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Perceived risk of neurodevelopmental outcomes in offspring related to psychotropic and mental illness exposures in pregnancy and breastfeeding: a cross-sectional survey of women with past or current mental illness

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ABSTRACT

Objectives To investigate the perceived risk of psychotropic and mental illness exposures (1) during pregnancy or (2) while breastfeeding on offspring neurodevelopment, and factors associated with this perception in women with past/current mental illness.

Design Cross-sectional, web-based study.

Setting Nationwide in Norway, June 2020–June 2021.

Participants Women aged 18–55 years who were pregnant, recent mothers or planning a pregnancy, and had been offered antidepressants in the last 5 years.

Primary and secondary outcome measures Perceived risk of prenatal and breastmilk exposure to psychotropic medications and maternal mental illness on offspring neurodevelopmental outcomes.

Results We included 448 women: 234 pregnant, 146 mothers and 68 planning a pregnancy. On a 0–10 scale, women perceived antidepressants as least harmful both (1) in pregnancy (mean score 4.2, 95% CI 3.6 to 4.8) and (2) while breastfeeding (mean score 3.8, 95% CI 3.3 to 4.4), relative to antipsychotics, anxiety/sleeping medication or antiepileptics (mean score range: 6.3–6.5 during pregnancy, 5.5–6.2 while breastfeeding). Many participants were unfamiliar with psychotropics other than antidepressants. The perceived risk of mental illness exposure exceeded that of antidepressants (mean score range 5.6–5.9) in both exposure periods. Using general linear models, factors associated with greater antidepressant risk perception in both exposure periods included having lower education, non-Norwegian native language, and employment status (range mean score difference (β): 2.07–6.07). For pregnant women and mothers, there was an inverse association between perceived risk and the perceived antidepressant effectiveness in both exposure periods (range of β: −0.18 to −0.25).

Conclusions In women with past/current mental illness, the perceived risk of antidepressant exposure on child neurodevelopment was lower than that for maternal mental illness. Other psychotropic medications were perceived as more harmful. As medication risk perception influences the decision-making regarding treatment of mental illness, pre- and pregnancy counselling should target women with characteristics associated with higher perceived risk.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first nationwide study in Norway about women's perceptions of child long-term neurodevelopmental risks following psychotropic medication and mental illness exposure during pregnancy and while breastfeeding.
⇒ The perceptions of risk measures were specific to long-term neurodevelopmental outcomes in offspring.
⇒ The study included only women with a current/past mental illness, who are possible end users of antidepressants and other psychotropic drugs.
⇒ Risk of bias due to self-selection cannot be excluded, although the results were made more generalisable in terms of age and county of residence by using survey weighting.
⇒ A specific definition of all possible neurodevelopmental outcomes was not provided to respondents, and women rated their perceived drug risk on the broad, unspecific spectrum of child neurodevelopment.

INTRODUCTION

Maternal mental illness occurs in 5%–15% of women during the perinatal period, most commonly major depression,[1] anxiety[2 3] and eating disorders.[4] In addition to the difficulties associated with mental illness for the affected women themselves, these perinatal disorders pose risks for short-term and long-term negative outcomes for the offspring.[5 6] Women with a perinatal mental illness may therefore require

psychotherapeutic or pharmacological treatment, or both, depending on the severity of the condition and therapeutic preference.

Antidepressants, particularly serotonin reuptake inhibitors, are the preferred pharmacological option for the above disorders during pregnancy.[7] Their estimated population prevalence, based on filled prescriptions during pregnancy, is 2.3%–3.7%.[8] Other psychotropics, such as benzodiazepines, z-hypnotics and antipsychotics, are less often used.[9 10] Even though multiple studies have shown that antidepressants are not major teratogens,[11–14] findings remain inconsistent about the risk of longer-term neurodevelopmental outcomes in children, for example, attention-deficit/hyperactivity disorders (ADHD), autism spectrum disorder or scholastic skills.[15 16] Current data about the reproductive safety of antipsychotics and benzodiazepines are limited,[17–19] while the short-term and long-term risk posed by the antiseizure drug valproate is now well acknowledged.[20 21]

In women with a perinatal mental illness, elevated risk perception of adverse outcomes in offspring due to psychotropic medication exposure often affects the decision-making regarding their treatment.[22–24] The ongoing debate concerning the reproductive safety of these medications may contribute to confusion and decisional conflicts regarding pharmacological treatment, both among women and healthcare providers.[25 26] Several studies have shown that the perceived teratogenic risk of psychotropic medication use may be unrealistically elevated among pregnant women or recent mothers.[27 28] In a multinational, web-based study across 18 countries, antidepressants were perceived as almost equally harmful for the developing fetus as alcohol.[28] However, such risk was rated by the general population of pregnant women, irrespective of their mental illness and current or previous treatment with psychotropics. Understanding the perception of the risk of antidepressants and other psychotropics specifically in women with a mental illness is crucial, as they are possible end users of such medications. Given the uncertainties about the longer-term safety of antidepressants in pregnancy and the high decisional conflicts faced by women considering this treatment,[15 29] quantifying the perceived medication risk specifically for long-term neurodevelopmental outcomes in children is clinically relevant.

