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Maternal mental health disorders associate with their child's asthma: A register-based study

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ABSTRACT

Background: Maternal perinatal mental health disorders contribute to the development of their child's asthma. We investigated the associations between maternal mental health disorders one year before and three years after childbirth to their child's non-allergic asthma and allergic asthma.

Methods: From 310701 children born in Finland from 2001 to 2006 and their 232240 mothers, health care registers were collected. Using the International Classification of Diseases 10th revision, a maternal mental health disorder was defined as any mental or behavioral disorder diagnosis (F00–99) from the one year before and three years after childbirth. The outcome was their child's asthma diagnosis (e.g., J45, J45.0, J45.1, J45.8, J45.9, or J46.0) at 7–12 years divided into allergic (J45.0) and non-allergic (J45.1) asthma.

Results: Of the children, 19000 (6.1 %) were diagnosed with asthma and 12953 (5.6 %) of the mothers with a mental health disorder. The child's asthma was associated with a maternal mental health disorder (adjusted odds ratio 1.24; 95 % confidence interval 1.16–1.33), smoking during pregnancy (1.08; 1.03–1.13), asthma history (2.94; 2.82–3.06), the mother having a production *vs*. higher management/executive occupational role (1.16; 1.10–1.23), or the child being male (1.47; 1.42–1.52), all $p < .001$. Maternal mental health disorders were associated more with their child's non-allergic asthma (1.37; 1.18–1.60) than allergic asthma (1.17; 1.05–1.30), both $p < .001$.

Conclusions: Maternal mental health disorders perinatally and during the early life of their child were associated with their child's asthma supporting intrauterine and early-life programming on the effects of maternal mental health on their child's respiratory morbidity risk.

1. Introduction

For children, asthma is a major health burden, as it is one of the major chronic childhood respiratory diseases (Guthold et al., 2021) with prevalences varying globally between 2.6 % and 30.5 % (Asher et al., 2020). In Finland, a program to reduce asthma and other allergic diseases was conducted resulting in diminishing costs of the treatment and hospital admission of children with asthma (Jantunen et al., 2021). Parental mental health problems are common. Up to 20 % of children live in a family where at least one of the parents suffers from a mental health disorder (Reupert et al., 2013). The most common mental health disorders in mothers during pregnancy are anxiety and depressive disorders with estimated prevalences of 18–25 % (Dennis et al., 2017) and 17 % (Underwood et al., 2016), respectively.

The etiology of childhood asthma remains uncertain. Asthma is a heterogeneous disease (Conrad et al., 2021), where children are mainly classified to have either an allergic or non-allergic phenotype of asthma. Historically, asthma was thought to be simply a psychosomatic disease, but modern studies now assess the biological risks modulated by environmental factors (Douwes et al., 2011). The prevalence of asthma is higher in children living in urban environments (Molnár et al., 2021), who are predisposed to perinatal smoking (Burke et al., 2012; Ding

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et al., 2022), in males (Hafkamp-de Groen et al., 2013), and in children whose parents have a lower educational level (Hafkamp-de Groen et al., 2013). Also, asthma runs in families (Paaso et al., 2013), and the effect seems to be stronger from the mother's side (Lim et al., 2010).

Immune responses begin *in utero* as a result from a genetic predisposition and/or factors during gestation or during early infancy that modify the infant's airway physiology or immune responses towards an atopy-prone state (Wright, 2010; Mathilda et al., 2012; Lukkarinen et al., 2017; Rosa et al., 2018). Interestingly, exposure of maternal perinatal psychological stress, such as maternal mental health disorders during and after pregnancy, elevates the risk for any type of asthma in their children (Brew et al., 2018; Magnus et al., 2018). Furthermore, maternal perinatal anxiety (Cookson et al., 2009; Kozyrskyj et al., 2008) and depressive symptoms (van der Leek et al., 2020) are associated with any type of their child's asthma phenotype (Flanigan et al., 2018), where the association grows with chronic perinatal symptoms compared to periodical pre- or postnatal symptoms (Brew et al., 2018; Magnus et al., 2018; van der Leek et al., 2020). Clinically diagnosed cases of maternal mental health disorders or of their child's asthma or both are scarce. The data are mainly based on population surveys and questionnaires or are subjective (Brew et al., 2018; Magnus et al., 2018; van der Leek et al., 2020; Teyhan et al., 2014; Ramratnam et al., 2021). Also, the research on prenatal risk factors and postnatal asthma phenotypes is limited. Our aim was to use a large, national, population-wide register and determine the association between maternal mental health disorders one year before and three years after childbirth with their child's asthma at the ages of 7–12 years, and moreover, the difference in allergic and non-allergic asthma phenotypes. We hypothesized that maternal mental health disorders elevate the risk of any type of asthma in their children.

