

# Gender differences in emotional reactions to in vitro fertilization treatment: a systematic review

Liying Ying<sup>1,2</sup> · Lai Har Wu<sup>1</sup> · Alice Yuen Loke<sup>1</sup>

Received: 2 November 2015 / Accepted: 10 December 2015 / Published online: 29 December 2015  
© Springer Science+Business Media New York 2015

## Abstract

**Purpose** The purposes of this paper are to provide a comprehensive picture of men and women's emotional reactions to infertility treatment, specifically In Vitro Fertilization (IVF) pursued by heterosexual couples, and to identify any differences between the genders.

**Methods** Nonexperimental studies exploring the psychological effects of IVF treatment on infertile couples were included. Six electronic databases were used to conduct a systematic search from the years 2000 to 2014. The references of the articles selected for review and other related systematic reviews were also screened to retrieve additional relevant articles. The quality of the included studies was assessed using the Joanna Briggs Institute Critical Appraisal Checklist. Descriptive analysis was adopted to synthesize the results.

**Results** A total of 22 quantitative and 4 qualitative studies were identified and included in this review. Although both men and women experienced psychological distress during the treatment, gender differences existed. Women had elevated anxiety and depression levels prior to the treatment, which became even higher on the day of the oocyte retrieval, pre- and post embryo transfer, and during the waiting period before the pregnancy test. Men of the infertile couples reported elevated depression scores before treatment, which usually increased during the time spent waiting for the outcome of the IVF treatment. Both men and women had lower scores on positive affect before the pregnancy test. A failed IVF cycle had long-term negative psychological consequences for both spouses.

**Conclusions** The results of this review pointed to the need for a couple-based support program, aimed at improving the psychological well-being of couples.

---

**Capsule** The results of this review pointed to the need for a couple-based support program, aimed at improving the psychological well-being of couples.

---

**Electronic supplementary material** The online version of this article (doi:10.1007/s10815-015-0638-4) contains supplementary material, which is available to authorized users.

---

✉ Alice Yuen Loke  
hsaloke@polyu.edu.hk; alice.yuen.loke@polyu.edu.hk

Liying Ying  
liying.ying@connect.polyu.hk

Lai Har Wu  
candy.wu@polyu.edu.hk

<sup>1</sup> School of Nursing, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China

<sup>2</sup> School of Nursing, Zhejiang Chinese Medical University, Hangzhou, Zhejiang, China

**Keywords** Anxiety · Depression · Gender difference · Infertility · In vitro fertilization · Systematic review

## Background

It is estimated that 1.9 and 10.5 % of women aged 20–44 worldwide suffer from primary and secondary infertility, respectively [1]. In their journey of seeking treatment, about 3 % of infertile couples resort to assisted reproductive technology (ART), of which In Vitro Fertilization (IVF) accounts for more than 99 % [2]. Fertilization with Intra Cytoplasmic Sperm Injection (ICSI) is used to treat sperm-related fertility problems. The success rate (delivery rate) of IVF treatments is low at 16.6–20.2 % (for fresh aspiration and frozen embryo transfers respectively) [2]. While infertility is a long-lasting source of stress that affects couples in their existential, physical, emotional, and interpersonal domains [3], IVF treatment is likely

to cause anxiety with its torturous nature in terms of bodily discomfort, and to evoke depression with the uncertainty of the treatment's outcome [4].

The psychological reactions of infertile women have received much attention in the literature, since women endure the majority of IVF procedures [5–8]. A systematic review of 27 studies focusing on the emotional adjustment of women to different stages of IVF treatment was conducted in 2007. The review indicated that women undergoing IVF reported a higher level of emotional distress than normal fertile women, and that the oocyte retrieval and the waiting period before the pregnancy test were the most stressful times of the IVF cycle [4]. It should be noted that more than half of the studies in the review (55.6 %) had been conducted before the year 2000, only three studies (11.1 %) were conducted in Asia, and that the emotional adjustment of men was not addressed in this review.

The emotional reactions of infertile couples and the effect that they have on each another has been recognized [9]. Although men were usually less involved in infertility treatment procedures, they also suffered from the IVF treatment together with their female partner as an infertile dyad. Studies on the psychological status of men before, during, and after the IVF cycle, have also been presented in a number of studies [7, 10, 11]. As the socialization process and expected gender role of men are different from those of women, one would expect there to be differences between genders in response to IVF treatment. However, there is no review that compares the differences of the journey between men and women undergoing IVF treatment. The psychological well-being of men is often neglected and also deserves attention.

The aim of this systematic review is to extend the abovementioned review in providing a comprehensive picture of men and women's emotional reactions to infertility treatment (IVF), and to identify any differences between the genders [4]. This will provide a better understanding of the emotional reactions of couples, and offer health care professionals the information that they need to help infertile couples to go through a vulnerable stage in their life. It might also lead to future research in related fields.

## Methods

### Literature search strategy

A systematic literature search was performed using the following databases: PubMed (1966+), CINAHL (1982+), PsycInfo (1806+), EMBase (1974+), CBM (Chinese BioMedical Literature Database, 1978+), and CAJ (China Academic Journal Full-text Database, 1915+). MeSH terms, key words, and free words such as *infertility AND fertilization in vitro OR sperm injections, intracytoplasmic AND psycholog\* OR anxiety OR depression OR emotions OR stress* were used to

conduct the search. Studies that were published in English or Chinese from the years 2000 to 2014 were included. Four selected searching strategies were listed in Supporting Information Table S1. The references of the articles selected for review and other related systematic reviews were also screened to retrieve additional relevant articles.

### Inclusion and exclusion criteria

The criteria for inclusion in this review were: studies that focused on infertile individuals or couples as the study population; those that examined the psychological effects of IVF treatment on infertile couples; and for articles in Chinese, inclusion in the Chinese Science Citation Database (CSCD). The exclusion criteria were: studies involving psychological responses relating to intrauterine sperm insemination (IUI); couples undergoing IVF with a surrogate, and studies that only explore the psychological impact on couples who became pregnant after IVF. The selection procedures for this study are presented in Fig. 1.

