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ORIGINAL RESEARCH ARTICLE

Risk of adverse perinatal outcomes in infants born to mothers with mental health conditions

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Abstract

Introduction: Maternal mental health conditions have been shown to affect perinatal outcomes negatively. However, knowledge on the impact of different types and severities of maternal mental health conditions is needed. The objective of this study was to determine the association between maternal mental health status and perinatal health outcomes in the infant.

Material and methods: This register-based cohort study included all live-born infants in Denmark born between 2000 and 2016. Exposed infants were grouped based on whether the mothers received mental health care in primary care settings only (minor conditions) or required specialized psychiatric intervention (moderate–severe conditions) within 12 months before childbirth. Modified Poisson regression analyses were applied to produce adjusted risk ratios (aRRs) for each perinatal outcome of interest. The primary outcomes were neonatal mortality, 5-minute Apgar scores <7 and <4 and newborn hospital admission during the neonatal period. Secondary outcomes included several neonatal morbidities such as respiratory distress syndrome and abstinence syndrome.

Results: A total of 952 071 infants were included in the analysis; 4.0% had mothers with minor mental health conditions and 2.9% had mothers with moderate–severe conditions. The risk of neonatal death in exposed infants was aRR 1.08 (95% CI 0.93–1.27) for minor mental health conditions and aRR 0.93 (95% CI 0.78–1.11) for moderate–severe conditions. Both exposure groups had increased risks of 5-minute Apgar scores <7 (minor: aRR 1.28, 95% CI 1.16–1.41; moderate–severe: aRR 1.49, 95% CI 1.34–1.66); 5-minute Apgar scores <4 (minor: aRR 1.10, 95% CI 0.93–1.30; moderate–severe: aRR 1.18, 95% CI 0.98–1.43), and hospital admission during the neonatal period (minor: aRR 1.20, 95% CI 1.17–1.23; moderate–severe: aRR 1.22, 95% CI 1.19–1.26) along with several neonatal morbidities. An explicit high risk was seen for abstinence syndrome (minor: aRR 10.30, 95% CI 8.40–12.63; moderate–severe: aRR 12.13, 95% CI 10.17–15.67).

Abbreviations: aRR, adjusted risk ratios; CI, confidence intervals; ICD-10, International Classification of Diseases, 10th revision.

Conclusions: Infants of mothers with moderate–severe and minor mental health conditions were at increased risks of multiple adverse perinatal outcomes. Effective supportive interventions to improve outcomes in both groups are needed.

KEYWORDS
Apgar score, child of impaired parents, infant, newborn, diseases, mental health, neonatal mortality, perinatology

1 | INTRODUCTION

Over the past few decades, mental health conditions in pregnant women have been found to affect not only the well-being of the mother, but also perinatal outcomes and the development of the child.[1-4] This is especially concerning as the prevalence of mental health conditions in women of childbearing age is high and believed to be increasing.[5] In Scandinavia, symptoms of mental health conditions have been reported in 14% of pregnant women.[6]

Psychiatric diagnostic criteria create well-defined groups for use in clinical research, and several studies have found associations between a range of psychiatric diagnoses in pregnant women, such as schizophrenia spectrum disorders and affective disorders, and adverse perinatal outcomes for their infants.[3,7,8] There is a lack of studies focusing on minor mental health conditions assessed by health professionals, for instance conditions not requiring specialist psychiatric care. Furthermore, the studies have mainly focused on depression.[2,4,9]

More knowledge is needed on perinatal health outcomes in infants born to mothers with mental health conditions of different types and severities to appropriately tailor and differentiate maternity care services.

We conducted a register-based, nationwide cohort study to determine the association between maternal mental health status and perinatal health outcomes in the infant. The comprehensive Danish national health and administrative registers and the organization of the mental healthcare services allowed us to differentiate maternal mental health conditions handled solely in primary-care settings from the more severe conditions that require psychiatric intervention.

Key message

This nationwide, register-based study showed that both minor and severe maternal mental health conditions increased the risk of multiple adverse perinatal outcomes such as low Apgar score, hospital admission, respiratory distress syndrome, feeding problems, jaundice, and abstinence syndrome.

2 | MATERIAL AND METHODS

2.1 | Study design and data sources

This nationwide cohort study was based on data from Danish registers. The data of individuals were linked across registers using the personal identification number that is assigned to all Danish residents at birth or upon the acquisition of Danish residency.

