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ORIGINAL RESEARCH ARTICLE

Perinatal antidepressant use and breastfeeding outcomes: Findings from the Norwegian Mother, Father and Child Cohort Study

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Abstract

Introduction: Antidepressant use is common in the perinatal period, but there are concerns that it can negatively impact on breastfeeding outcomes. The aim of this study was to examine the effects of perinatal antidepressant use on breastfeeding initiation and duration.

Material and methods: This was a retrospective analysis of 80 882 mother–infant dyads in the Norwegian Mother, Father and Child Cohort Study (MoBa). Women were first classified according to self-reported mental disorders and timing of antidepressant use before and/or after gestational week 28 (i.e., early-mid–gestation and/or late-gestation use). We subsequently classified women according to self-reported mental disorders and antidepressant use postpartum and whether antidepressants were continued from late gestation or were new/restarted. Breastfeeding outcomes included breastfeeding initiation as well as predominant or any breastfeeding and abrupt breastfeeding discontinuation until 6 months.

Results: Late-gestation antidepressant use was associated with a reduced likelihood of breastfeeding initiation (adjusted relative risk [aRR] 0.93; 95% confidence interval [CI] 0.90–0.97) but not predominant (aRR 0.96; 95% CI 0.67–1.39) or any (aRR 1.00; 95% CI 0.93–1.07) breastfeeding at 6 months compared with unexposed women with mental disorders. When examined according to postnatal antidepressant use, no differences in predominant (aRR 0.94; 95% CI 0.60–1.48) or any breastfeeding (aRR 0.99; 95% CI 0.91–1.07) at 6 months were evident among women who continued antidepressant use from late gestation into the postpartum period compared with unexposed women with mental disorders. In contrast, new/restarted antidepressant use postpartum was associated with a reduced likelihood of predominant (aRR 0.37; 95% CI 0.22–0.61) and any (aRR 0.49; 95% CI 0.42–0.56) breastfeeding at 6 months,

Abbreviations: ATC, Anatomical Therapeutic Chemical Classification System; BMI, body mass index; GW, gestational week; MBRN, Medical Birth Registry of Norway; MoBa, Norwegian Mother, Father and Child Cohort Study; Q1, first questionnaire; Q4, fourth questionnaire; RR, relative risk.

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as well as increased risk of abrupt breastfeeding discontinuation (aRR 2.64; 95% CI 2.07–3.37) compared with the unexposed women with mental disorders.

Conclusions: A complex relation exists between depression, antidepressant use, and breastfeeding outcomes. Antidepressant use in late pregnancy was associated with a reduced likelihood of breastfeeding initiation but not breastfeeding duration or exclusivity. In contrast, initiating or restarting antidepressants postpartum was associated with poorer breastfeeding outcomes. Overall, women taking antidepressants and women with a mental disorder may benefit from additional education and support to improve breastfeeding rates and promote maternal and infant health and wellbeing.

KEYWORDS

antidepressants, breastfeeding, mental health problems, MoBa, postpartum, pregnancy

1 | INTRODUCTION

Antidepressants are commonly required to treat preexisting or new-onset mental disorders during pregnancy and postnatally, with estimates of use ranging from 1 to 4% in Europe[1] to up to 8% in the USA.[2] Many studies have investigated the impacts of antidepressant use during pregnancy on perinatal outcomes and child development,[3] but the impacts of antidepressant use during breastfeeding are less well explored. The need to take antidepressants could negatively impact on breastfeeding outcomes in a number of ways. First, concerns regarding infant exposure to antidepressants through breast milk may result in some women choosing either not to breastfeed or to breastfeed but discontinue their antidepressant.[4] Second, serotonin has been identified as an important regulator of lactation homeostasis, suggesting that medications that inhibit serotonin reuptake may disrupt the normal physiological process associated with lactation.[5]

Few studies have investigated breastfeeding outcomes among women taking antidepressants.[6–10] Despite the fact that the risks to the breastfed infant are considered low,[11] the choice to breastfeed when taking an antidepressant may pose a dilemma for some women and their clinicians.[8,12,13] It has previously been suggested that women taking antidepressants have lower rates of breastfeeding intention and initiation,[8,9] but the role of underlying maternal mental illness remains unclear. Further, studies have largely focused on investigating short-term breastfeeding outcomes (i.e., <3 months). As such, the relation between antidepressant use and longer-term breastfeeding outcomes remains uncertain.

Given the well-known maternal and infant benefits of breastfeeding, a better understanding of modifiable risk factors, such as antidepressant use, on breastfeeding outcomes is crucial. Therefore, given the paucity of existing evidence, this study aimed to evaluate the association between antidepressant use during and following pregnancy on breastfeeding outcomes up to 6 months postpartum, accounting for underlying maternal mental health status.

Key message

In this study, late-gestation antidepressant use was independently associated with a reduced likelihood of breastfeeding initiation. Restarting or initiating antidepressant use in the postpartum period was also associated with an increased risk of abrupt breastfeeding discontinuation.

2 | MATERIAL AND METHODS

2.1 | Study design and data source

The present analyses are based on data from the Norwegian Mother, Father and Child Cohort Study (MoBa), a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health linked to the Medical Birth Registry of Norway.[14] Participants were recruited from all over Norway from 1999 to 2008. The women consented to study participation in 41% of the pregnancies. The cohort now includes 114 500 children, 95 200 mothers, and 75 200 fathers.[15] The current study is based on version 7 of the quality-assured data files released for research.

