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The impact of postpartum depressive symptoms on self-reported infant health and analgesic consumption at the age of 12 months: A prospective cohort study

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ABSTRACT

The infants of mothers with elevated depressive symptoms (EDS) postpartum appear to be at increased risk of somatic health problems during their first 12 months of life in low- and lower-middle-income countries. However, in higher-income countries, knowledge of this association is scarce. We sought to examine whether maternal reports of infant health problems, adherence to vaccination schedules and analgesic supply to the infant during the first 12 months of life differ between mothers with and without postpartum EDS. Altogether, 969 women who were enrolled in the Kuopio Birth Cohort study (www.kubico.fi) during 2012–2017 were included in this investigation. Depressive symptoms were measured with the Edinburgh Postnatal Depression Scale during pregnancy (1st and/or 3rd trimester) and at eight weeks postpartum. Infant health data were collected as a part of a 12-month online follow-up questionnaire for mothers and were based on self-reports of either maternal observations or physician-determined diagnoses. Postpartum EDS were associated with a 2- to 5-fold increased likelihood of abnormal crying and paroxysmal wheezing (based on parental observations), as well as gastroesophageal reflux and food allergy (based on physician-determined diagnoses). Mothers with postpartum EDS also supplied their infants with analgesic medication for longer periods. Adherence to vaccination schedules was similar between the examined groups. In conclusion, infants of mothers with postpartum EDS may be more likely to experience health problems or to be perceived by their mother as having health problems, and thus receive more medications.

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1. Introduction

The postpartum period is a common time frame for the onset of a major depressive episode, a condition responsible for most of the disability worldwide (WHO, 2018). The prevalence of postpartum depression (PPD) has been estimated to be between 10 and 15 percent (PACT, 2015), although estimates are dependent on the population, the methods used for evaluating depression or its symptoms and the time of assessment (O'Hara and McCabe, 2013). Several risk factors have been identified for PPD, such as being a single mother, abnormal infant crying, maternal psychiatric history, as well as maternal depression and anxiety during pregnancy (O'Hara and McCabe, 2013; Räisänen et al., 2013; Vik et al., 2009). Untreated maternal depression or depressive symptoms during pregnancy have also been linked to numerous adverse effects on the foetus (e.g., irregular foetal heart rate) and the offspring (e.g., premature deaths, neonatal intensive care unit admissions, increased salivary cortisol concentrations and central adiposity) (Gentile, 2017). Furthermore, maternal psychological distress during pregnancy has been associated with numerous somatic child health concerns such as wheezing, rhinitis, asthma, atopic eczema, inflammatory diseases and gastrointestinal complaints (Cheng et al., 2015; El-Heis et al., 2017; Krause et al., 2017; Van De Loo et al., 2016), possibly moderated by child sex, with more robust effects among girls (Alton et al., 2016; Rosa et al., 2016).

Similarly, PPD can have detrimental effects on the child and the whole family (Letourneau et al., 2012). For example, it may interfere with healthy bonding between the mother and infant, leading to impaired breastfeeding behaviour (Dias and Figueiredo, 2015; Moehler et al., 2006). Additionally, persistent postpartum maternal depressive symptoms have been shown to negatively impact on cognitive functioning in children (NICHD Early Child Care Research Network, 1999; van der Waerden et al., 2017). The possible influence of PPD on infant physical health has been studied to a more limited extent. An association between maternal PPD and increased acute health care visits due to infant-related health concerns was already described in 1999 (Mandl et al., 1999), although the findings have remained inconsistent (Anderson et al., 2008; Farr et al., 2013). More recent studies have further suggested decreased attendance at preventive child health care visits among depressed mothers (Chee et al., 2008; Lyngsøe et al., 2018; Minkovitz et al., 2005).

However, the majority of the studies reporting an association between postpartum depressive symptoms and infant somatic health concerns have been carried out in low- and lower-middle income countries (Agoub et al., 2005; Murray et al., 2015; Nakku et al., 2006; Patel et al., 2002; Rahman et al., 2004; Weobong et al., 2015) or in low-income minorities (Gress-Smith et al., 2012). A few studies carried out in higher-middle and high-income settings have found suggestive associations between perinatal depression and poorer infant health (Ban et al., 2010; Groer and Morgan, 2007), while Finnish and Australian cohort studies (Clout and Brown, 2015; Punamäki et al., 2006) have detected no association between postpartum depressive symptoms and self-reported poorer infant health. Moreover, most studies examining the relationship between maternal PPD and infant health have in fact measured mother-reported symptoms or concerns about their infants' health, and have not been based on more objective measures of infant health, such as physician-determined diagnoses. However, a recent meta-analysis revealed associations between prenatal and postnatal maternal depression and a higher risk of infant hospitalization and mortality in the first year of life (Jacques et al., 2019). The results of this meta-analysis were, nonetheless, limited by the small number of studies available for inclusion. Moreover, while there is evidence that maternal over-the-counter analgesic use is associated with their use in school-age children (Jensen et al., 2014), whether a similar relationship also exists in PPD mother–infant dyads has not yet been examined.

