

# Conception by means of in vitro fertilization is not associated with maternal depressive symptoms during pregnancy or postpartum

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**Objective:** To study whether conception by means of in vitro fertilization (IVF) is associated with maternal depressive symptoms during pregnancy or postpartum.

**Design:** Longitudinal observational study.

**Setting:** University hospital.

**Patient(s):** A total of 3,283 women with singleton pregnancies receiving antenatal care and delivering in Uppsala from 2010 to 2015.

**Intervention(s):** A web-based self-administered structured questionnaire including sociodemographic, clinical and pregnancy-related items, and the Edinburgh Postnatal Depression Scale (EPDS) was delivered at 17 and 32 gestational weeks and at 6 weeks and 6 months postpartum.

**Main Outcome Measure(s):** Prevalence of significant depressive symptoms (EPDS  $\geq 12$ ) and EPDS scores.

**Result(s):** A total of 167 women (5%) had conceived via IVF and 3,116 (95%) had a spontaneous pregnancy. IVF mothers were more frequently  $\geq 35$  years of age (46.1% vs. 22.6%) and primiparous (71.7% vs. 49.9%) and had a higher cesarean delivery rate (22.4% vs. 14.2%). Demographic and clinical characteristics were otherwise similar between the two groups. Significant depressive symptoms were reported by 12.8%, 12.4%, 13.8%, and 11.9% of women at 17 and 32 gestational weeks and 6 weeks and 6 months postpartum, respectively. The prevalence of depressive symptoms and the EPDS scores during pregnancy and postpartum were similar between women conceiving spontaneously or through IVF. The mode of conception was not associated with significant depressive symptoms at any time point, even when adjusting for several possible confounders in multivariable logistic regression analysis.

**Conclusion(s):** Despite the psychologic distress characterizing subfertility and its treatment, conception by means of IVF is not associated with maternal depressive symptoms during pregnancy or postpartum. (Fertil Steril® 2017;108:325–32. ©2017 by American Society for Reproductive Medicine.)

**Key Words:** In vitro fertilization, assisted reproductive technologies, pregnancy complications, depression, postpartum depression

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In vitro fertilization (IVF) was an acknowledged breakthrough in medical history (1, 2), and its scope has been successfully extended far beyond the initial indications due to multiple factors, including social,

technical, and commercial ones (3, 4). In 2012 it was estimated that 5 million children had already been born worldwide (5), and in some countries a considerable, and increasing, share of newborns are conceived via IVF (6, 7).

Although most of the research in this field has its natural focus on the desired reproductive outcomes, namely, pregnancies and live births, the question of whether conception by IVF is associated with perinatal depression has been addressed more rarely. Yet maternal depressive symptoms, whether occurring during pregnancy or culminating in the postpartum period, are a common and major contributor to maternal morbidity and mortality (8). Furthermore, psychologic distress is, unsurprisingly, associated with subfertility (9), and several studies show a high prevalence of anxiety and