The study cohort consisted of all 85 530 mother–infant dyads in MoBa who had delivered a singleton live-born infant and who had information available in the Medical Birth Registry of Norway (MBRN) as well as from one prenatal (Q1) and one postnatal (Q4) self-administered questionnaire (Figure 1).Women who did not answer questions about breastfeeding duration (n = 4575) or provide details of timing of antidepressant use during or following pregnancy (n = 73) were excluded, leaving a final cohort of 80 882.

The first questionnaire (Q1) was sent out during pregnancy (weeks 13–17), and the fourth (Q4) was sent out at 6 months postpartum. English translations of the questionnaires can be found on the MoBa website (https://www.fhi.no/en/studies/moba/). Pregnancy

and birth records from the MBRN are linked with the MoBa cohort using each women's unique identification number.

2.2 | Ascertainment of exposure

Information on antidepressant exposure was collected from Q1 and Q4. In Q1, women reported the name of the medication taken and timing of use either pre-pregnancy and/or during pregnancy, whereas in Q4 use was reported in three categories: late pregnancy, 0–3 months postpartum, or 4–6 months postpartum. Drug classification was based on the anatomical therapeutic chemical (ATC) classification system, with antidepressant exposure defined as exposure to a drug belonging to the ATC group N06A.

Information on mental health was collected from Q1 and Q4. In Q1, women were given a list of previous/concurrent illnesses, including specifically depression, anxiety, or other mental disorders, and asked whether they had experienced them "before pregnancy" or "during pregnancy." In Q4, women were asked if they had experienced "mental health problems" in the "last part of pregnancy" or "after birth."

Utilizing data on both timing of antidepressant use and mental disorders, we constructed two study samples for our analysis.

Study sample 1 was based on antenatal exposures only. Two antidepressant-exposed groups were defined.

1. Early-mid–gestation antidepressant use only: use only prior to <29 gestational weeks (GW).
2. Late-gestation antidepressant use: any use >29 GW, can include use <28 GW.
3. Unexposed mental disorder comparison. This group included women with self-reported mental disorders in the 6 months prior to or during pregnancy but no antidepressant use during pregnancy.
4. Population comparison: This group included women with no self-reported mental disorder in the 6 months prior to or during pregnancy and no reported antidepressant use in the 6 months prior to or during pregnancy.

Study sample 2 group allocation was based on antenatal and postnatal exposures and consisted of the following groupings:

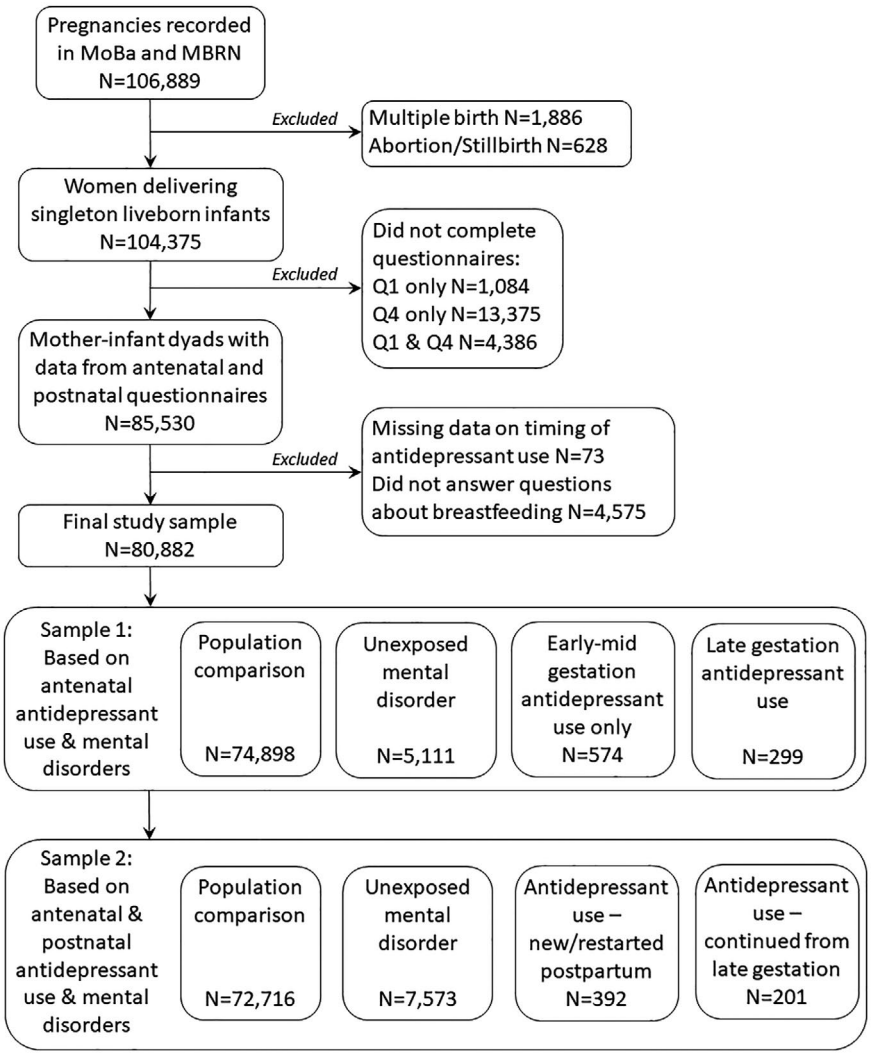

FIGURE 1 Study flow chart. MBRN, Medical Birth Registry of Norway; MoBa, Norwegian Mother, Father and Child Cohort Study

