Women’s emotional adjustment to IVF: a systematic review of 25 years of research

C.M.Verhaak1,3, J.M.J.Smeenk2, A.W.M.Evers1, J.A.M.Kremer2, F.W.Kraaimaat1 and D.D.M.Braat2

1Department of Medical Psychology and 2Department of Obstetrics and Gynaecology, Radboud University Nijmegen, Medical Centre, Nijmegen, The Netherlands

3To whom correspondence should be addressed at: Radboud University Nijmegen, Medical Centre, 818 Department of Medical Psychology, PO Box 9101, 6500 HB Nijmegen, The Netherlands. E-mail: c.verhaak@eukz.umcn.nl

This review provides an overview of how women adjust emotionally to the various phases of IVF treatment in terms of anxiety, depression or general distress before, during and after different treatment cycles. A systematic scrutiny of the literature yielded 706 articles that paid attention to emotional aspects of IVF treatment of which 27 investigated the women’s emotional adjustment with standardized measures in relation to norm or control groups. Most studies involved concurrent comparisons between women in different treatment phases and different types of control groups. The findings indicated that women starting IVF were only slightly different emotionally from the norm groups. Unsuccessful treatment raised the women’s levels of negative emotions, which continued after consecutive unsuccessful cycles. In general, most women proved to adjust well to unsuccessful IVF, although a considerable group showed subclinical emotional problems. When IVF resulted in pregnancy, the negative emotions disappeared, indicating that treatment-induced stress is considerably related to threats of failure. The concurrent research reviewed, should now be underpinned by longitudinal studies to provide more information about women’s long-term emotional adjustment to unsuccessful IVF and about indicators of risk factors for problematic emotional adjustment after unsuccessful treatment, to foster focused psychological support for women at risk.

Key words: anxiety/depression/emotional response/fertility treatment/IVF

Introduction

From the treatment’s launch, the emotional adjustment to IVF has received ample attention in clinical, descriptive and empirical studies (Menning, 1980; Greenfeld et al., 1984; Freeman et al., 1985; Mahlstedt, 1985; Hearn et al., 1987; Callan and Hennessey, 1988; Dennerstein and Morse, 1988; Kemeter, 1988; Kentenich, 1989; Mazure and Greenfeld, 1989; Edelmann, 1990). The descriptive studies have predominantly addressed the stressful consequences of infertility and its treatment, thus solely focusing on a selective sample of help seekers. Using representative samples and standardized measures, empirical research conducted in the 1980s, however, demonstrated that, in general, infertile women do not differ significantly from control or norm groups on emotional aspects (Dunkel-Schetter and Lobel, 1991). This review concluded that longitudinal and prospective studies were needed to support these results and to uncover information about groups at risk of emotional problems as a result of unsuccessful fertility treatment. Recent years have seen a substantial expansion of research efforts into women’s emotional adjustment to IVF.

With this review, we provide a systematic and comprehensive overview of the empirical research into women’s emotional adjustment to IVF over the last 25 years with a special emphasis on directions for future research. Because our review specifically targets the process and the multidimensional character of emotional adjustment to unsuccessful treatment, it extends earlier reviews (Wright et al., 1989; Dunkel-Schetter and Lobel, 1991; Eugster and Vingerhoets, 1999; Pasch, 2001). We consider the psychological adjustment process in relation to the various characteristics and stages of the medical procedure by differentiating between the different cycles of an IVF treatment because, in line with Beaurepaire et al. (1994), we assume that the number of treatment options left could easily determine the emotional response to the treatment and its outcome. For the same reason, this review exclusively focuses on IVF as it is nearly always the last treatment option for couples with fertility problems. Accordingly, we do not consider studies on emotional adjustment to less invasive treatment options such as intrauterine insemination.

IVF is a multidimensional stressor; the treatment itself constitutes the primary stressor and is most likely to evoke anxiety. The unpredictable outcome of the treatment is another major stress-inducing agent, more likely to evoke feelings of depression (Dunkel-Schetter and Lobel, 1991). To do justice to the course and varying
C.M. Verhaak et al.

impact of consecutive IVF cycles and its multidimensional character as a stressor, we have looked at how women tend to emotionally adjust to their infertility problems and treatment in relation to the following four phases of treatment: before the start of the treatment, within one treatment cycle, before and after treatment cycles (comparing differences) and after abandoning treatment.

Following stress-coping models on adjustment to a chronic stressor, our review regards the emotional response to IVF in terms of anxiety, depression and general distress. Aspects of coping skills, social support and personality characteristics are considered determinants of the emotional response and are thus taken into account as risk and protective factors to explain individual differences in emotional response to unsuccessful IVF based on stress-coping models (Abramson et al., 1978; Beck et al., 1979; Eysenck, 1981; Lazarus and Folkman, 1984; Leventhal et al., 1984; Cohen and Wills, 1985; Holahan and Moos, 1985; Ormel and Wohlfart, 1991; Edelmann, 1992; Clark et al., 1994; Costa et al., 1996; Holahan et al., 1996; Alloy et al., 1999). A sound insight into such risk and protective factors would facilitate the identification of women at risk of experiencing emotional problems and foster the development of preventative and tailored support.

In summary, this paper reviews empirical research on the emotional adjustment of women to IVF treatment published in the past 25 years with special emphasis on (i) the different phases in the treatment process and the various aspects of the emotional response in terms of anxiety, depression or general distress and (ii) specific risk and protective factors that are assumed to contribute to the emotional adjustment to IVF, i.e. the role of personality characteristics, coping skills, cognitions with respect to fertility problems and social support.