In a sample of women with current or past mental illness, we aimed to examine the perception of risk of long-term neurodevelopmental outcomes in offspring associated with prenatal and breastmilk exposure to antidepressant and other psychotropic medications, food items (alcohol and cranberries) and the mental illness itself. To contrast how women rated the perceived risk of antidepressant medication versus that of the mental illness itself, we sought to identify maternal factors associated with how these two risks were perceived.

METHODS

Study design and participants

Participants were recruited from the HEALTHx2 study. HEALTHx2 is a cross-sectional, sequential mixed-methods study, in which data were collected from all regions of Norway between June 2020 and June 2021. The quantitative component preceded the qualitative one. This study used solely quantitative cross-sectional data, which were collected using an electronic questionnaire administered via 'Nettskjema' provided by the University of Oslo. Participants could choose to access the questionnaire anonymously or by using their national ID number. Information about the study was posted on multiple pregnancy and motherhood-related websites and apps, on social media, and brochures with the study information were distributed at various psychiatric polyclinics, hospital psychiatric departments, and maternity health clinics (see online supplemental eTable 1 for further detail). The complete questionnaire is presented in online supplemental 1. A pilot study was carried out in May 2020, which elicited no major changes to the questionnaire. Women were eligible to participate in the study if they: (1) were between the ages of 18 and 55 years; (2) were planning a pregnancy, were pregnant or had given birth within the last 5 years (hereafter, recent mothers) and (3) have or had previously had a mental illness and been offered antidepressant treatment within the last 5 years.

Patient and public involvement

The research team attempted to involve patient representatives in the development of the study protocol and the questionnaire, with the support of national mental health patient organisations. No patient representatives were willing to be involved in this study.

Perception of risk

Participants were asked to rate (from 0 to 10, where 0 corresponded to 'not harmful' and 10 to 'very harmful') the perceived harmfulness of substances taken during gestation or while breastfeeding for the long-term neurodevelopment of the child in two separate questions: (1) in pregnancy and (2) while breastfeeding. To enhance reliability, the question specified examples of long-term outcomes in offspring, specifically autism, motor development, language skills and ADHD. The listed substances included antidepressants, antipsychotics, anxiety and sleeping medication, antiepileptics (eg, valproate), mental illness per se, cranberries and alcohol (eg, wine, beer, spirit). The latter two exposures were listed to act as reference for not harmful and harmful exposures, respectively. Women were asked to check 'unknown substance' if they were unfamiliar with the substance. The risk perception measures were adapted from a prior study of perceived risk among pregnant women and new mothers.[28]

Mental health factors

Previous and current mental health was measured via using self-report items in which participants could indicate the mental illness they currently or previously had within a predefined list including depression, anxiety, obsessive–compulsive disorders, eating disorders, other mental illness and no mental illness. Participants were also asked to indicate the time points at which they had a mental illness according to their pregnancy status at the time of questionnaire completion. (ie, planning a pregnancy, currently pregnant or recent mother; online supplemental e Table 2). To measure women's mental health burden, we counted the number of different illnesses reported across the available periods.

Active depressive symptoms were measured using the Edinburgh Postnatal Depression Scale (EPDS), a self-rating 10-item scale validated in pregnancy and postpartum with satisfactory Cronbach's alpha reliability (0.87).[30] The EPDS has been previously validated in a Norwegian sample.[31] Women were asked to rate whether each item reflected how they had been feeling in the past 7 days. Each item response scored 0–3 on an ordinal scale, producing a total EPDS score of 0–30. Higher scores indicate worse symptomatology. A cut-off score of 13 was used to determine the presence of active depressive symptoms; the choice of cut-off 13 is conservative, as it reflects the higher end of the validated cut-off for 'probable depression'.[30]

Current broadly defined eating disorder subtypes (ie, anorexia nervosa, bulimia nervosa, binge-eating disorder (BED), eating disorder not otherwise specified purging type) were measured via items according to the DSM-IV criteria, by applying an algorithm used in a previous pregnancy cohort study in Norway[4] (online supplemental 2).

Perceived stigma related to mental illness was measured using four selected items from the 'Attitudes Toward Seeking Professional Psychological Help Scale'[32] (ATSPPHS). Participants could indicate the extent to which they agreed or disagreed on each item, with a score ranging from 0 to 4. Scores across items were summed (range 0–20) and a greater score corresponded to more indifference to stigma (ie, more positive attitudes). This was modelled as a numeric variable. The ATSPPHS was translated to Norwegian and back-translated using two independent translators.