1. Antidepressant use continued from late pregnancy: late gestation and postnatal antidepressant use.
2. New/restarted antidepressant use: postnatal antidepressant use, but no use in late gestation.
3. Unexposed mental disorder comparison: self-reported mental disorder during pregnancy or following pregnancy, but no antidepressant use in postnatal period.
4. Population comparison: no history of mental disorder during or after pregnancy and no reported antidepressant use postpartum.

2.3 | Ascertainment of outcomes

Data on the infant feeding variables came from Q4, administered at 6 months postpartum. The three questionnaire items used in this analysis described infant feeding during the first week after birth; the kinds of liquids (i.e., milk, formula, water, or sugar water) that the infant received at months 0, 1, 2, 3, 4, 5, and 6; and the month in which the child started receiving complementary solids. We evaluated women's reports of full or any breastfeeding for 6 months postpartum as well as abrupt breastfeeding discontinuation.

Categorization of breastfeeding outcomes is consistent with previous MoBa studies.[16,17] We could not define exclusive breastfeeding because not all versions of the questionnaire included questions about use of water, water-based drinks, and fruit juice beyond the first week of the infant's life.

Breastfeeding practices were classified as follows:

- No breastfeeding: Infants received only an infant formula or other milk or solid food
- Partial/mixed breastfeeding: infants received breast milk along with any infant formula or other milk and/or solid food
- Predominant breastfeeding: infants received breast milk only without any infant formula or other milk and/or solid food
- Any breastfeeding: both full/predominant and partial breastfeeding at 6 months.

In our analysis, "abrupt breastfeeding discontinuation" was defined as cessation of predominant and any breastfeeding within the same month postpartum.

Information on nipple pain, mastitis, or other breastfeeding problems within the first month postpartum were ascertained from Q4.

2.4 | Covariates

Maternal age, pre-pregnancy body mass index (BMI; underweight <18.5 kg/m^2, normal weight 18.5–25 kg/m^2, or overweight >25 kg/m^2 according to World Health Organization guidelines), education (primary or secondary vs. university or higher), income (low, average, high), marital status (married or cohabiting vs other), parity (multiparous vs. primiparous), and illicit substance use during pregnancy were all ascertained from Q1. Smoking (ever during pregnancy vs. not during pregnancy) was ascertained by combining information from self-report and linkage to the MBRN. Method of delivery (vaginal vs. cesarean section) and preterm birth (delivery <37 weeks' completed gestation) were ascertained from the MBRN. Co-medication with other psychotropic medications during pregnancy and/or postpartum was defined as exposure to a drug belonging to the ATC group N05, including antipsychotics, anxiolytics, and hypnotics/sedatives.

The severity of maternal depressive and anxiety symptoms was measured at 30 weeks' gestation using the short version of The Hopkins Symptom Checklist_25 (SCL-25), namely, the 5-item (SCL-5).[18] Scores were averaged across the five items and standardized using *z*-scores. Lifetime history of major depression was measured in Q1 via five key depressive symptoms closely corresponding to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-III criteria for lifetime major depression.[19]

No imputation was undertaken for missing data, and all analyses were performed as complete case analyses.

2.5 | Statistical methods

The association between antidepressant use and breastfeeding outcomes was evaluated using a generalized linear model (Poisson distribution) with robust variance estimates, estimating relative risks (RRs) and 95% confidence intervals (CIs). Impact of antidepressant use on breastfeeding initiation was investigated within the whole study sample, whereas effects on other breastfeeding outcomes were restricted to women who initiated breastfeeding.

Confounders were identified through literature review and selected through the use of directed acyclic graphs (Figure S1).[20] Analyses of antenatal antidepressant use patterns were adjusted for possible confounders, including maternal age, BMI at conception, parity, marital status, education level, income, smoking status, use of other psychotropic medications during pregnancy, use of illicit drugs, and lifetime history of major depression. Analyses of postnatal antidepressant use patterns included further adjustment for preterm birth and cesarean section delivery.

We examined the robustness of our findings in a set of sensitivity subanalyses. These included adjustment for antenatal mental health symptoms during pregnancy (SCL in questionnaire 3) and restricting the analysis to those participating in MoBa for the first time. Additional sensitivity analyses for the postnatal exposure cohort included adjustment for postnatal mental health problems and breastfeeding problems in the first month postpartum and restricting the analysis to those reporting antidepressant use within 0–3 months postpartum. All statistical analyses were undertaken using STATA SE 16 (Stata).

2.6 | Ethical approval

This study obtained a license from the Norwegian Data Inspectorate (01/4325) and approval from the Regional

Committee for Medical Research Ethics (S-97045, S-95113; October 9, 1998). Ethics approval was also obtained from the Human Ethics Committee, La Trobe University, Australia (No. FHEC13/015; April 15, 2013). All participants gave written informed consent before participation.