The four treatment phases that were taken into account are schematically represented in Figure 1. The status and course of the patients’ emotional adjustment was assessed (i) pretreatment, i.e. before the start of the treatment, (ii) within cycle, i.e. during one treatment cycle, (iii) before and after treatment, i.e. from the pretreatment phase up to and including one or more treatment cycles and (iv) post-treatment, i.e. after treatment was abandoned.

Methodology

Selection of eligible studies

This review comprises studies published between 1978 (the introduction of IVF) and December 2005 in peer reviewed journals in English, German, Dutch and French. The electronic databases of Medline, PubMed and PsychInfo and the snowball method were used to identify relevant articles. To identify those articles that specifically paid attention to issues relating to emotional aspects of IVF (including ICSI treatment) in women, we used the search terms IVF, ICSI and infertility treatment in combination with the terms anxiety, depression, emotional, distress, stress, psychosocial, psychological and psychology. The selection criteria thus excluded studies focusing on the emotional aspects of assisted reproductive treatment (ART) in general, i.e. those which did not differentiate between IVF (including ICSI) and other ARTs such as intruterine sperm insemination.

Assessment of study quality

Study quality was determined by using criteria based on the protocols of the Cochrane Database of Systematic Reviews. We adjusted the criteria to fit the research questions of this review:

(i) Database: studies should be published in English, Dutch, French or German with an abstract presented in an electronic database.

(ii) Selection of subjects: the participants invited to take part in the study should be selected randomly or consecutively.

(iii) Outcome measures: the studies should make use of outcome measures defined in terms of anxiety or depression or in terms of general distress indicative of emotional adjustment, with proven reliability and validity, and compared with norm groups.

(iv) Sample size: the sample size should be sufficient to indicate medium effect sizes (d = 0.50) with a power of 0.80 (Cohen, 1977).

(v) Statistical analyses: preferably, effects should be expressed in significance levels or t- or F-values.

The additional criteria for prospective studies were as follows:

(i) Sample sizes of prospective studies needed to be sufficient and in relation to the number of predictors (at least 10 subjects for each predictor, see Cohen, 1977).

(ii) Studies should be of longitudinal design predicting changes in emotional factors out of predictive factors assessed at baseline.

Presentation of the results

The results are presented per treatment phase investigated, and prospective studies are discussed at the end. Information about statistics (t- or F-values) and mean scores on the instruments used,
e.g. Spielberger State in Trait Anxiety Inventory (STAI) scores are only presented when studies performed comparable analyses and used comparable assessment tools.

Results

The search of the literature yielded 706 articles that paid attention to a broad range of topics related to psychology and IVF. Two independent raters subsequently conducted a further selection to identify those studies that fit the contents and methodological criteria for this review (intrarater agreement was 92%). The focal points of the studies are summarized in Table I.

Thirty-one articles did not provide an abstract and 27 were not published in the target languages. A considerable proportion of the remaining studies focused on ethical, legal or sociological issues (24%), on medical aspects (16%), on the effects for the children conceived by IVF (11%), on relationships between psychological factors and treatment outcome (5%) or on the effects of psychosocial interventions, e.g. counselling (3%). Of the studies, 4% focused on a special group (e.g. women recovering from a severe disease), 5% addressed aspects of new reproductive technologies (e.g. surrogacy) and 1% of the studies dealt with treatment satisfaction or alternative treatments or concerned animal studies. Of the remaining 87 studies, 27 met the contents and methodological criteria for this review, presenting data on anxiety, depression or the effects of psychological interventions, e.g. counselling (3%). Of the studies, 4% focused on a special group (e.g. women recovering from a severe disease), 5% addressed aspects of new reproductive technologies (e.g. surrogacy) and 1% of the studies dealt with treatment satisfaction or alternative treatments or concerned animal studies. Of the remaining 87 studies, 27 met the contents and methodological criteria for this review, presenting data on anxiety, depression or the effects of psychological interventions, e.g. counselling (3%).

<table>
<thead>
<tr>
<th>Focus of attention</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focus on ethical or legal aspects</td>
<td>125</td>
<td>18</td>
</tr>
<tr>
<td>Medical aspects of IVF</td>
<td>110</td>
<td>16</td>
</tr>
<tr>
<td>Characteristics of parents and or children after IVF</td>
<td>80</td>
<td>11</td>
</tr>
<tr>
<td>Emotional adjustment before IVF</td>
<td>56</td>
<td>8</td>
</tr>
<tr>
<td>Qualitative/case studies</td>
<td>50</td>
<td>7</td>
</tr>
<tr>
<td>Focus on sociological aspects of IVF</td>
<td>44</td>
<td>6</td>
</tr>
<tr>
<td>New technology</td>
<td>39</td>
<td>5</td>
</tr>
<tr>
<td>Relationship between psychological factors and outcome</td>
<td>35</td>
<td>5</td>
</tr>
<tr>
<td>Special groups</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>Focus on counselling</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Reviews</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Course of the emotional response</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Long-term response</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Genetics</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Prospective studies</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Studies with animals</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Satisfaction with treatment</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Dropout</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Alternative treatment</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>No abstracts available</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>706</td>
<td>100</td>
</tr>
</tbody>
</table>

Table I. Subject of studies revealed by search and snowball method (n = 706)

Studies with focus of attention in italics met the criteria for the first selection for this review, based on content.