The project was approved by Statistics Denmark before gaining access to the data. The following registers,[10] were used:

- The Danish National Patient Register, which holds information on patient admissions, registered International Classification of Diseases, 10th revision (ICD-10) diagnoses, and infant Apgar scores in all Danish public hospitals.
- The Danish National Health Service Register, which holds information on services received by mothers in general practices and from private psychologists and psychiatrists.
- The Danish National Prescription Register, which holds information on all redeemed prescriptions and uses the anatomical therapeutic chemical classification.
- The Danish Medical Birth Register, which holds data on parity, maternal smoking status during pregnancy, and infant gestational age at the time of delivery.
- The Danish Death Register, which contains data on neonatal deaths.
- The Population Education Register, which holds information on maternal educational level.[11]
- The Population Statistics Register, which contains information on maternal age at the time of delivery, country of origin, and cohabitation status.

Overall, these national registers offer high-quality data. Data are collected prospectively on a routine basis across the entire country, and their completeness and validity are, in general, considered to be high.[10]

2.2 | Setting and participants

The study population included all live-born infants born in Denmark between January 1, 2000 and December 31, 2016. The infants were

followed through the neonatal period, from birth until the 28th day of life. Gestational age was determined either by use of Naegels Rule or first-trimester ultrasonography (2000–2003) in the first trimester of pregnancy,[12] and from 2004 routinely by use of first-trimester ultrasonography as part of the national maternity care program.[13] This program is offered free of charge to all pregnant women in Denmark as part of a universal, publicly funded healthcare system in which general practitioners provide first contact care and serve as gatekeepers to practicing specialists such as psychiatrists and specialized, secondary healthcare services. Infants were excluded if they were born to mothers with a mental disorder caused by psychoactive substance use (ICD-10 F1 diagnoses), if their mothers did not live in Denmark during the exposure period, or if the mother's personal identity number was missing.

2.3 | Exposure

Based on the level of mental health care, exposure was defined as maternal mental health conditions treated solely at primary healthcare settings (minor) or requiring a higher level of mental health care (moderate–severe) registered within the 12 months before childbirth (Table 1). The reference group included infants of mothers without any registered mental health conditions during the exposure period.

2.4 | Perinatal outcomes

The primary outcomes were neonatal mortality, 5-minute Apgar scores <7, 5-min Apgar scores <4, and hospital admission during the neonatal period for at least one night. These outcome measures are important indicators of the health of the child immediately after birth and during the neonatal period.[14,15]

Secondary outcome measures were neonatal morbidities including respiratory distress syndrome, abstinence syndrome, hypoglycemia, neonatal seizures, neonatal bacterial sepsis, jaundice and feeding problems, dehydration and/or failure to thrive.

2.5 | Covariates

The following covariates were included: country of origin (Nordic, other Western, and non-Western countries), cohabitation status (living with a partner or not), educational level (postsecondary education or not), gestational diabetes (yes/no), and maternal smoking during pregnancy (smokers/nonsmokers). Mothers were considered nonsmokers if they did not smoke during pregnancy or stopped smoking during the first trimester.[16] Finally, maternal age at the time of birth and gestational age at birth were included. To minimize residual confounding when adjusting for a continuous variable, maternal age and gestational age were adjusted for using a restricted cubic spline with three knots.[17]

This cohort includes births over several years, which leads to structural changes during the follow-up period, for example the guideline for perinatal care in 2009,[18] and an increase in prevalence of poor mental health in Danish adults.[19] This issue was handled in the analyses by controlling for calendar year using a restricted cubic spline with three knots.[17]

2.6 | Statistical analyses

For each overall exposure group, absolute numbers and proportions for all covariates and outcome variables of interest were determined. To accommodate the correlation between infants of the same mother, we used a generalized estimating equation with an exchangeable correlation structure to fit a generalized linear model with log link function assuming a Poisson distribution using robust variance estimation. Unadjusted and adjusted risk ratios (aRR) with 95% confidence intervals (CI) for all primary and secondary

