OXFORD

human reproduction

Human Reproduction, 2023, **38(9)**, 1755–1760

https://doi.org/10.1093/humrep/dead133

Advance Access Publication Date: June 24, 2023

Original Article

Psychology and counselling

Anxiety and depression in expectant parents: ART versus spontaneous conception

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ABSTRACT

STUDY QUESTION: Do expectant parents experience increased anxiety and depression during pregnancies conceived through ART compared to spontaneous conception?

SUMMARY ANSWER: Among all expectant parents in the sample, those who conceived through ART reported overall lower levels of anxiety and depression in pregnancy compared to expectant parents who conceived spontaneously, while in the subsample of parents who conceived both through ART and spontaneous conception, expectant mothers experienced increased anxiety and depression in early pregnancy following ART compared to spontaneous conception.

WHAT IS KNOWN ALREADY: Previous research on expectant parents' psychosocial adjustment in response to ART has found mixed results, with some studies suggesting ART is associated with increased anxiety and depression, and other studies suggesting improved mental health or no relationship. Mixed findings may relate to the use of cross-sectional designs that do not account for confounding differences between groups, or variability in the timing of assessment.

STUDY DESIGN, SIZE, DURATION: This prospective cohort study used data from the Norwegian Mother, Father and Child Cohort Study (MoBa), which includes 2960 pregnant women who underwent ART and 108 183 women who conceived spontaneously. Of these, a subsample of expectant parents had two consecutive pregnancies with one pregnancy resulting from ART and one conceived spontaneously (n = 286 women, n = 211 partners). Women self-reported their composite symptoms of anxiety and depression at two timepoints during each pregnancy (gestational weeks 17 and 30). Their partners self-reported composite symptoms of anxiety and depression at 17 weeks gestation during each pregnancy. Couples reported their relationship satisfaction at 17 weeks gestation.

MAIN RESULTS AND THE ROLE OF CHANCE: Using a conventional full-cohort analysis we found that ART was associated with less total anxiety and depression and greater relationship satisfaction, compared to spontaneous conception among both women and men. However, in the subsample of parents who experienced both ART and spontaneous pregnancies, ART was associated with increased levels of maternal anxiety and depression at gestational age 17 weeks ($M = 1.19$), compared to spontaneous pregnancies ($M = 1.15$), 95% CI of the mean difference 0.006, 0.074. At 30 weeks gestation, anxiety and depression were similar across both types of pregnancies. Expectant fathers reported similar levels of anxiety and depression at 17 weeks gestation during both pregnancies. Among women relationship satisfaction was higher following ART conception than spontaneous conception.

LIMITATIONS, REASONS FOR CAUTION: There is potential for selection effects in the sample, as women who have conceived through both ART and spontaneous conception in their first two pregnancies are rare. In addition, several factors that may be important predictors of mental health in this context, such as previous miscarriages and long-term infertility, were not assessed in the current study.

WIDER IMPLICATIONS OF THE FINDINGS: Our findings indicate that previous discrepancies in the literature may be related to inherent differences between the groups of parents receiving reproductive treatment and those who do not. This study addresses that limitation by prospectively comparing different types of pregnancies within the same expectant parents. Earlier inconsistencies may also relate to variations in gestational age when anxiety and depression were assessed. By examining symptoms at two timepoints in each pregnancy, we were able to examine the relation between gestational age and symptoms of anxiety and depression.

STUDY FUNDING/COMPETING INTEREST(S): The MoBa is supported by the Norwegian Ministry of Health and the Norwegian Research Council/FUGE (grant number 151918/S10). This work was also supported by the Research Council of Norway grant number 288083 and 301004. The authors have no conflicts of interest to declare.

TRIAL REGISTRATION NUMBER: N/A.

Keywords: anxiety / depression / pregnancy; ART / IVF / relationship satisfaction

Received: December 14, 2022. **Revised:** June 05, 2023. **Editorial decision:** June 09, 2023.

Introduction

Pregnancy is a period associated with increased mental distress for many expectant parents (Philpott et al., 2019; Montagnoli et al., 2020). In particular, couples who struggle with infertility and conceive a child through ART may be at increased risk for perinatal mental health difficulties such as elevated levels of stress, anxiety, and depression (Seok Kee et al., 2000; Souter et al., 2002; Klemetti et al., 2010). In addition to affecting parents' psychological wellbeing, perinatal mental health difficulties may have concomitant adverse effects on the offspring (Aktar et al., 2019). Such effects may include an increased risk of preterm birth and lower birth weight (Schetter and Tanner, 2012), child neurodevelopmental problems (Gentile, 2017), and increased emotional problems across the lifespan (Rice et al., 2007).