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depression among couples undergoing IVF (9–11). Treatment failures are particularly linked to psychologic distress (12), but even successful IVF mothers may experience a complex transition to parenthood with intense fetal attachment and anxiety (13–15). Nevertheless, relatively few well controlled studies with heterogeneous design have focused on the association between successful IVF and maternal depression. Some authors have documented a positive association between depressive perinatal maternal symptoms and conception by IVF (16), and related factors, such as multiple pregnancies, have been suggested to increase the risk (17). However, a recent meta-analysis of observational studies rejected the hypothesis that pregnancies conceived through medically assisted conception or assisted reproductive technologies (ART) are associated with postpartum depressive symptoms (18). Unfortunately, only six studies specifically focusing on ART were available for inclusion in analysis (16, 19–23), four of them originating from Australia (19, 20, 22, 23), accounting for a total of 1,773 women (18). A further obstacle to the synthetic interpretation of the few available studies is a substantial heterogeneity in case selection, design, and outcome measurements. Many include women conceiving with the use of ART treatments other than IVF (e.g., gamete intrafallopian transfer), or through gamete donation. The outcome variables also differ across published studies and have not always been measured by validated instruments. The internationally validated Edinburgh Postnatal Depression Scale (EPDS) (24) was sometimes used, albeit at different or unspecified time points. A study reported significantly higher EPDS scores among ART mothers at 30–32 gestational weeks and at 1 week and 3 months postpartum (16). The same authors found more depressed subjects, defined by EPDS >12, among the ART mothers during the 3rd trimester (16% vs. 0%) as well as at 1 week (12% vs. 7.9%) and 3 months (8% vs. 0%) postpartum, although only the antenatal difference was statistically significant (16). No significant differences in prevalence of depressive symptoms (EPDS ≥ 13) between ART (5%) and non-ART (7%) mothers were reported by another study at 12 months postpartum (19). Clinically relevant depressive symptoms (EPDS >12) among patients of a mother-baby unit, who presented with infant sleeping/feeding problems or maternal psychologic distress during the 1st year postpartum, were unsurprisingly frequent (>45% of women) regardless of the mode of conception (ART or spontaneous) (20). However, ART mothers were significantly overrepresented in that selected group of women (6% vs. 1.52% in the general population), and the mode of conception was not recorded for 219 cases (29.4%), which were included as spontaneous (20). McMahon et al. (22) observed no differences at 4 months postpartum between IVF and spontaneous mothers in the rate of major depressive disorder as diagnosed by a structured interview (Mini-Plus International Neuropsychiatric Interview). However, the prevalence of major depression was higher among IVF mothers in the age stratum of ≥ 31 to <37 years (11.6% vs. 3.6% in spontaneous pregnancies) (22), which is a well represented age group among ART patients. Through telephone interviews conducted up to 2 years after delivery, no significant differences between ART and

spontaneous mothers were found when asking “whether they believed that they had postnatal depression” during the first 4 weeks (23).

Registry studies including large populations also have failed to show an association between fertility treatments and postpartum depression (25, 26). However, they may be limited by a cross-sectional design, the inability to differentiate between different kinds of fertility treatments (25), or the need to rely retrospectively on registered treatments and coded diagnoses of depression (26).

Finally, most studies on postpartum depression, as well as the only available meta-analysis (18), neglect antenatal symptoms, although these are known as a significant risk factor (27) if not an earlier manifestation of the same condition (8). Findings from studies specifically addressing antenatal depressive symptoms among IVF mothers have so far been contrasting, including similar, higher, or even lower rates compared with spontaneously pregnant women (16, 28–30).

Clearly, the question of whether exposure to IVF conception alone is associated with perinatal depression has not been explored thoroughly. Therefore, our current view on this relevant and complex topic is neither as broad nor as deep as it should be, particularly in a context of evolving and cross-nationally heterogeneous IVF practices. Ideally, larger prospective studies, measuring depressive symptoms with the use of validated instruments both during pregnancy and postpartum and focusing on IVF patients while removing or controlling for potential confounders or effect modulators, would be needed. Furthermore, prospective data from so far under-represented geographic regions as well as from modern single embryo transfer (SET) contexts would be desirable. The aim of the present study was to evaluate whether conception by IVF is associated with maternal depressive symptoms, both during pregnancy and postpartum, in a large prospective cohort of pregnant women receiving obstetrical care at a Swedish university hospital.

## MATERIALS AND METHODS

### Study Population

This study was conducted at the Department of Obstetrics and Gynecology of Uppsala University Hospital, Uppsala, Sweden, as a part of the BASIC (Biology, Affect, Stress, Imaging, Cognition) project, a population-based longitudinal study on psychologic well-being during pregnancy and postpartum (31). From 2010 to 2015, pregnant women undergoing routine fetal ultrasound screening at gestational week 17 were informed about the project and asked to give their consent to participate. Exclusion criteria at this stage included: age <18 years, protected identity, inability to adequately communicate in Swedish, and pathologic findings at the routine ultrasound scan. Participation was not compensated, and the original BASIC cohort had a participation rate of 22%. Participants were asked to complete a web-based self-administered structured questionnaire containing questions on sociodemographic, clinical and pregnancy-related variables, and a Swedish validated version of the EPDS (24, 31), at 17 and 32 gestational weeks and 6 weeks and 6 months

postpartum. The questionnaires were self-paced (requiring an estimated 20 minutes to complete). At the first questionnaire, BASIC participants were asked whether they had conceived through a fertility treatment or not. For the aims of the present study, all respondents were initially included and grouped according to the mode of conception (spontaneous or via fertility treatment). Subjects with multiple pregnancies were excluded. Furthermore, the authors scrutinized medical records to exclude women who had received gamete donation or any treatment other than IVF with or without intracytoplasmic sperm injection.

