

# Are severe depressive symptoms associated with infertility-related distress in individuals and their partners?

Brennan D. Peterson<sup>1,\*</sup>, Camilla S. Sejbaek<sup>2</sup>, Matthew Pirritano<sup>3</sup>, and Lone Schmidt<sup>2</sup>

<sup>1</sup>Faculty of Psychology, Crean School of Health and Life Sciences, Chapman University, Orange, CA, USA <sup>2</sup>Department of Public Health, Section of Social Medicine, University of Copenhagen, Copenhagen K, Denmark <sup>3</sup>Children's Hospital of Orange County Health Alliance, Orange, CA, USA

\*Correspondence address. Faculty of Psychology, Crean School of Health and Life Sciences, Schmid College of Science, Chapman University, One University Drive, Orange, CA 92866, USA. E-mail: bpeterson@chapman.edu

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**STUDY QUESTION:** Are severe depressive symptoms in women and men associated with individual and dyadic infertility-related stress in couples undergoing infertility treatment?

**SUMMARY ANSWER:** Severe depressive symptoms were significantly associated with increased infertility-related distress at both the individual and partner level.

**WHAT IS KNOWN ALREADY?:** An infertility diagnosis, the stress of medical treatments and a prior history of depression are risk factors for future depression in those undergoing fertility treatments. Studies examining the impact of severe depressive symptoms on infertility-related distress in couples are lacking.

**STUDY DESIGN, SIZE, DURATION:** This cross-sectional study included 1406 couples who were consecutively referred patients undergoing fertility treatments in Denmark in the year 2000. A total of 1049 men and 1131 women were included in the study.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** Participants were consecutively referred patients undergoing a cycle of medically assisted reproduction treatment at five Danish public and private clinics specializing in treating fertility patients. Severe depressive symptoms were measured by the Mental Health Inventory 5 from the Short Form Health Survey 36. Infertility distress was measured by the COMPI Fertility Problem Stress Scales. Multilevel modelling using the actor–partner interdependence model was used to study the couple as the unit of analysis.

**MAIN RESULTS AND THE ROLE OF CHANCE:** Severe depressive symptoms were reported in 11.6% of women and 4.3% of men, and were significantly associated with increased infertility-related distress at the individual and partner level. There was no significant interaction for gender indicating that men and women did not differ in how severe depressive symptoms were associated with infertility distress.

**LIMITATIONS, REASON FOR CAUTION:** Because of the cross-sectional study design, the study findings only show an association between severe depressive symptoms to individual and partner distress at a single point in time; however, nothing is known about causality.

**WIDER IMPLICATIONS OF THE FINDINGS:** This study adds to the growing body of literature using the couple as the unit of analysis to study the relationship between depression and infertility distress. Recommendations for medical and mental health professionals that underscore the potential risk factors for depressed men and women who are pursuing infertility treatments are provided. Additional studies using a longitudinal study design to track the impact of depression on distress over the course of the infertility treatment cycle would be valuable for increasing our understanding of the complex relationship that exists between these psychosocial factors.

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**Key words:** depressive symptoms / infertility distress / couples / cross-sectional study

## Introduction

The experience of infertility is commonly linked with unexpected stressors that can impact one's personal life, social support networks and marital relationships (Newton *et al.*, 1999). These stressors can cause significant disruption in one's life and be related to increased psychological distress in men and women (Wichman *et al.*, 2011). One of the key types of distress reported in infertility patients is depression. An infertility diagnosis and the stress of medical treatment can put women at risk of depressive symptoms, particularly after treatment failure (Newton *et al.*, 1990; Domar *et al.*, 1992; Verhaak *et al.*, 2007; Volgsten *et al.*, 2010). On the other hand, women with depressive symptoms may be more likely to experience infertility due to depression's impact on the biological mechanisms that influence hormone production and ovulation (Lapane *et al.*, 1995; Williams *et al.*, 2007). Adding to the already complicated relationship that exists between these variables, a prior history of depression is a risk factor for future depression in women undergoing fertility treatments (Vahratian *et al.*, 2011; Pasch *et al.*, 2012).