3 | RESULTS

The study sample included 80 882 mother–infant dyads (Figure 1). Baseline sociodemographic, lifestyle, and health characteristics of the study sample according to timing of antidepressant use during pregnancy are shown in Table 1. Women reporting early-mid– or late-gestation antidepressant use were more likely to be overweight/obese, primiparous, have a lower income, use other psychotropic medications, and to smoke cigarettes than women in the unexposed mental disorder comparison and population comparison groups.

The unadjusted and adjusted differences in breastfeeding outcomes according to timing of antidepressant use during pregnancy are presented in Table 2. Compared with the unexposed mental disorder comparison group, late pregnancy antidepressant use (adjusted RR [aRR] 0.93; 95% CI 0.90–0.97) was associated with a reduced likelihood of breastfeeding initiation. Compared with the unexposed mental disorder comparison group, early-mid–gestation antidepressant use only was associated with a reduced likelihood of predominant (aRR 0.73; 95% CI 0.54–0.97) and any (aRR 0.95; 95% CI 0.90–0.99) breastfeeding at 6 months. Sensitivity analyses, which included adjusting for antenatal depressive symptoms or restricting the analysis to the first participation in MoBa (Table S1), resulted in no appreciable changes in the risk estimates.

Baseline sociodemographic, lifestyle, and health characteristics of the study sample according to timing of antidepressant use following pregnancy are shown in Table 3. In general, women reporting postnatal antidepressant use or mental health problems were more often disadvantaged (eg lower educational level and income, higher smoking rates). The unadjusted and adjusted differences in breastfeeding outcomes according to timing of antidepressant use postpartum are presented in Table 4. Compared with the unexposed mental disorder comparison group, new/restarted antidepressant use was associated with a reduced likelihood of predominant (aRR 0.37; 95% CI 0.22–0.61) and any (aRR 0.49; 95% CI 0.42–0.56) breastfeeding at 6 months as well as increased risk of abrupt breastfeeding discontinuation (aRR 2.64; 95% CI 2.07–3.37). No differences in outcomes were evident among those who continued antidepressant use from late gestation. Sensitivity analyses, which included adjustment for postnatal mental health problems and breastfeeding problems experienced in the first month postpartum (Table S2), as well as those adjusting for antenatal depressive symptoms or restricting the analysis to the first participation in MoBa (Table S3), resulted in no appreciable changes in the risk estimates.

4 | DISCUSSION

Our analysis of women in the MoBa birth cohort study demonstrates that, following adjustment for underlying maternal illness, women using antidepressants in late pregnancy are less likely to initiate breastfeeding but appear to be at no greater risk of experiencing breastfeeding problems or ceasing breastfeeding before 6 months postpartum. Further, we found that women who restarted or initiated antidepressant use postpartum were almost 3-fold more likely to abruptly discontinue breastfeeding. The consistent findings of suboptimal breastfeeding outcomes among women with an underlying mental health problem, irrespective of antidepressant use, highlights the importance of tailored educational and clinical measures to improve breastfeeding as part of a comprehensive postpartum support package.

Previous studies evaluating associations between antidepressant use and breastfeeding outcomes have suffered from a number of limitations, including small sample size, no adjustment for underlying maternal illness, or being restricted to evaluating short-term breastfeeding outcomes. Our study addresses these limitations to provide the most comprehensive longer-term evaluation of breastfeeding outcomes associated with antidepressant use during pregnancy and postnatally and substantially build on previous research findings.

The initial finding that women taking antidepressants in late pregnancy are less likely to initiate breastfeeding is supported by previous findings by Bogen et al. and Gorman et al.[8,9] Although the overall risk appears low, decisions regarding whether to breastfeed while taking an antidepressant may pose a dilemma for some women and their health care providers. Most antidepressants have a relatively well-documented safety profile for breastfeeding mothers and, in the majority of circumstances, are widely considered compatible with lactation.[21] Although antidepressant medications pass into breast milk to varying degrees, only a small amount is present, with levels substantially lower than those occurring in utero.[21]

Our novel approach, which involved restricting the analysis to women who initiated breastfeeding, did not support a direct negative physiological effect of antidepressant use on lactation, in contrast to previous study findings.[5] This concern was initially raised by Marshall et al., who studied a small cohort of just eight women taking selective serotonin reuptake inhibitors during lactation and found a 2-fold increased risk of delayed secretory activation.[5] However, a subsequent study that used the dispensing of domperidone as a surrogate for lactation insufficiency, failed to demonstrate any relation between antidepressant use and breastfeeding problems.[22] Although our findings from the MoBa cohort do not rule out an important role for serotonin in lactation, the growing body of literature suggests that interference of serotonin signaling through antidepressant use is unlikely to directly impact on breast milk production.