### Outcome Variable

The main outcome variable in this study was the prevalence of maternal depressive symptoms. This was evaluated by means of the EPDS, an internationally validated ten-item self-reported questionnaire designed to screen for depressive symptoms in the peripartum period (24). The questionnaire investigates the presence of symptoms during the previous 7 days, and different cutoffs have been used in clinical and research practice internationally. In the present study, significant depressive symptoms were defined by an EPDS score  $\geq 12$ , because this cutoff is validated and used in Sweden to screen for postpartum depression (32). Further analyses were based on a 9/10 threshold, which has been used in biologic research to potentially increase the test's sensitivity (31). EPDS scores during pregnancy were also analyzed with a 12/13 threshold, which showed 77% sensitivity and 94% specificity in a Swedish validation study (33).

In addition, the EPDS scores were considered as a secondary continuous outcome variable, acknowledging the dimensional nature of psychologic symptoms and in agreement with previous studies (16).

### Potential Confounders

Several sociodemographic and clinical variables were considered as potential confounders. Age, body mass index (BMI), and parity were dichotomized for statistical analysis (age  $<35$  or  $\geq 35$  years; BMI  $<25$  or  $\geq 25$  kg/m<sup>2</sup>; primipara or multipara). We also collected self-reported data about education, which was dichotomized as "higher" (college/university degree) and "lower" (primary/high school degree), and employment status (employed/unemployed). A history of depression and the use of selective serotonin-reuptake inhibitors (SSRI) were recorded and treated as categorical variables (yes/no). Obstetrical data included mode of delivery (vaginal or cesarean section) and length of pregnancy ( $<259$  or  $\geq 259$  days). Additional self-reported variables were collected at 6 weeks postpartum, including breastfeeding (yes/no), partner support (yes/no), sleep ( $<6$  or  $\geq 6$  hours per night), and stressful life events (SLEs) occurring during the previous 12 months (fewer than or at least three). Partner support was addressed by three possible answers to the closed-ended question, "Do you think that your partner helps you with the baby?" (yes, a lot; yes, a little; no). The first alternative was categorized as "partner support." The assessment of SLEs was performed with the use of a ten-item scale devel-

oped by Rosengren et al. (34) including the following: serious illness in family member, serious concern about family member, death of family member, divorce or separation, involuntary change of residence, involuntary change of work, feelings of redundancy, feelings of insecurity at work, serious financial trouble, and legal prosecution.

### Statistical Analyses

Pearson chi-square or Fisher exact test were used to examine differences in demographic and clinical characteristics in women with spontaneous or IVF pregnancies. Differences in rates of significant depressive symptoms between spontaneous and IVF pregnancies, during pregnancy and postpartum, were evaluated by means of Pearson chi-square test. Differences in EPDS scores were evaluated by means of Mann-Whitney *U* test because of their nonnormal distribution.

Logistic regression was used to measure the association between significant depressive symptoms as the dependent variable and the mode of conception (spontaneous or IVF) as the independent variable. Potential confounding factors were included in multivariable logistic regression analyses.

The software IBM SPSS Statistics for Windows, version 20, was used for data analysis. Statistical significance was set at a *P* value of  $<.05$ .

### Ethical Approval and Consent

Ethical approval was obtained from the Regional Ethical Review Board in Uppsala. Written informed consent was obtained from each woman before recruitment.