In summary, it remains unclear whether the association between maternal PPD and concerns about infant somatic health is also observable in higher-income countries, and whether such findings can also be detected when utilising external evaluations of child health (i.e., physician-determined diagnoses). Moreover, it is not known whether PPD also influences maternal health behaviour practices regarding their infants, such as adherence to vaccination schedules and the supply of analgesic medications. It is also unclear whether the suggested associations between PPD and infant health concerns or practices are independent or are observable irrespective of depressive symptoms during pregnancy, and whether the associations are moderated by infant sex.

Thus, our first aim was to investigate whether elevated depressive symptoms (EDS) at eight weeks postpartum were associated with any maternal reports of either self-perceived or physician-diagnosed health conditions in their infants at the age of 12 months. Secondly, we sought to examine whether analgesic medication supply to infants, infant health care visits and immunization habits were linked to EDS at eight weeks postpartum. Thirdly, in order to investigate the possible intermediary role of postpartum EDS, we examined whether EDS during pregnancy were associated with the 12-month infant health outcomes that were associated with postpartum EDS. Fourthly, we examined whether infant sex acts as a moderator for the examined associations. We hypothesized that infants of mothers with postpartum EDS would have an increased number of infant health care visits, physician-diagnosed health conditions and a longer period of analgesic medication supply, but lower adherence to vaccination schedules, compared to infants of mothers without postpartum EDS. In addition, we hypothesized that postpartum EDS would act as a mediator of the possible associations between EDS during pregnancy and infant health concerns, and that the association with infant wheezing would be more robust among girls (Alton et al., 2016; Rosa et al., 2016).

2. Methods

2.1. Study sample

This study utilized data from the ongoing Kuopio Birth Cohort study (KuBiCo; www.kubico.fi), which started in 2012 with the aim of recruiting and following up 10 000 mother–infant pairs until the child reaches 18 years of age (Huuskonen et al., 2018). All women who are likely to give birth at Kuopio University Hospital are invited to participate in the study through a prerequisite online questionnaire prior to routine prenatal care. The mean of the annual participation rates was 37% during 2012–2016. The demographics of the participants did not substantially differ from the nationwide Finnish delivery demographics regarding the following variables: maternal age, duration of pregnancy, infant gender and birth weight (Huuskonen et al., 2018). The research ethics committee of the Central Finland Health Care District has approved the KuBiCo study (December 8, 2011, K–S SHP Dnro 18U/2011). Informed consent of the participants was obtained after the nature of the procedures had been fully explained.

Data were extracted from the KuBiCo database in January 2017 (n = 4144). All the singleton mother–infant pairs who were first timers in the KuBiCo study with complete data on the Edinburgh Postnatal Depression Scale (EPDS) at postpartum and on a follow-up questionnaire when their child was aged 12 months were included in the analyses (n = 969) (Fig. 1).

2.2. Postpartum depressive symptoms (predictor)

Postpartum EDS were assessed with the EPDS questionnaire, completed online 8 weeks after delivery. The EPDS is a 10-item 4-level Likert-scale questionnaire used for screening postpartum depression in clinics (range 0–30). A cut-off of 10 points or more was used to indicate EDS (Cox et al., 1987).

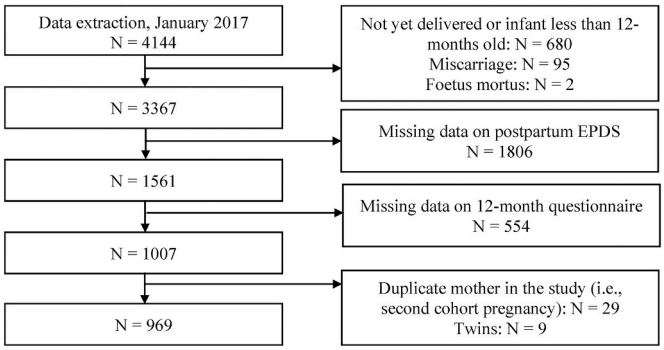

Fig. 1. Flow chart for the inclusion of study participants. EPDS: Edinburgh Postnatal Depression Scale.