The majority of studies examining the relationship between depression and infertility have examined the impact of depression on pregnancy and live birth rates. While some studies have found that depression is linked with lower pregnancy rates in couples pursuing assisted reproductive technologies (ART) (Klonoff-Cohen, 2005), two recent meta-analyses have found that depression was not associated with a reduced chance of pregnancy outcome (Boivin *et al.*, 2011; Matthiesen *et al.*, 2011). However, a recent study using a national register-based cohort found that of the 42 880 Danish women participating in ART treatments, women with a depression diagnosis prior to fertility treatments participated in fewer ART cycles and had fewer ART live births when compared with the non-depressed group (Sejbaek *et al.*, 2013). This supports a previous research finding that women with major depression reported the lowest live birth rate among study participants (Volgsten *et al.*, 2010).

For infertility patients who undergo ART, a prior depression history is the strongest risk factor for future depression (Vahratian *et al.*, 2011; Pasch *et al.*, 2012). Men and women with depression prior to infertility treatment likely have less physical, emotional and social resources to cope with the stress of infertility treatments and treatment failure, and thus may be considered an 'at risk' group. In a Swedish study of 545 couples undergoing *in vitro* fertilization (IVF), 10.9% of women and 5.1% of men had major depression at treatment initiation (Volgsten *et al.*, 2008). In this study, major depression was measured by the Primary Care Evaluation of Mental Disorders (PRIME-MD) based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). This is a substantial percentage of the patients seen for infertility treatments, and because we currently know very little about the association between pre-existing depressive symptoms and infertility-related distress in infertility patients, it is important to establish a baseline if such an association exists.

In addition to our limited understanding of the association between severe depressive symptoms and infertility-related distress, we know very little about how depression is associated with infertility distress at the dyadic level. In other words, is there an association between an individual's severe depressive symptoms and a partner's levels of infertility-related distress? To address the lack of studies using the couple as the unit of analysis, researchers have begun to use a data analytic technique called the actor-partner interdependence model (APIM)

(Kenny *et al.*, 2006), to study how the stressors of infertility are related to individual and partner outcomes (Peterson *et al.*, 2008, 2009, 2011; Benyamini *et al.*, 2009). A small number of these studies have used depression as a study variable and have examined its relationship with coping (Berghuis and Stanton, 2002), marital conflict (Proulx *et al.*, 2009) and the transmission of depressive symptoms between partners undergoing fertility treatments (Knoll *et al.*, 2009). However, few studies have examined how depression is associated with infertility distress, and particularly how depressive symptoms are associated with both the individual's and partner's levels of distress. Because infertility is ultimately a shared stressor that exists between both members of the couple, more studies are needed to utilize dyadic analyses in order to provide a more complete picture of the infertility experience.

The current study attempted to examine how severe depressive symptoms in women and men are associated with individual and dyadic infertility-related distress. The study asked the following research questions: (i) Prior to fertility treatments, do men and women with severe depressive symptoms experience higher levels of infertility distress when compared with men and women who do not report severe depressive symptoms? (ii) Are an individual's severe depressive symptoms associated with increased infertility-related distress in the individual and in their partner?

## Materials and Methods

### Procedure

This study is part of The Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme (Schmidt, 2006), a prospective longitudinal cohort study of infertile couples in fertility treatment. Patients who were consecutively referred at one of the four public hospital-based tertiary fertility clinics and one private clinic between January 2000 and August 2001 received a questionnaire for each spouse before attending their first treatment. The study complied with the Helsinki II Declaration was assessed by the Scientific Ethical Committee of Copenhagen and Frederiksberg Municipalities (KF 01-107/99), and was approved by the Danish Data Protection Agency (J. nr. 1999-1200-233; 2001-41-1486; 2005-41-5694).

### Measures

The 5-item Mental Health Inventory 5 (MHI-5) from the 36-item Short-Form Health Survey (SF-36), Medical Outcomes Study, was used to measure severe depressive symptoms (Bjorner *et al.*, 1998a,b; Strand *et al.*, 2003). Previous studies comparing MHI-5 with other (validated) mental health scales have shown MHI-5 to be a good measure of severe depressive symptoms (Berwick *et al.*, 1991; Strand *et al.*, 2003). The five items in the MHI-5 measure the mood of the participants in the past 4 weeks (e.g. felt so down in the dumps that nothing could cheer you up, felt downhearted and blue). The response key was a 6-point scale ranging from (1) all of the time to (6) none of the time. The scores for two of the items were reversed and the answers were summed up to a raw score ranging from 5 to 30 (Bjorner *et al.*, 1997). The raw score was then transformed to a scale ranging from 0 to 100. The scale was dichotomized with a cut-off point at 52 and participants scoring  $\leq 52$  were categorized as having severe depressive symptoms. This cut-off point was chosen in agreement with previous studies comparing other scales measuring depressive symptoms to the MHI-5, and investigating different cut-off points for the MHI-5 (Holmes, 1998; Strand *et al.*, 2003). Studies in other research fields also use a cut-off point at  $\leq 52$  (Rugulies *et al.*, 2012). Therefore, choosing the same cut-off point as other studies makes it possible to compare results. The MHI-5 has