TABLE 1 Criteria for exposure

Exposure group	Specifications (at least one criterion)	Exclusion criteria
Minor mental health conditions (treated in primary care)	At least two prescriptions of antidepressants (ATC N06AB, N06AX)	Meeting any of the moderate–severe mental health condition criteria
	At least two prescriptions of benzodiazepines (ATC N03AE, N05BA, N05CD, N05CF)	
	At least two therapy talks in a general practice	
	At least two psychometric tests in a general practice	
	At least one contact with a private psychologist	
Moderate–severe mental health conditions (treated in specialized care)	Any psychiatric diagnosis (ICD-10 F00–09, F20–99) registered at psychiatric hospital, excluding mental and behavioral disorders due to psychoactive substance use (F10–19)	None
	Mental health conditions treated at psychiatrist practicing outside psychiatric hospital (including child and adolescent psychiatrist)	

Note: Consensus definition of groups of mental health conditions.

Abbreviations: ATC, anatomical therapeutic chemical; ICD-10, International Classification of Diseases, 10th revision.

outcomes were calculated. The adjusted regression analyses were based on complete case data. We performed a sensitivity analysis with two mutually exclusive exposure periods, one of active mental health condition measured 0–12 months and another of previous mental health condition measured 12 to 24 months before birth. To further examine whether the presence of siblings affected the results, a sensitivity analysis including only firstborn infants was made. Subgroup analyses were performed to estimate the risks of maternal mental health conditions across subtypes. All analyses were carried out using STATA version 16.1.

2.7 | Ethical approval

According to Danish legislation, approval from an ethics committee is not required for register-based research when it does not involve human biological material.[20]

3 | RESULTS

During the study period, 1 050 385 infants were born alive in Denmark. After the exclusion of infants born to mothers with an ICD-10 F1 diagnosis (n = 7759) and/or whose exposure status could not be ascertained (n = 21 553), 1 021 126 (97.2%) infants were included in the analyses. About 4.0% (n = 40 435) of infants had mothers with minor mental health conditions, and 2.9% (n = 29 919) were born to mothers with moderate–severe mental health conditions (Figure 1).

The educational level of mothers with mental health conditions was on average lower than the level for women with no record of mental health conditions (Table 2). A higher number of mothers with mental health conditions smoked during pregnancy, suffered from gestational diabetes, and lived without a partner than mothers without mental health conditions.

Mothers with minor mental health conditions tended to be older, more frequently multiparous, and born in a Nordic country; whereas mothers with moderate–severe mental health conditions were younger, more frequently primiparous, and born in non-Western countries. Infants of mothers with mental health conditions were more often born preterm.

3.1 | Primary outcomes

Frequencies and risk ratios for primary outcomes in the overall study groups are presented in Figure 2. The associations between mental health conditions and neonatal mortality were not statistically significant. For infants whose mothers had minor mental health conditions, the risk tended to be increased (aRR 1.08, 95% CI 0.93–1.27) compared with infants whose mothers were in the reference group. For infants, whose mother had moderate–severe mental health conditions the risk tended to be decreased (aRR 0.93, 95% CI 0.78–1.11) compared with the reference group.

The risk of a 5-min Apgar score <7 was increased for both infants of mothers with minor (aRR 1.28, 95% CI 1.16–1.41) and infants of mothers with moderate–severe mental health conditions (aRR 1.49, 95% CI 1.34–1.66), and this risk was stronger in magnitude for the latter group.

The risk of a more severe 5-min Apgar score (ie <4) was also increased for both exposure groups, but this was not statistically significant (minor: aRR 1.10, 95% CI 0.93–1.30; moderate–severe: aRR 1.18, 95% CI 0.98–1.43).

Infants of mothers with mental health conditions were admitted more frequently to the hospital during the neonatal period compared with the reference group (minor: aRR 1.20, 95% CI 1.17–1.23; moderate–severe: aRR 1.22, 95% CI 1.19–1.26).

3.2 | Secondary outcomes

Infants born to mothers with mental health conditions, regardless of the severity level, were at significantly higher risks of respiratory distress syndrome, bacterial sepsis, abstinence syndrome, seizures, jaundice (except for the minor mental health condition exposure group), hypoglycemia and feeding problems, dehydration, and/or failure to thrive during the neonatal period compared with to infants in the reference group (Figure 3). Estimates for these outcomes

