controls N = 924		Snorers N = 23		*p*-value		Controls N = 1362		Snorers N = 31		*p*-value	
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Age (yrs)	2.06	0.12	2.10	0.14	0.109		2.05	0.05	2.05	0.04	0.687	
Weight (kg)	12.35	1.90	12.65	1.89	0.483		12.67	1.47	13.06	1.85	0.164	
Height (cm)	86.61	6.26	87.25	5.45	0.652		87.81	3.67	88.12	3.21	0.664	
BMI	16.37	1.29	16.55	1.44	0.550		16.41	1.45	16.86	1.87	0.116	
BMI-SDS	0.07	1.06	0.26	1.06	0.505		0.10	1.10	0.36	1.32	0.214	
Gestational age (wk)	40.03	1.27	39.88	1.06	0.607		39.75	1.65	39.76	1.67	0.976	
Total sleep time (hr)	11.87	0.87	11.65	1.01	0.238		10.71	0.87	10.85	0.83	0.369	
	n	%	**n**	%	OR (95% CI)	*p*-value	n	%	n	%	OR (95% CI)	*p*-value
Male sex	486	52.6	13	56.5	1.17 (0.51–2.69)	0.833	728	53.5	23	74.2	**2.46 (1.11–5.46)**	**0.028**
Overweight	120	13.0	4	17.4	1.41 (0.47–4.22)	0.528	277	20.3	7	22.6	1.14 (0.49–2.68)	0.821
Obesity	21	2.3	1	4.3	1.96 (0.25–15.18)	0.421	54	4.0	6	19.4	**5.81 (2.29–14.76)**	**0.002**
Only formula in the first months[a]	98	10.6	5	21.7	2.34 (0.85–6.45)	0.095	48	3.5	2	6.5	1.89 (0.44–8.14)	0.307
Use pacifier at the age of two years	182	19.7	5	21.7	1.11 (0.41–3.05)	0.792	NA					
Milk allergy	30	3.2	2	8.7	2.72 (0.67–11.12)	0.180	NA					
Other allergy	63	6.8	3	13.0	2.00 (0.61–6.57)	0.212	NA					
Allergic rhinitis	NA						14	1.0	1	3.2	3.14 (0.46–21.59)	0.282
Atopic dermatitis	NA						289	21.1	11	35.5	1.89 (0.92–3.90)	0.085
Asthma	16	1.7	1	4.3	2.48 (0.36–17.40)	0.344	31	2.3	3	9.7	**4.30 (1.37–13.50)**	**0.037**
Recurrent cycle of infections	32	3.5	3	13.0	**3.91 (1.22–12.54)**	**0.049**	151	11.1	4	12.9	1.20 (0.41–3.48)	0.769
Gastroesophageal reflux	15	1.6	0	0	NA	1.000	8	0.6	1	3.2	5.64 (0.68–46.54)	0.184

BMI = body mass index; BMI-SDS = body mass index standard deviation score; CS=CHILD SLEEP; FB=FinnBrain; NA = not available. Bold font indicates statistical significance.
[a] CS the first three months of life, FB the first four months.

higher proportion of obese children in the snorer group (19.4% vs. 4.0%, OR 5.8, 95% CI 2.3–14.8, p = 0.002).

In the FB cohort, there were more boys in the group of habitual snorers compared to children snoring less (74.2% vs. 53.5%, OR 2.5, 1.1–5.5, p = 0.028). In the CS cohort, a recurrent cycle of infections was distinctly more common in the snorer group (3.5% vs. 13.0%, OR 3.91, 1.22–12.54, p = 0.049). Correspondingly in the FB cohort, there were proportionately more children suffering from asthma among habitual snorers (9.7% vs. 2.3%, OR 4.30, 1.37–13.50, p = 0.037).

In the FB cohort, the fathers of habitually snoring children had a higher BMI compared to fathers in the control group (27.95 vs. 25.97, p = 0.043). Between the snoring group and the controls, there was no statistically significant difference in the mothers' BMI in both cohorts nor in the fathers' BMI in the CS cohort.

In the CS cohort, the mother's (21.7% vs. 7.9%, OR 3.24, 1.17–8.97, p = 0.034) and father's (39.1% vs. 15.9%, OR 3.40, 1.44–8.00, p = 0.007) snoring every night was significantly more common in the habitual snorer group. In the group of habitual snorers in the CS cohort, there was more often someone smoking in the family (43.5% vs. 22.6%, OR 2.63, 1.14–6.09, p = 0.041).

In both birth cohorts, the educational level of mothers in the snorer group was more frequently lower compared to the mothers in the control group (43.5% vs. 20.3%, CS OR 3.01, 1.30–6.97, p = 0.016, FB 48.4% vs. 26.75%, OR 2.57, 1.26–5.25, p = 0.013). In the FB cohort, the mother's monthly income was more often below 2000 euros (35.5% vs. 14.3%, OR 3.29, 1.55–6.98, p = 0.003) in the habitual snorer group.