### Quality assessment of the reviewed papers

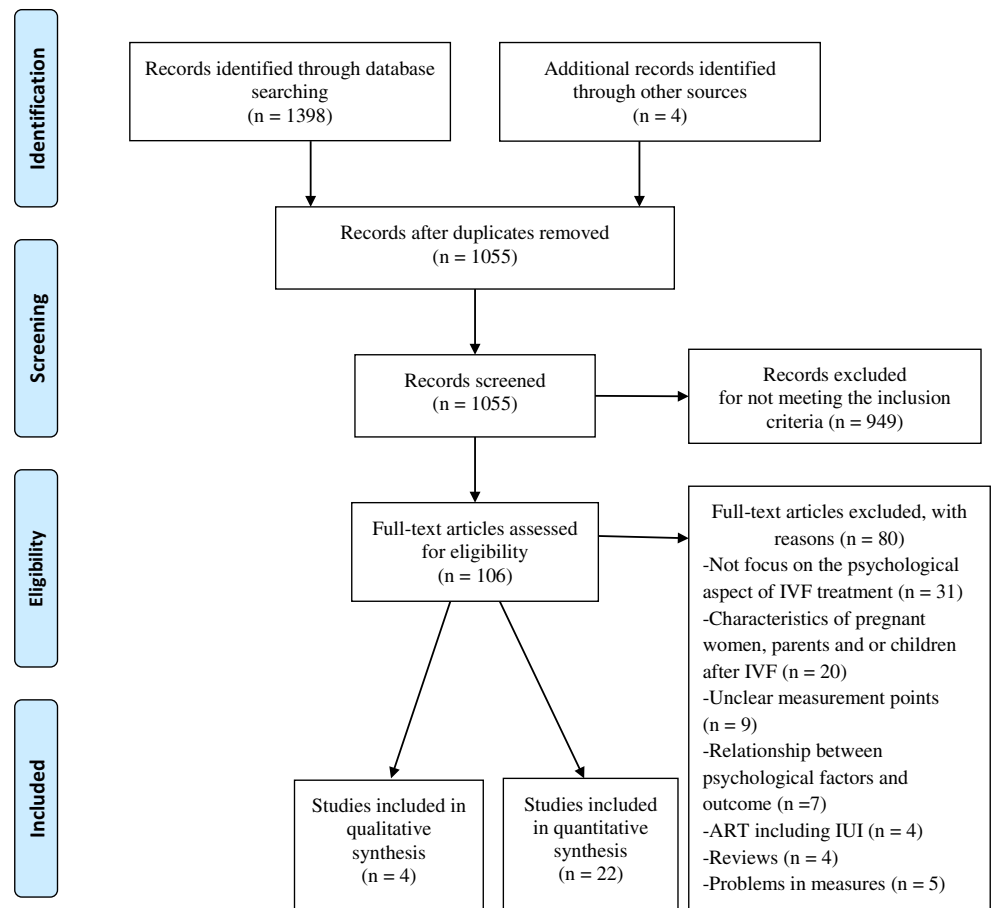
Two reviewers independently reviewed the included studies, and then conducted the quality assessment using the Joanna Briggs Institute Critical Appraisal Checklist for Descriptive/Cohort/Qualitative Studies [12]. There are nine or ten items (for qualitative studies) used to assess the quality of different studies. Each item can be evaluated as *yes*, *no*, or *unsure*, in which *yes* refers to the low risk of bias [13]. Although the item can be scored (*yes*=2; *no*=0; *unsure*=1), there is no priori cut-off score suggested by JBI for study selection. The scores are for reference in this review.

## Results

### General information of the studies

The comprehensive literature search yielded a total of 1398 citations, with 4 additional records identified through a hand search. After duplicate entries were removed, 1055 articles remained. The abstracts of these publications were screened and 949 papers that did not meet the inclusion criteria were excluded. The remaining 106 articles were further assessed for eligibility, and 80 were excluded: not focused on the psychological aspect of IVF treatment ( $n=31$ ), characteristics of pregnant women, parents, and or children after IVF ( $n=20$ ), unclear measurement points ( $n=9$ ), relationship between psychological factors and outcome ( $n=7$ ), ART including IUI ( $n=4$ ), reviews ( $n=4$ ), and problems in

**Fig. 1** Literature search and study selection



measures (n=5). As a result, a total of 22 quantitative and 4 qualitative studies were included in this review.

Of the total of 26 studies that were included, the majority had been conducted in Europe (n=11) and Asia (n=11), followed by North America (n=3), and Oceanic countries (n=1). Two of the studies were published in Chinese.

Of the 22 quantitative studies, 11 were cross-sectional, 9 were longitudinal descriptive, and 2 were cohort correlational studies. The studies focused on infertile couples (n=8), women of infertile couples (n=13), and men of infertile couples (n=1). These studies had an average sample size of 292 (range, 37–1,731), with a mean age of 33.45 years for females (range, 30–35.45 years old), and 34.46 years for males (32.41–36.30 years old). Five studies provided information on the cause of the infertility, with less than one-third involving female factors (28.73 %, range: 23.0–32.5 %), almost 40 % male factors (37.11 %, range 30.7–42.7 %), combined factors (about one out of four couples, 23.46 %, range: 8.0–35.3 %), and the rest involved unknown causes (10.72 %, range 2.5–29 %).

The approaches adopted in the qualitative studies were grounded theory [14], interpretative phenomenological analysis [15], thematic analysis [16], and content analysis [17]. Sample sizes of these four studies ranged from 14 to 22.

**Methodological quality and risk of bias of the included studies**

The results of the quality assessment indicated that the average scores on the quality of the included studies were 13.5 (range, 11–16; maximum possible score 18) for the quantitative studies, and 14 (range, 12–16; maximum possible score 20) for the qualitative studies. The two reviewers held a discussion meeting to resolve any disagreements. Although it was clear that the studies had methodological limitations, such as unclear inclusion criteria for the samples, a lack of objective outcome criteria, and insufficient descriptions of the subject groups in the studies, both reviewers considered all of the studies to be of good quality and suitable for inclusion in this review.

**Data extraction**

The key components of the 22 quantitative studies were extracted and tabulated according to a standard format: authors, country of the study, participants, instruments, and significant findings. In these studies, anxiety and depression were the two main indicators of the couples’ emotional reactions to IVF treatment. This is attributed to the fact that the two indicators were regarded as sensitive to the stress-induced activation of

the hypothalamic-pituitary-adrenal (HPA) axis [18]. The gender differences in depression, anxiety, and other forms of distress are presented in this review. The findings of these studies are grouped and presented according to three treatment periods: pre-, during, and in the long-term following IVF treatment.

### Pretreatment emotional reactions

A total of nine out of the 22 studies reported the psychological effects (depression and anxiety) of infertility in the pre-IVF treatment period, with four of the studies focusing on women, one on men, and four on the couples. The findings of these studies are presented in Table 1.

#### Depression

The depression levels of women and/or men were investigated in the nine studies using a variety of instruments: the Beck Depression Inventory (BDI) [11, 20, 24], the Symptom Check List (SCL-90) [5, 23], the Self-Rating Depression Scale (SDS) [19], the Psychological General Well-Being Index (PGWB) [6], the Patient Health Questionnaire-9 (PHQ-9) [21], and the Lubin's Depression Adjective Checklist Scale (DACL) [22].

The depression levels of women before proceeding with IVF treatment were presented in seven studies. Five of these studies revealed that compared with fertile women, infertile women reported more depressive symptoms [5, 20, 22, 23], or a higher prevalence of moderate and severe depression ( $\text{BDI} \geq 10$ , IVF vs. ICSI vs. control = 48 % vs. 52 % vs. 12 %) [11]. A study that analyzed the pretreatment data after the results of the pregnancy test had been disclosed did not identify significant differences in depression levels between women who finally succeeded in conceiving and those who failed [22]. However, one of the seven studies found no significant difference in depression scores between infertile and normal women (subscale of PGWB,  $m = 15.4$  vs. 15.3) [6], with the measurement point at 2–4 weeks before treatment. Contradictory findings were presented in a study conducted in the USA, indicating that incidences of major depressive disorders (MDD) and other depressive disorders (ODD) among IVF women were lower than among the primary care population (PHQ-9, MDD, 1 % vs. 10 %; ODD, 2 % vs. 6 %) [21], where the PHQ instruments were first developed and published [25]. A possible explanation for this finding proposed by the author was that the PHQ might not be an appropriate/sensitive measure of distress for women at the pre-IVF treatment period [21].

Two of the four studies that examined the depression status of infertile men also showed that these men exhibited more symptoms of depression than fertile men [19], or a higher incidence of moderate and severe depression ( $\text{BDI} \geq 10$ , IVF vs. ICSI vs. control = 44 % vs. 26.7 % vs. 24 %) [11].

However, a study that examined the depressed mood of men 2–4 weeks prior to treatment showed that they were less depressed than other men, indicated by the higher mean scores in subscale of PGWB ( $m = 16.3$  vs. 15.8) [6].