2. Methods

2.1. Study subjects and design

Retrospective data were collected from registers by the National Institute of Health and Welfare (THL) on Finnish children born between January 1st, 2001 and December 31st, 2006 (n = 341632) and their mothers (n = 232240). The data were collected by the end of year 2018. We excluded children born with severe syndromes (n = 11746), an unknown gestational age (n = 1248), perinatal deaths (n = 599), and premature birth before 37 gestational weeks (n = 17338) (Fig. 1 A). There were no exclusion criteria for the mothers. The study protocol was conducted in accordance with the Declaration of Helsinki and approved by THL (THL/595/5.05.00/2019) and the Ethics Committee of Turku University Hospital (J44/19). This was a retrospective register-based study needing no informed consent from the participants. The legal basis for processing personal data is public interest and for scientific research (EU General Data Protection Regulation 2016/679 [GDPR], Article (1)(e), and Article 9 (2)(j); Data Protection Act, Sections 4 and 6).

2.2. Maternal mental health, asthma, and occupational data

Diagnoses for maternal mental health disorders and asthma were collected from the Finnish Hospital Discharge Register (Sund, 2012). In Finland, the International Classification of Disorders (ICD)(World Health Organization, 2019) 10th (ICD-10) revision is used. Mothers were categorized to have a mental health disorder if they had received any diagnosis from the ICD-10 chapter on mental or behavioral disorders including all diagnoses of F00−99 based on the ICD-10 code one calendar year before until three calendar years after childbirth (Fig. 1, B). Subgroups for the mental health diagnoses categories F00−99 are specified in the Online Data Supplement (see Table E1 in the online supplement). Respectively, mothers were categorized to have lifetime asthma if they had received asthma diagnoses: J45.0 (allergic asthma), J45.1 (non-allergic asthma), J45.8 (mixed asthma), J45.9 (other or unspecified asthma), J45 without a phenotype, or J46 (status asthmaticus) categorized by the ICD-10 code or 493.xx (e.g., extrinsic, chronic obstructive, intrinsic, unspecified, or other forms of asthma) categorized by ICD-8 or ICD-9 codes during their lifetime (Global Initiative for Asthma, 2021; Asthma. Current Care Guidelines, 2022).

Data for maternal smoking during pregnancy, occupational status, and prior births were retrieved from the Medical Birth Register (MBR) (Gissler and Shelley, 2002) using the categorization of dichotomous "yes" or "no." Maternal occupational status was used as a proxy for family socioeconomic status (SES), as a low SES is a known risk factor for atopic diseases (Schyllert et al., 2020). It was originally retrieved from the MBR, but was later categorized using the International Standard Classification of Occupations (Alex) of Statistics Finland. The occupational status was categorized into four classes with the highest status and the reference group first: highest-level managers or executives, lower-level managers and salaried workers, manual-labor hourly wage workers, and others (e.g., homemakers, students, pensioners).

4.3. Child asthma data

The children met asthma criteria if they had received an asthma diagnosis coded: J45.0 (allergic asthma), J45.1 (non-allergic asthma), J45.8 (mixed asthma), J45.9 (other or unspecified asthma), and J46 (status asthmaticus) based on the ICD-10 code at ages 7–12 years (Fig. 1, B). To avoid double-diagnosing, the children were categorized by their latest asthma diagnosis. Children with a J46.0 status asthmaticus as their latest asthma diagnosis were categorized by their latest phenotype diagnosis (i.e., non-allergic or allergic asthma), and if there were no other asthma-related diagnoses, they were categorized in the subgroup of "other asthma" including J45.8 and J45.9. Also, children diagnosed only with "J45" were categorized in the same subgroup of "other asthma" with J45.8, J45.9, and J46.0. Data on offspring sex, birth weight, and gestational age were retrieved from the MBR.