Participants were also asked if they had previously received or were currently receiving psychological therapy (dichotomised as yes/no) and, if yes, the type of therapy and when they received it. Lastly, participants were asked to indicate the perceived effectiveness of antidepressants for treating mental illness both in general and during pregnancy, by rating this on a scale from 0 ('not at all') to 10 ('very useful'). See online supplement 2 for further details.

Sociodemographic and lifestyle characteristics

These included a participant's age, county of residence, number of prior children, marital status, educational attainment and work situation at the time of conception (or current for pregnancy planners), body mass index (BMI) at time of conception (or current for pregnancy planners), having the Norwegian language as mother tongue, information about future pregnancies (if participants were planning to become pregnant shortly), the current pregnancy or the latest pregnancy. The questions were based on a prior web-based, cross-sectional study conducted among pregnant women in Norway.[33] To avoid data sparsity, maternal variables were categorised as shown in table 1.

Statistical analysis

Mean risk perceptions and their 95% CIs were ashad active depressive symptsessed descriptively both for exposure in pregnancy and while breastfeeding, with survey weight adjustment (reported in the manuscript) and without survey weight adjustment (reported in online supplemental e Table 3). The survey weight was based on the most recent data available from the Norwegian Directorate of Health, which describes the proportion of female patients having had contact with psychiatric clinics in each health region of Norway (South-East, West, Middle, North) within each relevant age group (18–29, 30–39 and 40–49 years).[34] The weights were calculated by dividing the population proportion by the sample proportion in each age-by-region strata. This implies that the survey weight of under-represented participants was larger than 1; that of overrepresented participants was smaller than 1. The mean survey weight of the sample was 0.7 (range=0.3–13.3). Data on the county were missing for seven participants, and the mean weight of the sample was assigned to these. There were no missing data for age. To appraise the impact of confounding by age and region on the perception of risk, we also conducted descriptive analyses with no survey weight.

Principal component analysis (PCA) was conducted to assess if the risk perception of the various substances could be grouped into fewer factors for analyses; due to the large proportion of women who indicated psychotropic drugs other than antidepressants as 'unknown', the PCA caused substantial data loss. As a result, the grouping of psychotropic drugs other than antidepressants was hindered, and we focused subsequent analyses on the perceived risk of antidepressant and maternal mental illness exposure only. A preregistration[35] including the statistical analysis plan is published on the Open Science Framework (some sample statistics had been conducted before the publication of this preregistration, but no analyses related to the outcomes).

Association analyses

To determine which factors were related to the rated risk of antidepressant and maternal mental illness during pregnancy and while breastfeeding, we conducted a series of multiple general linear models with a robust standard error, using the survey weight. These models were built following the 'purposeful selection' approach.[36]

Table 1 Sociodemographic and health-related characteristics of the study sample (N=448)

	N	%
Sociodemographic characteristics		
Age (years)		
18–29	170	38
30–49	278	62
Pregnancy status		
Planning a pregnancy	68	15
Currently pregnant	234	52
Recent mothers (within the last 5 years)	146	33
Geographical health region		
South-East Norway	261	59
West Norway	98	22
Mid-Norway	50	11
North Norway	32	7
Marital status		
Married or cohabiting	415	93
Single or divorced/separated	25	6
Other	8	2
Educational attainment (current or at time of conception)		
Primary school	21	5
High school	96	21
University/college	316	71
Other	14	3
Missing	<5	—
Work situation (current or at time of conception)		
Student	32	7
Home maker	25	6
Health worker (eg, medical doctor, nurse, pharmacist)	76	17
Other paid work	255	57
Jobseeker	14	3
Other	46	10
Norwegian as main language		
Yes	405	91
No	42	9
Missing	<5	—
Health-related characteristics		
Self-reported number of mental illnesses*		
1	110	25
2	172	38
3 or more	166	37
Current symptoms of depression/anxiety		
Yes (EPDS≥13)	118	26
Missing	<5	—
Current broadly defined BED (yes)†	85	19
Had received or was currently receiving therapy		
Yes	230	51
No	208	46
Missing	10	2
	Mean	SD
Perceived stigma for mental illness‡§	9.1	4.1
Perceived effectiveness of antidepressant in general¶	6.9	3.2
Perceived effectiveness of antidepressant in pregnancy‡	5.3	3.9

*Participants were asked about their history of mental illness; this figure comprises number of psychiatric illnesses from more than 1 year before to the time of questionnaire completion.
†Other EDs were also measured, but had low prevalence in the sample.
‡Missing data were present for 4 (stigma scale), 7 (health region of residency), 85 (effectiveness of antidepressants in general) and 147 (effectiveness of antidepressants in pregnancy) women.
§Greater score corresponds to more indifference to stigma (ie, more positive attitudes).
¶Greater score corresponds to higher perceived effectiveness of antidepressants.
BED, binge-eating disorders; EPDS, Edinburgh Postnatal Depression Scale.

