

Parents' anxiety and depression symptoms after successful infertility treatment and spontaneous conception: does singleton/twin pregnancy matter?

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STUDY QUESTION: Does mode of conception [spontaneous/after infertility treatment (IT)], type of pregnancy (singleton/twin) and parent gender have an effect on anxiety and depression levels and trajectories during pregnancy and the post-partum period?

SUMMARY ANSWER: Conception after IT was associated with a transitory increase in anxiety during the perinatal period for parents of singletons, while for IT parents of twins higher levels of psychopathological symptoms tended to persist during pregnancy and the post-partum period.

WHAT IS KNOWN ALREADY: Most previous studies have shown that successful IT is not associated with poor psychological well-being during pregnancy and the post-partum period, but there is also some evidence for heightened pregnancy-related anxiety, lower self-esteem and lower self-efficacy. Parents of twins experience increased postnatal anxiety and depression.

STUDY DESIGN, SIZE, DURATION: This prospective longitudinal study assessed 267 couples ($N = 534$) at each trimester of pregnancy, after childbirth and at 3 months post-partum.

PARTICIPANTS/MATERIALS, SETTING, METHOD: The sample comprised 36 couples who had conceived after IT (19 twin pairs and 17 singletons) and 231 couples who had conceived spontaneously (SC; 28 twin pairs and 203 singletons). Couples were recruited at four public hospitals in Portugal, and self-report measures of anxiety and depression symptoms were administered.

MAIN RESULTS AND THE ROLE OF CHANCE: IT parents reported higher anxiety after childbirth than parents who SC, regardless of pregnancy type. IT parents of twins showed higher anxiety at mid-pregnancy, as well as higher anxiety and depression at 3 months post-partum than IT parents of singletons. Among IT mothers, those who had twins exhibited higher depression after childbirth than those who had singletons. Differences according to mode of conception, pregnancy type and parents gender over time were also noted. During pregnancy, IT parents of twins showed no significant change in depression scores, while the other groups depression scores statistically significantly decreased over time. From pregnancy to the post-partum period, (i) IT parents showed an increase in anxiety scores, whereas SC parents exhibited no changes in anxiety scores; (ii) IT women exhibited an increase in depression scores, while SC women depression scores decreased. During the post-partum period, IT and SC parents of twins showed no changes in anxiety scores, while IT and SC parents of singletons anxiety scores declined.

LIMITATIONS, REASONS FOR CAUTION: Due to the small number of IT couples, the interpretation and generalization of the results should be done with caution.

WIDER IMPLICATIONS OF THE FINDINGS: The adverse impact of IT on psychopathological symptoms depends mostly on time and type of pregnancy, and is greater for twin pregnancies. These findings are important for tailoring interventions that address parents' specific needs at different moments.

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Key words: twins / depression / anxiety / infertility treatment / couples / longitudinal / dyadic growth models

Introduction

Evidence concerning parents' psychological well-being after successful infertility treatment (IT) is mixed (Hammarberg *et al.*, 2008). Most studies have shown that IT parents report similar or lower levels of anxiety and depression than controls who conceived spontaneously (SC) (Colpin *et al.*, 1999; Klock and Greenfeld, 2000; Cohen *et al.*, 2001; Baor *et al.*, 2004; Repokari *et al.*, 2005; Vilksa *et al.*, 2009; Jongbloed-Pereboom *et al.*, 2012; Gressier *et al.*, 2015). Nevertheless, some studies have found that women who conceive after IT display higher levels of anxiety and depression during late pregnancy and after childbirth (McMahon *et al.*, 1997; Monti *et al.*, 2008, 2009), higher pregnancy-focused anxiety (McMahon *et al.*, 1997, 2011, 2013; Hjelmsstedt *et al.*, 2003), lower self-efficacy and self-esteem (Gibson *et al.*, 2000) during the post-partum period than SC women. Previous findings have also indicated that IT parents are more likely to under-report negative effect (McMahon *et al.*, 2003) as they may feel less entitled to complain about the difficulties experienced (Hammarberg *et al.*, 2009).

Parents of twins display similar or higher levels of prenatal anxiety and depression (Vilksa *et al.*, 2009; Jahangiri *et al.*, 2011) than parents of singletons. Evidence from studies with large samples suggests that parents of young twins (≤ 5 years old) show increased levels of anxiety and depression (Thorpe *et al.*, 1991; Ellison *et al.*, 2005; Olivennes *et al.*, 2005; Vilksa *et al.*, 2009).

Most studies on multiple births do not control for IT and vice versa, and this is problematic because there is an association between the use of IT and multiple births (Ross *et al.*, 2011). It is important to examine the independent and the combined effects of IT and multiple birth on parents' psychological well-being. Results from a previous study suggest that twin parenthood, but not IT, is associated with poor psychological well-being during the post-partum period both for mothers and fathers (Vilksa *et al.*, 2009). Even though this study followed couples from mid-pregnancy to 1-year post-partum, no longitudinal data analysis was described.

The purpose of this study was to examine the effects of mode of conception, type of pregnancy and parent gender on anxiety and depression levels at each trimester of pregnancy, childbirth and 3 months post-partum. The effects of these factors on anxiety and depression symptoms trajectories over time were also examined.