Another study, analyzing the pretreatment data after the results of the pregnancy test had been disclosed, revealed that the depression score of men in couples who succeeded in conceiving was not different from the score of normal men (DACL,  $m = 10.0$  vs. 8.5). Indeed, those men in couples who failed to conceive even showed a lower level of depression than was the norm (DACL,  $m = 7.3$  vs. 8.5) [22]. Thus, the depression levels of infertile men were not significantly higher than the norm. It may also be worth noting that some of these men had children from a previous marriage, which might result in more men who did not feel stressed for not having a second child [22].

Of the nine studies that were identified, only one included statistical testing for gender differences in pretreatment emotional reactions [24]. This study, consisting of 160 infertile couples, reported that women had a significantly higher score than men in symptoms of depression (BDI,  $m = 4.0$  vs. 2.7) [24].

#### Anxiety

The anxiety levels of women and/or men of infertile couples were assessed in eight studies that adopted different inventories: the State Trait Anxiety Inventory (STAI) [11, 20, 22, 24], the Symptom Check List (SCL-90) [5, 23], the Self-Rating Anxiety Scale (SAS) [19], and the Psychological General Well-Being Index (PGWB) [6].

A total of six studies measured the anxiety levels of females during the pre-IVF treatment period. Five studies revealed that infertile females reported higher levels of anxiety than fertile counterparts [5, 6, 22, 23], or higher rates of moderate and severe anxiety ( $\text{STAI} \geq 40$ , IVF vs. ICSI vs. control = 88 % vs. 76 % vs. 44 %) [11]. However, a study conducted in Korea revealed that females of infertile couples scored higher only in trait anxiety than fertile women at the time when the infertile females were entering the IVF program ( $\text{STAI-T}$ ,  $m = 46.23$  vs. 43.56), but there was no difference in the score of state anxiety [20].

Four studies examined the levels of anxiety in men at the pre-IVF treatment period. Two studies identified differences in anxiety, with men of infertile couples demonstrating higher levels of anxiety than fertile men (subscale of PGWB,  $m = 23.1$  vs. 24.5; SDS,  $m = 44.0$  vs. 41.88) [6, 19]. Two studies showed that there were no differences in the prevalence of anxiety prior to the initiation of treatment between the IVF or ICSI group and fertile men [11], and in the scores for state anxiety between infertile males and normal males [22]. The levels of trait anxiety in men at the pretreatment period were not higher than the norm [22].

**Table 1** Pretreatment emotional reactions to IVF treatment

Authors (country of study)	Sample size	Measurement point	Reference group	Significant findings		Anxiety	
				Depression		Women	Men
Dong et al. [19] (China)	502 men of infertile couples, inducees	At the beginning of treatment	Normative data	–	IVF > norm (SDS, $m = 44.00$ vs. 41.88)	–	IVF > norm (SAS, $m = 39.75$ vs. 37.23)
Holter et al. [6] (Sweden)	117 couples, inducees	2–4 weeks before the first treatment	Norm values from a Swedish population of matched age and gender 77 fertile women	IVF = norm (PGWB <sup>a</sup> , $m = 15.4$ vs. 15.3)	IVF < norm (PGWB <sup>a</sup> , $m = 16.3$ vs. 15.8)	IVF < norm (PGWB, $m = 21.6$ vs. 23.1)	IVF > norm (PGWB <sup>a</sup> , $m = 23.1$ vs. 24.5)
Kee et al. [20] (Korea)	138 IVF women	At the time of entering the IVF program	7860 postpartum patients, 3000 published primary care patients, and 4836 patients from the general population	IVF > norm (BDI, $m = 27.24$ vs. 26.32)	–	Trait anxiety: IVF > norm (STAI, $m = 46.23$ vs. 43.56); State anxiety: IVF = norm (the exact value was not provided)	–
Lewis et al. [21] (USA)	321 IVF women	Prior to undergoing IVF treatment	–	–	–	–	–
Merari et al. [22] (Israel)	113 couples, inducees and veterans	10–15 days prior to the initiation of the treatment	Population norm	–IVF < primary care group (PHQ-9, incidences of MDD: 1 % vs. 10 %; ODD: 2 % vs. 6 %; –No depressive symptoms: IVF > postpartum and general population group (PHQ-9, 45.2 % vs. 19.9 % vs. 34 %) Group C (succeeded in conceiving) = Group NC (failed to conceive) > Norm (DACL, $m = 11.35$ vs. 9.87 vs. 8.59)	Group C = Norm > Group NC (DACL, $m = 10.0$ vs. 8.5 vs. 7.3)	Trait: Group C = Norm > Norm (STAI, $m = 41.04$ vs. 41.44 vs. 38.3); State: Group C = Norm > Norm (STAI, $m = 43.04$ vs. 39.18 vs. 33.8)	Trait: Group C = Norm > Group NC (STAI: $m = 38.26$ vs. 37.4 vs. 34.99); State: Group C = Norm > Norm (STAI: $m = 35.6$ vs. 31.8 vs. 32.5)
Salvatore et al. [23] (Italy)	101 women, inducees and veterans	At the first visit of index treatment cycle	75 fertile women	IVF > fertile women (MMPPI, $m = 59.61$ vs. 49.56)	–	–	–
Wang et al. [5] (China)	100 IVF women, 100 ICSI women	During their first visits to the IVF clinic	100 fertile women	IVF > ICSI > control (SCL-90, $m = 0.70$ vs. 0.58 vs. 0.47)	–	–	–
Yassini et al. [11] (Iran)	25 IVF couples, 25 ICSI couples	Waiting for their first treatment cycle of IVF or ICSI	25 couples with a history of fertility	Moderate and severe: IVF < ICSI > control (BDI) $\geq 10$ , (BDI) $\geq 10$ , IVF vs. ICSI vs. control = 48 % vs. 52 % vs. 12 % Women > Men (BDI, $m = 4.0$ vs. 2.7)	Moderate and severe: IVF > ICSI > control (BDI) $\geq 10$ , ICSI vs. control = 44 % vs. 26.7 % vs. 24 %	Moderate and severe: IVF > ICSI > control (STAI) $\geq 40$ , IVF vs. ICSI vs. control = 88 % vs. 76 % vs. 44 % Women > Men, state anxiety (STAI-S, $m = 32.8$ vs. 30.4)	Moderate and severe: IVF = ICSI = control ( $P > 0.05$ )
Wichman et al. [24] (USA)	160 couples	Before proceeding with IVF	No	–	–	–	–

BDI the Beck Depression Inventory, DACL the Lubin's Depression Adjective Checklist Scale, MDD major depressive disorder, MMPPI the Welsh anxiety and depression sub-scale of the Minnesota multiphasic personality inventory, ODD other depressive disorders, PGWB the Psychological General Well-Being Index, PHQ-9 the Patient Health Questionnaire-9, PSS Perceived Stress Scale, SAS the Self-Rating Anxiety Scale, SCL-90 the Symptom Check List, SDS the Self-Rating Depression Scale, STAI the State Trait Anxiety Inventory