2.3. Outcome variables

Variables related to infant health conditions were based on maternal reports gathered as part of the 12-month follow-up questionnaire. The following questions, with a response option of yes/no, were asked: "Has your child experienced the following condition during his/her first year of life?": anaesthesia, dry cough (other than during a common cold), dry skin, fever (i.e., body temperature more than 38 °C), febrile seizures, gastrointestinal infection, hay fever, itchy rash, respiratory infection, rhinitis (other than during a common cold) and paroxysmal wheezing (i.e., acute episodes of wheezing). Additional questions (yes/no) were asked regarding colic ("During the first year of life, has a doctor or a nurse defined that your child has colic?"), doctor visits ("During the first year of life, has your child visited a doctor due to a health issue [other than routine doctor inspections at a child welfare clinic]?"), hospital treatment ("During the first year of life, has your child been treated in a hospital ward [other than treatments linked to delivery]?") and lacking regular vaccinations ("Has your child received all the regular vaccinations?") The variable 'abnormal crying' was defined as affirmative responses to all three of the following: 1) a period of abnormal crying lasting for at least three weeks; 2) during the three-week period, abnormal crying has occurred at least three times a week; 3) when crying, the infant has cried at least 3 h a day during the three-week period.

Physician-determined conditions (yes/no) were inquired as follows: "Has a doctor diagnosed any of the following conditions in your child during his/her first year of life?": asthma, atopic eczema, bacterial dermatitis, conjunctivitis, food allergy, gastroesophageal reflux, laryngitis, obstructive bronchitis or bronchiolitis, otitis, pneumonia, pertussis, tonsillitis, undescended testicle and urinary tract infection.

Each of the outcome variables was analysed separately as a binary outcome, with the exception of the count variable 'analgesic medication supply to the infant', which measured the number of days when the infant received analgesic medications (ibuprofen, naproxen or paracetamol) during the first year of life, as reported by the mother.

2.4. Covariates and potential moderators

Infant-related covariates. Information on gestational age, birth weight, infant sex, neonatal intensive care unit (NICU) admission and Apgar scores was recorded in an electronic database at the delivery ward of Kuopio University Hospital. Infant weight gain (as a continuous variable) was calculated as the difference between infant weight at eight months and one month of age, as recorded on the child welfare clinic card. The variable 'infant sex' was also tested as a moderator in the study.

Maternal covariates. Depressive symptoms during pregnancy were assessed with the EPDS. Of the study sample, 494 women completed the EPDS during the first trimester, 680 women during the third trimester and 343 women both during the first and third trimesters. Thus, altogether, 831 women completed the EPDS during pregnancy. The variable 'EPDS score during pregnancy' refers to either the first or third trimester score for women with only one measure during pregnancy, or to the mean score for women who completed the EPDS twice during pregnancy. A cut-off of 10 points or more in either the first trimester or third trimester was considered to indicate EDS during pregnancy (Cox et al., 1987). Maternal mental health problems before the index pregnancy were defined as either a self-report, during routine prenatal care, of previous mental health problems/mental illness ("Have you suffered from mental health problems/mental illness before pregnancy?" [yes/no]) or as self-reported earlier use of psychotropic medication.

The body mass index (BMI) in early pregnancy was calculated from the self-reported weight and height at the first prenatal care visit, which on average took place during pregnancy week 8 (mean 8.6 weeks, SD 1.5). In addition, data on maternal age and gestational diabetes mellitus were gathered from the Kuopio University Hospital delivery ward records. The variable 'diabetes mellitus' indicated either gestational diabetes or self-reported type I or type II diabetes. The other maternal covariates, based on the 12-month follow-up questionnaire, included: exclusive breastfeeding (number of months [0–6]), smoking (yes/no; either the mother or her partner), relationship status (living without a partner [yes/no]), maternal alcohol use (Alcohol Use Disorder Identification Test-C (AUDIT-C) (Levola and Aalto, 2015) with the 12-month questionnaire) and occupation (requiring tertiary education [yes/no] according to the International Standard Classification of Education, 1997).

2.5. Statistical methods

Differences between the groups of mothers with and without postpartum EDS were assessed with the chi-squared test for dichotomous variables, the Student's t-test for continuous variables and the Mann-Whitney *U* test for count variables. Non-normally distributed continuous variables (i.e., infant weight gain and BMI in the first trimester) were transformed to a normal distribution (Templeton, 2011) before using the Student's t-test. Health conditions for which the observed prevalence was less than 2% (asthma, bacterial dermatitis, fever seizure, hay fever, pertussis, pneumonia, tonsillitis, undescended testicle and urinary tract infection) were excluded from the analysis due to the lack of statistical power.