Materials and methods

Participants

Consecutive sampling of couples with <15-week twin pregnancies was carried out. Couples were invited by the researchers to participate in a

prospective longitudinal study at the antenatal Obstetrical Units of three public hospitals in Northern Portugal. Couples who did not speak Portuguese were excluded. Of the 55 couples contacted, 51 agreed to participate in the study (92.7%). Four of these couples were excluded due to death of one or both twins during the study period. Therefore, data from 47 couples were available for analysis.

Couples with singletons were derived from a larger prospective longitudinal study conducted in an Obstetrics Out-patients Unit in Oporto, Portugal. Mothers and fathers of at least 18 years of age who completed socio-demographic and clinical measures at baseline were selected. Detailed information on this study design is described elsewhere (Figueiredo and Conde, 2011).

Procedure

The Ethics Committee of the participating hospitals gave their approval for the study. The aims and procedures were explained to couples attending routine antenatal care appointments at 8–14 weeks of pregnancy and those who were willing to participate provided written informed consent. Information on parents' anxiety and depression symptoms was collected at each trimester of pregnancy (T1, 8–15 weeks; T2, 20–24 weeks; T3, 28–34 weeks) in the clinic, during hospital stay after childbirth (T4) and at 3 months post-partum (T5) during a home visit. Socio-demographic and clinical information of mothers and fathers was collected at T1 and T4. Mothers and fathers completed the paper-based measures separately.

Measures

Socio-demographic, clinical and perinatal data

Information on parents' age, ethnicity, parity, occupational and marital status, education level, history of infertility, mode of conception, pregnancy type, duration of pregnancy, medical complications, type of childbirth and singletons'/twins' birth weight was collected by self-administered questionnaires.

Anxiety symptoms

The 20-item state subscale of the State-Trait Anxiety Inventory Form Y (STAI, Spielberger *et al.*, 1983) is a screening instrument used to measure current anxiety symptoms. Items are scored on a four-point Likert scale (1–4). The scores range from 20 to 80, with higher scores indicating higher anxiety. STAI Portuguese version has shown excellent internal consistency and high criterion validity (Tendais *et al.*, 2014). In this study, STAI was used at each time point and Cronbach's α s ranged from 0.92 and 0.95 for women and 0.91 and 0.95 for men. A score of 40 or higher was considered clinically significant.

Depression symptoms

The Edinburgh Postnatal Depression Scale (EPDS, Cox *et al.*, 1987) is a self-report questionnaire composed of 10 items addressing depression symptoms within the previous 7 days. The scores range from 0 to 30, with higher scores indicating more severe depression symptoms. The

Portuguese version of this screening tool has shown good internal consistency and reasonable criterion validity (Tendais et al., 2014). In the present study, EPDS was used at each time point and Cronbach's α s ranged from 0.77 and 0.85 for women and 0.72 and 0.79 for men. A score of 12 or higher was considered clinically significant.

Data analysis

Multilevel modeling was used to assess the effect of mode of conception, type of pregnancy and parent gender and their interactions on anxiety and depression symptoms at each time point while controlling for age, parity and couples' interdependence. Pairwise comparisons were performed when the interactions were significant. One-sided Fisher's Exact Test was also used to test the association between group membership and high anxiety (STAI ≥ 40) or depression symptoms (EPDS ≥ 12) when significant between-group mean differences were found.

Examination of mean scores over time revealed a linear change in anxiety and depression scores during pregnancy and the post-partum period. However, a significant increase was observed for some groups from T3 to T4. To capture this discontinuity, piecewise dyadic growth models were estimated using multilevel modeling to assess changes in anxiety and depression levels from the first trimester of pregnancy (T1) to the first assessment post-partum (T4), from pregnancy to post-partum (pre-postnatal transition) and from childbirth (T4) to 3 months post-partum (T5). In these models, observation is level 1 and couple is level 2. Time 0 was defined at T1 and time was scored in months. Model selection is described in [Supplementary data](#).

Data were analyzed with IBM SPSS 23 Windows version (PASW Statistics for Windows, SPSS, Inc., Chicago, IL, USA). *Post hoc* power calculations showed that the attained sample size permitted the detection of medium to large effects (effect size $f^2 = 0.18$) in full models with all predictors (power > 0.80 , G * Power, [Faul et al., 2007](#)).

Results

Participants' characteristics

The sample included 267 couples, 36 who had conceived after IT (19 with twins and 17 with singletons) and 231 who had SC (28 with twins and 203 with singletons) ([Supplementary data](#), Fig. S1). In the IT group, 12 conceived by intracytoplasmic sperm injection (ICSI), 11 by *in vitro* fertilization (IVF), 8 after ovulation induction (OI), 4 by artificial insemination (AI) and 1 after surgery. All couples in this group had previous infertility.

On average, participants were 30 years old (SD = 5.6, range 18–46 years), the majority were Caucasian (95.3%), married (62.8%), employed (86.1%), primiparous (56.4%), had < 12 years of education (60.5%), and had medium to medium-low socio-economic level (53.5%). The mean gestational age was 38.4 weeks (SD = 2.1, range 27.7–42.0). IT couples had a mean duration of infertility of 3.6 years (SD = 2.7, range 0–10.0).