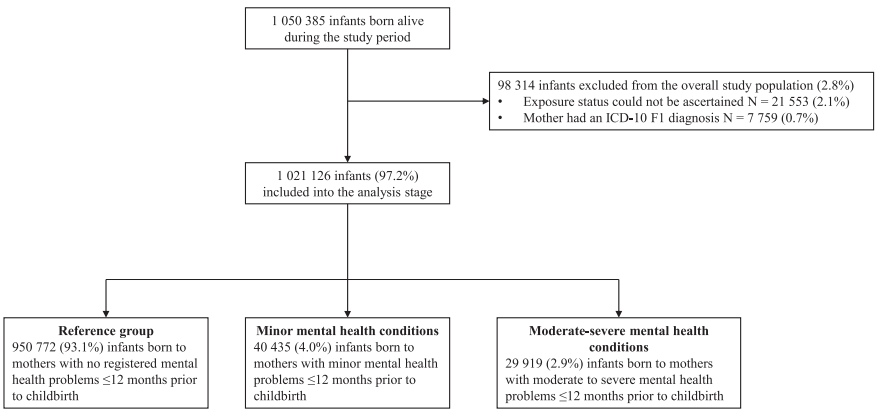


FIGURE 1 Flow diagram of the study population

TABLE 2 Baseline sociodemographic and clinical characteristics by exposure status

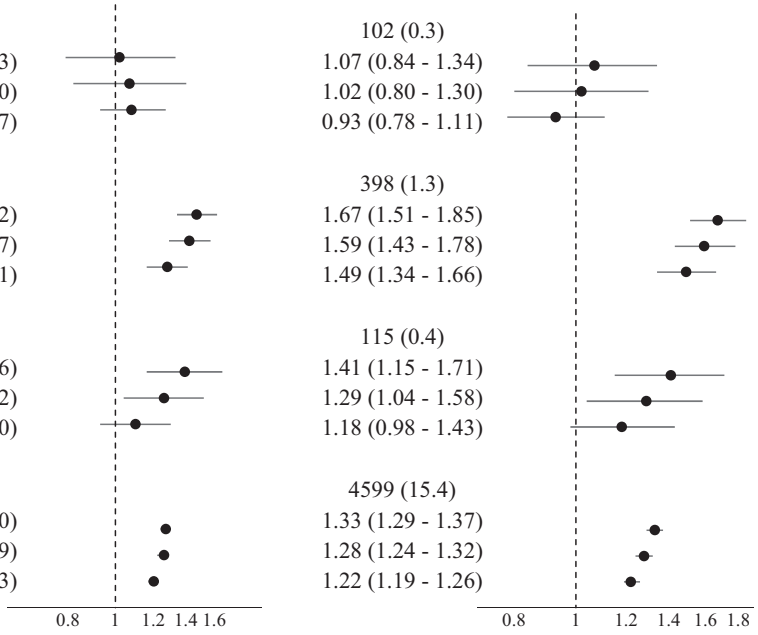
	Reference group	Minor mental health condition	Moderate–severe mental health condition
	N = 950 772	*N* = 40 435	*N* = 29 919
	%	%	%
Age			
≤20 years	1.2	1.0	2.7
21–34 years	73.8	69.8	71.2
≥35 years	25.0	29.2	26.1
Parity			
Primiparous women	44.1	42.6	48.1
Multiparous women	54.7	56.4	50.6
Missing	1.2	1.0	1.3
Gestational age			
<28 weeks	0.4	0.6	0.5
28–31 weeks	0.7	1.1	1.1
32–36 weeks	5.4	7.6	7.8
≥37 weeks	93.4	90.5	90.4
Missing	0.1	0.1	0.1
Country of origin			
Nordic country	84.6	90.1	84.1
Other Western country	0.5	0.4	0.4
Other	7.2	4.6	8.6
Missing	7.7	4.8	6.9
Cohabitation status			
Living with partner	93.6	88.9	84.1
Not living with partner	6.1	11.0	15.8
Missing	0.3	0.1	0.1
Educational level			
Post-secondary education	45.3	42.9	31.7
No post-secondary education	54.7	57.1	68.3
Missing	1.4	0.9	1.3
Smoking status			
Non-smokers	86.1	80.9	75.5
Smokers	11.9	16.9	22.3
Missing smoking status	2.0	2.2	2.2
Gestational diabetes			
No	98.5	97.7	97.6
Yes	1.5	2.3	2.4

were higher among infants of mothers with moderate–severe mental health conditions than for children of mothers with minor mental health conditions, except for seizures and sepsis. A particularly strong association was found with neonatal abstinence syndrome (minor: aRR 10.30, 95% CI 8.40–12.63; moderate–severe: aRR 12.63, 95% CI 10.17–15.67).