Candidate variables were first selected based on a p<0.15 in a univariable linear regression model. Selected candidate variables were then included in the multivariable model; at this stage, variables having no role (p>0.05) or yielding a change smaller than 15% in the beta coefficients of the retained variables were removed. We examined a vast array of mental health and sociodemographic factors on risk perceptions. Candidate mental health variables included: current and active depressive symptoms, BED at the time of questionnaire completion, number of self-reported past or current mental illnesses, perceived stigma related to mental illness, psychological therapy and perceived effectiveness of antidepressant treatment in general and during pregnancy. BED was the sole eating disorder included with a sufficient number of women to be included in the association analysis. Candidate demographic variables comprised marital status, work situation, education, having Norwegian as the main language and woman's BMI. Missing data on mental health factors ranged from <1% to 33%, while this issue was minimal (<0.5%) for sociodemographic variables.

The final multiple regression model included statistically significant and clinically relevant factors (ie, age, education). We replicated the multiple regression model in the three strata of women: planning a pregnancy at the time of questionnaire completion, being pregnant or recent mothers. Among pregnancy planners, only demographic variables were included due to low sample size. Results are presented as mean difference in risk

perception with the corresponding 95% CI, where positive coefficients indicated higher perceived risk and negative coefficients the converse.

Under the assumption that data were missing at random, we imputed incomplete data on the candidate explanatory variables and risk perception of antidepressants and maternal mental illness via multiple imputation with chained equation (twenty replications). The imputation model included the survey weight, baseline and health-related factors and auxiliary variables. As sensitivity analysis, we ran mixed-effects models[37] to account for dependence within different regions of Norway (North, South, East and West), and examined the distribution of key maternal variables by the number of 'unknown' psychotropics reported. The intraclass correlation was below 0.05 in all models, indicating that similarity was low within regions. All statistical analyses were conducted using STATA MP V.16.

RESULTS

Of the 753 women who indicated their willingness to participate in the study, 500 (66% response rate) consented. After excluding participants with missing data for all risk perception substances, age <18 years, and/or with no self-reported or proxies for current or previous mental illness, we reached a final study sample of 448 women. The data flow to achieve the final study sample is available in online supplemental eFigure1. The background characteristics of the participants are summarised in table 1. Most participants were either currently pregnant (52%) or recent mothers (33%). The mean gestational week of pregnant participants was 18.5 (SD=9.8). The majority of recent mothers (61%) had a child between four and twelve months of age. Most planners (59%) were actively trying to conceive at the time of questionnaire response. The overall mean age was 30.8 years (*SD*=4.6). The majority of women (75%) reported that they have or have had more than two psychiatric illnesses (see online supplemental e Table 2) and 118 (26%) had active depressive symptoms. Broadly defined BED was observed in 85 (19%) women, and few (<15) were classified as having another eating disorder type.

As shown in table 2, cranberry and alcohol were perceived as the least and most harmful substances both in pregnancy and while breastfeeding, respectively. Among the psychotropic drugs, antidepressants were perceived as least harmful both in pregnancy (mean score 4.2, 95% CI 3.6 to 4.8) and breastfeeding (mean score 3.8, 95% CI 3.3 to 4.4). Participants rated the mental illness itself as somewhat more harmful than antidepressants in both exposure periods (mean scores of 5.9 and 5.6). The risk perception scores were lower in the survey-weighted analysis relative to the non-weighted (see online supplemental e Table 3).

A large number of participants were unfamiliar with the risk of exposure to antipsychotics, anxiety and sleeping medication and antiepileptics. online supplemental e Table 4 shows the descriptive statistics of risk perception excluding participants with missing or 'unknown' responses to the risk perception items. The distribution of key characteristics according to rating as 'unknown' none, one or more than one psychotropic is given in online supplemental e Table 5.

Exposure to most substances was perceived as slightly less harmful in breastfeeding compared with during pregnancy, but the differences were small. The consistency of

Table 2 Descriptive statistics of the risk perception scores for seven items in relation to exposure during pregnancy and while breastfeeding