Socio-demographic and perinatal characteristics according to mode of conception and pregnancy type for mothers and fathers are presented in Table I. No differences were found for marital status, education level, occupational status and socio-economic level. No differences were found for infertility duration between those who delivered singletons and twins. However, there were significant differences in parity for both mothers and fathers between the four groups and in age for mothers while for fathers differences in age were close to statistical significance. Further analysis showed that IT mothers of

twins were more likely to be older (≥ 30 years of age) than SC mothers of singletons or twins (both P s = 0.01). IT mothers and fathers of twins were more likely to be primiparous than SC mothers and fathers of singletons (both P s = 0.05).

One-hundred and eighty-nine couples (70.8%) completed all questionnaires. No differences were found between IT and SC parents on full response rate (75.0% versus 70.1%, $P > 0.10$). Additional analysis showed that parents of twins had a lower response rate than parents of singletons [$\chi^2_{(1,267)} = 6.60$, $P < 0.001$].

Anxiety

At each pregnancy trimester, childbirth and 3 months post-partum

Mean anxiety scores at each time point for the different groups are displayed in Table II. The prevalence of anxiety is depicted in Table III.

During pregnancy and the post-partum period, significant mode of conception \times pregnancy type interactions emerged. At T2 and T5, IT parents of twins showed higher anxiety scores than IT parents of singletons and were also more likely to score above the cut-off (all P s < 0.05). Among SC parents, no differences were found between parents of singletons and twins (both P s > 0.05). No significant differences were found between IT and SC parents of twins (both P s > 0.05). At T3, no significant difference was found between IT parents of twins and singletons ($P > 0.05$).

At T4, mode of conception and parent gender were significantly related with anxiety. IT parents reported higher scores than SC parents and were also more likely to score above the cut-off ($P < 0.001$). Women had higher scores than men, but were not more likely to score above the cut-off than men ($P > 0.05$).

Trajectories over time

As shown in Table IV, a significant mode of conception \times pregnancy type interaction predicted change in anxiety from pregnancy to the post-partum period and over the post-partum period. IT parents of singletons had a higher increase in anxiety from pregnancy to the post-partum period than IT parents of twins (both P s < 0.001), while SC parents of singletons and twins showed a non-significant increase (both P s > 0.05 ; Fig. 1). Over the post-partum period, IT parents of singletons showed a steeper decrease in anxiety than SC parents of singletons (both P s < 0.001), whereas no significant changes were found for IT and SC parents of twins (both P s > 0.05 ; Fig. 1). Gender also predicted change in depression during the post-partum period, with women reporting greater decreases than men.

After accounting for the predictors in the final model, couples' residuals were positively correlated ($r = 0.14$, $Z = 3.13$, $P < 0.001$) suggesting that if one member of the couple was more anxious at a particular time point, the other tended to be more anxious at that time. The final model explained 63.3% and 53.1% of the variance of change for mothers and fathers, respectively.

Depression

At each pregnancy trimester, childbirth and 3 months post-partum

Mean depression scores at each time point for the different groups are displayed in Table II. The prevalence of clinically significant depression is depicted in Table III.

Table 1 Comparison of socio-demographic and perinatal characteristics according to mode of conception (SC $n = 231$ or IT $n = 36$ couples) and pregnancy type for mothers and fathers.

	Mothers				χ^2	Fathers				χ^2
	SC		IT			SC		IT		
	Singletons n (%)	Twins n (%)	Singletons n (%)	Twins n (%)		Singletons n (%)	Twins n (%)	Singletons n (%)	Twins n (%)	
Age (years)					7.93*					7.72 [†]
<30	115 (56.7)	18 (64.3)	8 (47)	5 (26)		83 (40.9)	11 (39.3)	3 (18)	3 (16)	
≥30	88 (43.3)	10 (35.7)	9 (53)	14 (74)		120 (59.1)	17 (60.7)	14 (82)	16 (84)	
Education (years)					1.56					2.67
<12	113 (55.7)	13 (46.4)	11 (65)	10 (53)		138 (68.0)	16 (57.1)	9 (53)	13 (68)	
≥12	90 (44.3)	15 (53.6)	6 (35.3)	9 (47.4)		65 (32.0)	12 (42.9)	8 (47)	6 (32)	
Parity					9.30*					11.08*
Primiparous	104 (51.2)	18 (64.3)	11 (65)	16 (84)		106 (52.2)	18 (64.3)	11 (65)	17 (90)	
Multiparous	99 (48.8)	10 (35.7)	6 (35)	3 (16)		97 (47.8)	10 (35.7)	6 (35)	2 (11)	
Employed					0.15					0.26
No	158 (77.8)	21 (75.0)	13 (77)	15 (79)		193 (95.1)	26 (92.9)	16 (94)	18 (95)	
Yes	45 (22.2)	7 (25.0)	4 (24)	4 (21)		10 (4.9)	2 (7.1)	1 (6)	1 (5)	
Cohabiting					3.48					
No	18 (8.9)	2 (7.1)	0 (0)	0 (0)						
Yes	185 (91.1)	26 (92.9)	17 (100)	19 (100)						
Socio-economic level					3.78					
≤Medium low	96 (47.3)	10 (35.7)	6 (35)	6 (32)						
≥Medium	107 (52.7)	18 (64.3)	11 (65)	13 (68)						

[†] $P < 0.10$; * $P < 0.05$. χ^2 3/267 degrees of freedom. IT, infertility treatment; SC, spontaneous.