Twenty-seven studies were not published in English, German, French or Dutch; Spanish (5), Swedish (4), Japanese (3), Chinese (3), Norge (4), Czech (2), Hebrew, Danish, Portuguese, Hungarian, Polish and Italian (all 1).

Emotional response to IVF

Pretreatment emotional adjustment

Nine studies investigated emotional adjustment before the start of fertility treatment (Table II). Six studies provided information about pretreatment depression levels using different inventories: three used the Beck Depression Inventory (BDI) (Beck et al., 1961), one the Symptom Checklist (SCL-90) (Derogatis et al., 1973), one the Centre for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977) and two the Profile of Mood States (POMS) (McNair et al., 1971). None of the studies reported differences in depression between the IVF patients and norm groups.

All studies also assessed anxiety, most frequently by use of the STAI (Spielberger, 1983) or SCL-90. With respect to state anxiety, four studies did not report differences with norm groups (Hearn et al., 1987; Edelmann et al., 1994; Verhaak et al., 2001; Felkes et al., 2003), whereas five showed enhanced pretreatment levels of state anxiety (Beaurepaire et al., 1994; Visser et al., 1994; Mori et al., 1997; Slade et al., 1997; Salvatore et al., 2001). Pretreatment anxiety scores on the STAI differed considerably, ranging from 50 to 33. This is partly explained by the differences in norms over countries. In Japan, the norm score for state anxiety was 42, whereas in other countries norms varied between 34 and 38; the differences may be because of cultural aspects and the type of norm group. As anxiety scores differ per age and sex, normative data should match these variables. However, most studies failed to provide information about the characteristics of the norm groups. Still, the differences in norm groups could not explain the considerable differences in pretreatment state anxiety levels even within one country (Visser et al., 1994; Verhaak et al., 2001).

The time in which the study was conducted (i.e. just after the introduction of IVF or more recently) could not explain the disparity in the state anxiety findings nor were there differences related to type of sample (only inductees versus inductees and veterans). In addition, the variations were also present in studies assessing state anxiety at more or less the same moment: immediately before the start of the medication. Nor could age differences explain the variations: the mean age of the women participating in the studies varied from 32 to 34 years. It is known that ways of communicating fertility problems and treatment possibilities, just as the method of delivering information, tend to influence the patients’ emotional responses before the start of IVF. The differences in pretreatment emotional adjustment may hence have been attributable to the different patient approaches the studies adhered to, but, unfortunately, the studies presented did not provide any details on these aspects of their procedures. Future studies should pay attention to these different treatment protocols.

All but one study assessed anxiety with general inventories that were unrelated to the fertility problem. Of special interest is the study by Felkes et al. (2003) that took both general and fertility-related emotional problems into account. The authors found no deviations from the norm groups on the general instruments but did report higher levels of emotional complaints for the fertility-related measures (Felkes et al., 2003).
C.M. Verhaak et al.

Table II. Studies investigating pretreatment emotional adjustment to IVF

<table>
<thead>
<tr>
<th>References</th>
<th>Sample size</th>
<th>Measurement point</th>
<th>Measures</th>
<th>Reference group</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fekkes et al. (2003), The Netherlands</td>
<td>n = 447, inductees</td>
<td>Before start of treatment, not clear how much</td>
<td>HSCL: general emotional complaints; SIP: infertility-related emotional complaints</td>
<td>Norms</td>
<td>HSCL: no differences with norms; SIP: more emotional complaints compared with norms (t = 7.17, P &lt; 0.01)</td>
</tr>
<tr>
<td>Salvatore et al. (2001), Italy</td>
<td>n = 176, inductees and veterans</td>
<td>Not defined</td>
<td>Anxiety, depression: SCL-90; general distress: GHQ-30</td>
<td>IVF versus matched controls</td>
<td>Anxiety: IVF &gt; controls (t = –2.01); depression: IVF = controls (t = –0.65); general distress: IVF = controls, no statistics given</td>
</tr>
<tr>
<td>Verhaak et al. (2001), The Netherlands</td>
<td>n = 207, inductees only, primary and secondary infertility</td>
<td>Just before starting medication of first treatment cycle</td>
<td>State anxiety: STAI (36–38); depression: BDI</td>
<td>Norm groups</td>
<td>State anxiety: IVF = norms; depression: IVF = norms, no statistics given</td>
</tr>
<tr>
<td>Mori et al. (1997), Japan</td>
<td>n = 102, inductees</td>
<td>Just before starting medication of first treatment cycle</td>
<td>State anxiety: STAI (50)</td>
<td>Norm groups</td>
<td>State anxiety: IVF &gt; norms</td>
</tr>
<tr>
<td>Slade et al. (1997), UK</td>
<td>n = 144, inductees only</td>
<td>Just before starting medication of first treatment cycle</td>
<td>State anxiety: STAI (44); depression: BDI; anxiety and depression: POMS</td>
<td>Norm groups</td>
<td>State anxiety: IVF &gt; norms; depression: IVF = norms; POMS: no comparisons with norms</td>
</tr>
<tr>
<td>Beaurepaire et al. (1994), Australia</td>
<td>n = 230, inductees versus veterans, primary and secondary infertility</td>
<td>Just before starting medication of treatment cycle</td>
<td>State anxiety: STAI (39); depression: CES-D</td>
<td>Norm groups</td>
<td>State anxiety: IVF &gt; norms; depression: IVF = norms</td>
</tr>
<tr>
<td>Edelmann et al. (1994), UK</td>
<td>n = 155, inductees, primary and secondary infertility</td>
<td>Just before starting medication of first treatment cycle</td>
<td>State anxiety: STAI (43); anxiety and depression: POMS</td>
<td>Norm groups</td>
<td>State anxiety: IVF = norms; depression: IVF = norms, no statistics given</td>
</tr>
<tr>
<td>Visser et al. (1994), The Netherlands</td>
<td>n = 150, inductees</td>
<td>Just before starting medication of first treatment cycle</td>
<td>State anxiety: STAI (44)</td>
<td>Norm groups</td>
<td>State anxiety: IVF &gt; norms</td>
</tr>
<tr>
<td>Hearn et al. (1987), Canada</td>
<td>n = 300, primary and secondary infertility</td>
<td>3 months before starting treatment</td>
<td>State anxiety: STAI (33); depression: BDI</td>
<td>Norm groups</td>
<td>State anxiety: IVF = norms; depression: IVF = norms</td>
</tr>
</tbody>
</table>