2.4. Statistics

Logistic regressions were used with and without adjusting for the following known risk factors for childhood asthma: maternal lifetime asthma history, maternal smoking during pregnancy, previous births (≥1) indicating older siblings, maternal education, and biological sex of the child (male/female). The same regressions were repeated separately for the asthma phenotypes of allergic asthma, non-allergic asthma, and other asthma. *p*-values <.05 were considered statistically significant. The analyses were carried out using SAS for Windows version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Study population and characteristics

In total, 310701 children were eligible and were followed until the age of 12 years (Table 1). Their 232240 mothers were included. Of the mothers, 12953 (5.6 %) had a mental health disorder one year before and up to three years after the child's birth, and 21104 (9.1 %) were diagnosed with lifetime asthma. The most common mental health diagnostic groups were in the categories of F30 to F39 with Mood (affective) disorders (n = 7718; 53.9 %); F40 to F49 with Neurotic, stress-related, and somatoform disorders (n = 7136; 49.8 %); and with F10 to F19 Mental and behavioral disorders due to psychoactive substance use (n = 1751; 12.2 %) (see Table E1, Supplementary data). The concomitant maternal mental health disorders and lifetime asthma were noticeable. 21104/232240 (9.1 %) of all mothers had asthma, whereas 1969/12953 (15.2 %) of mothers with any mental health disorder also had asthma (see Table E2, Supplementary data).

Of the children, 19000 (6.1 %) had received an asthma diagnosis between 7 and 12 years of age. Of the asthmatics, 3196 (16.8 %) children had received the diagnosis of non-allergic asthma (J45.1) as their

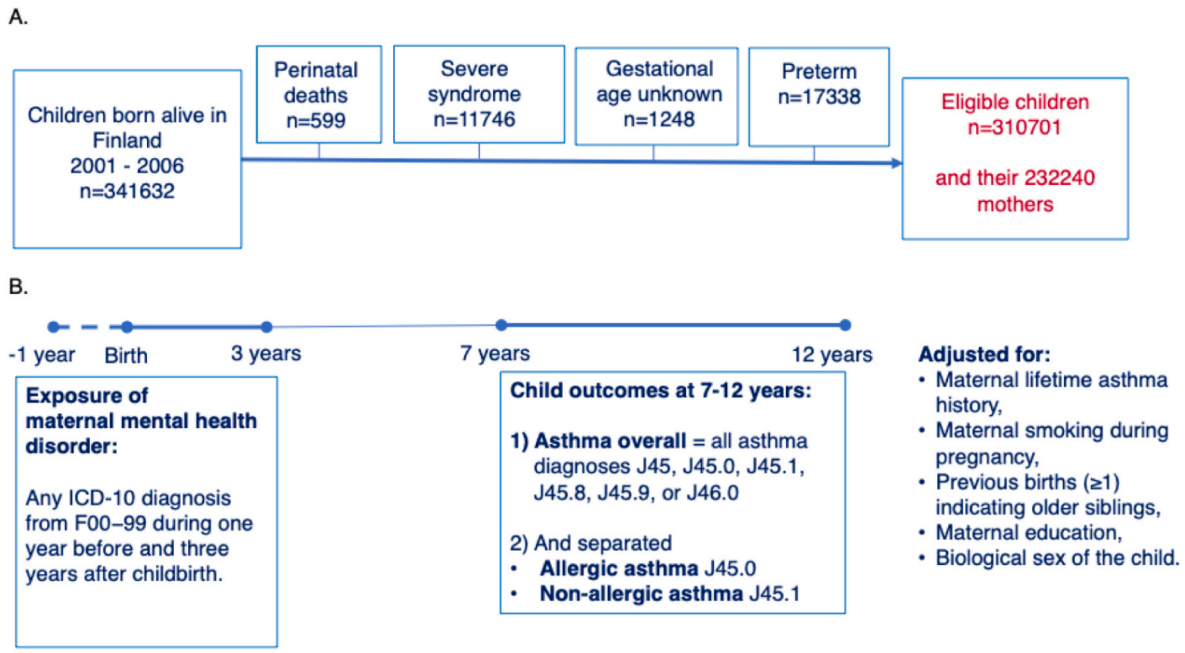

Fig. 1. A) Study flow chart. B) Study timeline and methods.