ART can be defined as 'all treatments or procedures that include the in vitro handling of both human oocytes and sperm, or embryos, for the purpose of establishing a pregnancy' (p. 2685) (Zegers-Hochschild et al., 2009). IVF is the most prevalent ART procedure globally, accounting for over 56% of all ART cycles in 2017 (Adamson, 2021). High costs, daily injections, blood samples, and the fear of failure may be significant sources of stress (Capuzzi et al., 2020). In particular, the oocyte retrieval, egg transfer, and waiting period for the pregnancy test have been identified as significant sources of stress among couples undergoing ART treatment (Boivin and Takefman, 1995). In addition, couples may experience self-worth difficulties, partially due to the stigma of infertility (Yilmaz and Kavak, 2019), or social difficulties and isolation (Schmidt, 2009). Even when successful, the conception following ART may involve emotional challenges, such as anxiety for a high-risk pregnancy or pregnancy loss (Covington, 1999; Souter et al., 2002).

Evidence on the psychological impact of ART has been mixed. While the use of ART has been associated with increased levels of anxiety and depression during pregnancy in some previous studies (Verhaak et al., 2007; Gourounti et al., 2013), other studies have found that couples seem to adjust well to the potential physical and emotional demands of the procedure (Hammarberg et al., 2008; McMahon et al., 2013). A recent review of 10 studies examining the association between IVF and anxiety and depression in pregnancy concluded that more research is needed to draw conclusions about this topic (Capuzzi et al., 2020). For example, Gourounti et al. (2013) found that women who conceived through IVF reported more anxiety during pregnancy compared to those who conceived spontaneously, while Velikonja et al. (2016) found no differences in anxiety and depression between women who used IVF and women who conceived naturally. In contrast, Repokari et al. (2005) found lower rates of anxiety and depression among women who conceived through ART than spontaneous conception.

One potential reason for the observed discrepancy in the previous literature may be due to the use of cross-sectional study designs that do not account for confounding factors, such as differences in socioeconomic status (SES), genetic effects, a history of mental illness, perceived self-efficacy, and quality of partner relationship between the groups (Rutter et al., 2007). Therefore, vulnerability or resilience to anxiety and depression may be independent of ART and instead relate to differences in the groups being studied. Thus, it is not clear whether differences in psychological distress are a result of ART itself, or other underlying factors that also influence psychosocial wellbeing. It is difficult to elucidate genetic effects and other confounders such as SES and lifestyle factors in observational studies (Rutter et al., 2007). However, using a quasi-experimental design comparing two pregnancies of the same mother, one conceived through ART and one through spontaneous conception, we are able to control for this. To our knowledge, no previous study has examined mental health difficulties in the same parents across different pregnancies that include both ART and spontaneous conception.

In addition, despite increasing paternal participation through pregnancy, childbirth, and infancy (Kvalevaag et al., 2013), very few studies have included the fathers in their evaluation of how parents adapt to ART (Hammarberg et al., 2008; Goldstein et al., 2020). Little is also known about how the relationship between the expectant mother and father may be affected. Given that infertility and the pursuit of parenthood are the shared experiences between the couple, it is important to consider not just how each parent is affected individually, but also the potential impact on the partner dyad. There is some evidence that successful ART may have a positive effect on the relationship between expectant parents (McMahon et al., 2013; Darwiche et al., 2015). In this context, to the best of our knowledge, the present study is the first of its kind, offering a unique opportunity to evaluate maternal and paternal mental health and relationship satisfaction in couples who had both a spontaneous pregnancy and one originated through ART, disentangling some of the mechanisms related to pregnancy-specific treatment.

The aims of this study are 2-fold. First, we will compare maternal and paternal mental distress (global anxiety and depression), and relationship satisfaction in a large sample of expectant parents both with and without ART pregnancies using a prospective cohort design. Second, we will look at only a subsample of parents with two successive pregnancies of spontaneous and ART conceptions and compare anxiety and depression, and relationship satisfaction in different types of pregnancies within the same parents.