In summary, it may be concluded that before the start of the treatment, in general, IVF patients did not differ from norm groups with respect to depression levels, whereas the results on state anxiety were equivocal: some studies showed elevated levels in the patients, other studies found no difference compared to norm groups.

**Within-cycle emotional adjustment**

Five studies (Table III) assessed women’s anxiety and general distress during the course of one treatment cycle (Merari et al., 1992; Boivin and Takefman, 1995; Ardenti et al., 1999; Yong et al., 2000; Kolonoff-Cohen et al., 2001). None of these studies presented statistics; all descriptions of the results were restricted to an indication whether differences were significant or not. The designs varied regarding the times of the assessments: from the start of the cycle to immediately before oocyte retrieval (OPU), shortly before embryo transfer and following the pregnancy test.

The study of Boivin and Takefman (1995) warrants special mention because they monitored the entire course of the IVF treatment cycle by having the women keep a daily record of subjective general distress, starting at day 1 of the cycle and ending after the result of the pregnancy test had been obtained. Distress levels did not show remarkable changes in the first segment of the treatment cycle, despite a slight increase at OPU. A more significant increase of distress was reported at the end of the cycle, just before the pregnancy test (Boivin and Takefman, 1995). Other studies, too, indicated a similar increase in distress during the course of the cycle. Overall, OPU and pregnancy test proved to constitute the most stressful stages of the IVF cycle (Merari et al., 1992; Ardenti et al., 1999; Yong et al., 2000; Kolonoff-Cohen et al., 2001).

**Pre- and post-treatment emotional adjustment**

Six studies repeated their assessments of women’s emotional response before and after one or more treatment cycles (Table IV). Three are of special interest because they discussed the results of women after both successful and unsuccessful treatments (Visser et al., 1994; Slade et al., 1997; Verhaak et al. 2001, 2005a). However, the subsamples of pregnant and non-pregnant women in two studies (Visser et al., 1994; Slade et al., 1997) were not sufficient to draw any firm conclusions. Three studies (Newton et al., 1990; Hynes et al., 1992; Lok et al., 2002) investigated the emotional response to unsuccessful treatment only.

Four studies used ANOVAs or MANOVAs to analyse the course of emotional adjustment between the various times of assessment and treatment outcomes. The most consistent finding reported by three studies was an increase in depression after one or more unsuccessful treatment cycles showing significant interaction effects between time and treatment outcome (Verhaak et al., 2005b).
**Table III.** Studies investigating emotional response during one treatment cycle

<table>
<thead>
<tr>
<th>References</th>
<th>Sample size</th>
<th>Moments of measurement</th>
<th>Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolonoff-Cohen et al. (2001), USA</td>
<td>n = 151, inductees and veterans</td>
<td>T1: at first visit; T2: before embryo transfer</td>
<td>Anxiety: POMS positive and negative affect: PANAS</td>
<td>Anxiety: T1 &lt; T2; positive affect: T1 &gt; T2; negative affect: T1 &lt; T2</td>
</tr>
<tr>
<td>Yong et al. (2000), UK</td>
<td>n = 37, inductees and veterans</td>
<td>T1: at first visit; T2: before embryo transfer; T3: before pregnancy test</td>
<td>Anxiety and depression: MAACL</td>
<td>Anxiety: T1 &gt; T2 = T3; depression: T1 = T2 &lt; T3</td>
</tr>
<tr>
<td>Ardenti et al. (1999), Italy</td>
<td>n = 200, inductees and veterans</td>
<td>T1: before oocyte pick-up; T2: between oocyte pick-up and embryo transfer; T3: at embryo transfer.</td>
<td>Anxiety: STAI</td>
<td>Anxiety: T1 &gt; T2 &lt; T3</td>
</tr>
<tr>
<td>Boivin and Takefman (1995), Canada</td>
<td>n = 40, inductees</td>
<td>Daily during cycle</td>
<td>Daily record</td>
<td>Highest distress at oocyte pick-up and pregnancy test</td>
</tr>
<tr>
<td>Merari et al. (1992), Israel</td>
<td>n = 113, inductees</td>
<td>T1: oocyte pick-up; T2: embryo transfer; T3: before pregnancy test</td>
<td>Anxiety: STAI; depression: DACL</td>
<td>Anxiety: T1 &gt; T2 &lt; T3; depression: T1 &gt; T2 &lt; T3</td>
</tr>
</tbody>
</table>

DACL, Depression Adjective Checklist (Lubin, 1981); MAACL, Mean Affect Adjective Checklist (Zuckerman and Lubin, 1965); PANAS, Positive and Negative Affect Scale (Watson et al., 1988); POMS, Profile of Mood States (McNair et al., 1971); STAI, Spielberger State in Trait Anxiety Inventory (Spielberger, 1983).