Table 2
The associations of parent-reported family background factors and snoring.

	Child sleep N = 947						FinnBrain N = 1393					
	Controls N = 924		Snorers N = 23		*p*-value		Controls N = 1362		Snorers N = 31		*p*-value	
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Mothers' BMI (kg/m^2)[a]	24.59	4.31	25.70	4.88	0.221		24.66	5.14	25.72	5.66	0.300	
Fathers' BMI (kg/m^2)[a]	26.16	3.52	26.89	2.54	0.436		25.97	3.78	27.95	6.22	**0.043**	
	n	%	n	%	OR (95% CI)	*p*-value	n	%	n	%	OR (95% CI)	*p*-value
Maternal snoring every night	73	7.9	5	21.7	**3.24 (1.17–8.97)**	**0.034**	116	8.5	3	9.7	1.15 (0.35–3.84)	0.744
Paternal snoring every night	147	15.9	9	39.1	**3.40 (1.44–8.00)**	**0.007**	112	8.2	5	16.1	2.15 (0.81–5.70)	0.176
Maternal smoking during pregnancy	40	4.3	3	13.0	3.32 (0.94–11.68)	0.082	157	11.5	7	22.6	2.24 (0.95–5.28)	0.082
Paternal smoking during pregnancy	240	26.0	8	34.8	1.52 (0.37–3.63)	0.342	225	16.5	6	19.4	1.21 (0.49–2.99)	0.628
Smoking in the family during previous 6 months or at the age of one year[b]	209	22.6	10	43.5	**2.63 (1.14–6.09)**	**0.041**	74	5.4	2	6.5	1.20 (0.28–5.13)	0.685
Maternal lower level of education	188	20.3	10	43.5	**3.01 (1.30–6.97)**	**0.016**	364	26.7	25	48.4	**2.57 (1.26–5.25)**	**0.013**
Paternal lower level of education	283	30.6	10	43.5	1.74 (0.76–4.02)	0.252	364	26.7	7	22.6	0.80 (0.34–1.87)	0.686
Maternal monthly income < 2000 €[c]	621	67.2	18	78.3	1.78 (0.65–4.78)	0.368	195	14.3	11	35.5	**3.29 (1.55–6.98)**	**0.003**
Paternal monthly income < 2000 €[c]	312	33.8	12	52.2	2.14 (0.93–4.91)	0.076	258	18.9	5	16.1	0.82 (0.31–2.16)	0.820

BMI = body mass index; CS=CHILD SLEEP; FB=FinnBrain. Bold font indicates statistical significance.
[a] CS when the child was two years old, FB when the child was one year old.
[b] FB information from 275 mothers and 168 fathers, CS previous 6 months, FB when the child was one year old.
[c] CS at the end of pregnancy, FB at the beginning of pregnancy.

3.1. The adjusted risk

After controlling for age, sex, prevalence of asthma, and recurrent infections in the logistic regression models, parental snoring, the mother's lower level of education, and the mother's lower income associated with the child's habitual snoring (see Table 3).

In the CS cohort, parental snoring every night (OR_a 2.75, 95% CI 1.11–6.78, p = 0.028) added to the risk of habitual snoring after adjustment. In the FB cohort but not in the CS cohort, the association of the mother's lower income and the child's habitual snoring remained statistically significant in the multivariable model (CS OR_a 2.12, 0.70–6.47, p = 0.182, FB OR_a 2.88, 1.31–6.34, p = 0.009).

Considering that the educational level (CS 38.3% vs. 22.3%, p < 0.001, FB 51.3% vs. 26.5%, p = 0.001) and monthly income (CS 79.9% vs. 67.3%, p = 0.004, FB 38.5% vs. 14.1%, p < 0.001) of smoking mothers were more often lower compared to non-smoking mothers in both cohorts, we added the maternal smoking status into the second model. In the CS cohort parents' snoring every night (OR_a 3.66, 1.34–10.01, p = 0.011) and mother's lower level of education (OR_a 2.78, 1.01–7.65, p = 0.048) remained significantly related to the child's snoring. In the FB cohort, the association of mothers' lower income and the child's habitual snoring was statistically significant in the second model as well (OR_a 2.82, 1.27–6.23, p = 0.011), see Table 3.

4. Discussion

Our results show that the prevalence of habitual snoring in Finland was lower than reported previously in other countries. The combined prevalence of habitual snoring in the two large birth cohorts was 2.3%, and the prevalence rates were virtually identical in both populations: 2.4% in the CHILD-SLEEP cohort and 2.2% in the FinnBrain cohort. In the CS cohort, the children not snoring at all during infancy had a persistent low risk for habitual snoring during the first two years of life. Habitual snoring was associated with several health and environmental factors such as parents' snoring, mother's lower socioeconomic status (SES), child's exposure to smoking, recurrent respiratory infections and asthma. Many of these factors can be altered and may provide important means to diminish the risk of the child snoring.