Substance	Mean risk score (SE)	95% CI	Median risk score	(Q1, Q3)	N	Unknown
Risk perception of exposures during pregnancy						
Alcohol	9.0 (0.1)	(8.7 to 9.2)	10	(8, 10)	442	5
Antiepileptics	6.5 (0.4)	(5.6 to 7.3)	7	(5, 9)	150	295
Antipsychotics	6.5 (0.3)	(5.9 to 7.1)	7	(5, 9)	245	198
Anxiety and sleeping medication	6.3 (0.2)	(5.8 to 6.7)	6	(5, 8)	328	116
Maternal mental illness per se	5.9 (0.2)	(5.4 to 6.3)	6	(4, 8)	423	22
Antidepressants	4.2 (0.3)	(3.6 to 4.8)	5	(3, 7)	383	63
Cranberry	0.9 (0.1)	(0.7 to 1.1)	0	(0, 1)	301	143
Risk perception of exposures while breast feeding						
Alcohol	7.0 (0.2)	(6.7 to 7.4)	8	(5, 10)	437	9
Anxiety and sleeping medications	6.2 (0.3)	(5.6 to 6.7)	6	(4, 9)	321	124
Antipsychotics	6.1 (0.3)	(5.5 to 6.6)	6	(4, 9)	248	198
Maternal mental illness	5.6 (0.3)	(5.0 to 6.2)	6	(3, 8)	417	26
Antiepileptics	5.5 (0.4)	(4.7 to 6.3)	6	(4, 8)	152	293
Antidepressants	3.8 (0.3)	(3.3 to 4.4)	4	(2, 6)	376	68
Cranberry	1.2 (0.2)	(0.7 to 1.7)	0	(0, 1)	298	147

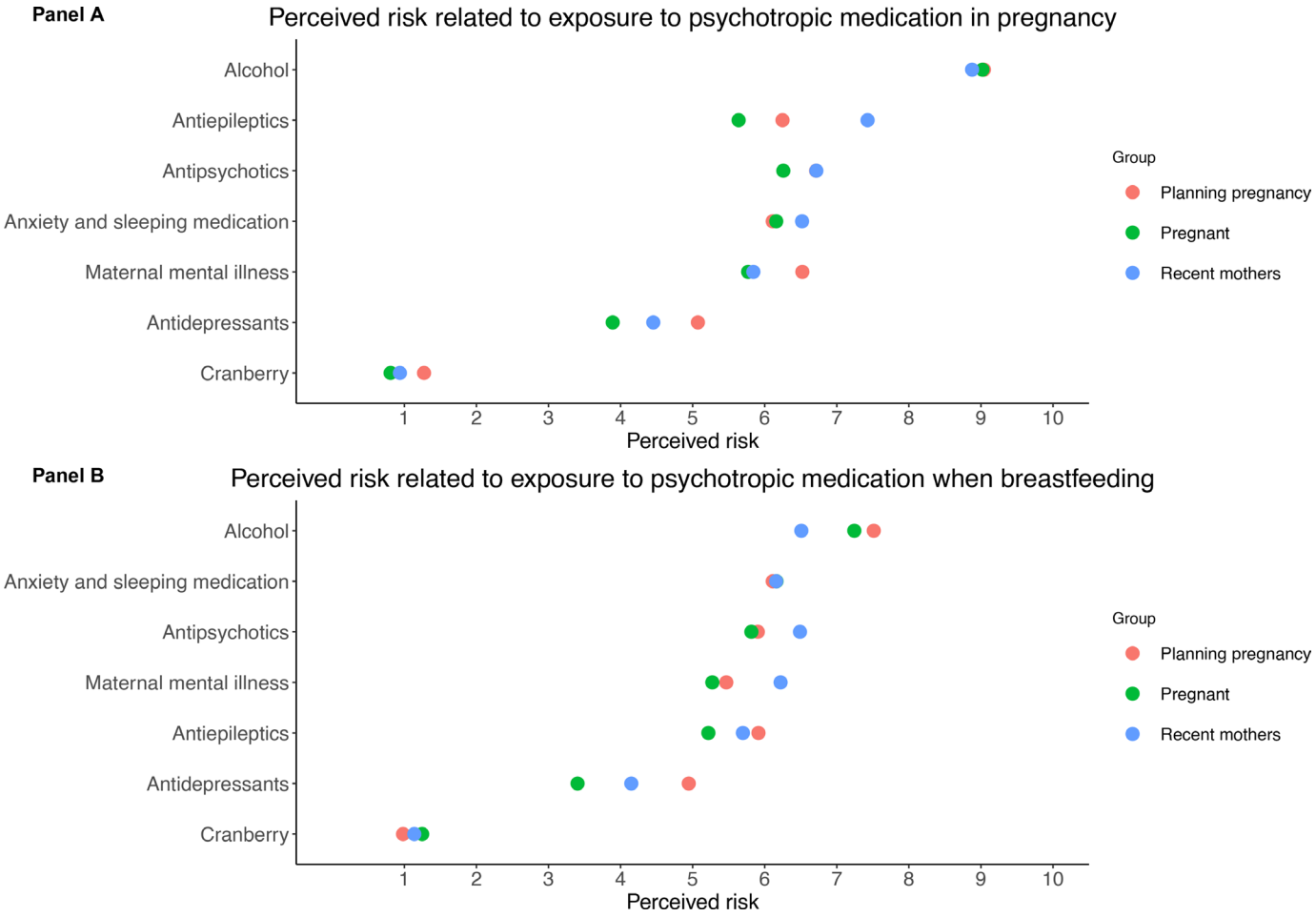

Figure 1 Perceived weighted risk related to exposure in pregnancy (A) and while breastfeeding (B).

women's responses across the risk perception scores for psychotropics were 0.73 (pregnancy exposure) and 0.78 (breastfeeding exposure).