Although no studies have previously examined abrupt breastfeeding discontinuation associated with antidepressant use, the

TABLE 1 Maternal characteristics according to mental illness and antenatal antidepressant use

	Late-gestation antidepressant use[a]	Early-mid–gestation antidepressant use only[b]	Unexposed mental disorder comparison[c]	Population comparison
N	299	574	5111	74 898
Age (y), mean (SD)	30.6 (5.2)	30.0 (5.0)	29.8 (5.0)	30.3 (4.5)
BMI (kg/m^2) at conception, *n* (%)				
<18.5	16 (5.6)	24 (4.3)	188 (3.8)	2129 (2.9)
18.5–25	161 (55.9)	333 (59.7)	3068 (61.9)	48 464 (66.3)
≥25	111 (38.5)	201 (36.0)	1698 (34.3)	22 503 (30.8)
Primiparous, *n* (%)	159 (53.2)	313 (54.5)	2297 (44.9)	34 223 (45.7)
Married/cohabiting, *n* (%)	272 (91.0)	505 (88.0)	4709 (92.1)	72 404 (96.7)
University/college education Level, *n* (%)	161 (53.9)	283 (49.3)	2751 (54.1)	49 614 (66.5)
Woman's gross yearly income, $US, *n* (%)				
Low (≤17 500)	88 (30.0)	164 (29.3)	1304 (26.5)	12 049 (16.6)
Average (17 501–46 800)	185 (63.1)	352 (63.0)	3222 (65.4)	51 769 (71.4)
High (≥46 801)	20 (6.8)	43 (7.7)	403 (8.2)	8715 (12.0)
Smoking status at GW 30, *n* (%)				
No	198 (69.7)	376 (68.5)	3637 (74.0)	60 719 (85.1)
Yes	51 (18.0)	90 (16.4)	627 (12.8)	4453 (6.2)
Stopped in pregnancy	35 (12.3)	83 (15.1)	648 (13.2)	6174 (8.7)
Other psychotropic medication use during pregnancy, *n* (%)[d]	75 (25.1)	74 (12.9)	255 (5.0)	934 (1.3)
Current or recent use of illicit drugs, *n* (%)	5 (1.7)	24 (4.2)	113 (2.2)	425 (0.6)
Lifetime history of major depression (yes), *n* (%)	139 (47.6)	234 (41.5)	996 (20.0)	3399 (4.7)
Depressive symptoms at GW 30 according to HSCL-5, *z*-score (SD)	1.58 (1.98)	1.42 (1.78)	1.45 (1.66)	−0.12 (0.82)

Note: Numbers do not always add up because of missing numbers: BMI, $n = 1986$; maternal education, $n = 339$, smoking status, $n = 3791$, income, $n = 2568$, lifetime history of depression, $n = 1989$; HSCL, $n = 4705$.

Abbreviations: BMI, body mass index; GW, gestational week; HSCL, Hopkins Symptom Checklist; SD, standard deviation.

[a] Late: use ≥29 week's gestation.

[b] Early-mid: use only <29 weeks' gestation.

[c] Women with self-reported mental disorder within 6 months prior to or during pregnancy.

[d] Psychotropics include antipsychotics, anxiolytics, and hypnotics/sedatives.

increased risk observed following new/restarted antidepressant use postpartum could be further reflective of concerns regarding their safety during breastfeeding, that is, women ceasing breastfeeding to start their antidepressant. However, abrupt breastfeeding discontinuation was also more common in women with underlying mental disorders than in the population comparison, suggesting possible underlying differences in breastfeeding intention and determination or differences in coping mechanisms in response to the breastfeeding challenges many women face. More broadly, beyond the initial decision of whether to breastfeed or not, the collective literature suggests that underlying maternal mental illness is likely to be a greater contributor to breastfeeding outcomes than antidepressant use. Maternal mental illness has itself been previously demonstrated to be associated with a reduction in breastfeeding intention, initiation, and duration.[16,23,24] In one study, reasons for breastfeeding discontinuation among women with postnatal depression were related to maternal lactation issues rather than psychosocial or convenience issues.[23] Notably, studies have demonstrated that breastfeeding discontinuation is associated with an increase in depression symptoms.[25] The increase was greater among those with preexisting depressive symptoms during pregnancy,[25] highlighting the importance of strategies aimed at supporting women to achieve their breastfeeding goals.

We used a rich dataset from one of the world's largest birth cohorts from Norway, where breastfeeding is established as the norm. We controlled for a broad range of covariates to reduce the effect of confounding and conducted a series of sensitivity analyses to evaluate the robustness of our findings. A major strength of this study is that we accounted for maternal depressive/anxiety disorders and measured their symptom severity. However, residual confounding by depression severity or genetic, environmental, or familial factors cannot be ruled out.

TABLE 2 Breastfeeding outcomes according to timing of antidepressant use during pregnancy