## RESULTS

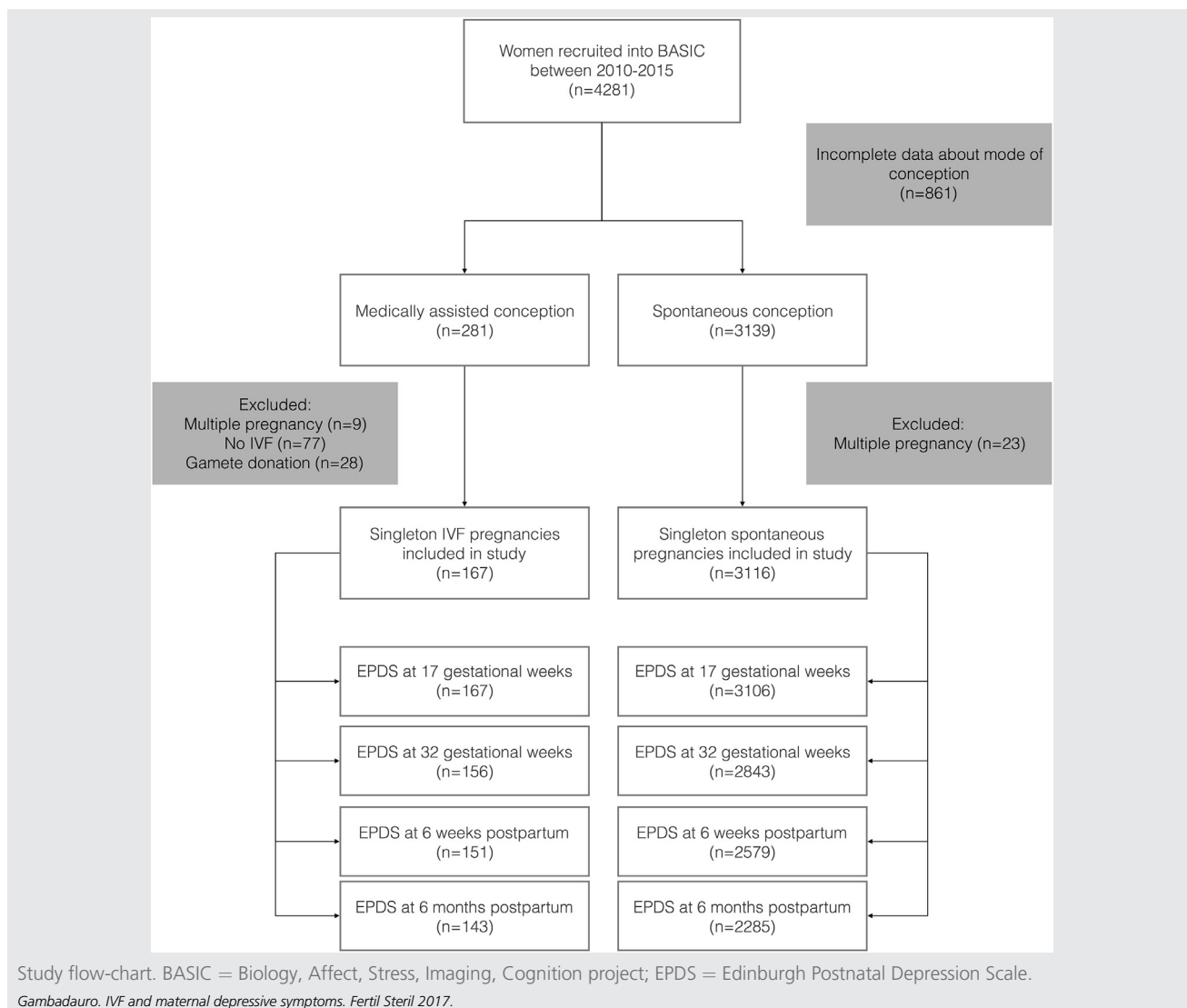
From 2010 to 2015, 4,281 women agreed to participate in BASIC, of whom 3,420 answered the question about mode of conception (spontaneous or by fertility treatment). After excluding multiple pregnancies and, for the IVF group, women who had received gamete donation or any other fertility treatment, 3,283 subjects were included in the present study. Of these women, 167 (5%) had conceived via IVF and 3,116 (95%) had a spontaneous pregnancy (Fig. 1).