The reason for the low prevalence of habitual snoring among Finnish infants [19] and toddlers in our cohorts is not known. Since breastfeeding is known to protect from snoring [1,19,40,41], the

Table 3
The adjusted risk for snoring of parent reported background factors.

	Child sleep N = 947			FinnBrain N = 1393		
	OR_a	95% CI	p	OR_a	95% CI	p
Model 1[a]						
Parental snoring every night	**2.75**	**1.11–6.78**	**0.028**	1.90	0.79–4.55	0.151
Maternal lower level of education	**2.93**	**1.15–7.46**	**0.024**	**2.14**	**1.01–4.51**	**0.047**
Maternal monthly income <2000 €	2.12	0.70–6.47	0.185	**2.88**	**1.31–6.34**	**0.009**
Model 2[b]						
Parental snoring every night	**3.66**	**1.34–10.01**	**0.011**	1.84	0.76–4.44	0.175
Maternal lower level of education	**2.78**	**1.01–7.65**	**0.048**	2.09	0.99–4.44	0.054
Maternal monthly income <2000 €	1.48	0.41–5.36	0.552	**2.82**	**1.27–6.23**	**0.011**

Bold font indicates statistical significance.
[a] Age, gender, recurrent cycle of infections and diagnosis of asthma controlled for.
[b] Age, gender, recurrent cycle of infections, diagnosis of asthma and mother's smoking status controlled for.

very high breastfeeding numbers in our country may explain some of this low snoring prevalence among infants.

Furthermore, in both our birth cohorts, the parents were relatively highly educated. Lower SES [2,22] is a risk factor for childhood snoring that has been identified in previous studies. In the CS cohort, the mother's lower monthly income associated with habitual snoring at two years. In addition, in both cohorts a lower maternal educational level was significantly related to the toddler's habitual snoring. We hypothesize that the low prevalence of snoring is connected to the fact that both of our cohorts are skewed toward higher socioeconomic classes. In line with this, Bonuck et al. reported a higher prevalence of snoring [1] where the proportion of mothers with lower education was considerably higher (62.3%) compared to our study populations (CS 20.9%, FB 27.2%). When we stratified the sample according to education, we found that the prevalence of snoring was 5.1% in the CS and 4.0% in the FB cohort in families with lower maternal education. These figures are somewhat closer to those reported previously, albeit at the lower end of the spectrum.

In addition, another explanation for the unexpectedly low prevalence of snoring among Finnish children could be the somewhat pure outdoor air, given the evidence that air pollution may affect the incidence of sleep-disordered breathing in children [42,43]. Further research is undoubtedly needed to clarify the background of the distinct SDB prevalence in different countries.

The first-line therapy for OSA in childhood is adenotonsillectomy. In our study population, adenoidectomy was performed in nine children in the CS cohort. None of these children were in the group of habitual snorers at the age of two years. In the FB cohort, there were 20 children who had had their adenoids removed, all of whom were in the group with no reported habitual snoring at 24 months. There was one child alone who snored habitually regardless of adenoidectomy. If we assume that all these aforementioned children would have snored without adenoidectomy, the prevalence of habitual snoring would have been 3.4% in the CS and 3.7% in the FB cohort. Even in this scenario, Finnish toddlers to date seem to snore markedly less than reported previously.

There are multifactorial mechanisms including environmental factors and genetic aspects behind childhood snoring. Additionally to socioeconomic status and environmental air quality, snoring in the family is a well-known risk factor for children's snoring [17–19] and these factors were established in our present study as well. In the CS cohort, parental snoring associated significantly with the toddler's habitual snoring. Inherited anatomic factors that determine facial structure and body composition explain the tendency to snore in some families. In addition, obesity runs in the family.

The high frequency of upper respiratory infections is a risk factor for snoring [13], and we found the same association in our study in the CS cohort, where children with a recurrent cycle of infection snored more often habitually compared to children without cyclic infections. However, the same association was not seen in the FB cohort. The prevalence of recurrent infections was markedly low (3.7%) in the CS cohort, considering that approximately 10% of children aged under two years are estimated to suffer from frequent infections [44]. In the FB cohort, the prevalence of recurrent infections was 11%. The more specific phenotype of these children with recurrent respiratory infections in the FB cohort has been reported previously [45]. Most of the children with cyclic infections had more than five respiratory infections before 2 years of age (77% vs. 16%) and more frequent antibiotic treatments compared to the comparison group in the FB cohort. In the CS cohort, information on antibiotic treatments was not available. Some 51% of the children with a recurrent cycle of infection had more than five infections. In total, a substantially limited proportion of children in the CS cohort had had more than five infections compared to the children in the FB cohort (4.8% vs. 26%) based on parental reports. The underlying reason for this difference remains unknown along with the lacking association of recurrent infections and children's snoring in the FB cohort.