	Unexposed mental disorder comparison		Late-gestation antidepressant use		Early-mid–gestation antidepressant use only		Population comparison	
Breastfeeding outcomes	***n*** **(%)**	**aRR (95% CI)**	***n*** **(%)**	**aRR (95% CI)**	***n*** **(%)**	**aRR (95% CI)**	***n*** **(%)**	**aRR (95% CI)**
Initiated breastfeeding	5041 (98.6)	Ref	276 (92.3)	**0.93 (0.90–0.97)**	560 (97.6)	0.99 (0.98–1.00)	74 317 (99.2)	1.00 (1.00–1.01)
Any breastfeeding until 6 months[a]	3942 (78.2)	Ref	211 (76.5)	1.00 (0.93–1.07)	406 (72.5)	**0.95 (0.90–0.99)**	63 158 (85.0)	**1.05 (1.03–1.06)**
Predominant breastfeeding until 6 months[a]	626 (12.4)	Ref	32 (11.6)	0.96 (0.67–1.39)	45 (8.1)	**0.73 (0.54–0.97)**	11 100 (15.0)	**1.09 (1.00–1.18)**
Abrupt breastfeeding discontinuation[a]	378 (7.5)	Ref	19 (6.9)	0.91 (0.56–1.46)	43 (7.7)	0.99 (0.72–1.36)	3535 (4.8)	**0.80 (0.71–0.89)**
Breastfeeding problems reported in first month postpartum								
Any breastfeeding problems[a]	889 (17.6)	Ref	43 (15.6)	0.76 (0.57–1.03)	117 (20.9)	1.08 (0.91–1.29)	10 568 (14.2)	**0.80 (0.75–0.86)**
Sore nipples[a]	354 (7.0)	Ref	14 (5.1)	0.64 (0.37–1.11)	54 (9.6)	1.25 (0.94–1.66)	4211 (5.7)	**0.82 (0.73–0.91)**
Mastitis[a]	445 (8.8)	Ref	22 (8.0)	0.88 (0.58–1.35)	54 (9.6)	1.08 (0.82–1.43)	5806 (7.8)	**0.87 (0.79–0.96)**
Other breastfeeding problems[a]	437 (8.7)	Ref	19 (6.9)	**0.60 (0.37–0.96)**	64 (11.4)	1.07 (0.83–1.38)	4169 (5.6)	**0.65 (0.59–0.72)**

Note: Adjusted for maternal age, body mass index at conception, parity, marital status, education level, income, smoking status, use of other psychotropic medications during pregnancy, use of illicit drugs, lifetime history of major depression.

Abbreviations: aRR, adjusted relative risk; CI, confidence interval.

Bold vlue indicates $p < 0.05$.

[a] Analysis restricted to those who initiated breastfeeding.

TABLE 3 Maternal characteristics according to maternal mental illness and antidepressant use during the 6 months postpartum

	Antidepressant use – continued from late gestation	Antidepressant use – new/ restarted postpartum	Unexposed mental disorder comparison	Population comparison
N	201	392	7573	72 716
Age (y), mean (SD)	30.9 (5.1)	30.1 (5.1)	29.8 (4.9)	30.3 (4.5)
BMI (kg/m^2) at conception, *n* (%)				
<18.5	10 (5.2)	10 (2.6)	264 (3.6)	2073 (2.9)
18.5–25	109 (56.2)	240 (62.3)	4549 (61.8)	47 128 (66.4)
≥25	75 (38.7)	135 (35.1)	2550 (34.6)	21 753 (30.7)
Primiparous, *n* (%)	99 (49.3)	179 (45.7)	3690 (48.7)	33 024 (45.4)
Married/cohabiting, *n* (%)	187 (93.0)	3664 (92.9)	7013 (92.6)	70 326 (96.7)
University/college education level, *n* (%)	110 (54.7)	198 (50.8)	4201 (55.7)	48 300 (66.7)
Woman's gross yearly income, $US *n* (%)				
Low (≤17 500)	50 (25.4)	105 (27.4)	1904 (26.1)	11 546 (16.4)
Average (17 501–46 800)	131 (66.5)	248 (64.8)	4789 (65.5)	50 360 (71.5)
High (≥46 801)	16 (8.1)	30 (7.8)	616 (8.4)	8519 (12.1)
Smoking status at GW 17, *n* (%)				
No	144 (75.0)	275 (74.3)	5428 (75.0)	59 083 (85.3)
Yes	28 (14.6)	59 (16.0)	865 (12.0)	4269 (6.2)
Stopped in pregnancy	20 (10.4)	36 (9.7)	941 (13.0)	5943 (8.6)
Use of other psychotropic[a] medications during pregnancy, *n* (%)	45 (22.4)	38 (9.7)	383 (5.1)	872 (1.2)
Use of other psychotropic[a] medications 0–6 months postpartum, *n* (%)	22 (11.0)	55 (14.0)	141 (1.9)	159 (0.2)
Current or recent use of illicit drugs, *n* (%)	4 (2.0)	6 (1.5)	155 (2.1)	402 (0.6)
Lifetime history of major depression (yes), *n* (%)	99 (50.5)	102 (26.7)	1471 (20.0)	3096 (4.4)
Depressive symptoms at GW 30 according to HSCL-5, *z*-score (SD)	1.59 (1.96)	1.14 (1.75)	1.18 (1.60)	−0.13 (0.80)
Preterm birth, *n* (%)	9 (4.5)	22 (5.6)	396 (5.3)	3214 (4.4)
Delivered by cesarean section, *n* (%)	37 (18.4)	76 (19.4)	1279 (16.9)	9660 (13.3)
Self-reported mental disorder postpartum, *n* (%)	121 (60.2)	345 (88.0)	3359 (44.4)	0 (0.0)

Note: Numbers do not always add up because of missing numbers: BMI, *n* = 1986; maternal education, *n* = 339; smoking status, *n* = 3791; income, *n* = 2568; lifetime history of depression, *n* = 1989; HSCL, *n* = 4705.

Abbreviations: BMI, body mass index; GW, gestational week; HSCL, Hopkins Symptom Checklist; SD, standard deviation.

[a] Psychotropics include antipsychotics, anxiolytics, and hypnotics/sedatives.