latest asthma diagnosis, and 7794 (41.0 %) had allergic asthma (J45.0). The remaining 8010 (42.2 %) children had received other asthma diagnoses: mixed asthma, other and unspecified asthma, asthma without any phenotype (J45), and/or status asthmaticus (Table 2). Asthma was more prevalent in male children than female children (Table 1).

3.2. Risk of asthma at the ages of 7 to 12 years

Mothers who were diagnosed with a mental health disorder, had smoked during pregnancy, had an asthma history, had no prior births, were young at labor, or who were lower educated were more likely to have children with asthma (Table 1). In the unadjusted analyses, maternal mental health disorders one year before and three years after their child's birth were associated with their child's asthma (odds ratio [OR] 1.40; 95 % confidence interval [CI] 1.32–1.49). In the adjusted analyses, the results remained unchanged. Maternal smoking during pregnancy, maternal asthma history, a lower education, and their child's sex being male were associated with their child's asthma, whereas previous births having older siblings had an inverse association with their child's asthma (Table 3).

3.3. Risk of asthma phenotypes at the age of 7 to 12 years

In the unadjusted analyses, a maternal mental health disorder was associated with their child's other asthma (OR 1.40; 95 % CI 1.28–1.53), non-allergic asthma (OR 1.55; 95 % CI 1.36–1.78), and allergic asthma (OR 1.28; 95 % CI 1.16–1.41). In the adjusted analyses, the results remained unchanged (Table 3).

4. Discussion

Here, we found that maternal mental health disorders during pregnancy and postnatally up to their child's age of 3 were associated with their child's asthma at the ages of 7–12 years. Moreover, we studied the association between maternal mental health disorders and their child's asthma phenotypes and found that maternal mental health disorders were associated more with non-allergic asthma. Despite extensive research and because this relation is multifactorial, there is no clear understanding of the mechanisms linking maternal mental health with their child's asthma. Unravelling the related associations and mechanisms is warranted.

Our results are in line with a study by Heuckendorff et al., which is a Danish register-based study on 925288 children, that found that maternal mental health disorders were associated with any type of asthma in their children, as exposed children were more likely to have asthma (10.6–12.0 %) compared with unexposed children (8.5–9.0 %) having an incidence rate ratio of 1.34 (95 % CI 1.34–1.38) for a moderate mental health disorder and a ratio of 1.38 (95 % CI 1.34–1.43) for a major mental health disorder (Heuckendorff et al., 2021). Their experimental setting was almost identical to ours by studying maternal mental health diagnoses two years before and until three years after childbirth and their child's asthma at the ages of three to six years. However, they did not have access to primary health care diagnoses, parental smoking status, or an asthma phenotype. In contrast, comparisons to previous, more survey-based studies, such as the study by Ramratnam et al. (2021), are challenging, as the diagnostic criteria for the disease may not be fulfilled even though symptom questionnaires met threshold values. Register-based studies may exclude mothers with mild symptoms and those not using health care services, but, still, these large population-wide studies based on clinically confirmed diagnoses play a major role in result interpretation.