Multivariable Poisson regression analyses with robust error variance (Zou, 2004) were performed to examine the adjusted risk ratios (RR) of each outcome variable that displayed statistical significance in bivariate chi-squared or Fisher's exact test analyses, comparing groups with and without EDS. Since multiple bivariate tests were performed for 22 outcome variables, statistical significance was defined using the Benjamini-Hochberg procedure (Benjamini and Hochberg, 1995) to control the false discovery rate (set to 0.05). To control for the effect of possible confounders, seven differently adjusted models (Basic model, Mental Health model, Metabolic model, Perinatal Status model, Lifestyle model, Breastfeeding model and Infant Sex model) were tested, as detailed in Table 3. For the non-dichotomous outcome variable 'analgesic medication supply to the infant', negative binomial regression with the log link was used to calculate incidence rate ratios (IRR) for women with EDS compared to the group without EDS. The models used in the negative binomial regression analyses were identical to those used in the modified Poisson regression analyses. All the covariates that displayed statistical significance in the bivariate analyses with postpartum EDS (i.e., previous maternal mental health issues, EPDS scores during pregnancy, diabetes, BMI in the first trimester, maternal alcohol consumption and breastfeeding) were included in the regression models as possible confounders. Furthermore, we included the following possible confounders in our regression models based on previous literature on the risk factors for both postpartum depression and infant health issues: maternal age (Kenny et al., 2013), living without a partner

(Crosier et al., 2007), occupation (Lorant et al., 2003), NICU admission (Blom et al., 2010), first delivery (Räisänen et al., 2013), parental smoking (Wootton et al., 2020) and infant sex (Xie et al., 2007). In the multivariable analyses, cases with missing values for any of the covariate variables were excluded.

To test the role of depressive symptoms during pregnancy in the possible associations between postpartum EDS and infant health outcomes, we utilized chi-squared tests and Mann-Whitney U-tests to examine differences in the prevalence of infant health outcomes that were significant in the bivariate analysis with postpartum EDS between mothers with and without EDS during pregnancy. Further mediation analyses (Hayes, 2017) were performed for outcomes that were found significant in the above-described analyses.

The possible moderating role of infant sex in the association between postpartum EDS and infant health outcomes was examined using bivariate analyses performed separately among boys and girls and by

Table 1
Basic characteristics of the whole sample and differences between the groups divided according to a postpartum Edinburgh Postnatal Depression Scale (EPDS) score cut-off of 10 or more. Test statistics and p-values refer to differences between the EPDS <10 vs. ≥ 10 cut-off groups.

	Whole sample	EPDS < 10	EPDS ≥ 10	Test statistics	P-value
		n (%)			
Occupation requiring tertiary education (n = 891)	487 (54.7)	438 (55.3)	49 (49.5)	$\chi^2 = 1.2$	0.274
Earlier mental health issues (n = 966)	80 (8.3)	56 (6.5)	24 (22.4)	$\chi^2 = 31.7$	<0.001
EPDS ≥ 10 in either the 1st trimester or 3rd trimester (n = 831)	99 (11.9)	52 (7.1)	47 (49.0)	$\chi^2 = 141.9$	<0.001
Parental smoking (n = 903)	191 (21.2)	165 (20.6)	26 (25.5)	$\chi^2 = 1.3$	0.255
Living without a partner (n = 933)	13 (1.4)	11 (1.3)	2 (2.0)	-	0.641[a]
Diabetes mellitus (incl. GDM) (n = 966)	171 (17.7)	138 (16.1)	33 (30.8)	$\chi^2 = 14.3$	<0.001
First child (n = 969)	506 (52.2)	447 (51.9)	59 (55.1)	$\chi^2 = 0.4$	0.521
Female infant (n = 969)	459 (47.4)	408 (47.3)	51 (47.7)	$\chi^2 < 0.1$	0.948
Neonatal intensive care unit admission (n = 969)	112 (11.6)	100 (11.6)	12 (11.2)	$\chi^2 < 0.1$	0.906
		Mean (SD)			
Postpartum EPDS score (n = 969)	4.5 (3.8)	3.6 (2.6)	12.4 (2.7)	Z = –17.0	<0.001
EPDS score during pregnancy (n = 831)	4.2 (3.6)	3.7 (3.0)	8.4 (4.6)	Z = –9.7	<0.001
BMI in the first trimester (kg/m^2) (n = 964)	25.0 (5.2)	24.8 (5.1)	26.4 (6.2)	t = –2.7	0.008
Maternal age at delivery (years) (n = 968)	30.4 (4.8)	30.4 (4.7)	30.4 (4.9)	t < 0.1	0.997
Exclusive breastfeeding (months) (n = 881)	3.8 (2.0)	3.9 (2.0)	3.2 (2.2)	Z = –2.9	0.004
Maternal alcohol use (AUDIT-C) (n = 852)	1.9 (1.3)	1.9 (1.3)	2.4 (1.5)	Z = –3.5	<0.001
Gestational age (weeks) (n = 968)	39.4 (1.6)	39.3 (1.6)	39.4 (1.6)	Z = –0.5	0.652
Apgar scores 1min (n = 968)	8.7 (1.1)	8.7 (1.1)	8.8 (0.9)	Z = –1.5	0.147
Apgar scores 5min (n = 968)	9.0 (0.8)	9.0 (0.9)	9.0 (0.6)	Z > –0.1	0.993
Birth weight (kg) (n = 951)	3.49 (0.51)	3.50 (0.50)	3.48 (0.53)	t = 0.2	0.806
Infant weight gain (months 1–8, kg) (n = 932)	4.28 (0.99)	4.27 (0.99)	4.31 (1.03)	t = –0.3	0.792

[a] Fisher's exact test; Abbreviations: AUDIT-C = Alcohol Use Disorders Identification Test, consumption questions; EPDS = Edinburgh Postnatal Depression Scale; GDM = Gestational diabetes mellitus.

determining multiplicative and additive estimates of interaction (Andersson et al., 2005; Knol and VanderWeele, 2012) for the outcomes that were found significant in the bivariate analyses with postpartum EDS.