Materials and methods

Study design and participants

This study used data from the Norwegian Mother, Father and Child Cohort Study (MoBa) (Magnus et al., 2016), a population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health. Participants were recruited from across Norway between 1999 and 2008, and women consented to participation in 41% of pregnancies (Schreuder and Alsaker, 2014). Maternal questionnaire response rates at 17 weeks gestation and 30 weeks gestation were 95.1% and 91.4%, respectively (Schreuder and Alsaker, 2014). This study was based on version 12 of the quality-assured data files released for research in 2020.

The MoBa cohort includes 111 143 mothers and 76 594 fathers. Of these, 2798 women and 2295 of their partners had at least one successful conception through ART. A subsample of 286 women had both an ART pregnancy and a spontaneous pregnancy in their first two pregnancies. Of these, 166 first had an ART pregnancy and then a spontaneous pregnancy, while 120 first had a spontaneous pregnancy and then an ART pregnancy. Among the partners, 211 fathers also participated with one ART pregnancy and one spontaneous pregnancy. Of these, 121 first had an ART pregnancy and then a spontaneous pregnancy, while 90 first had a spontaneous pregnancy and then an ART pregnancy.

Measures

Sample characteristics

Sociodemographic information regarding marital status and education was collected using self-report questionnaires at 17 weeks gestation. Medical information including parity and maternal age

at birth was collected using the Medical Birth Registry of Norway (Irgens, 2000).

Symptoms of anxiety and depression

Mothers reported global symptoms of anxiety and depression using two validated short versions of the Hopkins Symptom Checklist (SCL-25): the SCL-5 (Tambs and Moum, 1993) and the SCL-8 (Tambs and Røysamb, 2014). Items from the SCL-25 such as feeling constantly frightened or anxious, worrying too much, and feeling blue are scored on a Likert scale ranging from 1 ('not bothered') to 4 ('very bothered') (Tambs and Røysamb, 2014). The SCL-5 has been validated with a correlation of 0.92 with the SCL-25 (Tambs and Moum, 1993) and the SCL-8 has been validated with a correlation of 0.94 (Tambs and Røysamb, 2014). Maternal anxiety and depression were assessed twice during pregnancy. First at 17 weeks gestation using the SCL-5 and again at 30 weeks gestation using the SCL-8. The mean scores for the 17th and 30th gestational weeks were calculated separately. Paternal anxiety/depression was assessed once at the 17th week of gestation using the SCL-8. Cronbach's alpha for the SCL-8 was 0.82 for men and 0.80 for women. Cronbach's alpha for the SCL-5 was 0.78 for women.

Partner relationship

Men and women reported their satisfaction with the relationship to their spouse/partner using the Relationship Satisfaction Scale (Røysamb *et al.*, 2014) at gestational age 17 weeks. The scale consists of ten statements such as 'I have a close relationship with my spouse/partner' and 'I believe my partner is satisfied with our relationship' where participants rate their agreement on a 6-point Likert scale, ranging from 'I completely disagree' to 'I completely agree'. Mean scores were calculated, and Cronbach's alpha for the measure was 0.87 for men and 0.89 for women.

Statistics

The power to detect a difference in maternal anxiety and depression when comparing their ART and spontaneous pregnancies in the quasi-experimental design was computed using R version 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria) with the package 'pwr' (Champely *et al.*, 2018). We found that with a sample size of 286 mothers, we would have 0.92 power to detect a small effect size and >0.99 power for medium or large effect sizes.

For descriptive statistics, we used parametric and non-parametric analyses as appropriate. Independent samples' *t*-tests were used to compare mean differences in anxiety and depression, and relationship satisfaction between expectant parents with and without ART pregnancies. To compare mean differences in anxiety and depression between ART and spontaneous pregnancies among women at 17 and 30 weeks gestation, and among men at 17 weeks gestation, three paired-samples' *t*-tests were conducted. In the entire cohort analyses, we examined the influence of age, education, and parity using univariate ANOVAs with the potentially confounding variables added as random factors one by one. In the subsample, the difference in anxiety and depression and relationship satisfaction between men and women across pregnancies were compared using mixed-design ANOVAs. This allowed for assessing whether there was any interaction with the type of pregnancy (ART versus spontaneous) and the order of pregnancy (ART first versus ART second). The analyses were performed using IBM SPSS version 27 (Statistical Package for the Social Sciences, IBM, Armonk, NY, USA) with alpha level 0.05.