Figure 1 illustrates the perceived risk in pregnancy (figure 1A) or while breastfeeding (figure 1B) by pregnancy status (ie, pregnancy planners, pregnant or recent mothers). The risk perception was rated similarly by participants with different pregnancy statuses. However, antidepressant and mental illness exposures during pregnancy were perceived as slightly more harmful by pregnancy planners compared with pregnant participants.

Tables 3 and 4 report maternal factors associated with the perceived risks in pregnancy or while breastfeeding, respectively. Having primary school as the highest achieved education level, a non-Norwegian native language and being a jobseeker or homemaker, were the factors most strongly associated with greater antidepressant risk perception in both exposure periods among pregnancy planners (range of β: 2.07–6.07). Health workers rated the risk posed by maternal illness in both exposure periods significantly higher than women with other paid work (β: 1.72–2.35), but this association was solely present among pregnancy planners.

In both pregnant women and recent mothers, a greater perception of antidepressant effectiveness was associated with a lower risk rating of antidepressants in pregnancy or while breastfeeding, although the effect size was small (range of β: −0.18 to −0.25). Mothers who were unmarried/not cohabiting rated the risk of mental illness exposure in pregnancy significantly lower than the reference group (β: −6.30, 95% CI −6.98 to −5.61).

DISCUSSION

This study is, to the best of our knowledge, the first to examine the perceived risk of neurodevelopmental outcomes in offspring following exposure to psychotropic drugs and maternal mental illness itself during pregnancy or while breastfeeding. By targeting the evaluation of risk to women who are possible end users of psychotropics, the study generates clinically relevant knowledge about barriers to the decision-making process regarding mental illness treatment in pregnancy or while breastfeeding.

We found that antidepressants were perceived as less harmful than other psychotropic drugs, alcohol and the maternal mental illness itself, both in pregnancy and when breastfeeding. This is in contrast with a prior study[28] where antidepressants were rated almost as harmful as alcohol. The perceived risk among participants from Northern Europe in the study by Petersen *et*

Table 3 Factors associated with risk perception score for antidepressant and mental illness exposures during pregnancy, by pregnancy status

	Antidepressants		Maternal mental illness	
Maternal predictive factor	**β (95% CI)**	**P value**	**β (95% CI)**	**P value**
Planning pregnancy				
Educational attainment				
High school	Ref		Ref	
Primary school	3.99 (2.62 to 5.35)	<0.001	1.42 (0.16 to 2.68)	0.027
University/college	1.59 (0.21 to 2.98)	0.024	N.S.	—
Occupational status				
Other paid work	Ref		Ref	
Home maker	1.89 (0.56 to 3.22)	0.005	N.S.	—
Health worker	N.S.	—	1.72 (0.19 to 3.26)	0.028
Jobseeker/others	2.49 (0.90 to 4.09)	0.002	N.S.	—
Not having Norwegian native language	3.30 (1.62 to 4.98)	<0.001	N.S.	—
Pregnant				
AD effectiveness in pregnancy	−0.24 (−0.37 to -0.10)	0.001	N.S.	—
Occupational status				
Other paid work	Ref		Ref	
Jobseeker/others	−1.89 (−3.75 to -0.02]	0.047	N.S.	—
Mothers				
Occupational status				
Other paid work	Ref		Ref	
Student	−1.73 (−3.14 to -0.32)	0.016	N.S.	—
Homemaker	−2.19 (−3.90 to −0.47)	0.012	N.S.	—
Marital status				
Married or cohabiting	Ref		Ref	
Other	N.S.	—	−6.30 (−6.98 to -5.61)	<0.001
Not having Norwegian native language	2.01 (0.53 to 3.50)	0.008	N.S.	—
AD effectiveness in pregnancy	−0.18 (−0.37 to -0.00)	0.049	N.S.	—

Notes. Only statistically significant factors are reported. All models were survey weighted, and adjusted for age and education, in addition to the variables listed in the table. Psychotherapy was retained in the model for pregnant women and antidepressant risk perception, as its removal changed the beta coefficients of retained variable substantially.
AD, antidepressant; N.S, non-significant statistically.

al was also higher than in the current study. There are several possible reasons for these differences. First, there is now greater availability of research data on the longer-term reproductive safety of antidepressants in 2020 compared with 2011, which may have reached the population to a larger degree.[11–15] Second, our study measured the perceived risk for neurodevelopmental outcomes in offspring, whereas prior work[28] focused on structural teratogenic risk. Third, our participants had prior/current mental illness, increasing the likelihood that they would have received tailored counselling on potential risks of antidepressant exposure to the offspring. This could have contributed to a lower assessment of antidepressant risks. This finding is encouraging, as an overestimation of risk may contribute to treatment discontinuation and poor adherence, even when the antidepressant is needed.[38]