**Table IV.** Studies investigating emotional response pre- and post-IVF

<table>
<thead>
<tr>
<th>References</th>
<th>Sample size</th>
<th>Moments of measurement</th>
<th>Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verhaak et al. (2001, 2005b), The Netherlands</td>
<td>n = 65 unsuccessful treatment, n = 83 successful treatment, inductees</td>
<td>T1: before cycle 1; T2: 4 weeks after last cycle; T3: 6 months after last cycle</td>
<td>Anxiety: STAI; depression: BDI</td>
<td>Unsuccessful treatment—anxiety: T1 &lt; T2 = T3; depression: T1 &lt; T2 = T3 ; successful treatment—anxiety: T1 &gt; T2 = T3 ; depression: T1 &gt; T2 = T3 ; MANOVA</td>
</tr>
<tr>
<td>Lok et al. (2002), China</td>
<td>n = 372 unsuccessful treatment, inductees and veterans</td>
<td>T1: before IVF; T2: 4 weeks after IVF</td>
<td>General health: GHQ; depression: BDI; Anxiety: STAI; depression: BDI; mood: POMS</td>
<td>Unsuccessful treatment—depression: T1 &lt; T2; general health: T1 &gt; T2; ANOVA No test on repeated measures, only cross-sectional Mann Whitney U-test</td>
</tr>
<tr>
<td>Slade et al. (1997), UK</td>
<td>n = 14 unsuccessful treatment*, n = 42 successful treatment, inductees</td>
<td>T1: before cycle 1; T2: 6 months after last cycle</td>
<td>Anxiety: STAI; general health: HSC</td>
<td>Unsuccessful treatment—anxiety: T1 = T2; depression: T1 &lt; T2; successful treatment— anxiety and depression: T1 = T2; Wilcoxon matched pairs test</td>
</tr>
<tr>
<td>Visser et al. (1994), The Netherlands</td>
<td>n = 53 unsuccessful treatment, n = 12 successful treatment* inductees</td>
<td>T1: before first cycle; T2: 4 weeks after first cycle</td>
<td>Anxiety: STAI; general health: HSC</td>
<td>Unsuccessful treatment—depression: T1 &lt; T2; ANOVA</td>
</tr>
<tr>
<td>Hynes et al. (1992), Australia</td>
<td>n = 100 unsuccessful treatment, n = 73 controls, inductees and veterans</td>
<td>T1: before treatment cycle; T2: 4 weeks after treatment cycle</td>
<td>Depression: Mitchell, Cronkite and Moos Depression Scale</td>
<td>Unsuccessful treatment—depression: T1 &lt; T2; ANOVA</td>
</tr>
<tr>
<td>Newton et al. (1990), Canada</td>
<td>n = 187 unsuccessful treatment, n = 26 successful treatment, inductees</td>
<td>T1: 3 months before cycle 1; T2: 4 weeks after cycle 1</td>
<td>Anxiety: STAI; depression: BDI</td>
<td>Unsuccessful treatment: increase anxiety and depression; successful treatment: no information; MANOVA</td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory (Beck et al., 1961); GHQ, General Health Questionnaire (Goldberg, 1972); HSC, Hopkins Symptom Checklist (Derogatis et al., 1974); POMS, Profile of Mood States (McNair et al., 1971); STAI, Spielberger State in Trait Anxiety Inventory (Spielberger, 1983).

*Sample too small to draw firm conclusions.

$F = 12.9; P < 0.01$; Hynes et al., 1992; Lok et al., 2002: $F = 12.0; P < 0.01$. Newton et al. (1990) only presented results after unsuccessful treatment and showed a significant effect of time ($F = 11.1; P < 0.01$). The results with respect to anxiety after unsuccessful treatment were less consistent: of the three studies that assessed anxiety, two showed an increase in anxiety levels relative to baseline after unsuccessful treatment (Verhaak et al., 2005b; time × outcome: $F = 6.5; P < 0.01$; Newton et al., 1990: time: $F = 25.2; P < 0.01$). Visser et al. (1994) did not find any pre-post-treatment differences. However, the results of the latter study are difficult to interpret because the researchers differentiated between subgroups based on the number of treatment cycles before pregnancy. This resulted in small sample sizes thus rendering too little power.

Only one study evaluated the course of anxiety and depression several months after treatment conclusion and reported no recovery from enhanced anxiety and depression levels in this period after unsuccessful treatment (Verhaak et al., 2005b). The results with respect to the emotional adjustment to successful treatment consistently showed equally low or decreased pre-to-post-treatment anxiety and depression levels, reflecting that negative emotions regarding IVF disappear after successful treatment.

In general, unsuccessful treatment tends to evoke an increase of at least depressive symptoms, which are not liable to diminish shortly after treatment. Successful treatment, on the contrary, tends to alleviate negative emotional responses.