All the statistical analyses were performed with IBM SPSS Statistics Version 25. All the performed tests were two-tailed with the alpha level set to 0.05.

3. Results

Background characteristics of the study sample are presented in Table 1. The mean postpartum EPDS score for the whole sample was 4.5 (standard deviation [SD] 3.8, range 0–21). A total of 107 women (11.0%) had postpartum EDS (EPDS ≥ 10). The mothers with postpartum EDS had a higher BMI in the first trimester and a higher prevalence of diabetes mellitus and earlier mental health issues compared to mothers without postpartum EDS. Mothers in the EDS group also had higher EPDS scores during pregnancy and higher AUDIT-C scores at 12

Table 2
Outcome prevalences and means for the whole sample and differences in infant health outcomes between the groups formed according to a postpartum EPDS-score cut-off of 10 or more. Test statistics and p-values refer to differences between the EPDS <10 vs. ≥ 10 cut-off groups.

	Whole sample	EPDS < 10	EPDS ≥ 10	Test statistics	P-value
Conditions based on self-reports of maternal observations					
		n (%)			
Abnormal crying (n = 954)	80 (8.4)	64 (7.5)	16 (15.4)	$\chi^2 = 7.4$	0.006
Anaesthesia (n = 961)	38 (4.0)	31 (3.6)	7 (6.6)	-	0.178[a]
Doctor visit (n = 958)	622 (64.9)	541 (63.5)	81 (76.4)	$\chi^2 = 6.9$	0.009
Dry cough during the night (n = 957)	73 (7.6)	65 (7.6)	8 (7.5)	$\chi^2 < 0.1$	0.973
Dry skin (n = 911)	315 (34.6)	276 (34.1)	39 (38.6)	$\chi^2 = 0.8$	0.366
Fever (n = 927)	512 (55.2)	455 (55.3)	57 (54.8)	$\chi^2 < 0.1$	0.926
Gastroenteritis (n = 958)	190 (19.8)	162 (19.0)	28 (26.4)	$\chi^2 = 3.2$	0.072
Hospital treatment (n = 958)	109 (11.4)	90 (10.6)	19 (17.9)	$\chi^2 = 5.1$	0.024
Itchy rash (n = 951)	205 (21.6)	177 (20.9)	28 (26.7)	$\chi^2 = 1.8$	0.177
Lacking regular vaccinations (n = 953)	91 (9.5)	84 (9.9)	7 (6.8)	$\chi^2 = 1.0$	0.314
Respiratory infection (n = 929)	854 (91.9)	759 (91.9)	95 (92.2)	$\chi^2 < 0.1$	0.904
Rhinitis (other than during a cold) (n = 958)	251 (26.2)	222 (26.1)	29 (27.4)	$\chi^2 = 0.1$	0.774
Paroxysmal wheezing (n = 957)	77 (8.0)	60 (7.1)	17 (16.0)	$\chi^2 = 10.3$	0.001
Conditions based on self-reports of physician-assigned diagnoses					
		n (%)			
Atopic eczema (n = 943)	146 (15.5)	124 (14.8)	22 (21.2)	$\chi^2 = 2.9$	0.090
Conjunctivitis (n = 955)	155 (16.2)	134 (15.7)	21 (20.2)	$\chi^2 = 1.3$	0.246
Colic[b] (n = 947)	46 (4.9)	37 (4.4)	9 (8.7)	$\chi^2 = 3.6$	0.056
Food allergy (n = 941)	42 (4.5)	31 (3.7)	11 (10.8)	-	0.003[a]
Gastroesophageal reflux (n = 959)	74 (7.7)	55 (6.4)	19 (17.9)	$\chi^2 = 17.4$	<0.001
Laryngitis (n = 959)	42 (4.4)	41 (4.8)	1 (1.0)	-	0.076[a]
Obstructive bronchitis / bronchiolitis (n = 957)	35 (3.7)	30 (3.5)	5 (4.7)	-	0.579[a]
Otitis (n = 956)	245 (25.6)	214 (25.2)	31 (29.2)	$\chi^2 = 0.8$	0.366
Non-dichotomous variables					
		Mean (SD)			
Analgesic medication supply to infant (days within the first 12 months of life) (n = 918)	13.6 (14.5)	13.1 (14.3)	17.3 (15.2)	Z = –3.1	0.002

[a] Fisher's exact test, [b] Condition recorded by a physician or a nurse.

months postpartum than mothers in the non-EDS group. Furthermore, mothers with postpartum EDS ceased exclusive breastfeeding earlier than mothers without postpartum EDS.