Table II Effects of mode of conception, pregnancy type and parents' gender on anxiety (STAI) and depression (EPDS) scores at each time point controlling for age and parity.

Group	Adjusted scores (Mean ± SE)				t values						
	Spontaneous conception (n = 192–231)		Infertility treatment (n = 31–36)		Main effects			Interaction effects			
	Singletons	Twins	Singletons	Twins	Mode of conception (A)	Type of pregnancy (B)	Gender (C)	A × B	B × C	A × C	A × B × C
<i>STAI</i>											
T1	34.6 (0.47)	34.2 (1.28)	33.9 (1.59)	37.0 (1.52)	1.00	1.19	−1.53	1.37	−0.59	1.01	−1.65
T2	33.1 (0.49)	31.8 (1.27)	30.0 (1.69)	34.8 (1.58)	0.21	1.60	−1.93 [†]	2.42*	−0.06	1.93 [†]	0.35
T3	34.9 (0.53)	33.9 (1.43)	31.6 (1.87)	36.5 (1.72)	0.20	1.67 [†]	−2.80**	2.09*	0.22	1.25	1.10
T4	34.1 (0.64)	36.1 (1.77)	41.8 (2.11)	39.8 (2.14)	3.10**	−0.08	−4.26***	−1.13	−0.92	−0.88	−0.30
T5	30.0 (0.52)	32.0 (1.37)	28.3 (1.65)	36.0 (1.71)	1.16	3.75***	−0.03	2.20*	−1.46	1.41	0.74
<i>EPDS</i>											
T1	5.5 (0.20)	5.5 (0.54)	5.6 (0.67)	5.2 (0.65)	0.42	0.01	−3.12**	−0.09	−0.64	0.14	−0.69
T2	5.1 (0.21)	3.8 (0.55)	4.8 (0.72)	5.1 (0.67)	1.13	−0.65	−2.73**	1.45	0.13	1.51	0.29
T3	4.8 (0.21)	4.5 (0.56)	3.7 (0.73)	5.5 (0.67)	0.33	1.69 [†]	−3.20**	1.87 [†]	−0.83	0.21	−0.09
T4	4.7 (0.24)	4.7 (0.67)	4.8 (0.82)	7.0 (0.81)	1.73 [†]	1.67 [†]	−5.47***	1.61	−1.34	−2.50*	−2.12*
T5	4.1 (0.24)	3.8 (0.62)	3.3 (0.77)	6.3 (0.79)	1.82 [†]	2.24*	−0.76	2.79**	−2.78**	−0.42	0.08

T1, 8–15 weeks of pregnancy; T2, 20–24 weeks of pregnancy; T3, 28–34 weeks of pregnancy; T4, during hospital stay after childbirth; T5, 3 months post-partum. Data are given as mean (standard error). [†]*P* < 0.10; **P* < 0.05; ***P* < 0.01; ****P* < 0.001. STAI, State-Trait Anxiety Inventory Form Y; EPDS, Edinburgh Postnatal Depression Scale.

Table III Prevalence of high anxiety (STAI ≥ 40) and high depression (EPDS ≥ 12) in SC and IT mothers and fathers at all time points.

	Mothers				Fathers			
	SC		IT		SC		IT	
	Singletons	Twins	Singletons	Twins	Singletons	Twins	Singletons	Twins
<i>STAI</i> ≥ 40								
T1	69 (34.0)	7 (25.0)	2 (12)	7 (37)	51 (25.1)	11 (39.3)	4 (24)	3 (16)
T2	62 (30.5)	4 (14.3)	2 (12)	6 (32)	58 (28.6)	3 (10.7)	2 (12)	5 (26)
T3	69 (34.0)	9 (32.1)	5 (29)	8 (42)	65 (32.0)	6 (21.4)	3 (18)	9 (47)
T4	78 (39.2)	15 (53.6)	9 (53)	13 (68)	60 (30.3)	10 (35.7)	9 (53)	11 (58)
T5	49 (25.7)	10 (35.7)	3 (18)	8 (42)	44 (23.0)	8 (28.6)	2 (12)	10 (53)
<i>EPDS</i> ≥ 12								
T1	22 (10.8)	4 (14.3)	1 (6)	4 (21)	23 (11.3)	4 (14.3)	1 (6)	0
T2	35 (17.2)	0	3 (18)	1 (5)	28 (13.8)	1 (3.6)	3 (18)	1 (5)
T3	25 (12.3)	2 (7.1)	3 (18)	4 (21)	31 (15.3)	2 (7.1)	2 (12)	2 (11)
T4	37 (18.6)	7 (25.0)	2 (12)	9 (47)	36 (18.2)	8 (28.6)	3 (18)	4 (21)
T5	37 (19.8)	4 (14.3)	2 (12)	7 (37)	37 (19.4)	6 (21.4)	1 (6)	6 (32)

Data are n (%).