The pre–post results are based on averages of the emotional adjustment observed in women after successful and unsuccessful treatment.
IVF. Women who may have clinical levels of emotional problems constitute a group that may also need additional psychological support during fertility treatment. Three studies reported proportions varying from 10 (Lok et al., 2002) to 25% (Verhaak et al., 2005b; Newton et al., 1990) of women with clinically relevant levels of depression after one or more unsuccessful treatment cycles. Although most of the women therefore seem to adjust well to unsuccessful treatment, a considerable number of patients might be eligible for supplemental counselling.

Long-term post-treatment emotional adjustment

The six studies we found on long-term emotional adjustment to IVF that met the criteria for review are summarized in Table V. There were no longitudinal studies on the emotional response of women after IVF treatment had been abandoned. There were two cross-sectional studies that compared the emotional adjustment of women after unsuccessful treatment with that of women after successful IVF (Freeman et al., 1987; Hammarberg et al., 2001). Remarkably, Hammarberg et al. (2001) did not report any differences in emotional status between these two contrasting groups several years after treatment cessation. In contrast, the earlier study by Freeman et al. (1987) did find higher levels of depression in the women who had not conceived following IVF compared with the controls (women with children). The discrepancy in findings may be because of the variations in the time elapsed since the final treatment cycle. In Hammarberg et al.?s (2001) sample this was 2.5–3.5 years, whereas, in the sample of Freeman et al. (1987), this was 6 months to 2.5 years. It is reasonable to suggest that the longer the time since the end of the treatment, the better the emotional adjustment will be. In addition, the comparison groups the studies used differed: pregnant and non-pregnant women after IVF (Hammarberg et al., 2001) and non-pregnant women after IVF versus spontaneously pregnant women and women having conceived after IVF (Freeman et al., 1987).

Table V. Studies investigating long-term emotional response post-treatment

<table>
<thead>
<tr>
<th>References</th>
<th>Sample size</th>
<th>Moment of measurement</th>
<th>Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hjelmstedt et al. (2004), Sweden</td>
<td>n = 55 IVF mothers, n = 40 non–IVF mothers</td>
<td>T1: early pregnancy; T2: 2 months post-partum; T3: 6 months post-partum</td>
<td>Parental stress: Swedish Parental Stress Questionnaire</td>
<td>No differences in parental stress between both groups</td>
</tr>
<tr>
<td>Sydsjo et al. (2002), Sweden</td>
<td>n = 110 pregnant women after IVF, n = 108 women after spontaneous pregnancy</td>
<td>T1: week 15–20 in pregnancy; T2: 12 months post-partum</td>
<td>Parental stress and life satisfaction</td>
<td>More favourable outcome in IVF women compared with women after spontaneous pregnancy</td>
</tr>
<tr>
<td>Hammarberg et al. (2001), Australia</td>
<td>n = 108 women after unsuccessful treatment, n = 121 women after successful treatment</td>
<td>T1: 2.5–3.5 years post-IVF</td>
<td>General Health: GHQ; life satisfaction: satisfaction with life scale</td>
<td>Both at week 12 and week 28, no differences in anxiety and depression between both groups</td>
</tr>
<tr>
<td>Klock and Greenfeld (2000), USA</td>
<td>n = 74 pregnant women after IVF, n = 40 pregnant women after spontaneous pregnancy</td>
<td>T1: 12 weeks pregnant; T2: 28 weeks pregnancy</td>
<td>Anxiety: STAI; depression: BDI</td>
<td>Descriptive analysis: anxiety and depression above norms, 50% of women will continue treatment</td>
</tr>
<tr>
<td>Van Balen and Trimbos-Kemper (1993), The Netherlands</td>
<td>n = 108 long-term infertile women</td>
<td>Last treatment at least 2 years ago</td>
<td>General health: SCL-90</td>
<td>Most depression in unsuccessful group</td>
</tr>
<tr>
<td>Freeman et al. (1987), USA</td>
<td>n = 87 women after unsuccessful IVF, n = 37 women who got spontaneously pregnant, n = 37 women pregnant after IVF</td>
<td>Last treatment at 6–32 months ago</td>
<td>General health: HSC</td>
<td></td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory (Beck et al., 1961); CES-D, Centre for Epidemiologic Studies Depression Scale (Radloff, 1977); GHQ, General Health Questionnaire (Goldberg, 1972); HSC, Hopkins Symptom Checklist (Derogatis et al., 1974); SCL-90, Symptom Checklist (Derogatis et al., 1973); STAI, Spielberger State and Trait Anxiety Inventory (Spielberger, 1983).
The determinants of psychological factors assessed at baseline were compared to the course of the emotional adjustment to unsuccessful treatment. One study limited its predictors to coping factors (Terry and Hynes, 1998), whereas the other two studies used a more comprehensive model (Lukse and Vacc, 1999; Verhaak et al., 2005a), but all the three models were based on stress-coping theory. Verhaak et al. (2005a) and Lukse and Vacc (1999) compared pretreatment outcomes to outcomes after unsuccessful treatment, but the former group did so by controlling for emotional adjustment at baseline which the latter group omitted. Terry and Hynes studied adjustment patterns for many weeks starting some weeks after treatment by controlling for pretreatment emotional adjustment. Because of these different study designs, the statistical data do not allow any firm conclusions. The significance of cognitive strategies in the adjustment to unsuccessful IVF was consistently underlined (Terry and Hynes, 1998; Verhaak et al., 2005a). Furthermore, evidence was found for the contribution of social factors and personality characteristics. Only a comprehensive model would allow a proper assessment of the relative importance of the various predictors of emotional adjustment to unsuccessful IVF, but none of the studies reviewed was sufficiently extensive.