<sup>a</sup>The higher value indicates less depression/anxiety

**Table 2** Emotional reactions of infertile couples during a treatment cycle

Authors (country of the study)	Sample size	Measurement point	Significant findings		Anxiety	
			Depression	Men	Women	Men
Chiaffarino et al. [9] (Italy)	872 women and 859 men, inductees and veterans	T1: at first visit; T2: at the time of the $\beta$ -HCG dosage (or at the moment of the suspension of the cycle)	T2 T1 (ZDS, $m = 34.62$ vs. 33.40)	T2 = T1 (ZDS, $m = 29.51$ vs. 29.78)	T2 T1 (ZAS, $m = 32.64$ vs. 31.95)	T2 = T1 (ZAS, $m = 27.55$ vs. 27.84)
Ismail et al. [10] (UK)	30 couples, veterans	T1: pretreatment; T2: before the embryo transfer; T3: before the pregnancy test	T2 < T1 < T3 (MAACL, $m = 50.6$ vs. 51.7 vs. 61.9)	T2 < T1 > T3 (MAACL, $m = 50.3$ vs. 54.6 vs. 61.8)	Similar for all visits	Similar for all visits.
Jin et al. [26] (China)	460 women, inductees	On the day their oocytes were retrieved	Prevalence: (ZDS $\geq 40$ , 14.8 %)	–	Prevalence: (ZAS $\geq 40$ : 33.3 %)	–
Li et al. [27] (China)	538 women, inductees and veterans	Within 2 h after the embryo transfer	Prevalence: (SDS, 12.3 %)	–	Prevalence: (SAS, 38.5 %)	–
Mahajan et al. [28] (Australia)	74 women, inductees	T1: before the start of the study, T2: before the ovum pick-up (OPU), T3: before the embryo transfer	–	–	State anxiety: T1 < T2 = T3 (STAI, $m = 44.00$ vs. 46.41 vs. 46.72)	–
Romano et al. [29] (Israel)	63 women with explained infertility (EIF), 42 women with unexplained infertility (UIF); inductees and veterans	T1: before entering treatment; T2: 2–4 weeks after baseline, at the end of the 2 weeks gonadotropin administration period; T3: 12 days after the embryo transfer but before the pregnancy test	EIF, T1 = T2 = T3 (CES-D, 31.36 vs. 34.43 vs. 35.7; $P > 0.05$ ); UIF, T1 = T2 = T3 (CES-D, 31.73 vs. 34.81 vs. 34.41, $P > 0.05$ )	–	EIF, T1 = T2 = T3 (STAI, $m = 39.53$ vs. 43.16 vs. 45.35; $P > 0.05$ ); UIF, T1 = T2 = T3 (STAI, $m = 38.95$ vs. 43.52 vs. 43.92; $P > 0.05$ )	–
Turner et al. [30] (USA)	44 women, inductees and veterans	T1: prior to ovarian stimulation; T2: 1 day prior to the oocyte retrieval; T3: 5–7 days after the embryo transfer	–	–	State anxiety: T1 = T2 = T3 > norm (STAI, $m = 41.45$ vs. 41.63 vs. 42.06 vs. 35.20) Trait anxiety: T1 = T2 = T3 (STAI, $m = 38.68$ vs. 38.87 vs. 37.81), T1 = T2 > norm (STAI, $m = 38.68$ vs. 38.87 vs. 34.79)	–
Volgsten et al. [7] (Sweden)	439 women, 423 men, inductees and veterans	On the day of the oocyte retrieval	Prevalence of major depression (PRIME-MD, 10.9 %)	Prevalence of major depression (PRIME-MD, 5.1 %)	Prevalence of anxiety disorder (PRIME-MD, 14.8 %)	Prevalence of anxiety disorder (PRIME-MD, 4.9 %)
Yong et al. [31] (UK)	37 women, inductees	T1: before treatment; T2: before the embryo transfer; T3: before the pregnancy test	T1 = T2 < T3 (MAACL, $m = 45.21$ vs. 45.21 vs. 57.12)	–	T1 < T2 = T3 (MAACL, $m = 60$ vs. 77.26 vs. 71.51)	–
Wu et al. [32] (China)	212 women	T1: pretreatment; T2: 1 h before the embryo transfer; T3: 9–10 days after ET; T4: 20 days after the embryo transfer	The prevalence of depression: T1 = T2 = T3 < T4 (CES-D, 32.1 % vs. 27.4 % vs. 30.2 % vs. 47.2 %)	–	The prevalence of anxiety: T1 = T2 = T3 < T4 (SAS, 15.1 % vs. 17.5 % vs. 18.4 % vs. 25.9 %)	–

A study that compared the men and women of 160 couples before they proceeded to undergo IVF treatment found that women scored significantly higher than men in state anxiety (STAI-S,  $m = 32.8$  vs.  $30.4$ ) and perceived stress (PSS,  $m = 11.2$  vs.  $9.9$ ) [24].

In summary, the studies that examined the emotional states of individuals and couples at the pre-IVF treatment period revealed that women experienced higher levels of depression and anxiety. Men in general also had elevated depression levels, while the results on the level of anxiety were inconsistent, with some showing elevated levels of anxiety and others reporting no differences between infertile men and their norm groups.

**The emotional reactions and psychological distress of infertile couples during the treatment cycle**

A total of 12 out of the 22 studies measured the emotional reactions (Table 2) and psychological distress (Table 3) of infertile women and/or men during the IVF treatment cycle. Eight of the 12 studies focused on females, and four on the couples.

*Depression*

Eight studies examined the depression suffered by women and/or men during the cycle of IVF treatment by employing a variety of instruments: the Zung Self-Rating Depression Scale (ZDS) [9, 26], the Center for Epidemiologic Studies Depression Scale

(CES-D) [29, 32], the Mean Affect Adjective Check-List (MAACL) [10, 31], the Self-rating Depression Scale (SDS) [27], and the Primary Care Evaluation of Mental Disorders (PRIME-MD) [7].

For women, the prevalence of depression was high on the day of the oocyte retrieval ( $ZDS \geq 40$ , 14.8 %; PRIME-MD, major depression: 10.9 %) [7, 26], or within 2 h after the embryo transfer (SDS 41, 12.3 %) [27], while the highest incidence of depression was detected 20 days after the embryo transfer (CES-D, 47.2 %) [32]. Compared with the stress level of that measured at baseline, women also scored higher in depression at the time of the  $\beta$ -HCG dosage (the pregnancy test) ( $ZDS, m = 34.62$  vs.  $33.40$ ) [9].

Two studies that measured depression levels at three different time points: pretreatment (T1), before the embryo transfer (T2), and before the pregnancy test (T3), revealed that women scored higher in T3 (MAACL, T1:T2:T3,  $m = 51.7$  vs.  $50.6$  vs.  $61.9$ ;  $m = 45.21$  vs.  $45.21$  vs.  $57.12$ ) [10, 31]. However, one study that adopted repeated measures ANOVA to analyze the level of depression at three different time points: pretreatment, at the end of the gonadotropin administration period, and before the pregnancy test, showed that there were no significant differences between women with either explained infertility (CES-D, T1:T2:T3,  $m = 31.36$  vs.  $34.43$  vs.  $35.71$ ) or unexplained infertility ( $m = 31.73$  vs.  $34.81$  vs.  $34.41$ ), while the higher scores were also present in T2 and T3 [29].