IVF mothers were more frequently older ( $\geq 35$  years; 46.1% vs. 22.6%) and primiparous (50.1% vs. 28.3%) than those who had conceived spontaneously. Delivery was by cesarean section in 22.4% of IVF pregnancies compared with 14.2% of spontaneous pregnancies. No other significant differences in demographic and clinical characteristics were observed between the two groups (Table 1).

EPDS response rates were 99.7% and 91.3%, respectively, at 17 and 32 gestational weeks, and 83.2% and 74%, respectively, at 6 weeks and 6 months postpartum (Fig. 1). Significant depressive symptoms (EPDS  $\geq 12$ ) were overall reported by 12.8% (419/3,273), 12.4% (371/2,999), 13.8% (376/2,730) and 11.9% (288/2,428) of women at 17 and 32 gestational weeks and 6 weeks and 6 months postpartum, respectively.

The prevalence of significant maternal depressive symptoms during pregnancy and postpartum was not significantly

FIGURE 1



different between IVF and spontaneous pregnancies (Table 2). Similarly, no differences were seen when comparing EPDS scores by means of the Mann-Whitney *U* test (Table 2).

The logistic regression analyses showed that the mode of conception was not associated with significant depressive symptoms (EPDS  $\geq 12$ ) at any of the considered time points during pregnancy and postpartum, even when adjusting for age, BMI, parity, education, depression history, and SLEs (Table 3).

All analyses were repeated with EPDS cutoff at  $\geq 10$  points for pregnancy and postpartum, as well as with pregnancy EPDS cutoff of  $\geq 13$  points, and the results remaining unaltered.

## DISCUSSION

This is so far, and to the best of our knowledge, the largest longitudinal study comparing singleton spontaneous and IVF

pregnancies, with own gametes, in terms of maternal depressive symptoms that were prospectively assessed by a validated scale and at multiple time points during pregnancy and postpartum. Our findings show no statistically significant differences in perinatal depressive symptoms between mothers conceiving spontaneously or via IVF. This was observed at several measurements, during pregnancy (17 and 32 gestational weeks) and postpartum (6 weeks and 6 months), as well as after controlling for many relevant confounders.

Despite the well known psychologic distress of patients coping with subfertility and its medical management (9), only few controlled studies with heterogeneous design have so far focused on the association between treatments and maternal depression. Although a higher risk for perinatal depressive symptoms for women conceiving by fertility treatments was previously suggested (16), a recent meta-analysis could not confirm the association when considering only the postpartum period (18). A limit of that otherwise

TABLE 1

**Sociodemographic and clinical characteristics of the study population in association with mode of conception (spontaneous or via IVF).**

Category	Mode of conception, n (%)		P value <sup>a</sup>
	Spontaneous	IVF	
Age, y			
<35	2,187 (77.4)	90 (53.9)	<.001
≥35	638 (22.6)	77 (46.1)	
BMI, kg/m <sup>2</sup>			
≤24.9	2,116 (72)	110 (66.3)	.11
≥25	862 (28)	56 (33.7)	
Parity			
Primipara	1,168 (49.9)	109 (71.7)	<.001
Multipara	1,174 (50.1)	43 (28.3)	
Education			
Higher	2,411 (77.8)	136 (81.4)	.272
Lower	687 (22.2)	31 (18.6)	
Employment			
Employed	2,813 (90.7)	153 (91.6)	.703
Unemployed	287 (9.3)	14 (8.4)	
Depression history			
No	2,130 (69.1)	117 (70.5)	.700
Yes	954 (30.9)	49 (29.5)	
Use of SSRI			
No	2,999 (98.1)	163 (97.6)	.561
Yes	58 (1.9)	4 (2.4)	
Delivery mode			
Vaginal	2,010 (85.8)	118 (77.6)	.006
Cesarean	332 (14.2)	34 (22.4)	
Pregnancy length, d			
≥259	2,244 (95.8)	141 (92.8)	.074
<259	98 (4.2)	11 (7.2)	
6 wk postpartum			
Stressful life events <sup>b</sup>			
0–2	2,448 (94.3)	144 (94.1)	.940
≥3	149 (5.7)	9 (5.9)	
Breastfeeding			
Yes	2,410 (92.7)	144 (93.5)	.717
No	189 (7.3)	10 (6.5)	
Partner support			
Yes	1,614 (62.3)	103 (67.8)	.179
No	975 (37.7)	49 (32.2)	
Poor sleep			
No	1,994 (77.2)	110 (71.9)	.133
Yes	590 (22.8)	43 (28.1)	

Note: SSRI = selective serotonin-reuptake inhibitor.