However, our study has several limitations. Maternal mental disorders were self-reported, as were data on antidepressant use. Although exposure misclassification could be an additional concern, a previous validation study showed that most women self-reporting antidepressant use in MoBa did fill prescriptions for these medications, with an associated sensitivity of 81.7% and specificity of 99.9%.[26] No data on antidepressant dosage were available. The participation rate in MoBa was moderate (41%),[15] possibly indicating self-selection of the healthiest women. The potential for selection bias was previously explored through comparisons of MoBa with the total Norwegian birthing population:[27] although prevalence estimates could not necessarily be generalized, the measures of exposure–outcomes associations tested remained valid. In addition, timing of antidepressant use postpartum was in 3-month intervals, meaning it was not possible to be certain that breastfeeding and antidepressant intervals

TABLE 4 Breastfeeding outcomes according to maternal mental illness and antidepressant use during the 6 months postpartum

	Unexposed mental disorder comparison		Antidepressant use – continued from late gestation		Antidepressant use – new/restarted postpartum		Population comparison	
	n (%)	aRR (95% CI)	*n* (%)	aRR (95% CI)	*n* (%)	aRR (95% CI)	*n* (%)	aRR (95% CI)
Any breastfeeding until 6 months[a]	5768 (77.3)	Ref	141 (75.8)	0.99 (0.91–1.07)	137 (36.7)	**0.49 (0.42–0.56)**	61 671 (85.5)	**1.06 (1.05–1.07)**
Predominant breastfeeding until 6 months[a]	874 (11.7)	Ref	20 (10.8)	0.94 (0.60–1.48)	16 (4.3)	**0.37 (0.22–0.61)**	10 893 (15.1)	**1.14 (1.07–1.22)**
Abrupt breastfeeding discontinuation[a]	577 (7.3)	Ref	13 (7.0)	0.98 (0.56–1.71)	84 (22.5)	**2.64 (2.07–3.37)**	3301 (4.6)	**0.75 (0.68–0.82)**
Breastfeeding problems reported in first month postpartum								
Any breastfeeding problems[a]	1410 (18.9)	Ref	30 (16.1)	0.75 (0.53–1.07)	99 (26.5)	**1.37 (1.14–1.64)**	10 078 (14.0)	**0.75 (0.71–0.79)**
Sore nipples[a]	555 (7.4)	Ref	11 (5.9)	0.70 (0.38–1.30)	37 (9.9)	1.35 (0.97–1.87)	4030 (5.6)	**0.78 (0.71–0.85)**
Mastitis[a]	700 (9.4)	Ref	17 (9.1)	0.93 (0.58–1.49)	45 (12.1)	1.26 (0.94–1.69)	5565 (7.7)	**0.82 (0.76–0.89)**
Other breastfeeding problems[a]	737 (9.9)	Ref	12 (6.5)	0.54 (0.30–0.96)	62 (16.2)	**1.60 (1.25–2.07)**	3878 (5.4)	**0.56 (0.52–0.61)**

Note: Adjusted for maternal age, body mass index at conception, parity, marital status, education level, income, smoking status, use of other psychotropic medications during and following pregnancy, use of illicit drugs, lifetime history of major depression, preterm birth, cesarean section.

Abbreviations: aRR, adjusted relative risk; CI, confidence interval.

Bold vlue indicates $p < 0.05$.

[a] Analysis restricted to those who initiated breastfeeding.

overlapped. Furthermore, breastfeeding duration was reported in monthly categories, rather than weekly. Lastly, we did not adjust for multiple comparisons and cannot rule out the potential for chance findings.

5 | CONCLUSION

Underlying maternal mental disorders appear to be strongly associated with suboptimal breastfeeding outcomes. The relation between antidepressant use and breastfeeding outcomes differs according to utilization patterns. That is, late-gestation antidepressant use is associated with a reduced likelihood of breastfeeding initiation but not breastfeeding duration or exclusivity. In contrast, antidepressants initiated or restarted postpartum were associated with poorer breastfeeding outcomes. These findings provide evidence of a complex relation between depression, antidepressant use, and breastfeeding outcomes. Overall, women taking antidepressants and those with a mental disorder may benefit from additional education and support to improve breastfeeding rates and promote maternal and infant health and wellbeing.

CONFLICT OF INTEREST

None.

AUTHORS' CONTRIBUTIONS

LEG developed the study protocol, conducted data analyses, and drafted the manuscript. MRS, LHA, EY, and HN critically reviewed the study protocol and analyses and contributed to the paper. All authors approved the final manuscript.

DATA AVAILABILITY STATEMENT

The consent given by the participants does not allow for storage of data at an individual level in repositories or journals. Researchers who want access to datasets for replication should submit an application to datatilgang@fhi.no. Access to datasets requires approval from The Regional Committee for Medical and Health Research Ethics in Norway and an agreement with MoBa.