3.3 | Supplementary analyses

Table 3 presents aRRs for primary outcomes in subgroups within minor and moderate–severe mental health condition exposure groups. Infants born to unaffected mothers served as the reference group.

	Maternal mental health conditions		
	None	Minor	Moderate-severe
Neonatal mortality			
N (%)	2737 (0.3)	187 (0.5)	102 (0.3)
Unadjusted RR (95% CI)	1	1.02 (0.79 - 1.33)	1.07 (0.84 - 1.34)
Adjusted* RR (95% CI)	1	1.07 (0.82 - 1.40)	1.02 (0.80 - 1.30)
Adjusted^ RR (95% CI)	1	1.08 (0.93 - 1.27)	0.93 (0.78 - 1.11)
Apgar score < 7/5 min			
N (%)	7455 (0.8)	483 (1.2)	398 (1.3)
Unadjusted RR (95% CI)	1	1.47 (1.34 - 1.62)	1.67 (1.51 - 1.85)
Adjusted* RR (95% CI)	1	1.42 (1.29 - 1.57)	1.59 (1.43 - 1.78)
Adjusted^ RR (95% CI)	1	1.28 (1.16 - 1.41)	1.49 (1.34 - 1.66)
Apgar score < 4/5 min			
N (%)	2508 (0.3)	164 (0.4)	115 (0.4)
Unadjusted RR (95% CI)	1	1.39 (1.16 - 1.66)	1.41 (1.15 - 1.71)
Adjusted* RR (95% CI)	1	1.26 (1.04 - 1.52)	1.29 (1.04 - 1.58)
Adjusted^ RR (95% CI)	1	1.10 (0.93 - 1.30)	1.18 (0.98 - 1.43)
Hospital admission			
N (%)	107621 (11.3)	5899 (14.6)	4599 (15.4)
Unadjusted RR (95% CI)	1	1.27 (1.24 - 1.30)	1.33 (1.29 - 1.37)
Adjusted* RR (95% CI)	1	1.26 (1.22 - 1.29)	1.28 (1.24 - 1.32)
Adjusted^ RR (95% CI)	1	1.20 (1.17 - 1.23)	1.22 (1.19 - 1.26)



**Adjusted for calendar year, maternal age, education, smoking during pregnancy, country of origin, cohabitation status and gestational diabetes*
^Adjusted for calendar year, maternal age, education, smoking during pregnancy, country of origin, cohabitation status, gestational diabetes and gestational age

FIGURE 2 Percentages and relative risks (95% CI) of the primary perinatal outcomes in each exposure group

For subgroups (antidepressant/benzodiazepine use, therapy talk/psychometric test in general practice, and/or contacts with psychologist) within the minor mental health conditions group, the trends in findings were consistent with those of the main analysis (Figure 2). However, statistical significance was not present for some outcomes in the subgroups of the minor mental health conditions group. For infants of mothers who had redeemed at least two prescriptions of antidepressants and/or benzodiazepines during the exposure period, the associations were consistently stronger compared with those observed in the main analysis.