We found that maternal mental health disorders had a notable association with non-allergic asthma compared to other asthma phenotypes, and the extent of these findings is new. Interestingly, our finding is consistent with the study by Ramratnam et al. (2021), who found that, during pregnancy, maternal stress and depression were associated with their child's asthma and with a non-allergic asthma phenotype in an at-risk population cohort (Ramratnam et al., 2021). Furthermore, we observed that the prevalence of concomitant mental health disorders and asthma in mothers was similar to previous research (Scott et al., 2007). In this study, the analyses were adjusted for known asthma risk factors, such as maternal smoking, asthma, and SES. The association between maternal mental health disorders and their child's asthma remained after adjusting for these, and we suggest that maternal mental health disorders may be an independent risk factor for the development of their child's asthma. Of note, asthma diagnostics in Finland relies on national and international guidelines using objective diagnostic lung function tests and is highly standardized, which, here, ensures a good

Table 1
Background characteristics of the children.

Characteristics	All children (n = 310701)	Any asthma (n = 19000, 6.1 %)	Non-asthmatics (n = 291701, 93.9 %)	$p^{\dagger}$
Maternal mental health disorder one year prior to three years after birth n (%)	14584 (4.7)	1197 (6.3)	13387 (4.6)	**<0.001**
Maternal smoking during pregnancy n (%)	45698 (14.7)	3210 (16.9)	42488 (14.6)	**<0.001**
Maternal lifetime asthma n (%)	28135 (9.1)	4015 (21.1)	24120 (8.3)	**<0.001**
Maternal previous births (≥1), n (%)	181821 (58.5)	10608 (55.8)	171213 (58.7)	**<0.001**
Age during labor years (SD)	29.4 (5.5)	29.0 (5.5)	29.5 (5.5)	**<0.001**[‡]
Maternal occupational status as: highest-level managers or executives n (%)	55987 (18.0)	2997 (17.9)	52990 (20.8)	**<0.001**[§]
Maternal occupational status as: lower-level managers and salaried workers n (%)	111614 (35.9)	7243 (43.3)	104371 (40.9)	
Maternal occupational status as: manual-labor hourly wage workers n (%)	47199 (15.2)	3023 (18.1)	44176 (17.3)	
Maternal occupational status as: other (e.g., homemaker, pensioner, student) n (%)	56972 (18.3)	3462 (20.7)	53510 (21.0)	
Children				
Male sex n (%)	158024 (50.9)	11390 (59.9)	146634 (50.3)	**<0.001**
Birth weight grams (SD)	3587 (480)	3584 (489)	3587 (480)	.420[‡]

Presented as numbers (percentages) or means (standard deviation, SD); $p < .05$ in bold text; [†]Comparison between asthmatics and non-asthmatics, Chi-Square test; [‡]Student's t-test; [§]Comparison between all occupational status subgroups, Chi-Square test.

reliability of diagnoses (Global Initiative for Asthma, 2021; Asthma. Current Care Guidelines, 2022). We included the group of older asthmatic children between 7 and 12 years, as this age group is capable of managing the diagnostic lung function tests, and the diagnosis of asthma is rather stable compared to the younger asthmatic children and more likely to predict asthma status during adulthood (Jenkins et al., 1994; Martinez et al., 1995).

Despite extensive research, there is no clear understanding of the

Table 2
Characteristics and the comparison between the children's asthma phenotypes of non-allergic and allergic asthma.

Characteristics	Other asthma (n = 8010, 42.2 %)	Non-allergic asthma (n = 3196, 16.8 %)	Allergic asthma (n = 7794, 41.0 %)	$p^{\dagger}$
Maternal mental health disorder one year prior to three years after birth n (%)	512 (6.4)	226 (7.1)	459 (5.9)	**<0.02**
Maternal smoking during pregnancy n (%)	1456 (18.2)	562 (17.6)	1192 (15.3)	**<0.003**
Maternal lifetime asthma n (%)	1627 (20.3)	679 (21.3)	1709 (21.9)	.43
Maternal previous births (≥1), n (%)	4480 (55.9)	1929 (60.4)	4199 (53.9)	**<0.001**
Age during labor, years (SD)	28.8 (5.5)	29.1 (5.5)	29.2 (5.5)	.34[‡]
Maternal occupational status as: highest-level managers or executives n (%)	1187 (14.8)	487 (15.2)	1323 (17.0)	**<0.04**[§]
Maternal occupational status as: lower-level managers and salaried workers n (%)	3042 (38.0)	1216 (38.0)	2985 (38.3)	
Maternal occupational status as: manual-labor hourly wage workers n (%)	1325 (16.5)	531 (16.6)	1167 (15.0)	
Maternal occupational status as: other (e.g., homemaker, pensioner, student) n (%)	1523 (19.0)	547 (17.1)	1392 (17.9)	
Offspring				
Male sex n (%)	4716 (58.9)	1803 (56.4)	4871 (62.5)	**0.001**
Birth weight grams (SD)	3590 (490)	3570 (500)	3584 (483)	.16[‡]