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REFERENCES

1. Charlton R, Jordan S, Pierini A, et al. Selective serotonin reuptake inhibitor prescribing before, during and after pregnancy: a population-based study in six European regions. *BJOG*. 2015;122:1010-1020.
2. Huybrechts KF, Palmsten K, Mogun H, et al. National trends in antidepressant medication treatment among publicly insured pregnant women. *Gen Hosp Psychiatry*. 2013;35:265-271.
3. Fischer Fumeaux CJ, Morisod Harari M, Weisskopf E, et al. Risk-benefit balance assessment of SSRI antidepressant use during pregnancy and lactation based on best available evidence–an update. *Expert Opin Drug Saf*. 2019;18:949-963.
4. Chabrol H, Teissedre F, Armitage J, Danel M, Walburg V. Acceptability of psychotherapy and antidepressants for postnatal depression among newly delivered mothers. *J Reprod Infant Psychol*. 2004;22:5-12.
5. Marshall AM, Nommsen-Rivers LA, Hernandez LL, et al. Serotonin transport and metabolism in the mammary gland modulates secretory activation and involution. *J Clin Endocrinol Metab*. 2010;95:837-846.
6. Grzeskowiak LE, Leggett C, Costi L, Roberts CT, Amir LH. Impact of serotonin reuptake inhibitor use on breast milk supply in mothers of preterm infants: a retrospective cohort study. *Br J Clin Pharmacol*. 2018;84:1373-1379.
7. Galbally M, Watson SJ, Ball H, Lewis AJ. Breastfeeding, antidepressants, and depression in the mercy pregnancy and emotional wellbeing study. *J Hum Lact*. 2019;35:127-136.
8. Bogen DL, Hanusa BH, Moses-Kolko E, Wisner KL. Are maternal depression or symptom severity associated with breastfeeding intention or outcomes? *J Clin Psychiatry*. 2010;71:1069-1078.
9. Gorman JR, Kao K, Chambers CD. Breastfeeding among women exposed to antidepressants during pregnancy. *J Hum Lact*. 2012;28:181-188.
10. Leggett C, Costi L, Morrison JL, Clifton VL, Grzeskowiak LE. Antidepressant use in late gestation and breastfeeding rates at discharge from hospital. *J Hum Lact*. 2017;33:701-709.
11. Molenaar NM, Kamperman AM, Boyce P, Bergink V. Guidelines on treatment of perinatal depression with antidepressants: an international review. *Aust N Z J Psychiatry*. 2018;52:320-327.
12. Bilszta JL, Tsuchiya S, Han K, Buist AE, Einarson A. Primary care physician's attitudes and practices regarding antidepressant use during pregnancy: a survey of two countries. *Arch Womens Ment Health*. 2011;14:71-75.
13. Turner KM, Sharp D, Folkes L, Chew-Graham C. Women's views and experiences of antidepressants as a treatment for postnatal depression: a qualitative study. *Fam Pract*. 2008;25:450-455.
14. Magnus P, Irgens LM, Haug K, Nystad W, Skjærven R, Stoltenberg C. Cohort profile: the Norwegian mother and child cohort study (MoBa). *Int J Epidemiol*. 2006;35:1146-1150.
15. Magnus P, Birke C, Vejrup K, et al. Cohort profile update: the Norwegian mother and child cohort study (MoBa). *Int J Epidemiol*. 2016;45:382-388.
16. Ystrom E, Niegel S, Klepp K-I, Vollrath ME. The impact of maternal negative affectivity and general self-efficacy on breastfeeding: the Norwegian mother and child cohort study. *J Pediatr*. 2008;152:68-72.
17. Grzeskowiak LE, Saha MR, Ingman WV, Nordeng H, Ystrom E, Amir LH. Incidence, antibiotic treatment and outcomes of lactational mastitis: findings from the Norwegian mother, father and child cohort study (MoBa). *Paediatr Perinat Epidemiol*. 2021. doi:10.1111/ppe.12824. Epub ahead of print.
18. Tambs K, Røysamb E. Selection of questions to short-form versions of original psychometric instruments in MoBa. *Norsk Epidemiol*. 2014;24:195-201.
19. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. The lifetime history of major depression in women: reliability of diagnosis and heritability. *Arch Gen Psychiatry*. 1993;50:863-870.
20. Textor J, van der Zander B, Gilthorpe MS, Liśkiewicz M, Ellison GT. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol*. 2016;45:1887-1894.
21. Sprague J, Wisner KL, Bogen DL. Pharmacotherapy for depression and bipolar disorder during lactation: a framework to aid decision making. *Semin Perinatol*. 2020;44:151224.
22. Grzeskowiak LE, Amir LH, Smithers LG. Longer-term breastfeeding outcomes associated with domperidone use for lactation differs according to maternal weight. *Eur J Clin Pharmacol*. 2018;74:1071-1075.

23. Bascom EM, Napolitano MA. Breastfeeding duration and primary reasons for breastfeeding cessation among women with postpartum depressive symptoms. *J Hum Lact*. 2016;32:282-291.
24. Stuebe AM, Meltzer-Brody S, Propper C, et al. The mood, mother, and infant study: associations between maternal mood in pregnancy and breastfeeding outcome. *Breastfeed Med*. 2019;14:551-559.
25. Ystrom E. Breastfeeding cessation and symptoms of anxiety and depression: a longitudinal cohort study. *BMC Pregnancy Childbirth*. 2012;12:36.
26. Skurtveit S, Selmer R, Tverdal A, Furu K, Nystad W, Handal M. Drug exposure: inclusion of dispensed drugs before pregnancy may lead to underestimation of risk associations. *J Clin Epidemiol*. 2013;66:964-972.
27. Nilsen RM, Vollset SE, Gjessing HK, et al. Self-selection and bias in a large prospective pregnancy cohort in Norway. *Paediatr Perinat Epidemiol*. 2009;23:597-608.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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