<sup>a</sup> Pearson chi-square or Fisher exact test (when >20% cells had expected count <5).

<sup>b</sup> During the previous 12 months.

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comprehensive work of synthesis was that only six studies comparing women conceiving via ART or spontaneously were identified and included in analysis (16, 19–23), for a total of 1,773 women (554 ART and 1,219 control), whereas our study was based on a cohort of 3,283 mothers giving birth at the same university hospital. Interestingly, four out of the six studies proceeded from a single country, Australia (19, 20, 22, 23). Furthermore, many studies did not limit their exposure of interest to IVF conception; they included women who had undergone other reproductive technologies or gamete donation or had multiple pregnancies. In some cases, even the exact definition of ART pregnancy appeared to be vague (21). As pointed out in our introductory review, the few available studies on ART and postpartum depression

are also heterogeneous for timing and outcome measurements, and their synthetic interpretation would seem therefore to be controversial. Although some authors have reported more depressive symptoms among ART mothers 1 and 3 months after delivery (16), others have reported no differences at 1 year postpartum (19). Other authors have reported similar prevalence of postpartum depressive symptoms although without specifying the time points and limiting their observations to women with specifically stressful experiences, such as exhaustion or neonatal feeding/sleeping problems (20). Yet another study, though not observing overall differences between ART and non-ART mothers, reported higher prevalence of major depression in an age stratum (31–37 years) that is well represented among IVF mothers (22).

Unfortunately, inconclusive findings also emerge from the sparse available literature on IVF and antenatal depressive symptoms, with both negative findings and positive findings of opposite direction having been reported (16, 28–30).

In this context of paucity and heterogeneity of data sources, our work has a number of strengths, the first being its size, making it the largest study including only singleton homologous IVF pregnancies and where depressive symptoms were prospectively measured by means of a validated instrument, namely, the EPDS. Our relatively large sample was facilitated by an established prospective cohort of pregnant women receiving obstetrical care and delivering at a single university hospital, allowing us to confirm our findings at several longitudinal measurements in the same study population, including during pregnancy and postpartum. Furthermore, we present prospective and robustly controlled data from the European region, which has so far been underrepresented in the related literature. Another strength of our study was the availability of several sample characteristics that were systematically measured in the whole cohort. Such breadth of analysis is important because, although postpartum depression is a serious outcome, antenatal depressive symptoms strongly predict it (27), and the whole perinatal period influences maternal and child health, in both the short and the long term (8).

The study's observational nature is a limitation, because women conceiving spontaneously or with the use of ART often have different characteristics. Nevertheless, we thoroughly considered several factors whose plausible effect on depressive symptoms may be difficult to separate from that of IVF (17). Only singleton pregnancies were included, because multiple pregnancies have been related to a higher risk of maternal depression, particularly after ART (17). Births by cesarean section in our study were more common among IVF mothers, but their rate (22%) was low compared with other studies on the same topic reporting rates up to 88% (21) and consistently >45% (16, 20, 22, 23). The two groups showed no statistically significant differences regarding employment, pregnancy length, breastfeeding, partner support, or poor sleep during postpartum. Furthermore, we considered multiple known risk factors for maternal depression that could be unevenly distributed between the IVF and spontaneous conception groups, such as age, BMI, parity, education, history of depression, and SLEs. These

TABLE 2

## Mode of conception and maternal depressive symptoms during pregnancy and postpartum.

Time point/conception mode	Prevalence of depressive symptoms (EPDS $\geq 12$ )		EPDS score	
	n (%)	P value <sup>a</sup>	Median (IQR)	P value <sup>b</sup>
Gestational week 17				
Spontaneous	404 (13)	.131	5 (6)	.182
IVF	15 (9)		4 (6)	
Gestational week 32				
Spontaneous	353 (12.4)	.746	5 (6)	.684
IVF	18 (11.5)		5 (5)	
Postpartum week 6				
Spontaneous	354 (13.7)	.770	5 (6)	.906
IVF	22 (14.6)		5 (5)	
Postpartum month 6				
Spontaneous	275 (12)	.291	5 (6)	.948
IVF	13 (9.1)		5 (6)	

Note: EPDS = Edinburgh Postnatal Depression Scale; IQR = interquartile range.