Although women presented higher depression scores than men at each pregnancy trimester, there was a similar proportion of women and men scoring above the cut-off (all *P*s > 0.05).

After childbirth (T4), a significant interaction effect was found between conception mode, type of pregnancy and parent gender. IT mothers of twins showed higher depression scores than IT mothers of

singletons and were also more likely to score above the cut-off (both *P*s = 0.01). No differences were found between mothers of SC singletons and twins (*P* > 0.05) or between IT and SC fathers of singletons and twins (both *P*s > 0.05). IT mothers of twins exhibited also higher depression scores than SC parents of twins (*P* = 0.001), but the proportion scoring above the cut-off in both groups was similar (*P* > 0.05).

Table IV Full and final trimmed piecewise growth curve models predicting anxiety and depression symptoms from pregnancy to the post-partum period as a function of mode of conception (spontaneous/ after IT), pregnancy type (singleton/twin) and parent gender.

Fixed effects	Anxiety				Depression			
	Full model		Final		Full model		Final	
	β	SE	β	SE	β	SE	β	SE
Intercept	34.74***	1.81	35.09***	1.79	4.91***	0.76	4.92***	0.75
Time pregnancy	-0.11	0.12	0.04	0.07	-0.21***	0.05	-0.19***	0.03
Pre-postnatal transition	3.88***	0.65	3.25***	0.53	1.06***	0.24	0.93***	0.19
Time post-partum	-3.08***	0.35	-3.07***	0.35	-0.44***	0.12	-0.42***	0.12
Mode of conception	0.36	0.63	0.09	0.58	0.11	0.28	0.06	0.26
Pregnancy type	1.16	0.63	0.34	0.51	-0.06	0.28	-0.17	0.24
Gender	-1.04	0.41	-1.39	0.23	-0.74***	0.18	-0.69***	0.10
Mode of conception × pregnancy type	1.17	0.63			0.18	0.28		
Mode of conception × gender	0.56	0.40			0.01	0.17		
Pregnancy type × gender	0.14	0.40			-0.14	0.17		
Mode of conception × pregnancy type × gender	-0.07	0.40			-0.09	0.17		
Time pregnancy × mode of conception	-0.13	0.12			-0.03	0.05		
Pre-postnatal transition × mode of conception	3.24***	0.65	2.30***	0.43	0.71**	0.24	0.59***	0.16
Time post-partum × mode of conception	-1.10**	0.35	-0.97**	0.34	-0.28*	0.12	-0.27*	0.12
Time pregnancy × pregnancy type	0.00	0.12			0.08†	0.05	0.04	0.03
Pre-postnatal transition × pregnancy type	-0.86	0.65			-0.31	0.24		
Time post-partum × pregnancy type	1.39***	0.35	1.14***	0.28	0.24†	0.12	0.17†	0.10
Time pregnancy × gender	-0.01	0.10			0.01	0.04		
Pre-postnatal transition × gender	-1.17*	0.57	-0.26	0.24	-0.39†	0.21	-0.40**	0.11
Time post-partum × gender	1.24*	0.37	1.11*	0.23	0.43**	0.15	0.40***	0.11
Time pregnancy × mode of conception × pregnancy type	0.03	0.10			0.10*	0.05	0.06*	0.03
Pre-postnatal transition × mode of conception × pregnancy type	-1.71**	0.65	-1.02*	0.40	-0.36	0.24		
Time post-partum × mode of conception × pregnancy type	1.08**	0.35	0.96**	0.33	0.08	0.12		
Time pregnancy × mode of conception × gender	0.03	0.10			0.04	0.04		
Pre-postnatal transition × mode of conception × gender	-0.92	0.57			-0.73**	0.21	-0.29**	0.09
Time post-partum × mode of conception × gender	0.60	0.37			0.16	0.15		
Time pregnancy × pregnancy type × gender	-0.09	0.10			-0.02	0.04		
Pre-postnatal transition × pregnancy type × gender	-0.39	0.57			0.29	0.21		
Time post-partum × pregnancy type × gender	-0.09	0.37			-0.33*	0.15	-0.29***	0.07
Time pregnancy × mode of conception × pregnancy type × gender	0.10	0.10			0.03	0.04		
Pre-postnatal transition × mode of conception × pregnancy type × gender	-0.59	0.57			-0.28	0.21		
Time post-partum × conception mode × pregnancy type × gender	0.36	0.37	0.09	0.15				

Mode of conception was coded as after IT = 1, spontaneous = -1. Pregnancy type was coded as twin = 1, singleton = -1. Gender was coded as men = 1, women = -1.

Models are adjusted for age and parity.