Presented as numbers (percentages) or means (standard deviation, SD). $p < .05$ in bold text. [†]Comparison between allergic and non-allergic asthma, Chi-Square test; [‡]Student's t-test; [§]Comparison between all occupational subgroups under allergic and non-allergic asthma; Chi-Square test.

mechanisms linking maternal mental health with their child's asthma, but the relationship is multifactorial. As for the environmental exposures and confounding factors for childhood asthma, mothers with poorer mental health generally have a lower SES, and parents from a lower SES are more often smokers, which both expose children to asthma (Ding et al., 2022; Shalowitz et al., 2006; Orton et al., 2014; Huuskonen et al., 2016). Here, maternal atopic diseases were a risk factor for their child's atopic diseases (Venter et al., 2021). Preterm children are predisposed to asthma symptoms (Nozawa et al., 2019) and were therefore excluded. One potential mechanism to explain the association between early-life maternal mental health disorders and offspring asthma, especially non-atopic asthma, could be that stress and depression related to maternal poorer mental health can alter the hypothalamic-pituitary-adrenal (HPA) axis resulting in increased glucocorticosteroid production. (O'Donnell et al., 2009), (Packard et al., 2016), (Glover, 2015)

Prenatally, the elevated levels of stress hormones can cause placental

Table 3
Risk of childhood asthma in 7–12-year-old children.

Exposures	Any asthma	Other asthma (J45/J45.8/J45.9/J46.0)	Non-allergic asthma (J45.1)	Allergic asthma (J45.0)
	aOR (95 % CI)	aOR (95 % CI)	aOR (95 % CI)	aOR (95 % CI)
Maternal mental health disorder one year prior to three years after birth	**1.24 (1.16–1.33)**	**1.22 (1.10–1.35)**	**1.37 (1.18–1.60)**	**1.17 (1.05–1.30)**
Mother smoking during pregnancy	**1.08 (1.03–1.13)**	**1.16 (1.09–1.24)**	**1.12 (1.01–1.24)**	.97 (.90–1.04)*
Maternal lifetime asthma	**2.94 (2.82–3.06)**	**2.57 (2.42–2.74)**	**2.72 (2.47–2.98)**	**2.96 (2.78–3.14)**
Previous births (≥1)	**0.87 (0.84–0.90)**	**0.88 (0.84–0.92)**	1.06 (.98–1.15)**	**0.81 (0.77–0.85)**
Highest-level managers or executives *vs.* lower-level managers and salaried workers	**1.19 (1.14–1.25)**†	**1.25 (1.16–1.34)**†	**1.20 (1.08–1.34)**†	**1.12 (1.05–1.20)**†
Manual-labor hourly wage workers *vs.* highest-level manager or executives	**1.16 (1.10–1.23)**†	**1.26 (1.16–1.37)**†	**1.21 (1.07–1.38)**†	**1.04 (0.95–1.13)**†
Other *vs.* highest-level managers or executives	**1.08 (1.03–1.14)**†	**1.18 (1.09–1.27)**†	**1.04 (0.91–1.17)**†	**1.00 (0.93–1.09)**†
Child male vs. female sex	**1.47 (1.42–1.52)**	**1.36 (1.30–1.43)**	**1.27 (1.18–1.37)**	**1.62 (1.54–1.70)**

aOR, adjusted Odds Ratio; CI, Confidence Interval; Results adjusted for confounding factors listed in the table. **bold** $p < .05$. *$p = .35$; **$p = .14$; †Comparison between all occupational subgroups under the same asthma phenotype, $p < .001$, tests done using the Wald Chi-Square Test.