**Discussion**

**Emotional adjustment to fertility treatment**

Apart from individual differences, 25 years of research into the psychological aspects of IVF has not yielded compelling evidence for significant negative emotional consequences of unsuccessful treatment. Most women seem to be able to deal effectively with the burden of the successive cycles. Most women seem to adjust well, even to unsuccessful treatment, but still a considerable number develops clinical relevant emotional problems as a result of ineffective IVF. These findings imply that psychological support should target on those women who are at risk of developing adjustment problems following failed cycles. However, prospective studies that have tried to delineate risk factors are scarce, leaving the identification of women at risk in an early treatment phase flawed. Accordingly, in addition to standardized assessments of emotional adjustment before the start of IVF, research into early risk factors is warranted because this will open new avenues for timely and tailored psychological support for those women likely to experience problems in an early phase of the treatment.

When IVF results in a pregnancy, negative emotions tend to disappear immediately, indicating that the stress of the treatment is predominantly determined by the threat of failure. It also justifies the conclusion that the IVF treatment itself evokes no long-term emotional problems. Comparisons of parental stress in IVF mothers and controls did not reveal any differences in emotional adjustment, precluding negative emotional consequences of IVF treatment in parenthood. However, any conclusion about the emotional impact of unsuccessful IVF should be interpreted with caution. Despite the ample number of studies into the psychological aspects of IVF, comprehensive, consistent knowledge about the course of the emotional response through the various stages and cycles of the treatment is scarce, as is univocal information about the factors that determine that course, which underscores the importance of longitudinal and prospective studies.

The lack of enhanced anxiety and depression levels in women starting fertility treatment was unexpected, as women’s history of several years of fertility problems represents a relatively chronic stressor (Stanton et al., 1992; Domar et al., 1993). Possibly, women embarking on IVF may see the treatment as a first step towards a solution of their fertility problems, a possibility to regain control over the fulfillment of an important life goal, which is likely to positively affect their emotional disposition. Preliminary support for this assumption can be found in longitudinal studies that investigated the course of the adaptation process starting before the actual IVF intervention (i.e., from the first consultation with a fertility specialist; Berg and Wilson, 1991; Boivin et al., 1995). This yielded a curvilinear course starting and ending with low distress scores after several years of infertility with a peak in between, which course may be explained by adaptation to the infertility (Boivin et al., 1995) or as the perceived regaining of control because of the focus on a new treatment option.

Regarding long-term emotional adjustment, a potentially complicating factor is the availability (at least in theory) of endless treatment options that may only be curbed by financial or medical treatment barriers (Smeenk et al., 2004). In the adaptation process to unsuccessful IVF and definitive childlessness, women will eventually have to shift from an active, treatment-focused coping style to a cognitive coping style (by adjusting important life goals). When the possibility to resolve the infertility through treatment is

### Table VI. Studies investigating prediction of emotional response after unsuccessful IVF

<table>
<thead>
<tr>
<th>Sample size and design</th>
<th>Predictors</th>
<th>Emotional response in terms of</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verhaak et al. (2005a)</td>
<td>Personality characteristics, infertility-related cognitions, coping, social support</td>
<td>Change in anxiety and depression</td>
<td>Personality characteristics, infertility-related cognitions and social support predicted change in anxiety and depression</td>
</tr>
<tr>
<td>Lukse and Vacc (1999)</td>
<td>Coping (general), demographic factors, life events</td>
<td>Depression, grief</td>
<td>No prediction of coping variables on depression and grief. No control for baseline levels of depression and grief</td>
</tr>
<tr>
<td>Terry and Hynes (1998)</td>
<td>Post-treatment coping (at T2, specific)</td>
<td>Composite of anxiety and depression T3 controlled for T1 levels</td>
<td>Problem appraisal, emotional approach and less avoidance coping predicted distress at T3 (controlled for distress at T1)</td>
</tr>
</tbody>
</table>
abandoned, woman has to adjust the meaning of her infertility (Folkman, 1984), for instance, by looking for other life goals, by acknowledging certain benefits of childlessness or by concentrating on other ways to care for one or more children, e.g. adoption or fostering. These shifts in coping efforts have been found to be beneficial to people dealing with different kinds of uncontrollable health-related stressors and to particularly induce positive mood (Evers et al., 2001). Similarly, on average, childless women are not characterized by an enhanced negative mood, but they do show lower positive mood and lower levels of life satisfaction (Weaver et al., 1997; Leiblum et al., 1998; Hammarberg et al., 2001) which may be because of a lack of cognitive coping efforts (see Predictors of adjustment to infertility). For women undergoing IVF treatment, the apparently unlimited treatment possibilities can prevent them from adopting more cognitive coping efforts: they may be more likely to persist in considering or trying different treatment options thus preventing themselves from truly facing the loss of their main life goal and making a start to accepting ultimate childlessness. This lack of a well-marked end of treatment may be an important aggravating aspect in women’s adaptation process to definitive childlessness.