† $P < 0.10$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

At T5, a significant mode of conception × pregnancy type interaction emerged. IT parents of twins showed higher depression scores than IT parents of singletons and SC parents of twins and were also more likely to score above the cut-off (all P s < 0.05). In contrast, no difference was found between SC parents of singletons and twins ($P > 0.05$). A significant pregnancy type × parent gender interaction was also found. Mothers of twins exhibited higher depression scores than mothers of singletons ($P = 0.01$), even though the proportion scoring above the cut-off in both groups was similar ($P > 0.05$). As for

fathers, no difference was found between those who had singletons and twins ($P > 0.05$).

Trajectories over time

As shown in Table IV, the predicted depression score decreased during pregnancy. This trend was statistically significant ($P < 0.05$) in all groups except the IT parents of twins (Fig. 2).

A significant mode of conception × parent gender interaction predicted change in depression from pregnancy to the post-partum

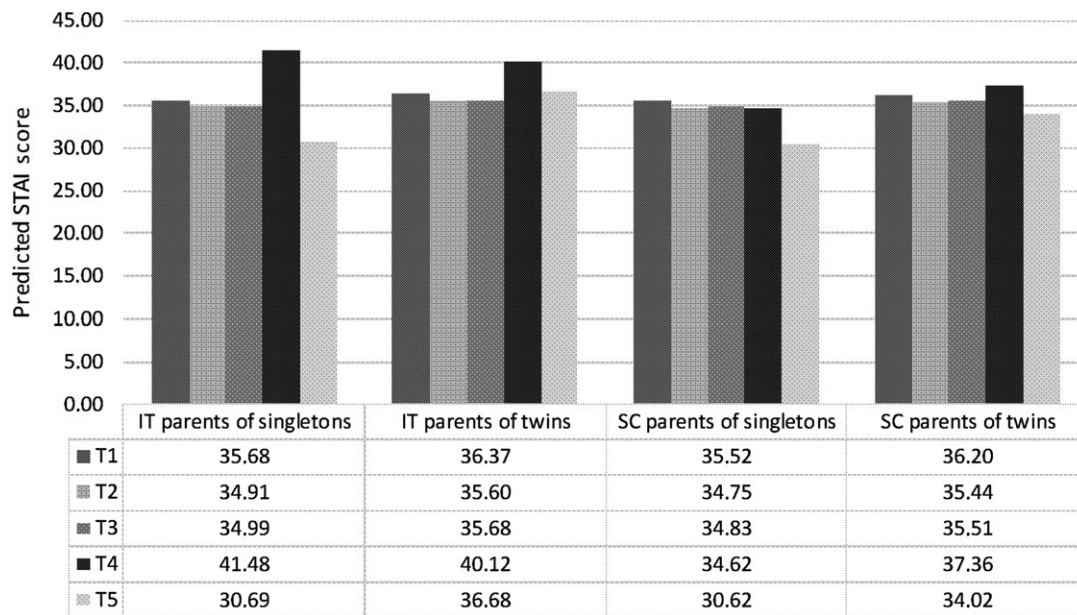


Figure 1 Predicted anxiety (STAI) scores in each trimester of pregnancy (T1–T3), the day of delivery (T4) and 3 months later (T5) as a function of mode of conception (IT versus SC) and pregnancy type. IT parents of singletons and IT parents of twins showed a significant increase in anxiety at T4 (both P s < 0.001), while the other groups showed a non-significant increase (P s > 0.05). Over the post-partum period, IT and SC parents of singletons showed a steep decrease in anxiety (both P s < 0.001), whereas the other groups showed a non-significant change (P s > 0.05). STAI, State-Trait Anxiety Inventory Form Y; IT, infertility treatment; SC, spontaneous conception.

period, such that IT mothers showed a statistically significant increase in depression from pregnancy to the post-partum period ($P < 0.001$), while the other groups showed a non-significant increase (all P s > 0.05) (Fig. 3).

Although all groups showed a decrease in depression scores during the post-partum period, IT parents decreased more quickly than SC parents. A significant pregnancy type \times parent gender interaction also predicted change in depression over the post-partum, such that mothers of singletons decreased ($P < 0.001$), whereas no significant changes were found for the other groups (both P s > 0.05).

After accounting for the predictors in the final model, couples' residuals were positively correlated ($r = 0.16$, $Z = 3.70$, $P < 0.001$) indicating that if one member of the couple was more depressed at a particular time point, the other tended to be more depressed at that time. The variance of change of depression explained by the final model was 64.1% for mothers and 60.9% for fathers.

Discussion

This prospective longitudinal study examined the effect of mode of conception, pregnancy type and parent gender on anxiety and depression levels and trajectories during pregnancy and the post-partum period. We observed that the effect of IT on parents' psychopathological symptoms depends mostly on time and type of pregnancy. IT parents of singletons exhibited no increased risk of clinically significant anxiety and depression during pregnancy and the post-partum period when compared to spontaneous controls (data not shown), except after childbirth. In contrast, IT parents of twins appear to be at higher risk for clinically significant psychopathological

symptoms during pregnancy and the post-partum period than IT parents of singletons, as well as at higher risk for postnatal depression than SC parents of twins.