Ethics

All participants have provided their informed consent prior to participation. The study was approved by the Regional Committees for Medical and Health Research Ethics (REK-2009/1899-7; 2013/2061) and the Norwegian Data Inspectorate.

Results

Description of sample

Sociodemographic variables describing the entire cohort and the subsample are shown in Table 1. In the entire cohort, ART women were on average older, more educated, more likely to be married or cohabiting, and more likely to be primiparous than women who conceived spontaneously. In the subsample of women who participated with both an ART and a spontaneous pregnancy, women were slightly younger during their ART pregnancy than their spontaneous pregnancy ($P < 0.05$). Other sociodemographic variables did not significantly differ between pregnancies.

Entire cohort comparison between couples with and without ART pregnancies

In the entire cohort analysis, expectant mothers who conceived through ART reported less anxiety and depression at 17 weeks gestation ($M = 1.23$, $SD = 0.37$) compared to expectant mothers with spontaneous conceptions ($M = 1.26$, $SD = 0.40$), $t(97\ 883) = 3.71$, $P < 0.001$. Similarly, among fathers, those who conceived through ART reported less anxiety and depression ($M = 1.13$, $SD = 0.26$) than those who conceived spontaneously ($M = 1.14$, $SD = 0.27$), $t(76\ 592) = 2.12$, $P < 0.0.01$ (Supplementary Fig. S1). At 30 weeks gestation, women who were pregnant through ART continued to report less anxiety and depression ($M = 1.21$, $SD = 0.30$) than those with spontaneous conceptions ($M = 1.26$, $SD = 0.35$), $t(88\ 451) = 6.60$, $P < 0.001$. Controlling for parity, age, or education did not significantly influence the results.

Mean relationship satisfaction at gestational age 17 weeks was higher among those women who were pregnant through ART ($M = 5.41$, $SD = 0.58$) than through spontaneous conception ($M = 5.31$, $SD = 0.68$), $t(99\ 053) = 7.43$, $P < 0.001$. Similarly, among men, mean relationship satisfaction was higher among those with ART pregnancies ($M = 5.33$, $SD = 0.62$) than those with spontaneous pregnancies ($M = 5.29$, $SD = 0.64$), $t(76\ 573) = 3.27$, $P < 0.001$.

Subsample comparison of pregnancies in couples with both ART and spontaneous conception

When comparing different types of pregnancies among women who had one pregnancy from ART and one from spontaneous conception, ART pregnancies were associated with more anxiety and depression at 17 weeks gestation than spontaneous conception ($M = 1.19$, $SD = 0.35$ versus $M = 1.15$, $SD = 0.29$), $t(256) = 2.00$, $P < 0.05$, with a mean difference 0.037, 95% CI [0.006, 0.074] (Supplementary Fig. S2). Adjusting for age, education, or whether ART was the first or second pregnancy did not significantly influence the results. At 30 weeks gestation, there was no significant difference in anxiety and depression depending on the type of pregnancy, $t(249) = -0.310$, $P = 0.756$ [mean ART pregnancy = 1.20 ($SD = 0.29$), mean spontaneous conception = 1.21 ($SD = 0.35$)]. Among men in the subsample, there was no difference in anxiety and depression between ART and spontaneous pregnancies at 17 weeks gestation, $t(183) = 0.784$, $P = 0.434$ [mean ART pregnancy = 1.13 ($SD = 0.23$), mean spontaneous conception = 1.12 ($SD = 0.18$)].

Table 1 Sociodemographic characteristics in the entire cohort of parents and in the subsample of men and women participating with two pregnancies, one conceived through ART and one through spontaneous conception (SC).