**Predictors of adjustment to infertility**

Compared with studies in the emotional adjustment to IVF, studies in the prediction of the emotional response to unsuccessful treatment are relatively scarce. This does not tally with the relevance of this type of research for the psychological support for IVF patients as it can provide essential information about protective and risk factors for adaptation problems facilitating the identification of women at risk at an early stage. Few studies with solid prospective designs showed that cognitive processes play an important role in the adjustment to unsuccessful treatment. To deal effectively with the uncontrollable stressor of infertility, women need to exert considerable effort to change or to adjust the meaning of their childlessness. This is in line with adjustment studies examining other uncontrollable health problems (Rothbaum et al., 1982; Taylor, 1983; Folkman, 1984; Carver et al., 1993; Osowiecki and Compass, 1999; Pakenham, 1999) and, more specifically, studies delineating the process of having to reconstruct one’s life after unsuccessful fertility treatment (Daniek, 2001) and adjustment to ART in general (Schmidt et al., 2005). Based on a qualitative interview assessment, the latter study describes an adaptive process from the first acknowledgement that the fertility problems will under no circumstances be solved, through grief about the unsuccessful treatment attempts, to turning towards the future and giving meaning to childlessness. Schmidt et al. (2005) also stressed the importance of cognitive processes in terms of changing the meaning of infertility. It would be interesting to see whether prospective, longitudinal studies would support these findings.

**Recommendations for future research**

This review provides several starting points for future research. First, there is a clear need for further longitudinal studies that follow women in the last phase of their IVF treatment through 2–3 years after abandoning treatment to shed more light on the final adaptation process, i.e. a cognitive shift from trying to get pregnant to trying to give meaning to one’s life without a child that is genetically one’s own.

Furthermore, future studies into the emotional response within one treatment cycle should differentiate between the stress of the treatment itself and the stress caused by the threat of infertility. Is the emotional response to the treatment itself related to that of the looming childlessness? Are the women who have difficulties in dealing with the fertility treatment the same as those that have difficulties in dealing with its failure?

It is also desirable to know more about how the adaptation process evolves in less invasive infertility treatments before IVF. What is the effect of the prospect of another treatment option (IVF) on the adaptation process to the fertility problems? Is the adjustment to unsuccessful IVF facilitated by the ability to shift coping efforts from more behavioural control (seeking treatment) to cognitive control (changing goals)?

Finally, the decision-making processes in connection with starting and abandoning IVF and the emotional consequences of these decisions should be addressed, possibly accompanied by research into how women could best be counselled in these stages of the treatment.

As to potential predictive factors, a crucial point in psychological research into the emotional impact of IVF is the identification of women who are at risk of developing severe emotional problems as a result of failed treatment. To date, very few studies have been dedicated to this group and even fewer to their long-term adjustment. As the reviewed research demonstrated, ~25% of women experience clinical or subclinical complaints (Verhaak et al., 2005b). Prospective, longitudinal studies testing the predictive value of a comprehensive set of risk and protective factors are warranted to foster the timely identification of at-risk women, preferably before they start treatment. The study focus should be on personality characteristics, on coping and cognitive factors and on social support.

**Clinical implications**

The conclusion that the vast majority of women adjust well to the treatment itself is of considerable clinical relevance. Negative emotional responses proved to be strongly related to the outcome of the treatment, i.e. to the threat of definitive childlessness. Accordingly, psychological support should be specifically targeted to help the woman adjust to the possibility of treatment failure and eventual childlessness rather than to help her to cope with the impact of the treatment itself. As prospective studies showed, especially the pretreatment cognitions of helplessness and acceptance with respect to possible childlessness are the factors that play a prominent role in determining the emotional response to treatment failure. From the start, additional psychosocial care should be dedicated to change the meaning of childlessness. Fertility professionals can advance the process of acceptance by discussing the infertility problems with the couples and by improving their communications about the issue, i.e. by asking about possible plans in the event of unsuccessful treatment and by gauging possible differences in motivation for treatment between the spouses (Boivin et al., 2001; Kentenich et al., 2002). Clinicians should also prepare their patients for possible emotional reactions to unsuccessful treatment. Indeed, Hammarberg et al. (2001) reported that the couples themselves indicated a need for information on the emotional aspects of their fertility problems. Such psychosocial education, e.g. explaining to the couple in advance that enhanced distress is a
natural reaction to unsuccessful treatment, might enhance their control over their emotional response to treatment failure. In most cases, the knowledge will reassure the couple that they are experiencing is part of a normal reaction and not an indication of dysfunctional adjustment.

As the majority of women and their partners seem to adjust well to the considerable stress of successive unsuccessful treatment cycles, standard psychological interventions for all patients are not indicated. However, as mentioned above, the early identification of women who might benefit from psychological intervention, i.e. those at risk of developing emotional problems as the result of unsuccessful treatment, merits close attention. Again, because permanent infertility and eventual childlessness constitute the most important stressor in IVF treatment, any psychological intervention should be aimed at the couple’s acceptance of their fertility problems and adjustment to the likelihood of childlessness.

To summarize, most women adjust well to unsuccessful IVF cycles, but there is a lack of knowledge about the process of adjustment to definitive unsuccessful treatment and childlessness as well as about the factors that contribute to the process. Beyond the considerable negative emotional response, most women experience after abandoning treatment, which represents a normal grief reaction that is expected to diminish over time, there is a sizeable experience after abandoning treatment, which represents a normal grief reaction. As well as about the factors that contribute to the process. Beyond the considerable negative emotional response, most women experience after abandoning treatment, which represents a normal grief reaction that is expected to diminish over time, there is a sizeable experience after abandoning treatment, which represents a normal grief reaction.

References


Submitted on February 15, 2006; resubmitted on June 25, 2006; accepted on July 27, 2006.