<sup>a</sup> Chi-square test.

<sup>b</sup> Mann-Whitney U test.

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were included in multivariable analyses and did not alter the results.

Another limitation is that the study cannot account for the potential effect of the care that may have been offered to those presenting with significant depressive symptoms at any time point. That possibility was intrinsic to the longitudinal design, but there is no reason to think that such care would differ depending on the mode of conception, considering the universal nature of Swedish health care. A further consideration is that not all of the recruited women responded to the EPDS questionnaire at every time point, although the response rate was consistently  $>90\%$  during pregnancy and  $>70\%$  postpartum.

Regardless of the above considerations, our findings are reassuring for those undergoing IVF and for their health care providers, considering the known psychologic burden of subfertility. Some factors could be argued to modulate

the potential risk of perinatal depression among IVF mothers, one of them being the joy and relief in finally achieving a desired pregnancy. This is not necessarily true for all women, because the transition to parenthood for IVF parents may be complex and characterized by intense fetal attachment, related anxiety, and lower self-esteem (13–15, 19). Even higher rates of sick leave during pregnancy or admission to residential early parenting services have been reported among mothers conceiving via fertility treatments (35, 36). We must, however, acknowledge how other studies have instead found that the self-esteem and psychologic status of women conceiving by IVF or spontaneously are similar, and that IVF mothers would even report improved self-esteem and lower anxiety as the pregnancy advances (37).

Another plausible modulator of the risk of maternal depression after IVF may be that, despite the association between subfertility and psychologic distress, women who

TABLE 3

Logistic regression derived crude and adjusted odds ratios (ORs and aORs) and 95% confidence intervals (CIs) for significant perinatal depressive symptoms (EPDS  $\geq 12$ ) in relation to mode of conception.

Analysis	Gestational week 17		Gestational week 32		Postpartum week 6		Postpartum month 6	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Mode of conception (IVF)	0.66	0.39–1.14	0.92	0.56–1.52	1.07	0.67–1.71	0.73	0.41–1.31
<b>Multivariable regression</b>	<b>aOR</b>	<b>95% CI<sup>a</sup></b>	<b>aOR</b>	<b>95% CI<sup>b</sup></b>	<b>aOR</b>	<b>95% CI<sup>c</sup></b>	<b>aOR</b>	<b>95% CI<sup>d</sup></b>
Mode of conception (IVF)	0.69	0.37–1.29	0.96	0.55–1.67	0.99	0.60–1.63	0.65	0.34–1.24
Age ( $\geq 35$ y)	0.78	0.56–1.08	0.80	0.57–1.10	1.19	0.89–1.61	0.83	0.59–1.16
BMI ( $\geq 25$ kg/m <sup>2</sup> )	0.88	0.65–1.18	1.08	0.81–1.45	1.12	0.85–1.47	0.81	0.59–1.11
Parity ( $>1$ )	1.26	0.96–1.65	1.23	0.94–1.62	0.74	0.57–0.97	1.13	0.85–1.49
Education (higher)	1.76	1.31–2.35	1.48	1.09–1.99	1.15	0.86–1.55	1.16	0.84–1.62
Depression history	4.04	2.95–5.53	4.22	3.07–5.81	2.96	2.24–3.92	3.88	2.80–5.37
Stressful life events ( $\geq 3$ )	1.38	0.88–2.16	1.37	0.87–2.16	1.62	1.07–2.47	1.38	0.85–2.23

Note: EPDS = Edinburgh Postnatal Depression Scale.

<sup>a</sup> n = 2,280.

<sup>b</sup> n = 2,215.

<sup>c</sup> n = 2,260.

<sup>d</sup> n = 2,091.