Three studies measured depression in men of infertile couples with IVF treatment. No difference was detected between the time points of the baseline and the  $\beta$ -HCG dosage (the

**Table 3** Psychological distress of infertile couples during a treatment cycle

Authors (country of the study)	Sample size	Measurement point	Significant Findings	
			Psychological Distress	
			Women	Men
Holter et al. [6] (Sweden)	117 couples, inductees	T1: 2–4 weeks before the first treatment, T2: 1 h before the oocyte retrieval	Psychological impacts: T2 > T1 (EIQ, $m = 34.2$ vs. $33.5$ )	Psychological impacts: T2 > T1 (EIQ, $m = 32.0$ vs. $30.8$ )
Ismail et al. [10] (UK)	30 couples, veterans	T1: pretreatment; T2: before the embryo transfer; T3: before the pregnancy test	Positive affect: T2 > T1 > T3 (MAACL, $m = 43.4$ vs. $40.8$ vs. $37.2$ )	Positive affect: T2 > T1 > T3 (MAACL, $m = 44.1$ vs. $42.8$ vs. $39.8$ )
Mahajan et al. [28] (Australia)	74 women, inductees	T1: before the start of the study, T2: before ovum pick-up (OPU), T3: before the embryo transfer	-Positive affect: T2 = T3 < T1 (PANAS, $m = 30.10$ vs. $29.90$ vs. $32.00$ ) -Negative affect: T1 < T2 < T3 (PANAS, $m = 26.44$ vs. $29.75$ vs. $31.89$ )	–
Yong et al. [31] (UK)	37 women, inductees	T1: before treatment; T2: before the embryo transfer; T3: before the pregnancy test	-Positive affect: T1 = T2 > T3 (MAACL, $m = 39.45$ vs. $41.92$ vs. $35.34$ )	–
Boivin & Lancaster, [33] (UK)	61 women, inductees and veterans	Active stage, waiting stage, outcome stage	–Active stage: positive affect with a lesser degree of anxiety; –Waiting stage: a combination of positive affect and anxiety symptoms versus depression; –Outcome stage: depression	–

*BDI* the Beck Depression Inventory, *CES-D* the Center for Epidemiologic Studies Depression Scale, *EIQ* the Effects of Infertility Questionnaire, *ICQ* the Illness Cognition Questionnaire, *MAACL* the Mean Affect Adjective Check-List, *PANAS* The Positive and Negative Affect Schedule, *PRIME-MD* the Primary Care Evaluation of Mental Disorders, *SAS* the Self-Rating Anxiety Scale, *SDS* the Self-Rating Depression Scale, *STAI* the State Trait Anxiety Inventory, *ZAS* Zung Anxiety Scale, *ZDS* the Zung Self-Rating Depression Scale

pregnancy test) (ZDS,  $m=29.78$  vs.  $29.51$ ) [9], while the incidence of major depression was about 5.1 % on the day of the oocyte retrieval [7]. Men also reported similarly higher levels of depression as women before the pregnancy test compared with pretreatment or before the embryo transfer (MAACL, T1:T2:T3,  $m=54.6$  vs.  $50.3$  vs.  $61.8$ ) [10].

### Anxiety

Women and/or men's anxiety was explored in ten studies using different instruments: STAI [28–30], the Zung Anxiety Scale (ZAS) [9, 26], MAACL [10, 31], SAS [27, 32], and PRIME-MD [17].

The incidence of anxiety in women was high on the day of the oocyte retrieval (ZAS  $\geq 40$ , 33.3 %; PRIME-MD, anxiety disorder: 14.8 %) [17, 26], within 2 h after the embryo transfer (SAS 40, 38.5 %) [27], and 20 days after the embryo transfer (SAS  $> 40$ , 25.9 %) [32]. The mean anxiety score for women was higher at the time of the  $\beta$ -HCG dosage (the pregnancy test) than at pretreatment (ZAS,  $m=32.64$  vs.  $31.95$ ) [9]. No differences in anxiety level were detected between women who had received the first cycle and those who had undergone a repeated cycle of IVF treatment [30].

Only three studies examined men's anxiety during the IVF cycle. The findings revealed that the anxiety levels of men at the time of the  $\beta$ -HCG dosage (the pregnancy test) [9], or before the embryo transfer and the pregnancy test were similar to those at baseline [10]. The prevalence of anxiety disorder on the day of the oocyte retrieval was 4.9 %, which was evaluated by the instrument PRIME-MD [7].

Although the scores for levels of anxiety on the day of the oocyte retrieval (T2), before the embryo transfer (T3), and before the pregnancy test (T4) were all higher than at baseline (T1), there were no differences between the three time points (STAI-S, T1 < T2 = T2,  $m=44.00$  vs.  $46.41$  vs.  $46.72$ ; MAACL, T1 < T3 = T4,  $m=60.00$  vs.  $77.26$  vs.  $71.51$ ) [28, 31]. Four of the studies reported that anxiety levels (or the prevalence of anxiety [32]) in T4 were higher than at pretreatment, but the differences were not significant [10, 29, 30]. One study also reported that the state anxiety of women in T1, 1 day before the oocyte retrieval, and T4 was higher than in normal people (STAI-S,  $m=41.45$  vs.  $41.63$  vs.  $42.06$  vs.  $35.20$ ) [30]. To conclude, women were more likely than men to show a higher level/incidence of anxiety at the time of the oocyte retrieval, pre- and post-embryo transfer, and before the pregnancy test.

### Psychological distress

Apart from depression and anxiety, the psychological distress of infertile couples, including positive and negative affect, and general psychological impacts and reactions, were assessed in five studies using different instruments: MAACL [10, 31], the

Positive and Negative Affect Schedule (PANAS) [28], the Effects of Infertility Questionnaire (EIQ) [6], and the Daily Record Keeping Chart (DRK) [33].

A study was conducted to explore the psychological impacts of IVF treatment on infertile couples using the 14-item EIQ (e.g., anger, frustration, anxiety, depression, powerlessness) [6]. The results revealed that both men and women had higher overall scores at 1 h before the oocyte retrieval than in pretreatment (EIQ, men:  $m=32.0$  vs.  $30.8$ ; women:  $m=34.2$  vs.  $33.5$ ). Compared with men, women reported significantly higher scores on psychological impacts before the oocyte retrieval (EIQ,  $m=34.2$  vs.  $32.0$ ) [6].

Two studies indicated that the positive affect scores of women during treatment before the pregnancy test were significantly lower than in the pretreatment period (MAACL,  $m=37.2$  vs.  $40.8$ ;  $m=35.34$  vs.  $39.45$ ) [10, 31]. A study examining the negative affect (NA) of women showed that the mean NA scores before the embryo transfer and oocyte retrieval were higher than that in the pretreatment period (PANAS,  $m=31.89$  vs.  $29.75$  vs.  $26.44$ ) [28]. It was reported that the men reacted in the same psychological pattern as their wives [10].

A study adopted the Daily Record Keeping (DRK) chart to monitor the course of women's affective reactions (e.g., anxiety, depression, and positive affect) to different stages of IVF treatment [33]. The results revealed that in the last 7 days of ovarian stimulation, women reported a positive affect with a lower level of anxiety. During the last 7 days before the pregnancy test, they became increasingly anxious and depressed, while the scores for positive affect were almost unchanged. However, after the pregnancy test a returned negative result, depression was the predominant emotion of women.

In summary, both women and men reported lower levels of positive affect and higher negative affect during the cycle than at the pre-IVF treatment period. A gender difference in the psychological effects of treatment was also identified, with women reporting more negative impacts than men. The treatment had a significant impact on the emotional and psychological distress of women, especially during the period prior to the disclosure of the results of the pregnancy test.

### Experiences of couples undergoing IVF

The results of the two qualitative studies that explored the experiences of couples undergoing IVF provided a more in-depth understanding of the couples. The studies revealed that couples were affected psychologically and in their sexual relationship. During each reproductive cycle, couples go through an emotional roller-coaster of hope, expectation, and despair [16]. Women reported a diminished self-image because they felt that their bodies were treated as a tool for the embryo [15]. Couples expressed difficulty in handling their sexual life, which had been compromised to meet the schedule



required because of the IVF treatment [16]. The unpredictable outcome of the treatment usually gives rise to feelings of anxiety and worry during the waiting period [15, 16].