3.1. Postpartum EDS and infant health

Mothers with postpartum EDS more often reported that their infants had paroxysmal wheezing, abnormal crying, physician-diagnosed gastroesophageal reflux and physician-diagnosed food allergy compared to mothers without postpartum EDS (Table 2). Furthermore, infants of mothers belonging to the postpartum EDS group were more likely to have visited a doctor than those of mothers belonging to the non-EDS group. Additionally, infants of mothers with postpartum EDS received analgesic medication for longer periods than those of mothers without postpartum EDS (Cohen's d = −0.29). No differences were detected between the postpartum EDS and non-EDS groups regarding regular vaccinations.

According to the Benjamini-Hochberg procedure, with the false discovery rate set to 0.05, the significance level for the bivariate tests was $P \leq 0.009$ (Supplementary Table 4). Based on this set p-value level, we included the following outcome variables in the multivariable analyses: Abnormal crying, Doctor visits, Food allergy, Gastroesophageal reflux, Paroxysmal wheezing and Analgesic medication supply to the infant.

In multivariable analyses, the associations between postpartum EDS and the following conditions remained significant in all the models: abnormal crying, food allergy, gastroesophageal reflux and paroxysmal wheezing (Table 3). The association between postpartum EDS and doctor visits lost its significance in the Mental Health model but remained significant in all the other models.

Postpartum EDS was associated with a longer supply of analgesic medication to the infant in all the models except for the Mental Health model, in which the association was borderline significant ($p = 0.062$) (Table 4). Belonging to the postpartum EDS group was associated with an up to 38% increase in the duration of analgesic supply to the infant during his/her first year of life compared to the non-EDS group.

3.2. EDS during pregnancy and infant health

Out of the 831 women who completed the EPDS during pregnancy, 99 (10.2%) had EDS during pregnancy. EDS during pregnancy was not associated with the following outcomes that were significantly associated with postpartum EDS in our analysis: abnormal crying, paroxysmal wheezing, gastroesophageal reflux, food allergy and analgesic medication supply to the infant (Supplementary Table 1). Mothers with EDS during pregnancy were more likely to report infant doctor visits than mothers without EDS during pregnancy.

Doctor visits was the only outcome variable that was associated with both postpartum EDS and EDS during pregnancy, indicating the possibility of a mediating role of postpartum EDS regarding the association between EDS during pregnancy and doctor visits. In the further mediation analysis, postpartum EDS did not mediate the association (Supplementary Figure).

3.3. Moderating effect of child sex

In analyses stratified by infant sex, the associations between postpartum EDS and a higher prevalence of paroxysmal wheezing and analgesic medication supply to the infant were significant among girls but not among boys (Supplementary Table 2). However, when testing for a modifying effect of infant sex on postpartum EDS, no significant moderation effect was detected (Supplementary Table 3).

4. Discussion

4.1. Main findings

The results of this study demonstrate an increased risk of both mother-reported (i.e., abnormal crying and paroxysmal wheezing) and physician-diagnosed (i.e., gastroesophageal reflux and food allergy) health problems among infants of mothers with postpartum EDS compared to those without postpartum EDS. Infants of mothers with postpartum EDS also received analgesic medication for longer periods during the first 12 months of life than infants of mothers without postpartum EDS. The results further suggest, contrary to our hypothesis, that the associations are independent of depressive symptoms during

Table 3
Risk ratios (RR) and 95% confidence intervals (CI) of reporting each infant health condition for mothers with elevated postpartum depressive symptoms (EPDS ≥ 10) compared to mothers with no elevated postpartum depressive symptoms.

	Abnormal crying			Doctor visit			Food allergy			Gastroesophageal reflux			Paroxysmal wheezing		
	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI
Basic Model	855	2.34[a]	1.40–3.91	857	1.19[b]	1.05–1.35	856	3.23[a]	1.67–6.25	860	3.12[a]	1.92–5.07	859	2.49[a]	1.48–4.19
Mental health Model	730	2.21[b]	1.06–4.62	732	1.09	0.93–1.28	731	3.30[b]	1.51–7.20	735	2.91[a]	1.56–5.43	734	2.74[b]	1.31–5.71
Metabolic Model	848	2.44[a]	1.47–4.07	850	1.17[b]	1.03–1.33	849	3.24[a]	1.71–6.13	853	3.12[a]	1.92–5.08	852	2.20[b]	1.31–3.70
Perinatal status Model	855	2.28[a]	1.38–3.76	857	1.19[b]	1.05–1.35	856	3.14[a]	1.63–6.06	860	3.09[a]	1.92–4.97	859	2.54[a]	1.51–4.26
Lifestyle Model	744	2.72[a]	1.61–4.60	745	1.24[a]	1.09–1.41	743	5.36[a]	2.65–10.83	747	3.37[a]	2.03–5.61	747	2.64[a]	1.57–4.44
Breastfeeding Model	792	2.26[b]	1.32–3.89	793	1.18[b]	1.03–1.35	791	3.51[a]	1.77–6.97	795	3.07[a]	1.85–5.07	794	2.97[a]	1.76–5.01
Infant sex Model	855	2.36[a]	1.41–3.95	857	1.18[b]	1.04–1.34	856	3.33[a]	1.72–6.42	860	3.15[a]	1.94–5.13	859	2.46[a]	1.46–4.16