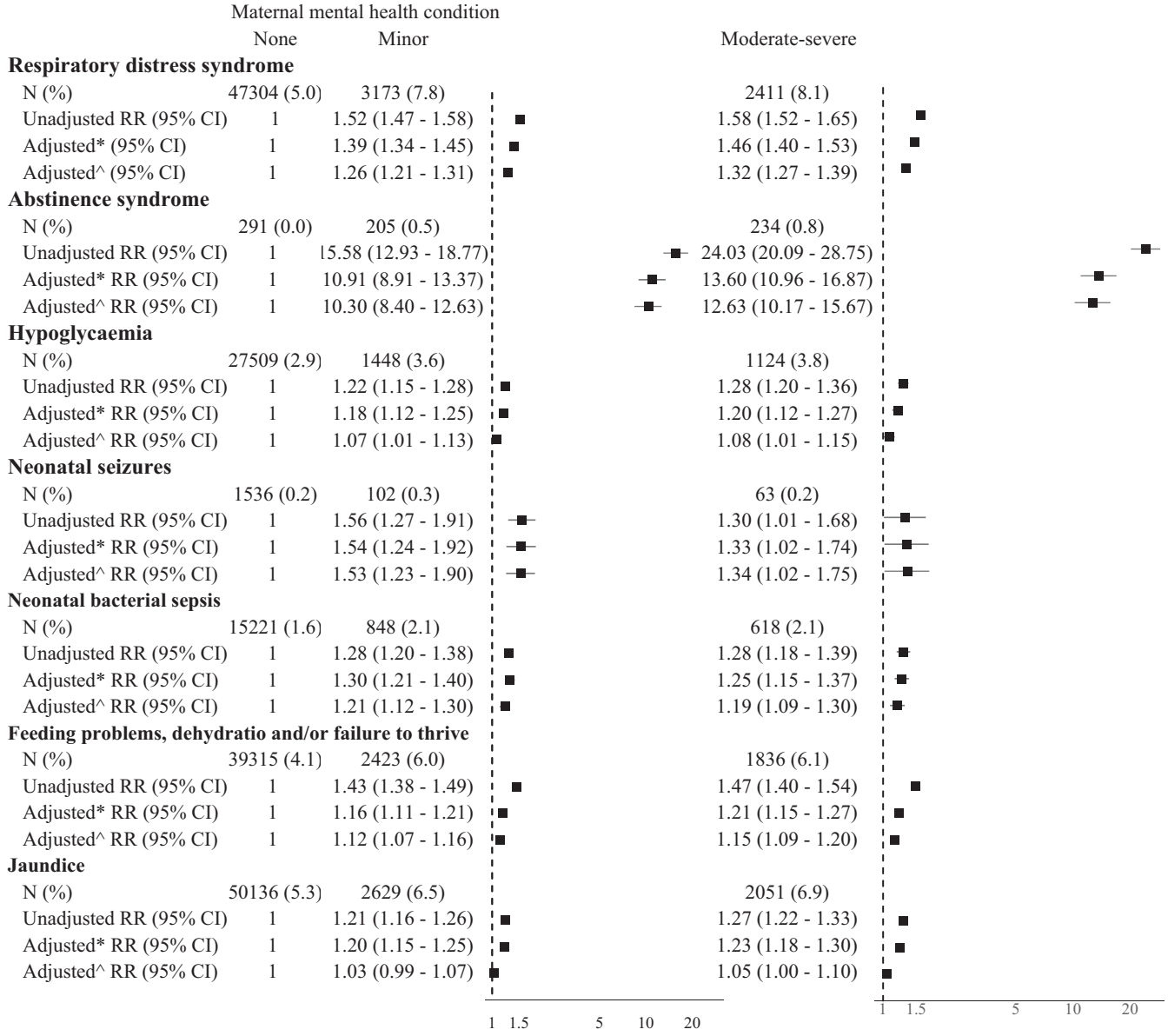
For all subgroups within the moderate–severe mental health conditions group, such as an ICD-10 diagnosis schizophrenia spectrum disorder (DF20–29), bipolar disorder (DF31), depression (DF32–33), or anxiety disorder (DF40–41), the trends in findings were consistent with those of the main analysis. For the subgroups of infants born to mothers diagnosed with a schizophrenia spectrum disorder, bipolar disorder, unipolar depression, or post-traumatic stress disorder, however, trends in risk estimates were even stronger compared with the overall risk estimates for the moderate–severe group.

For previous maternal mental health 12–24 months before birth, the associations were weakened and only statistically significant for hospital admission (Supporting Information Table S1). Overall, the association between adverse perinatal outcomes and maternal mental health conditions was slightly stronger when including only firstborn infants (Supporting Information Table S2). The estimates of the analysis including only firstborn infants were slightly higher than those of the main analysis; most evident for Apgar score <7 and moderate–severe mental health conditions: aRR 1.63, 95% CI 1.39–1.91.

4 | DISCUSSION

Both infants of mothers with minor as well as moderate–severe mental health conditions were at higher risks of 5-min Apgar scores <7 and of hospital admission during the neonatal period than infants born to unaffected mothers. Infants born to mothers with minor mental health conditions were also at risk of having 5-min Apgar scores <4. Higher risks were found for respiratory distress syndrome, abstinence syndrome, hypoglycemia, bacterial sepsis, jaundice, and problems related to hydration and nutrition during the neonatal period in both exposure groups.