It can be concluded that during the course of the IVF cycle, the stressful time points for women are the time of the oocyte retrieval, the embryo transfer, and the period prior to the pregnancy test. Men only reported feeling a higher level of depression before the pregnancy test, with anxiety levels being generally similar across the cycle.

**Long-term emotional reactions after the IVF failure**

Two quantitative and two qualitative studies explored the long-term emotional impact after the IVF failure in women and couples. The findings of the quantitative studies are presented in Table 4.

A longitudinal descriptive study identified gender differences in terms of the psychological adjustment of couples 6 months after the IVF treatment [8]. Women scored higher both in depression (BDI,  $m = 1.5$  vs. 2.3) and state anxiety (STAI,  $m = 37.3$  vs. 39.0) after an unsuccessful cycle, and lower in depression and anxiety after a successful cycle (STAI,  $m = 36.7$  vs. 34.2; BDI,  $m = 1.5$  vs. 0.5) than at pre-treatment. However, the difference in men was only found in those with pregnant wives, with such men reporting significantly lower levels of depression (BDI,  $m = 0.7$  vs. 0.4).

Another study examined the psychological adjustment of women 4 to 9 years after failing to conceive after IVF treatment [34]. The findings showed that compared with the women who became parents, those women who remained childless had a higher level of stress (Perceived Stress Scale, PSS,  $m = 14.88$  vs. 18.44) and depression [The Anxiety and Depression subscale of the Minnesota Multiphasic Personality Inventory (MMPI),  $m = 1.71$  vs. 4.56], and less satisfaction with life [The Satisfaction With Life Scale (SWLS),  $m = 26.29$  vs. 21.58].

A qualitative study conducted in Sweden revealed that the grieving process for both men and women was unresolved even 3 years after unsuccessful IVF [17]. Women were more likely to express grief than their husbands, who tended to assume the supportive roles and suppress their own feelings. However, positive experiences were revealed as well. In a qualitative study in Hong Kong, infertile couples with ineffective IVF reported gains in positivity, in personality, or knowledge, in relationships with their partners, children, parents, friends, colleagues, and fellow patients, and in transpersonal relationships (e.g., spirituality) [14].

In short, women in couples who had experienced a failed cycle felt greater stress than those with successful cycles, had higher levels of anxiety and depression, and lower self-esteem and satisfaction with life even years after the treatment. In contrast, for men, there were no significant differences in anxiety and depression pre- and post-treatment. Couples were

**Table 4** Long-term emotional reactions after IVF failure

Authors (country of the study)	Sample size	Measurement point	Significant findings		Anxiety/Other emotional reactions			
			Depression		Women		Men	
			Women	Men	Women	Men	Women	Men
Verhaak et al. [8] (The Netherlands)	148 women, 71 men, inductees	T1: Pre-treatment; T2: 4–6 weeks after the pregnancy test; T3: 6 months after the treatment cycle	Pregnant women: T1 > T2 = T3 (BDI, $m = 1.5$ vs. 0.8 vs. 0.5); non-pregnant women: T1 < T2 = T3 (BDI, $m = 1.5$ vs. 2.3 vs. 2.3)	In couples with pregnant women: T1 = T2 < T3 (BDI, $m = 0.7$ vs. 0.6 vs. 0.4) In couples with non-pregnant women: T1 = T2 = T3 (BDI, $m = 1.0$ vs. 1.5 vs. 0.8)	State anxiety; pregnant women: T1 > T2 = T3 (STAI, $m = 36.7$ vs. 33.5 vs. 34.2); non-pregnant women: T1 < T2 = T3 (STAI, $m = 37.3$ vs. 40.2 vs. 39.0)	State anxiety; in couples with pregnant women: T1 = T2 = T3 (STAI, $m = 32.8$ vs. 32.3); in couples with non-pregnant women: T1 = T2 = T3 (STAI, $m = 33.5$ vs. 34.9 vs. 32.4)		
Bryson et al. [34] (UK)	76 women whose treatment had failed 4–9 years ago	4–9 years after the failure of the IVF treatment	Those who became parents < those who remained childless (MMPI, $m = 1.71$ vs. 4.56)		Other emotional reactions – Stress: < those who became parents (PSS, $m = 14.88$ vs. 18.44) – Satisfaction with life: those who became parents > those who remained childless (SWLS, $m = 26.29$ vs. 21.58)			

BDI Beck Depression Index, MMPI the Welsh anxiety and depression sub-scale of the Minnesota multiphasic personality inventory, PSS the perceived stress scale, STAI State and Trait Anxiety Inventory, SWLS the satisfaction with life scale

together experiencing unresolved grief in the long term after the IVF failure.

## Discussion

In the present review of the literature, the emotional reactions of infertile couples to IVF treatment were explored from the perspective of gender. The findings from the literature were organized into three categories: pre-, during, and long-term after IVF treatment.

### Pretreatment emotional reactions of infertile couples

Before the start of IVF, women reported higher levels of depression and anxiety than fertile women. In general, our findings are consistent with those in the previous review, in which the authors concluded that women who started the treatment were emotionally distressed compared with fertile women, although the disparity was slight [4]. Such findings are to be expected, considering the physical, social, and emotional pain that they suffer. Women in the modern society still regard motherhood as an important role and a respected identity, although they now have other ways to find value in life [35]. In their desire to fulfill their dream of motherhood, infertile women are exposed to the majority of IVF procedures, including injections, medications, blood tests, and scans [36]. IVF offers them new hope of having a baby, but it also adds a great psychological burden on women because of its poor success rate of 16.6–20.2 % [2]. Therefore, it is not surprising to note that infertile women reported psychological distress even prior to the IVF treatment.

Infertile men also experienced depression before the IVF treatment, while the effects on their anxiety levels were inconsistent. Men, as well as women, suffered from the fact of being infertile, and were more likely to experience depression [4]. However, men suffered less from the procedures of the IVF treatment, and their anxiety levels were less affected.

### Emotional reactions of infertile couples during the treatment cycle

Compared with the pretreatment stage, infertile women presented higher levels/incidences of depression and anxiety at the time of the oocyte retrieval, the embryo transfer, and before the pregnancy test. These findings are supported by the results of a previous review [4]. Men of infertile couples reported a higher level of depression only during the time that couples were waiting for the outcome of the IVF treatment. A study also found that, compared with the pretreatment period, both men and women had lower scores on positive affect before the pregnancy test.

When entering the cycle, infertile couples, especially women, suffer from painful procedures including routine injections and tests. The oocyte retrieval was regarded as the most tortuous procedure [16], which was accompanied by abdominal cramping, bloating, and general fatigue. The period of embryo transfer, although less painful, saw the couples worrying about the quality and quantity of the embryos, or the loss of the transferred embryo(s). Some women suffered from a disturbance to their self-image, feeling that their body was being instrumentalized for the embryos. During the waiting period before the pregnancy test, both women and men reported psychological distress. In a qualitative study conducted in China, a participant actually described this period as facing *an impending death sentence* [37]. The outcome of the IVF treatment is unguaranteed and uncontrollable. The couples find themselves powerless to do anything but wait for the results, knowing that their chance of conceiving is only one fifth [2]. It is understandable that the couples would experience psychological distress before the pregnancy test.

Although both men and women reported psychological distress, gender differences existed during the treatment. Women of infertile couples usually had higher levels of anxiety and depression, while men only exhibited higher levels of depression. The anxiety levels of men were similar across the cycle. Apart from the involvement of fewer men than women in the treatment procedures, the socialization processes of men might also play a role in the interpretation of the results. During their life cycle, men are usually expected to be strong and to suppress their emotions when encountering adversity, which might contribute to a higher prevalence of depression and hardly any changes in anxiety level [38].