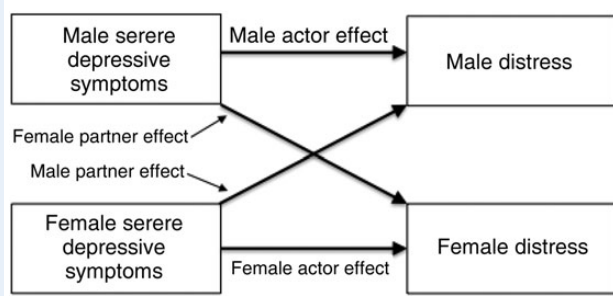
been widely used in studies assessing mental health, as well as general health, and has had a Cronbach's alpha of 0.82 (Strand *et al.*, 2003).

Infertility-related distress was measured by the COMPI Fertility Problem Stress Scales, a 14-item instrument based on The Fertility Problem Stress Inventory (Abbey *et al.*, 1991) and qualitative interviews of Danish infertile patients regarding the psychosocial consequences of infertility and fertility treatment (Schmidt, 1996). The measure includes questions regarding one's personal distress (six items, e.g. how much stress the individual felt in their life as a result of the childlessness), marital distress (four items, e.g. how much stress the childlessness placed on marriage and sexual relationship) and social distress (four items, e.g. how much stress the fertility problem placed on relationships with family, friends and workmates). The response key for 10 of the 14 items is based on a 4-point scale from (1) a great deal to (4) none at all, while four items are based on a 5-point scale from (1) strongly agree to (5) strongly disagree. An exploratory factor analysis produced a set of parsimonious factors (Schmidt *et al.*, 2003). In the exploratory factor analysis, items with factor loadings  $>0.45$  were assigned to the factor (personal, marital or social distress) for which they had the greatest loading. As mentioned above, the three domains were uncovered in accordance with Abbey *et al.* (1991) and the interviews conducted by Schmidt (1996). The range, mean and Cronbach alpha coefficients differed depending on the subscale: personal distress (range 0–20, mean 6.86, SD 4.48, Cronbach alpha 0.82); marital distress (range 0–14, mean 3.86, SD 3.16, alpha 0.73) and social distress (range 0–12, mean 1.87, SD 2.43, alpha 0.82) (Schmidt *et al.*, 2003).

## Data analysis

This study was cross-sectional. Multilevel modelling using the APIM (Kenny *et al.*, 2006; Kashy and Donnellan, 2008) was used to study the association between a partner's severe depressive symptoms and his or her partner's distress (personal, marital and social) (see Fig. 1). The APIM allows for the simultaneous estimation of actor effects (individual effects) and partner effects (the effects of another closely associated person) to shared stressors in dyads, thus providing a more complete picture of how severe depressive symptoms are related to distress in couples.

Data were analysed with the couple as the unit of analysis. This was done by conducting multilevel analyses using the SAS 9.2<sup>®</sup> mixed procedure. A multilevel analysis involves more than one regression model calculated at different levels of a nested design. In the current set of analyses, level 1 was the individual level that was nested within level 2, the couple. Multilevel analyses estimate the model independently at each of these levels. The design of the analysis is very similar to a multiple regression with one dependent variable and a set of predictors, or independent variables. Analyses provide unstandardized estimates of path coefficients for actor and partner effects.



**Figure 1** General model of actor and partner effects of severe depressive symptoms on distress.

The analyses were cross-sectional with severe depressive symptoms (dichotomous) as the independent variable, and personal, marital and social distress as the dependent variables. Three analyses were conducted, one for each of the three types of distress. Because previous research has found infertility diagnosis (i.e. male or female factor infertility) to be related to other psychosocial consequences of infertility (Peronace *et al.*, 2007), infertility diagnosis based on five categories [i.e. male factor, female factor, both male–female factor, other causes (not specified), unknown] was therefore tested as a covariate in the analyses. However, no statistical association between infertility diagnosis and severe depressive symptoms and personal and marital distress was found, so it was not included in the final analyses.