The findings indicate that maternal mental health conditions can adversely impact the health of the child at birth and during the neonatal period, regardless of whether these conditions are handled in primary care settings only (minor conditions) or require psychiatric specialist care (moderate–severe conditions). Moderate–severe maternal mental health conditions were found to be more strongly associated with the risk of 5-min Apgar scores <7 and hospital admission during the neonatal period than minor maternal mental health conditions, suggesting a potential dose–response relationship. The more severe risk of 5-min Apgar scores <4 was, however,



**Adjusted for calendar year, maternal age, education, smoking during pregnancy, country of origin, cohabitation status and gestational diabetes*

^Adjusted for calendar year, maternal age, education, smoking during pregnancy, country of origin, cohabitation status, gestational diabetes and gestational age

FIGURE 3 Percentages and relative risks (95% CI) of the secondary perinatal outcomes in each exposure group

only non-significantly increased. A similar relationship was observed for neonatal death. One possible explanation is that minor mental health conditions managed only in primary care may be easily overlooked. In Denmark, pregnant women are offered psychosocial risk assessment in early pregnancy and women with mental health conditions are offered a higher level of care and tailored services.[21] Women with more severe mental health conditions may, however, be more easily identifiable in patient records and receive more clinical attention compared with women with minor mental health conditions. Our findings indicate that increased clinical and research attention should be directed towards both groups and that more effective preventive strategies are needed.

As several types of psychotropic medications have been associated with low 5-min Apgar scores,[22,23] it is likely that at least some of the observed increase in the risk of low Apgar scores among infants born to mothers with mental health conditions was mediated through the maternal use of psychotropic drugs during pregnancy. The results for infants of mothers with previous mental health conditions 12–24 months before birth indicate an effect not related to in utero exposure but also suggest impact of general psychosocial vulnerability.

Perinatal maternal mental health is a complex construct, and the exact mechanisms by which mental health conditions mediate adverse perinatal outcomes remains to be elucidated. It is likely that

TABLE 3 Primary perinatal outcomes in subgroups of minor and moderate–severe mental health conditions

		Neonatal mortality		Apgar score <7 at 5 min		Apgar score <4 at 5 min		Hospital admission	
	N	%	aRR	%	aRR	%	aRR	%	aRR
Minor mental health condition									
Antidepressant and/or benzodiazepine use	15 120	0.6	1.11 (0.91–1.36)	1.7	1.59 (1.39–1.83)	0.5	1.13 (0.88–1.44)	14.6	1.34 (1.28–1.40)
Therapy talk/psychometric test in GP	11 853	0.5	1.23 (0.93–1.64)	1.1	1.23 (1.02–1.47)	0.4	1.13 (0.83–1.54)	11.5	1.15 (1.09–1.22)
Contact with private psychologist	19 122	0.3	0.93 (0.70–1.23)	0.9	1.02 (0.87–1.19)	0.3	1.03 (0.79–1.34)	11.4	1.16 (1.11–1.21)
Moderate–severe[b]									
Schizophrenia spectrum disorder (F20–29)	1018	[a]	[a]	1.9	1.80 (1.11–2.92)	[a]	[a]	13.8	1.30 (1.10–1.54)
Bipolar disorder (F31)	532	[a]	[a]	1.5	1.32 (0.57–3.06)	[a]	[a]	15.2	1.30 (1.03–1.64)
Depression (F32–33)	7838	0.4	1.20 (0.86–1.68)	1.7	1.99 (1.67–2.38)	0.5	1.92 (1.41–2.61)	13.9	1.32 (1.24–1.40)
Anxiety disorders (F40–41)	5311	[a]	[a]	0.9	1.07 (0.79–1.46)	0.3	0.95 (0.53–1.68)	11.6	1.10 (1.02–1.20)
Obsessive compulsive disorder (F42)	847	[a]	[a]	1.8	2.19 (1.32–3.64)	[a]	[a]	12.6	1.20 (1.00–1.45)
Post-traumatic stress disorder (F43.1)	676	[a]	[a]	2.1	1.92 (0.95–3.87)	[a]	[a]	13.8	1.27 (0.99–1.62)
Eating disorder (F50)	1532	[a]	[a]	1.4	1.69 (1.10–2.60)	[a]	[a]	12.1	1.24 (1.08–1.42)
Personality disorder (F60–62)	3371	[a]	[a]	1.5	1.39 (1.06–1.82)	[a]	[a]	13.1	1.17 (1.07–1.29)
Intellectual disabilities (F70–79)	116	[a]	[a]	[a]	[a]	[a]	[a]	14.7	1.09 (0.68–1.76)

Note: Adjusted for calendar year, maternal age, education, smoking during pregnancy, country of origin, cohabitation status, gestational diabetes, and gestational age.