dysregulation then cross the placenta and affect fetal development by impairing fetal maturation of HPA axis and altering fetal glucocorticoid levels that can all potentially lead to altered immune responses and airway hyperresponsiveness in the child. Glucocorticoids might then inhibit type 2 inflammatory responses in the fetus and decrease allergic sensitization in children (Fahy, 2015; Belvisi, 2004). Exposure of maternal prenatal stress may partly explain the non-genetic variability seen in childhood asthma phenotypes by interfering with the immune system and inducing the shift away from Th2 dominant predisposition. Postnatally, the first three years of life represent a critical window in the biological development of the child. An unpredictable and unsupportive caregiving environment is, in part, due to poorer parental mental health and partner relationship satisfaction, lack of parental skills, less socio-economic resources, or stressful life events and daily hassles. These challenges in family life already influence fetal development, although the mechanisms differ prenatally and postnatally. Studies show that an alteration in offspring biological stress reactivity and cortisol levels are altered in children who have been predisposed to maternal mental health disorders, postnatal stress, and depression early in life (Barry et al., 2015; Essex et al., 2002). The effect may be mediated also through epigenetic changes due to diminished abilities to sustain healthy caregiver-child interactions (Barry et al., 2015). Other mechanisms that could include detrimental effects of stress on airway development or lung maturation or altered airway tone are possibly through autonomic nervous system pathways.

The present study has several strengths. The quality and quantity of Finnish health care registers are validated and comprehensive. On this scale prior, a population-wide register study distinguishing the risk between different asthma phenotypes was not conducted. We were also able to include an extended follow-up. Compared to previous studies, we included primary health care diagnoses covering all children born between 2004 and 2006, and, partially, to the rest covering our study period. In this study, the childhood asthma case prevalence of 6.1 % was similar to previous studies (Asher et al., 2020), which, in interpreting our data and results, supports generalizability. There are also limitations. Since the diagnoses were recorded from any of the health care visits, the diagnosis could be a summary of medical history during a health check-up, even though the subject did not fulfill the diagnosis criteria at the time of examination. Due to a lack of medication and pharmacy records, we could not include those who were currently using antidepressant or asthma medication, but who had not yet received a diagnosis. There might be mothers with symptoms of mental health disorders or children with asthma symptoms who did not seek medical care during the study period and were not included. Mothers with mental health disorders and diagnosed and treated in the primary health care clinics were included in the reference group of healthy subjects, as we did not have access to the primary health care diagnoses before 2011. Therefore, the number of mothers with mental health disorders may be insufficient, as the total amount of mothers with mental health disorders (5.6 %) was less than shown in previous studies in a general population and of pregnant women (Vesga-López et al., 2008; Pirkola et al., 2005). Some children (n = 1375; 7.2 % of children with asthma) were diagnosed with "J45" without a more specific asthma phenotype. This may be due to technical differences among health care systems used in Finland and/or human error in mistyping the diagnosis into the system and both of which could result in incomplete data.

In conclusion, maternal mental health disorders before birth and postnatally up to their child's age of three years were associated with their child's school-age asthma and especially with a non-allergic asthma phenotype. These findings highlight the influence of prenatal and early-life exposure of maternal mental health disorders on their child's immune system and support the theory of an intrauterine programming effect of maternal mental health disorders leading to asthma (Brew et al., 2018; van der Leek et al., 2020; Flanigan et al., 2018). Special attention towards maternal mental health is recommended at family planning clinics and not only during pregnancy but also prenatally and postnatally.

CRediT authorship contribution statement

Eetu P. Kanerva: Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Minna M. Lukkarinen:** Conceptualization, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Marika H. Leppänen:** Investigation, Visualization, Writing – review & editing. **Bernd K. Pape:** Data curation, Formal analysis, Writing – review & editing. **Päivi T.K. Rautava:** Project administration, Writing – review & editing. **Max R.J. Karukivi:** Conceptualization, Investigation, Methodology, Visualization, Writing – review & editing.

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Declaration of competing interest

There were no conflicts of interest among all authors.

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Appendix A. Supplementary data

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