Our findings suggest that IT parents, regardless of pregnancy type, may experience more adjustment difficulties to the perinatal period than SC parents as they experience an increase in anxiety from pregnancy to the post-partum and higher anxiety than SC parents after childbirth. Monti *et al.* (2008) also found a significant increase in manifest anxiety among IT mothers both during the third trimester of pregnancy and 1 week after childbirth. Previous research has shown that IT mothers present more child-related worries than SC mothers (McMahon *et al.*, 2011), namely, about the survival, normality and well-being of the baby and separation from the child after birth (McMahon *et al.*, 1997). IT parents are likely to be confronted with most of their fears after childbirth and these feelings may increase their anxiety. An increase in levels of depression from pregnancy to the post-partum period was observed among IT mothers, whereas SC mothers, IT and SC fathers showed smaller, statistically non-significant changes. Our findings confirm that changes in depression levels from pregnancy to post-partum are moderated by mode of conception (Hammarberg *et al.*, 2008) and gender (Repokari *et al.* 2005). Previous studies have shown that IT mothers report less confidence in parental competence than SC mothers (Gibson *et al.*, 2000), and this may have a negative effect on mood.

Our longitudinal study provides evidence for the combined effects of IT and twin pregnancy on anxiety and depression levels and trajectories over time. IT parents of twins experienced higher anxiety than IT parents of singletons during pregnancy and the post-partum period. In addition, IT parents of twins exhibited higher depression than IT

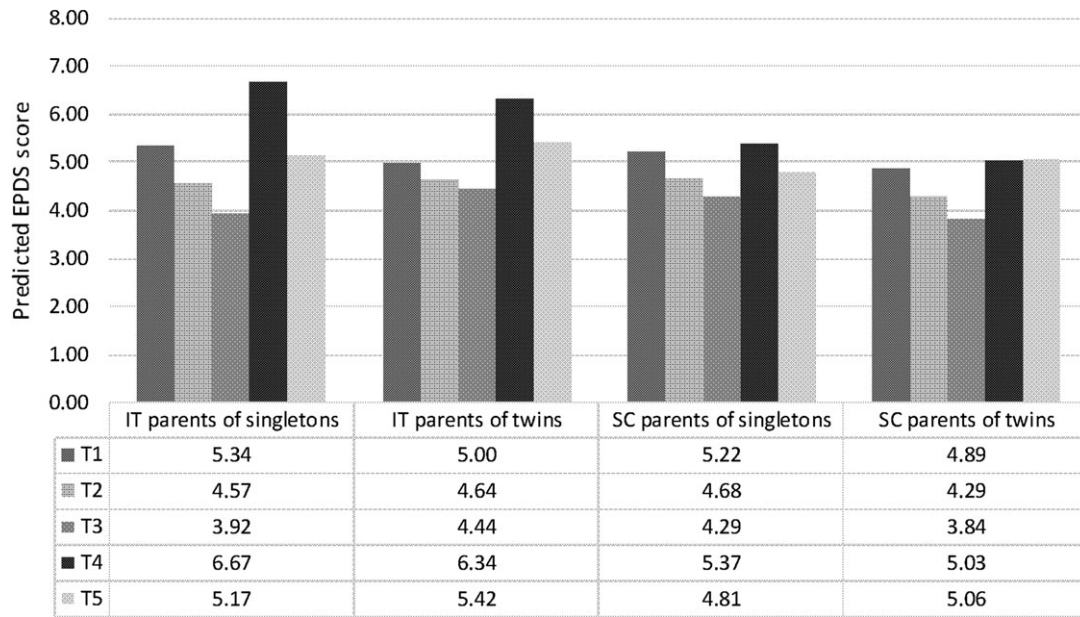


Figure 2 Predicted depression (EPDS) scores in each trimester of pregnancy (T1–T3), the day of delivery (T4) and 3 months later (T5) as a function of mode of conception (IT versus SC) and pregnancy type. All groups showed a significant decrease in depression scores during pregnancy (all P 's < 0.05) except the parents of twins conceived after IT (IT parents of twins). EPDS, Edinburgh Postnatal Depression Scale.