Basic Model: maternal age, living without a partner, occupation; Mental Health Model: Basic Model + previous maternal mental health issues, EPDS scores during pregnancy; Metabolic Model: Basic Model + diabetes, BMI in the first trimester; Perinatal Status Model: Basic Model + NICU admission, first delivery; Lifestyle Model: Basic Model + maternal alcohol consumption, parental smoking; Breastfeeding model: Basic model + breastfeeding; Infant sex model: Basic model + infant sex.
[a] $p \leq 0.001$; [b] $0.001 < p \leq 0.05$.

Table 4
Incidence rate ratios (IRR), 95% confidence intervals and p-values of analgesic medication supply to infants of mothers with elevated postpartum depressive symptoms (EPDS ≥ 10) compared to mothers with no elevated postpartum depressive symptoms.

	N	IRR	95% confidence interval	P-value
Basic Model	822	1.37	1.12–1.67	0.002
Mental Health Model	703	1.25	0.99–1.57	0.062
Metabolic Model	815	1.32	1.08–1.62	0.006
Perinatal Status Model	822	1.38	1.14–1.69	0.001
Lifestyle Model	717	1.36	1.11–1.68	0.003
Breastfeeding Model	763	1.36	1.10–1.68	0.005
Infant Sex Model	822	1.36	1.12–1.66	0.002

Basic model: maternal age, living without a partner, occupation; Mental health model: Basic model + previous maternal mental health issues, EPDS scores during pregnancy; Metabolic model: Basic model + diabetes, BMI in the first trimester; Perinatal status model: Basic model + NICU admission, first delivery; Lifestyle model: Basic model + maternal alcohol consumption, parental smoking; Breastfeeding model: Basic model + breastfeeding; Infant sex model: Basic model + infant sex.

pregnancy. Similarly, contrary to our hypothesis, no association was found between postpartum EDS and altered vaccination habits.

4.2. Comparison with previous literature

In line with our findings, three earlier studies carried out in higher-middle and high-income countries, although among ethnically distinct samples compared to our sample, have reported an association between postpartum depressive symptoms and poorer mother-reported infant health (Gress-Smith et al., 2012; Groer and Morgan, 2007; Wan et al., 2009).

In contrast, two other studies have reported no association between postpartum depressive symptoms and maternal self-reported infant health concerns (Clout and Brown, 2015; Punamäki et al., 2006). However, in one of these (Clout and Brown, 2015), the number of available postpartum mothers was rather modest (n = 105), and 99 of them reported either excellent or very good health of their infants. Both the smaller sample size and the narrow distribution of outcome variable values could have led to the observed lack of associations between EDS and infant health outcomes. Furthermore, a Finnish longitudinal study (Punamäki et al., 2006) found no association between depressive symptoms at 2 months postpartum and mother-reported infant health at 12 months. Here, infant health outcomes included reports of infant infectious illnesses during the first 12 months, infant hospital treatment during the first 12 months and maternal worries of infant health at 12 months postpartum. In our study, infant health was assessed in connection with a larger variety of conditions in addition to infectious diseases, hospitalizations and maternal worries.

A large population-based cohort study carried out in the UK examined infant health through register-based information on childhood infectious diseases during the first four years of life (Ban et al., 2010). The study found an association between a maternal diagnosis of depression or prescriptions of antidepressants during the perinatal period (i.e., during pregnancy or the first six months postpartum) and both infant gastrointestinal and lower respiratory tract infections also when limiting the analyses to the first 12 months of life. In our study, infant gastroenteritis was indeed associated with EDS during pregnancy, but not postpartum. However, the UK study pooled together depression during pregnancy and postpartum.