A key result is that exposure to mental illness itself in pregnancy and when breastfeeding was perceived as more harmful than antidepressants, and almost at par with other psychotropics. In pregnant women, having BED was associated with a greater perceived risk of mental illness exposure in pregnancy and while breastfeeding, relative to women with no BED, which could be indicative of fears and concerns related to passing on the illness to the child and/or whether maternal eating patterns negatively affect the child.[39] Comparing this finding with prior research is difficult due to the lack of similar data. Nevertheless, it could point to greater awareness in women about the possible negative consequences of perinatal mental illness for offspring. This finding is important from both a public health and patient-specific perspective.

Table 4 Predictors of risk perception of antidepressant and mental illness exposures when breastfeeding, by pregnancy status

	Antidepressants		Maternal mental illness	
Maternal predictive factor	β (95% CI)	P value	β (95% CI)	P value
Planning pregnancy				
Education				
High school	Ref		Ref	
Primary school	6.07 (4.38 to 7.77)	<0.001	−2.34 (−4.08 to -0.61)	0.008
University/college	1.66 (0.14 to 3.17)	0.033	N.S.	—
Other	N.S.	—	4.75 (0.47 to 9.03)	0.030
Occupational status				
Other paid work	Ref		Ref	
Homemaker	2.07 (0.69 to 3.46)	0.003	−1.96 (−3.36 to −0.57)	0.006
Health worker	N.S.	—	2.35 (−0.04 to 4.74)	0.054
Jobseeker or other	2.53 (0.77 to 4.30)	0.005	N.S.	—
Not having Norwegian native language	3.66 (1.75 to 5.56)	<0.001	N.S.	—
Pregnant				
AD effectiveness in pregnancy	−0.24 (−0.39 to -0.08)	0.003	N.S.	—
Stigma*	N.S.	—	−0.20 (-0.33 to -0.07)	0.003
BED (yes vs no)	N.S.	—	1.66 (0.44 to 2.88)	0.008
Mothers				
Occupational status				
Other paid work	Ref			
Student	−1.82 (−3.18 to -0.47)	0.008	N.S.	—
Home maker	−2.69 (−4.87 to -0.51)	0.015		
Health worker	−1.31 (−2.61 to -0.02)	0.047	N.S.	—
AD effectiveness in pregnancy	−0.25 (−0.45 to -0.05)	0.014	N.S.	—

Notes. Only statistically significant factors are reported. All models were survey weighted, and adjusted for age and education, in addition to the variables listed in the table.
*Perceived stigma related to mental illness was measured using four selected items from the 'Attitudes Toward Seeking Professional Psychological Help Scale'.
AD, antidepressant; BED, binge-eating disorder; N.S., non-significant statistically.

Confounding by maternal mental illness severity, genetic and familial environment remains a concern when interpreting the associations between prenatal antidepressant exposure and child development.[15] Maternal perinatal mental illness has been linked to negative health outcomes in the mother,[7] her offspring[5 40 41] and the family as a whole.[42 43] Negative sequelae include fewer mother–child interactions[44 45] and poorer long-lasting attachment bonds.[46] Therefore, in treating a perinatal mental illness, the potential risks of treatment with psychotropic medication must be balanced against the negative consequences of untreated maternal mental illness for each woman. Psychotherapy has moderate effectiveness on postpartum depression,[47 48] and should always be offered as first-line and/or alongside psychotropic medication. Interventions which aim to strengthen social support have also been found to have moderate effects on postpartum depression.[49]

Our observed heightened risk perceptions for antipsychotics and sleeping and anxiety medication in both pregnancy and while breastfeeding may be attributable, at least in part, to the scarcity of research on the longer-term reproductive safety of these medications.[17–19] For many women with psychotic episodes and bipolar disorders, antipsychotics constitute important treatment components.[1 6 7] Yet, scarcity of safety data poses serious challenges for clinicians, and women themselves.[49] Even though antidepressants are often taken together with other psychotropics,[38 50] many women in our study were unfamiliar with antipsychotics and sleeping and anxiety drugs, and could not rate their risks. This unfamiliarity was more common in women not working as healthcare professionals and those with lower education.

In line with current recommendations and the available evidence,[20 21] antiepileptics, in specific valproate, were correctly rated as moderately harmful in pregnancy. This

greater awareness can be attributable to the nation-wide restrictions on valproate prescribing in fertile women, in force since 2018.[51 52] Other antiepileptic drugs such as lamotrigine, have a more favourable safety profile in pregnancy, and their benefits outweigh the risk posed by untreated epilepsy on maternal–child health.[53] Because our questionnaire listed only valproate as an example of antiepileptics, the observed perceived risk most certainly relates to valproate only, and not to other antiepileptic drugs.