### Long-term emotional reactions after IVF failure

The study showed that women who had a successful cycle reported lower negative emotions than at pretreatment [8]. Women who remained childless 4 to 9 years after unsuccessful IVF treatment reported less satisfaction with life than those who finally became parents [34]. The results indicated that it is the unsuccessful outcome of IVF instead of IVF itself that would have long-term psychological consequences [8]. Infertile couples who had failed cycle experienced unresolved grief 3 years after treatment [17]. The findings of this review are consistent with the statement that the grieving process in the IVF cycle is often long [39].

It was interesting in this review to note that there was a difference between the persistence of infertile couples in the West from those in China. A study in the USA showed that about 34 % of insured patients who underwent IVF would terminate their treatment cycle after one or two unsuccessful trials [40]. However, infertile couples in China were more persistent, and not many couples were willing to drop out of treatment until the desired pregnancy was achieved. The

repeated IVF treatments would result in a long-lasting negative impact on the couple's emotions, and would also hinder them from moving on to a childfree life or from adopting a child [5, 26, 41].

### Methodological issues of the reviewed studies

There are methodological shortcomings to the studies that were included in this review. First, it is noteworthy that the studies only compared the pretreatment psychological status of infertile individuals prepared to undergo IVF treatment with their fertile counterparts or the general population as the norm, but not with other infertile patients who are not undergoing IVF treatment. Therefore, the impact of infertility vs. the impact of the IVF treatment cannot be distinguished. Moreover, anxiety and depression were assessed using various instruments, including general and fertility-specific measures of depression, which might have influenced the interpretation of the findings. The assessment points also varied in the studies, ranging from 2 to 4 weeks to immediately before the treatment, and the waiting period was not defined, which might also have influenced the levels of emotional reactions. In future studies, researchers should consider these matters, including the selection of a reference group, instruments, and measurement points.

### Limitations

Several limitations in the present literature review should be considered. First, only articles published in English and Chinese were included. This resulted in biases in publications and sources. However, the published papers were generally regarded as being of better quality than grey literature. Another limitation is that there were far fewer studies identified on the emotional reactions of men to IVF than on women, which might led to some biases in our conclusion. A further exploration of the psychological reactions of men is needed to confirm the results.

### Recommendations for future research/program

This review provided some starting points and insights for future research in related fields. First, when examining the pretreatment emotional responses of infertile couples, the reference groups selected in these studies were mostly fertile couples or the normal population. There is a need to compare these couples with those involved in first-line infertility treatments before IVF. It is in comparing two equivalent groups with infertility but with or without treatment that the impacts of pre-IVF treatment can be accurately depicted. Also, the personal factors, such as personality, individual coping strategies, social economic status, and social support, should be considered.

Second, infertility-specific instruments are more sensitive than other instruments in assessing the emotional states of infertile couples and should be adopted. Third, as this review has shown that a considerable number of infertile couples experienced emotional distress when undergoing IVF treatment, a screening system to identify those at risk for emotional disturbances and a support program should be developed and provided. Finally, since it was revealed that IVF treatment affects both men and women as couples, and the negative emotions of one affected the other in the couple, the emotional reactions to IVF treatment of both men and women should be attended to.

### Clinical implications

The better understanding of the impacts of IVF treatment on infertile couples has significant clinical implications for health care providers. From the beginning, clinicians should clarify to couples the fact that elevated negative emotions in women are natural under the circumstances and will not affect the pregnancy rate [42]. The couples should also be provided with information and support, which will give them a better understanding of the process, more realistic expectations about the outcome of the treatment, and the strength to go through the treatment.

During the cycle, psychological support should be provided on the day of the oocyte retrieval, the embryo transfer, and especially during the stage leading up to the pregnancy test. As both men and women experienced elevated levels of depression, such support should target the couple as a dyad. Men of infertile couples should also be encouraged to express their feelings and demands. The support could include information on the procedures, relaxation skills, and coping strategies.

Counseling or therapy should be made available, particularly for couples with failed cycles. It has been found that unsuccessful treatment will not only lead to immediate heart-break but also to long-term unresolved grief [17]. Counselors should help the couples to accept and adjust to the undesirable outcomes. Advice and counseling should be given on whether the couple should proceed with the next treatment.

It is recommended that a support program should be developed, aimed at enhancing the partnership in couples undergoing IVF treatment. It has been reported that both women and men of infertile couples experience a stressful married life [3], and those seeking IVF treatment are more likely to have an unstable marital relationship because of the prolonged nature and demands of the treatment [5, 43]. However, a supportive marital relationship can play a protective role for couples during the period of the IVF cycle [44], especially when the woman is not adapting effectively to IVF [45]. An intervention program aimed at enhancing the partnership in couples, helping the couples to support each other while undergoing IVF treatment, is needed.

## Conclusion

Although both men and women experienced psychological distress during IVF treatment, gender differences existed. Compared with their fertile counterparts, women of infertile couples had higher levels of anxiety and depression, while men usually had a higher level of depression. Women had higher anxiety and depression prior to the treatment, and became even worse on the day of the oocyte retrieval, the pre- and post embryo transfer, and during the waiting period before the pregnancy test. Before the treatment, men of the infertile couples reported elevated depression scores, which rose further during the time that couples waited to learn the outcome of the IVF treatment. Both men and women had lower positive affect scores before the pregnancy test. A failed IVF cycle had long-term negative psychological consequences for both spouses. A couple-based support program aimed at improving the psychological well-being and marital relationship of infertile couples should be provided.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