Similarly to our finding of an association between postpartum EDS and infant paroxysmal wheezing, a Canadian longitudinal study found that postpartum depressive symptoms at eight weeks after delivery were associated with an increased risk of wheezing in 3-year-old girls, but not in boys (Alton et al., 2016). The authors also suggested that postpartum depressive symptoms would act as a mediator in the association between maternal distress during pregnancy and childhood wheezing (Alton et al., 2016; Rosa et al., 2018). Similarly, a Mexican study found a sex-specific association between maternal postnatal stress and child wheezing in girls, but not in boys (Rosa et al., 2016). Conversely, a large Canadian population-based study demonstrated an association between maternal recurrent and late-onset postnatal distress and childhood asthma at age of 7 years among boys, but not among girls (van der Leek et al., 2020). In our study, postpartum EDS, but not EDS during pregnancy, were associated with infant paroxysmal wheezing during the first 12 months of life. The association was more robust in girls, but attenuated to non-significant in boys. However, infant sex did not act as a significant moderator in the further moderation analysis.

Our novel finding of an association between maternal postpartum EDS and infant gastroesophageal reflux supports the results of a previous Australian study on 51 infant–mother dyads admitted to a residential unit due to infant irritability (Armstrong et al., 2000). The authors reported an 88% prevalence of high maternal EPDS scores (≥12) and an 82% prevalence of a pre-admission diagnosis of gastroesophageal reflux.

Finally, we observed that infants of mothers with postpartum EDS received an increased supply of analgesic medication during the first 12 months of their lives. Two European studies have suggested an association between the maternal prenatal psychological burden and infant antibiotic, antipyretic, pain and digestive medication (Beijers et al., 2010; Krause et al., 2017). In our study, however, EDS during pregnancy were not associated with an increased supply of analgesics to the infant.

4.3. Possible mechanisms

In our study, EDS during pregnancy and postpartum were associated with different profiles of infant health concerns during the first year of life. Thus, it is unlikely that depression during pregnancy and its physiological effects on the foetus could explain the associations between postpartum EDS and an increased risk of infant health concerns. Hence, other mechanisms could be hypothesized, such as 1) maternal fatigue due to early infant morbidity, in turn increasing maternal depressive symptoms, 2) a negatively altered maternal perception of infant health due to depressive symptoms and 3) a combination of 1 and 2. Regarding

the conditions based on maternal reports of a physician-determined diagnosis (e.g., gastroesophageal reflux and food allergy), a negatively altered maternal perception of infant health might lead to an increased number of doctor visits and the consequent diagnoses. It is notable that if this is the case, the possibility of over-diagnosis cannot be ruled out (Armstrong et al., 2000; Oberklaid, 2000). Furthermore, the diagnosis of both gastroesophageal reflux and food allergy is mostly clinical and strongly based on maternal anamnesis. Additionally, symptoms such as inconsolable crying might increase maternal depressive symptoms, which in turn may reduce the ability of the mother to soothe the infant (Radesky et al., 2013), thus increasing the perceived infant symptoms (Mäntymaa et al., 2003). This vicious circle might lead to increased supplies of analgesic medication to the infant, which was associated with postpartum EDS in our study.

4.4. Strengths and limitations

The large sample size and the broad spectrum of infant health conditions examined (more than 20) is a strength of our study. Additionally, the availability of data on previous mental health and depressive symptoms during pregnancy allowed us to control for the effect of earlier-onset depressive symptoms.

The study also had some limitations, which need to be taken into consideration when interpreting our findings. Missing answers in both postpartum EPDS and the 12-month follow-up questionnaire may have weakened the observed associations; more severely depressed mothers, who may be more likely to report infant conditions, might also be more likely opt out from filling in the questionnaires. The outcome variables aimed to assess infant health during the first year of life, and postpartum EDS were measured 8 weeks after delivery, a time period that partially overlaps with the time period for which the infant outcomes were reported. Therefore, our data cannot be used to evaluate causal relationships between the observed associations. Some of the outcome variables were exclusively based on maternal self-reports (e.g., paroxysmal wheezing, abnormal crying and primary care visits), and as such possibly reflected maternal perceptions rather than being an objective measure of the infant's health. However, mothers have a generally good recall of postpartum acute health care visits (D'Souza-Vazirani et al., 2005), indicating that self-reports are likely to be accurate. Furthermore, variables such as food allergy and gastroesophageal reflux were based on self-reports of physician-determined diagnoses. Similarly, early-pregnancy maternal BMI was based on self-reported measures of weight and height. In our study, it was not possible to determine the specific number of infant doctor visits, but only whether a doctor had been visited during the first life year, leading to a generalised estimate of the health care received by the infant. Nevertheless, we had data on self-reported hospital treatments, which reflect more serious conditions. Analgesic medication supply was based on a self-report of the number of days when analgesics were supplied to the infants during the previous 12 months, and the use of this variable may possibly introduce recall bias. Furthermore, we had no information on the dosages of the supplied analgesics.

5. Conclusions

Our findings highlight the importance of recognizing women with postpartum EDS, as their children may be at higher risk of having or being perceived by their mother to have a health problem, and thus of receiving more medications. However, based on our results, postpartum EDS did not negatively impact on vaccination habits.

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CRediT authorship contribution statement

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Declaration of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2021.02.036.

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