Abbreviations: aRR, adjusted risk ratio; GP, general practitioner.

[a]Too few observations.

[b]International Classification of Diseases, 10th revision, codes used for conditions.

the causal pathways include socioeconomic, psychosocial, biological, and behavioral factors. There is plenty of evidence that disadvantageous maternal socioeconomic circumstances influence both the maternal mental well-being and infant perinatal outcomes negatively.[24,25] Other mechanisms are related to psychosocial factors, such as social support and social stigma, which may explain some of the observed associations in this study. Plausible biological pathways include the neuroendocrine and inflammatory alterations induced by psychosocial stress that may impact fetal development and health, but there is also evidence of shared genetic susceptibility to some mental disorders and adverse perinatal outcomes.[26] Furthermore, smoking, substance abuse, unhealthy nutrition, a general lack of self-care, and non-attendance at antenatal care have been suggested to be mediating mechanisms.[9,27] The possible risks of this study might therefore be even higher as we adjusted for smoking during pregnancy.

The statistically significant associations reported in this study (except for neonatal abstinence syndrome) are relatively modest. A noticeable association with neonatal abstinence syndrome was also reported by Rusner et al (adjusted odds ratio [aOR] 52.2, 95% CI 36.5–74.7),[7] and Vigod et al (aOR 53.7, 95% CI 36.8–78.4).[3] However, the estimates should be interpreted in light of the high prevalence of

mental health conditions among expecting mothers (as documented in this study) and the severity of the investigated neonatal outcomes. With approximately 1 in 15 infants being exposed to maternal mental health conditions in our nationally representative study sample, even modestly increased risks of severe and/or common adverse perinatal outcomes may produce a high burden at the population level and be relevant to maternal and perinatal health.

Overall, our findings emphasize the relevance of universal perinatal mental health screening in early pregnancy and preventive, supportive services for women with moderate–severe as well as minor mental health conditions. Preventive strategies should address maternal mental well-being, underlying social determinants, and modifiable risky health behaviors.[28]

The major strengths of this study are a large sample size, providing high statistical power to detect even modest but potentially clinically relevant associations as well as the use of data from multiple Danish nationwide registers, ensuring individual follow up and high data validity. Furthermore, free access to health care, which includes a national maternity care program, limits the risk of confounding due to differences in clinical practices and access to care.

Limitations include the observational study design with its inherent possibility of residual confounding. Despite the ability to control for a wide range of potential confounders, data were not available for maternal pre-pregnancy body mass index. However, we were able to control for gestational diabetes, which is strongly associated with maternal pre-pregnancy body mass index,[29] and can therefore be expected to make up for some of this unmeasured potential confounding. Additionally, infants born to women with mental health conditions who received no services could have been erroneously included in the reference group. The prevalence of mental conditions and the reported associations are therefore likely to be somewhat underestimated. Further, both mild and moderate severities of, for example, depression and anxiety are treated in general practice. The minor category might therefore reflect less severe and less complicated conditions rather than only those of minor severity. Moreover, psychotropic drug use is based on redeemed prescriptions and not actual knowledge of drug use. Finally, as the overall study population only included live-born infants, no data on stillbirths were available.

5 | CONCLUSION

Regardless of whether the maternal mental health conditions had been treated in primary care settings only (minor conditions, 4.0%) or had required psychiatric specialist care (moderate to severe conditions, 2.9%), these infants were at significantly increased risk of multiple adverse neonatal outcomes compared with infants born to unaffected mothers.

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CONFLICTS OF INTEREST

None.

AUTHOR CONTRIBUTIONS

SH, LFC, KF and CO participated in the design of the study. SH and LFC planned the analyses. SH managed the data, performed the analysis. LFC, SH, KF, and CO contributed to interpreting the data. LFC wrote the first draft of the manuscript, that was further thoroughly edited by SH. SH, LFC, KF and CO gave input to all phases of the study, contributed to critical revision of the manuscript and approved the final version.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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