## References

- Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. *PLoS Med*. 2012;9(12):e1001356.
- Sullivan E, Zegers-Hochschild F, Mansour R, Ishihara O, de Mouzon J, Nygren K, et al. International committee for monitoring assisted reproductive technologies (ICMART) world report: assisted reproductive technology 2004. *Hum Reprod*. 2013;28(5):1375–90. **doi:10.1016/j.ijnurstu.2015.05.004**.
- Ying LY, Wu LH, Loke AY. Gender differences in experiences with and adjustments to infertility: a literature review. *Int J Nurs Stud*. 2015. **doi:10.1016/j.ijnurstu.2015.05.004**.
- Verhaak CM, Smeenk JM, Evers AW, Kremer JA, Kraaijmaat FW, Braat DD. Women's emotional adjustment to IVF: a systematic review of 25 years of research. *Hum Reprod*. 2007;13(1):27–36. **Update**.
- Wang K, Li J, Zhang JX, Zhang L, Yu J, Jiang P. Psychological characteristics and marital quality of infertile women registered for in vitro fertilization-intracytoplasmic sperm injection in China. *Fertil Steril*. 2007;87(4):792–8.
- Holter H, Anderheim L, Bergh C, Möller A. First IVF treatment—short-term impact on psychological well-being and the marital relationship. *Hum Reprod*. 2006;21(12):3295–302.
- Volgsten H, Svanberg AS, Ekselius L, Lundkvist Ö, Poromaa IS. Prevalence of psychiatric disorders in infertile women and men undergoing in vitro fertilization treatment. *Hum Reprod*. 2008;23(9):2056–63.
- Verhaak CM, Smeenk JM, van Minnen A, Kremer JA, Kraaijmaat FW. A longitudinal, prospective study on emotional adjustment before, during and after consecutive fertility treatment cycles. *Hum Reprod*. 2005;20(8):2253–60.
- Chiapparino F, Baldini MP, Scarduelli C, Bommarito F, Ambrosio S, D'Orsi C, et al. Prevalence and incidence of depressive and anxious symptoms in couples undergoing assisted reproductive treatment in an Italian infertility department. *Eur J Obstet Gynecol Reprod Biol*. 2011;158(2):235–41.
- Ismail W, Menezes M, Martin C, Thong K. A comparison of psychological functioning in couples undergoing frozen-thawed embryo replacement in various stages of treatment using the mean affect adjective check list (MAACL). *J Assist Reprod Genet*. 2004;21(9):323–7.
- Yassini M, Khalili M, Hashemian Z. The level of anxiety and depression among Iranian infertile couples undergoing in vitro fertilization or intra cytoplasmic sperm injection cycles. *J Res Med Sci*. 2005;10(6):358–62.
- Institute JB. Joanna Briggs Institute reviewers' manual: 2014 edn. Adelaide, Australia: JBI; 2014.
- Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane back review group. *Spine*. 2009;34(18):1929–41.
- Lee GL, Choi WH, Chan CH, Chan CL, Ng EH. Life after unsuccessful IVF treatment in an assisted reproduction unit: a qualitative analysis of gains through loss among Chinese persons in Hong Kong. *Hum Reprod*. 2009;24(8):1920–9.
- Cipolletta S, Faccio E. Time experience during the assisted reproductive journey: a phenomenological analysis of Italian couples' narratives. *J Reprod Infant Psychol*. 2013;31(3):285–98.
- Widge A. Seeking conception: experiences of urban Indian women with in vitro fertilisation. *Patient Educ Couns*. 2005;59(3):226–33.
- Volgsten H, Svanberg AS, Olsson P. Unresolved grief in women and men in Sweden three years after undergoing unsuccessful in vitro fertilization treatment. *Acta Obstet Gynecol Scand*. 2010;89(10):1290–7.
- Sandi C, Richter-Levin G. From high anxiety trait to depression: a neurocognitive hypothesis. *Trends Neurosci*. 2009;32(6):312–20.
- Dong YZ, Yang XX, Sun YP. Correlative analysis of social support with anxiety and depression in men undergoing in vitro fertilization embryo transfer for the first time. *J Int Med Res*. 2013;41(4):1258–65.
- Kee BS, Jung BJ, Lee SH. A study on psychological strain in IVF patients. *J Assist Reprod Genet*. 2000;17(8):445–8.
- Lewis AM, Liu D, Stuart SP, Ryan G. Less depressed or less forthcoming? Self-report of depression symptoms in women preparing for in vitro fertilization. *Arch Womens Ment Health*. 2013;16(2):87–92.
- Merari D, Chetrit A, Modan B. Emotional reactions and attitudes prior to in vitro fertilization: an inter-spouse study. *Psychol Health*. 2002;17(5):629–40.
- Salvatore P, Gariboldi S, Offidani A, Coppola F, Amore M, Maggini C. Psychopathology, personality, and marital relationship in patients undergoing in vitro fertilization procedures. *Fertil Steril*. 2001;75(6):1119–25.
- Wichman CL, Ehlers SL, Wichman SE, Weaver AL, Coddington C. Comparison of multiple psychological distress measures between men and women preparing for in vitro fertilization. *Fertil Steril*. 2011;95(2):717–21.
- Spitzer RL, Kroenke K, Williams JB, Group PHQPCS. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. *JAMA*. 1999;282(18):1737–44.
- Jin X, Wang G, Liu S, Zhang J, Zeng F, Qiu Y, et al. Survey of the situation of infertile women seeking in vitro fertilization treatment in China. *Biomed Res Int*. 2013;2013:1–7.
- Li YC, Xu HL, Gao SY. Anxiety and depression in women with in vitro fertilization and embryo transfer treatment (in Chinese). *Chin Ment Health J*. 2012;26(4):241–6.

28. Mahajan NN, Turnbull DA, Davies MJ, Jindal UN, Briggs NE, Taplin JE. Changes in affect and state anxiety across an in vitro fertilization/intracytoplasmic sperm injection cycle. *Fertil Steril*. 2010;93(2):517–26.
29. Romano GA, Ravid H, Zaig I, Schreiber S, Azem F, Shachar I, et al. The psychological profile and affective response of women diagnosed with unexplained infertility undergoing in vitro fertilization. *Arch Womens Ment Health*. 2012;15(6):403–11.
30. Turner K, Reynolds-May MF, Zitek EM, Tisdale RL, Carlisle AB, Westphal LM. Stress and anxiety scores in first and repeat IVF cycles: a pilot study. *PLoS One*. 2013;8(5):e63743.
31. Yong P, Martin C, Thong J. A comparison of psychological functioning in women at different stages of in vitro fertilization treatment using the mean affect adjective check list. *J Assist Reprod Genet*. 2000;17(10):553–6.
32. Wu Z, Zhang H, Cong L. Study on symptoms of anxiety, depression in women with in vitro fertilization and embryo transfer (in Chinese). *Prog Obstet Gynecol*. 2008;17(3):205–8.
33. Boivin J, Lancaster D. Medical waiting periods: imminence, emotions and coping. *Women's Health (Lond Engl)*. 2010;6(1):59–69.
34. Bryson CA, Sykes DH, Traub AI. In vitro fertilization: a long-term follow-up after treatment failure. *Hum Fertil*. 2000;3(3):214–20.
35. Loke AY, Yu PL, Hayter M. Experiences of sub-fertility among Chinese couples in Hong Kong: a qualitative study. *J Clin Nurs*. 2012;21(3–4):504–12.
36. Infertility BC. *Obstetrics and gynecology*. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014. p. 371–80.
37. Ying LY, Wu LH, Loke AY. The experience of Chinese couples undergoing in vitro fertilization treatment: perception of the treatment process and partner support. *PLoS One*. 2015;10(10):e0139691. doi:10.1371/journal.pone.0139691.
38. Beevers CG, Wenzlaff RM, Hayes AM, Scott WD. Depression and the ironic effects of thought suppression: therapeutic strategies for improving mental control. *Clin Psychol Sci Pract*. 1999;6(2):133–48.
39. Alesi R. Infertility and its treatment: an emotional roller coaster. *Aust Fam Physician*. 2005;34(3):135–8.
40. Domar AD, Smith K, Conboy L, Iannone M, Alper M. A prospective investigation into the reasons why insured United States patients drop out of in vitro fertilization treatment. *Fertil Steril*. 2010;94(4):1457–9.
41. Lau JT, Wang Q, Cheng Y, Kim JH, Yang X, Yi TH. Infertility-related perceptions and responses and their associations with quality of life among rural Chinese infertile couples. *J Sex Marital Ther*. 2008;34(3):248–67.
42. Boivin J, Griffiths E, Venetis CA. Emotional distress in infertile women and failure of assisted reproductive technologies: meta-analysis of prospective psychosocial studies. *BMJ*. 2011;342(7795):1–9.
43. Newton CR. Counseling the infertile couple. *Infertility counseling: a comprehensive handbook for clinicians*. New York: Parthenon; 2006. p. 143–55.
44. Lowyck B, Luyten P, Corveleyn J, D'Hooghe T, Buyse E, Demyttenaere K. Well-being and relationship satisfaction of couples dealing with an in vitro fertilization/intracytoplasmic sperm injection procedure: a multilevel approach on the role of self-criticism, dependency, and romantic attachment. *Fertil Steril*. 2009;91(2):387–94.
45. Chochovski J, Moss SA, Charman DP. Recovery after unsuccessful in vitro fertilization: the complex role of resilience and marital relationships. *J Psychosom Obstet Gynaecol*. 2013;34(3):122–8.