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choose and undergo treatments are different from those who avoid them. Actually, depressed subfertile women are less likely to seek medical care (38). Among those who eventually start fertility treatments, psychologic distress is a major reason for discontinuation (39). Accepting the burden of undergoing multiple treatments until success could also be a sign of resilience or adaptive coping strategies (40). It is therefore not paradoxical that IVF parents show less trait anxiety and better mental health if they have experienced more cycles or a longer time to pregnancy (41). In addition, recent evidence shows that depression is associated with reduced odds of IVF success (42). All these findings support the hypothesis that those who pursue fertility treatments and eventually achieve a pregnancy constitute a subset of subfertile women who are less likely to suffer from depressive symptoms. This may contribute to explain the findings of the present study and supports future research to explore whether perinatal depressive symptoms are instead more prevalent among subfertile women who conceive spontaneously.

The main implication of our findings for clinical practice is that conception by IVF alone does not justify specific screening for depressive symptoms. This is important because it allows for an effective use of available resources as well as preventing mothers, who have already gone through stressful treatments, from receiving unjustified care only because of their mode of conception. However, as for any other pregnant woman or mother, the risk of perinatal depression should never be underestimated, because significant symptoms are common. Furthermore, given the demographics of IVF mothers, caution should be exercised when considering risk factors for developing perinatal depressive symptoms. Our findings confirm a history of depression as a strong predictor regardless of mode of conception, but further research is needed before assuming that other risk factors apply similarly to spontaneous and IVF pregnancies.

Regarding the generalizability of our findings, it should be noted that our sample proceeded from a population-based project and that participation was offered to nearly all women receiving antenatal care in Uppsala County. The participation rate for the original BASIC cohort was relatively low (22%), and women with higher education and primiparae were slightly overrepresented (31). These circumstances are not surprising for a population study, but they suggest caution due to our inability to measure depressive symptoms among nonparticipants. However, there is no plausible reason to think that the prevalence of depression among nonparticipants would be associated with the mode of conception to a different extent than among participants.

The proportion of IVF pregnancies included in the present study (5%) was also slightly higher than is reported at the national level in Sweden (7), although this small variation may be explained by the generally high cultural and socioeconomic status of the population of Uppsala, which is also one of the few Swedish counties (8 of 21) with local IVF clinics.

Because generalizability also relates to a broader context of research, we wish finally to discuss some health care provision aspects that may contribute to narrowing the gap between subfertile and fertile mothers in Sweden. As IVF's

success rates and patient-friendliness improve, treatments become increasingly common and thus less subject to stigma. In our specific national context, fertility treatments are generously funded by the regional health services, which generally offer childless couples up to three full IVF treatments, including any resulting frozen embryo transfer cycle. Couples are offered rapid access to treatment, with a national target of a maximum 3 months' waiting time, and counseling is offered as part of standard care. Such economic and clinical conditions arguably decrease the burden of treatment on patients, with potential benefits on their psychologic well-being. Sweden was also among the first to introduce a national single-embryo transfer (SET) policy, which makes it the country with the highest proportion of SETs (>75%) and the lowest rate of multiple pregnancies after ART in Europe (6, 7). This strategy has clearly shown to pay off in terms of reduced obstetrical risks and unaffected cumulative success rates (43). In addition, the routine care of pregnant women conceiving by means of IVF is not different from that received by those who spontaneously conceive, because it is largely unmedicalized and managed by midwives. With this in mind, it seems interesting to highlight how the study suggesting an increased risk of depressive symptoms in ART mothers was conducted in Italy (16), a country with medicalized obstetrical care (44) and in a period (2005–2006) during which a debated ART legislation was determining specific practices, such as the forced transfer of multiple embryos (45). Although factors such as an SET policy or antenatal care are specific to the context, they also belong to a positive movement toward safer treatments and patient-centered care. Therefore, while our results may already be generalizable to specific parts of the world, they are in our opinion also future-proof for any other country or context where similar developments are highly desirable.

## CONCLUSION

Despite the psychologic distress characterizing subfertility and its medical management, conception by means of IVF in an SET policy context is not associated with maternal depressive symptoms during pregnancy and postpartum, even when controlling for several potential confounders.

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