Despite the absent association between infections and snoring, the diagnosis of asthma associated with habitual snoring in the FB cohort. Since the diagnosis of asthma is usually made based on a history of recurrent wheezing during respiratory infections, we think that the association of snoring and asthma in the FB cohort might reflect the association of snoring and cyclic infections in the CS cohort. However, the number of children with a diagnosis of asthma in both cohorts was rather low, so it is troublesome to establish the statistical significance.

Some studies have reported a higher incidence of snoring in boys compared to girls [13,17]. In the FB cohort, there were significantly more boys among the group of habitual snorers, but we did not find the same difference in the CS cohort. In our study, this can be explained by the fact that boys in the FB cohort were significantly more often overweight or obese than girls (25.4% vs 14.5%, OR 1.51, 1.27–1.80, $p < 0.001$). In the CS cohort the prevalence of overweight was somewhat lover (15.0% in boys and 11.0% in girls). The protective effect on female gender concerning childhood snoring remains to be established in further studies.

A meta-analysis of 24 studies among children indicates that tobacco smoke exposure increases the risk of habitual snoring [46]. The specific pathways by which exposure to tobacco smoke induces snoring are not known. It has been hypothesized that upper airway inflammation caused by chronic irritant exposure could be one explanation. In the CS cohort, the children of smoking parents snored habitually significantly more often compared to children living in smoke-free families. This association could serve as a supplementary tool for healthcare workers to be used in counselling and encouraging parents to quit smoking.

Previous longitudinal studies concerning snoring during early childhood are scarce. During the first two years of life, the prevalence of habitual snoring remained low among Finnish children in the CS cohort. The children not snoring at all during infancy seemed to have a persistent low risk for habitual snoring subsequently at the age of eight and 24 months, and vice versa. Overall, as many as half of the children (47%) in the CS cohort did not snore at any measurement point.

Despite the paucity of longitudinal information regarding toddlers' habitual snoring, there is a reasonable amount of data that parent-reported snoring may represent multiple phenotypes. Kamal et al. [16] reported four different SDB symptom trajectories up to two years of age; no-SDB, early SDB, late SDB, and persistent SDB. In every trajectory, they found different risk factors for SDB symptoms. Rhinitis and prior day-care seemed to add to the risk of snoring, daytime sleepiness, and attention deficit hyperactivity disorder symptoms in all trajectories. In addition, Freeman and Bonuck [47] defined five clusters during childhood; early snoring, early apnea, late snoring and mouth-breathing, normal, and all SDB after infancy. Children in the clusters of early snoring and early apnea alone developed the symptoms during the first two years of life. Some 50% of children were classified in the normal cluster, and these families were characterized by higher SES and a lower prevalence of smoking by the mothers.

The various phenotypes of SDB symptoms and the different risk factors in each cluster can explain the differences in the associations with habitual snoring in the CS and FB cohorts. Since the amount of habitually snoring children in our birth cohorts was limited (CS $N = 23$, FB $N = 31$) due to the low snoring prevalence, the evaluation of different phenotypes in our study population was not possible. Considering the low prevalence of snoring during early childhood in Finland, it would be interesting to study these phenotypes in a case control study in the future.

This study is based on comprehensive questionnaire surveys from two large birth cohorts, the CS (N = 947) and the FB (N = 1393). Further along in the CS cohort, we report the longitudinal aspect of snoring during early childhood. Comparable to our previous study covering snoring in infancy, the number of habitual snorers remained small in this study, and even larger samples or case–control study settings are needed in the future.

Polysomnography is considered to be the gold standard for diagnosing sleep disorders, and the absence of an objective measurement of snoring is a limitation in a community-based survey study. However, in this kind of large cohort study, overnight sleep recording is remarkably difficult to accomplish. We used standardized scales to assess the children's snoring in the questionnaires. As the snoring prevalence was practically identical in the two independent cohorts, we assume that the result of our study demonstrates rather accurately the prevalence of snoring among children in Finland.

In conclusion, our study suggests that the prevalence of habitual snoring among Finnish toddlers is notably lower (2.3%) than reported previously. Furthermore, risk for habitual snoring remained low from infancy to toddlerhood. Screening and administering preventive interventions for risk factors for snoring in early childhood may apply a tool to reduce the well-documented negative health consequences of SDB in later life.

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Credit author statement

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Conflict of interest

None declared.

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PUBLICATION III

The association of snoring, growth, and metabolic risk factors at the age of two years

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