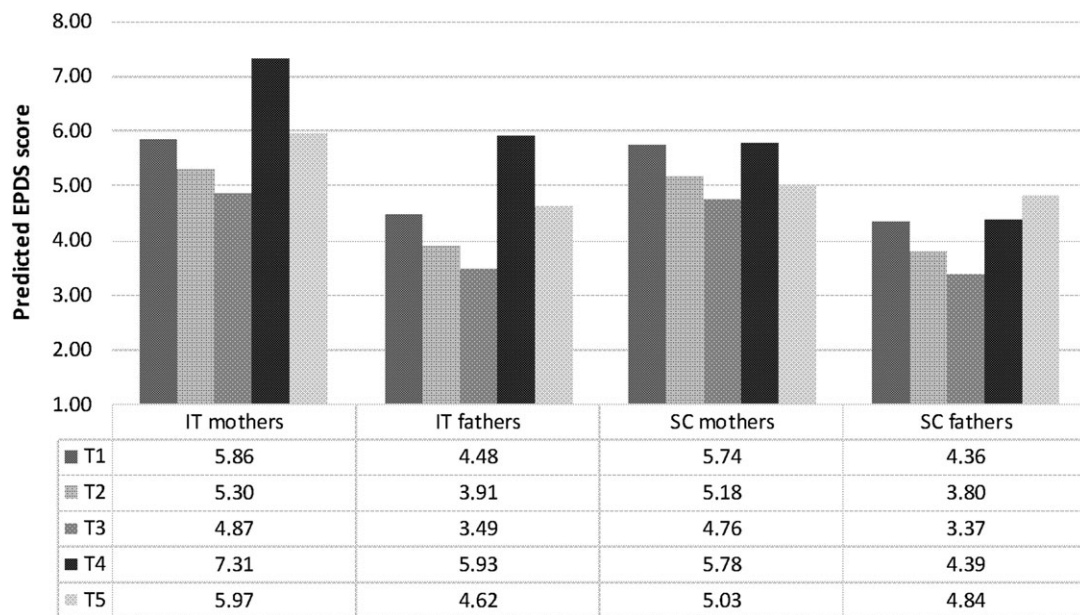


Figure 3 Predicted depression (EPDS) scores in each trimester of pregnancy (T1–T3), the day of delivery (T4) and 3 months later (T5) according to conception mode (IT versus SC) and parent gender. Mothers who conceived after IT (IT mothers) showed a significant increase in depression at T4 (P s < 0.001), while the other groups showed a non-significant increase (P s > 0.05).

parents of singletons and SC parents of twins during the post-partum period. Our results are consistent with previous research showing that primiparous IT mothers of 9–12-month-old twins report lower psychological well-being than primiparous mothers of SC twins (Colpin

et al., 1999; Baor *et al.*, 2004). In contrast, Vilksa *et al.* (2009) found no interaction effects between IT and type of pregnancy on mothers' and fathers' well-being during pregnancy and the post-partum period. Ross *et al.* (2011) acknowledged that IT multiple birth is associated with

increased risk for post-partum maternal depression. With regard to change over time, even though IT parents of singletons experienced a higher increase in anxiety than IT parents of twins from pregnancy to the post-partum period, anxiety levels of IT parents of singletons decreased over the post-partum period, while those reported by IT parents of twins remained stable. In contrast to the results of Jahangiri *et al.* (2011), we found that depression levels of parents declined significantly during pregnancy except for IT parents of twins, for whom the apparent trend was less steep and failed to achieve statistical significance. While expectations of parents of twins are focused on two infants, those of parents of singletons are concentrated on one child only. If the most feared thoughts related to childbirth injury and the well-being of the child would have been confirmed, the investment would have been lost. For most parents, these worries were not confirmed, and their anxiety level decreased sharply. However, for IT parents of twins, these worries are likely to have been followed by concerns regarding caring for two new-born infants (Jahangiri *et al.*, 2011), a decreased ability to provide each child with warmth and reciprocity (Feldman *et al.*, 2004), feelings of low self-efficacy and self-esteem (Gibson *et al.*, 2000).

This study has several limitations that need to be considered. Due to the small number of couples in the IT group, the interpretation and generalization of the results should be done with caution. This number was insufficient to compare the psychological well-being between those who conceived with IT (IVF, ICSI) and those who conceived with other methods (OI, AI). Because IT parents tend to under-report negative effect (McMahon *et al.*, 2003), the use of self-reported measures may have increased the reporting bias in the IT group. In addition, we were unable to distinguish the effects of previous infertility and use of IT on parents' well-being. Finally, in this study the extension of the trajectory during pregnancy to childbirth included in the model described in Table IV is an extrapolation and not a measurement. This extrapolation ignores the possibility that anxiety/depression may increase in the last weeks of pregnancy as birth becomes imminent.

Despite these limitations, the present study also has several important strengths. The inclusion of four different groups (parents of singletons and twins SC and after IT), into a prospective longitudinal design allowed us to study between-person differences in within-person change. The study yielded important and novel information about the effect of mode of conception on psychopathological symptoms over time according to the type of pregnancy. To date, little was known about the changes in psychological well-being experienced by these groups during the transition to parenthood. It also notes the specific time periods in which parents experience more psychopathological symptoms and extends previous research by assessing their clinical significance. In addition, by including both mothers and fathers, we were able to confirm that couples' psychological well-being is interdependent (Galhardo *et al.*, 2016).

Our findings underscore the need to provide special support to IT parents of twins to ensure the early detection and provision of psychosocial or specialized mental health care services to those experiencing poor psychological well-being. It should be noted that parents' depression and anxiety symptoms have been consistently associated with adverse outcomes on the fetus, neonate and child, including early emotional regulation and social problems and impairments in child cognitive development (Ross *et al.*, 2011; Stein *et al.*, 2014).

In conclusion, our results suggest that for those who conceived after IT, a twin pregnancy appears to be associated with more psychopathological symptoms over time. In contrast, the negative effects of IT on parents of singletons appear to be limited to increased anxiety during the perinatal period. These findings are important to the debate on the number of embryos for transfer.

Supplementary data

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

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Authors' roles

I.T. and B.F. designed the study. I.T. collected the data, undertook the statistical analysis interpreted the results and wrote the first draft of the manuscript. Both authors contributed to and have approved the final manuscript.

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Conflict of interest

None to declare.

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