Generally, women did not seem to differentiate between risks of exposure in pregnancy and when breastfeeding to a substantial degree, which is surprising. Clinicians should be aware of this perception, so that they can adequately inform women about the difference in risk during pregnancy or while breastfeeding. Although data on psychotropic excretion into breastmilk and possible effects on the breastfed infant are sparse, most psychotropics are considered compatible with breastfeeding.[53] Breastfeeding is strongly recommended to improve maternal and child health outcomes.[54] . However, for specific drugs, for example, lamotrigine or second-generation antipsychotics, an individual assessment needs to be performed, which includes consideration of infant age, maternal wish to breastfeed and safer treatment alternatives.[53]

Among pregnancy planners, sociodemographic characteristics such as having primary school as the highest education level, non-Norwegian native language and being unemployed or a homemaker, were associated with increased perceived risk of antidepressant exposure in pregnancy and breastfeeding. Differential access to healthcare and evidence-based counselling, as well as the ability to obtain and interpret health information, could in part contribute to these results. These groups of women should be primary targets for preconception intensified counselling. The association between greater perception of antidepressant effectiveness and lower risk rating of these drugs in pregnancy may point to an increased emphasis on the woman's needs regarding treatment in the perinatal period. Even though the available evidence on antidepressant effectiveness in pregnancy is limited,[55] the psychiatric history of the woman, her response to prior and/or ongoing antidepressant treatment, and outcomes following prior attempts to discontinue the medication, must be part of the individual risk-benefit assessment of antidepressants in pregnancy and while breastfeeding. Such assessment should always be done together with the woman as part of the shared decision-making.

Strengths and limitations

One major strength of our study is that risk perceptions were measured using the same methodology as in prior research,[28] with the added advantage of being specific to perceived risk of neurodevelopmental outcomes in offspring. The study had a considerable study size given the difficult-to-reach population, from all regions of Norway. Several recruitment strategies were implemented to minimise the risk of selection bias. To make the sample more representative, analyses were corrected using survey weight adjustment based on the most recent data from the Norwegian Health Directorate; however, this affected our results only minimally.[34] The study used screening tools and diagnostic algorithms validated and/or used in prior research in Norway.[4 31] We also conducted multiple imputation for missing data on both explanatory and outcome variables. The primary analyses of the current study were preregistered,[35] although some sample descriptive statistics had been conducted before the preregistration.

Our study also has limitations. The sample size for women planning a pregnancy was low, and a large proportion of participants were unfamiliar with antipsychotics, antiepileptics and anxiety and sleeping medication. It is possible that naming branded products could have enhanced recall. Unfamiliarity with these psychotropics was more common among women not working as a healthcare professional and those with lower education. This could have influenced our descriptive and association results, although the latter were all adjusted for maternal educational level. An important limitation of the study is that we did not provide a specific definition of all individual 'neurodevelopmental outcomes' in the questionnaire, but rather presented a few substantially heterogeneous examples. This may have affected the accuracy of women's reporting on the perceived risk of psychotropics and mental illness related to the broader, unspecific domain of child neurodevelopment. We cannot rule out the possibility that the lack of clarity in these items influenced our estimates of perceived risk and associations. The mental illnesses were self-reported by the participants, and thus dependent on the accuracy of the woman's reporting. However, the eligibility criteria included being offered antidepressant treatment in the last 5 years, thus targeting primarily moderate to severe mental illness cases. Women with no proxy of current/past mental illness were excluded from the analysis. Use of an electronic questionnaire and multiple recruitment strategies did not permit calculation of a conventional response rate, and bias due to self-selection cannot be ruled out. However, among the women expressing their willingness to participate or not in the study, the response rate was satisfactory (66%). The validity of web-based recruitment methods is now well acknowledged,[56 57] and the internet penetration rate is almost 100% in women of childbearing age in Norway.[58] We did not consider how patterns of psychotropic medication use were related to the woman's assessment of their risk. We assumed data to be missing at random when conducting the association models; however, this assumption is not testable and it was only based on the patterns of missingness in our population. Finally, we cannot exclude the possibility that the women who decided to participate in the study differed from the general birthing population of women with mental illnesses in ways that our analysis could not control for.

CONCLUSION

In this population, the perceived risk of maternal mental illness exposure during pregnancy or while breastfeeding on child neurodevelopment exceeded that for antidepressants. Exposure to antiepileptics, antipsychotics, anxiety and sleeping medication was perceived as most harmful, together with alcohol. Specific sociodemographic variables and perceived effectiveness of antidepressants were significantly associated with rated risk of antidepressants and mental illness. Our findings underline the importance of providing tailored, evidence-based information about the benefits and risks of both psychotropic and mental illness exposure during pregnancy or while breastfeeding, to facilitate complex shared decision-making.

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