	Women			Men		
	ART pregnancy N (%)	SC pregnancy N (%)	P-value	ART pregnancy N (%)	SC pregnancy N (%)	P-value
Entire cohort	**N = 2960**	**N = 108 183**		**N = 2243**	**N = 74 299**	
Age, M (SD)	32.38 (3.68)	30.5 (19.9)	**<0.001**			
Married or cohabiting	2912 (98.3)	103 208 (95.5)	**<0.001**	2237 (99.6)	73 915 (97.9)	**<0.001**
Education			**<0.001**			**<0.001**
High school or vocational school	830 (31.0)	33 360 (35.7)		976 (44.7)	35 562 (48.7)	
University/college up to 4 years	1142 (42.7)	38 216 (40.9)		658 (30.1)	19 634 (26.9)	
University/college >4 years	704 (26.3)	21 909 (23.4)		550 (25.2)	17 819 (24.4)	
First pregnancy	1977 (66.5)	84 195 (64.1)	**0.001**			
Subsample	**N = 286**	**N = 286**		**N = 211**	**N = 211**	
Age, M (SD)	32.14 (3.50)	33.15 (3.89)	**0.012**			
Married or cohabiting	285 (99.7)	284 (99.3)	0.551	209 (99.1)	211 (100)	0.155
Education			0.768			0.912
High school or vocational school	68 (26.8)	63 (24.2)		70 (35.4)	75 (37.3)	
University/college up to 4 years	120 (46.2)	130 (50.0)		69 (34.8)	69 (34.3)	
University/college >4 years	66 (25.4)	67 (25.8)		59 (29.8)	57 (28.4)	
First pregnancy	166 (58.0)	120 (42.0)	0.171			

Different pregnancies were compared using independent t-tests, paired-samples t-tests, and chi-square statistics as appropriate. Significant differences are highlighted in bold.

Mean relationship satisfaction at 17 weeks gestation among expectant mothers was 5.44 (SD = 0.55) during the ART pregnancy and 5.32 (SD = 0.63) during the spontaneouspregnancy (Supplementary Fig. S3). Among expectant fathers, the mean relationship satisfaction was 5.34 (SD = 0.68) in the ART pregnancy and 5.36 (SD = 0.74) in the spontaneous pregnancy. Parental sex significantly interacted with the type of pregnancy, $F(1, 389) = 5.91$, $p < 0.05$, such that women experienced increased relationship satisfaction during their ART pregnancy, while there was no difference between pregnancies among men.

Discussion

Interpretation of main findings

Using a large population-based longitudinal cohort study, we compared anxiety and depression in pregnancies conceived through ART and spontaneously. The conventional full-cohort analysis showed that ART pregnancies were associated with less anxiety and depression and greater relationship satisfaction than spontaneous pregnancies. However, when comparing different types of pregnancies in a subsample of couples who conceived both through ART and spontaneously, we found that in contrast ART pregnancies were associated with more maternal symptoms of anxiety and depression than spontaneous pregnancies at 17 weeks gestation. Among men and women at 30 weeks gestation, there was no difference in symptoms of anxiety and depression between ART and spontaneous conception using this design.

The differing findings between the analyses using the full cohort and the subsample of parents with both ART and spontaneous pregnancies suggest that the findings in the full cohort may be influenced by inherent differences in the populations being studied. Specifically, parents who conceive through ART may represent a particularly resourceful population who may be less vulnerable to experiencing elevated anxiety and depression in pregnancy (McMahon et al., 2013). However, it does appear that within this group, ART is associated with more distress in early pregnancy compared to spontaneous pregnancies. Conceiving a child through ART is often a long and stressful process that can cause emotional strain (Souter et al., 2002). Several earlier studies have documented that ART is associated with increased pregnancy-specific anxiety (McMahon et al., 2013; Capuzzi et al., 2020), which includes worries about the health of the fetus and the pregnancy. It is estimated that around 26% of pregnancies end in miscarriage and more than 80% of these occur in the first trimester (Dugas and Slane, 2021). Thus, the viability of the pregnancy is a much greater concern for women in early pregnancy. By gestational week 30, we did not see a difference in symptoms of anxiety and depression between women with ART pregnancies and women who conceived spontaneously. This may indicate that once the viability of the pregnancy is established and the stress of the procedure becomes more distant, the emotional response to ART pregnancies is similar to that of other pregnancies.

Among women, ART pregnancies were associated with slightly higher relationship satisfaction compared to spontaneous pregnancies both in the full cohort and in the subsample. A previous study showing higher marital satisfaction following ART compared to spontaneous conception hypothesized that the difference may be due to ART patients being particularly motivated and competent parents (McMahon et al., 2013). This may in part explain the difference we observed when looking at the entire cohort. In addition, it may be that the shared challenge of going through infertility and reproductive treatment necessitates enhanced communication, intimacy, and closeness between the partners (Pasch and Sullivan, 2017).

Strengths and limitations

This study is the first to compare anxiety and depression and relationship satisfaction during ART and spontaneous pregnancies using both a longitudinal study design and a quasi-experimental design. By looking prospectively at the same parents across two types of pregnancies we were able to rule out unmeasured confounding variables for example due to genetic liability, SES, lifestyle factors, and other environmental differences that may vary between families (Lahey and D'Onofrio, 2010). Given the impossibility of randomizing mothers according to ART and spontaneous pregnancies, this study design solves some of the methodological

problems inherent in population comparison designs (Kendler, 2017).

Another important addition of this study to the literature is the repeated measure of anxiety and depression at two time-points among women during each type of pregnancy and the inclusion of a relationship satisfaction variable. The difference in anxiety and depression between early and late pregnancy may partially explain some of the inconsistencies reported by earlier research, as the effect of ART on anxiety and depression in the subsample differed between gestational age 17 and 30 weeks. In addition, the prospective nature of the study reflects the direction of effects and enhances the validity of measurements.

A limitation of the study includes the potential for selection effects in the sample when we included only those parents who have had both an ART and a spontaneous pregnancy in their first two pregnancies. This is an unusual cohort, and for that reason, the vast majority of MoBa participants could not be included in the quasi-experimental design. Thus, the findings may not be representative of the whole target population. Furthermore, the women participating in MoBa with several pregnancies might also represent a biased selection as has been suggested by Sjölander (2016) and Frisell *et al.* (2012).

Several factors that may be important predictors of mental health, specifically in the context of ART pregnancies, such as previous miscarriages and long-term infertility, were not assessed in the current study. Future studies should further explore the role of these experiences in the context of ART versus spontaneous conception. In addition, earlier literature suggests that early pregnancy may be a particularly stressful period due to the fear of miscarriage (Boivin and Takefman, 1995). It would therefore have been beneficial to examine anxiety and depression prior to week 17 of pregnancy. With additional assessment timepoint, we could have further examined the influence of gestational age on parental anxiety and depression. Lastly, self-report questionnaires were used to measure maternal anxiety/depression and partner relationship satisfaction. Social stigma about mental health problems and partner conflicts, paired with a desire to appear healthy for the expected baby, could potentially lead to the under-reporting of these difficulties.

Conclusion

The association between ART and mental and social wellbeing in pregnancy depended on whether we compared ART pregnancies to spontaneous conception in the cohort overall or to spontaneous pregnancies within the same group of parents. These differing results suggest that there are unmeasured differences between families that influence psychosocial wellbeing. Overall, couples undergoing ART appeared to experience lower levels of mental and social distress compared to the cohort as a whole. Among women, there may be some emotional strain associated with the treatment of infertility through ART, but the impact on emotional wellbeing seems temporary. Men did not report any difference in anxiety and depression between ART and spontaneous pregnancies, indicating that women's emotional health may be more responsive to these specific reproductive health challenges than men's emotional health.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

The data contain sensitive information and therefore cannot be made publicly available (General Data Protection Regulation). Since the participants have not given their consent that the data can be made publicly available, data sharing is restricted by the informed consent and the regulations in the Health Research Act (01 July 2009), regulated by the Regional Committees for Medical and Health Research Ethics of Norway. The dataset analyzed during the current study may be requested by contacting project leader Mona Bekkhus (mona.bekkhus@psykologi.uio.no) at Promenta Research Center, Department of Psychology, University of Oslo, Forskningsveien 3A, 0373 Oslo. Data access can be given via the services for sensitive data provided by the University of Oslo, after application and approval from the Regional Committees for Medical and Health Research Ethics of Norway and the MoBa administration. Researchers will then be able to replicate the findings presented by following the protocol in the methods section.

Authors' roles

A.O. wrote the manuscript with input from all authors. A.O. and D.S. conducted the statistical analyses. S.T. and L.J.K.M. conducted a literature review and read and reviewed the manuscript. M.B., A.K., and E.R. conceptualized the study and reviewed and edited the manuscript. T.G.T. read and reviewed the manuscript. M.B. was the project administrator and participated with data curation and funding acquisition.

Funding

The Norwegian Mother and Child Cohort Study is supported by the Norwegian Ministry of Health and the Norwegian Research Council/FUGE (grant no. 151918/S10). This work was partly supported by the Research Council of Norway through its Centers of Excellence funding scheme, project number 262700 and grant numbers 288083 and 301004.

Conflict of interest

No conflicts of interest were declared.

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