## Results

In total, 2812 fertility patients (1406 couples) received a baseline questionnaire for each partner and 80.0% ( $n = 2250$ ) participated. Couples who had a child together prior to inclusion in COMPI and participants without a severe depressive symptoms score were excluded from the analyses. Thus, 1049 men and 1131 women were included in the overall study. At baseline the mean age of women was 31.9 years ( $SD = 3.6$  years) while their male partners mean age was 34.3 years ( $SD = 5.1$  years). Couples had been together for an average of 7.7 years ( $SD = 3.7$ ) and had been infertile for  $\sim 4.2$  years ( $SD = 2.3$ ). Nearly 60% had been in fertility treatment prior to inclusion in the COMPI Research Programme.

As shown in Table I, 11.6% of women in the sample reported severe depressive symptoms compared with 4.3% of men ( $\chi^2 = 39.0$ ,  $P < 0.001$ ). Women with severe depressive symptoms had significantly higher distress levels for all three measures compared with women with no severe depressive symptoms. The same relationship was also found for men (see Table I). Women reported significantly higher levels of personal distress ( $t = -15.9$ ,  $P < 0.001$ ) and social distress ( $t = -7.73$ ,  $P < 0.001$ ) when compared with men. However, no difference was found between women and men with respect to marital distress.

Table II shows the results of APIM analyses (multilevel modelling). The results are displayed in the form of unstandardized regression coefficients. Severe depressive symptoms were significantly associated with increased personal, marital and social distress in both men and women (i.e. significant actor effects). There were no interaction effects with gender, indicating that the association between depression and distress did not differ between men and women. There were also significant partner effects for men and women in that an individual's severe depressive symptoms were associated with higher levels of personal and marital distress in one's partner. However, for social distress only a female partner effect was found, showing that a male's severe depressive symptoms were significantly associated with a female partner's social distress. None of the interaction effects between partner effects and gender were significant, indicating that the association between severe depressive symptoms and effects on the partner's distress did not differ between males and females.

## Discussion

This study adds to the growing body of literature that examines the dyadic impact of a partner's response to infertility (Berghuis and Stanton, 2002; Benyamini *et al.*, 2009; Knoll *et al.*, 2009; Peterson *et al.*, 2009, 2011) by

**Table I** Descriptive analysis.

	Male n (%)	Female n (%)	P-value for gender diff
No depressive symptoms	1004 (95.7%)	1000 (88.4%)	<0.001
Severe depressive symptoms	45 (4.3%)	131 (11.6%)	
	<b>No depressive symptoms</b>	<b>Severe depressive symptoms</b>	<b>P-value<sup>b</sup></b>
Personal distress, n	970	124	
Mean (std)	5.14 (3.65)	12.56 (3.68)	<0.001 <sup>b</sup>
Marital distress, n	969	121	
Mean (std)	3.65 (3.05)	6.08 (3.17)	<0.001 <sup>b</sup>
Social distress, n	975	126	
Mean (std)	1.39 (2.16)	3.91 (3.03)	<0.001 <sup>b</sup>

<sup>a</sup>P-value comparing distress among males with no severe depressive symptoms to males with severe depressive symptoms.

<sup>b</sup>P-value comparing distress among females with no severe depressive symptoms to females with severe depressive symptoms.

<sup>c</sup>Gender difference for personal distress, marital distress and social distress.

**Table II** Actor and partner effects of severe depressive symptoms on distress presented as unstandardized regression coefficients.

	Personal distress	Marital distress	Social Distress
Severe depressive symptoms			
Actor effects			
Male	4.75 <sup>c</sup>	3.47 <sup>c</sup>	1.61 <sup>c</sup>
Female	4.71 <sup>c</sup>	2.43 <sup>c</sup>	1.78 <sup>c</sup>
Actor effects by gender	-0.04	-1.04	0.18
Partner effects			
Male	1.36 <sup>c</sup>	1.74 <sup>c</sup>	0.13
Female	1.88 <sup>b</sup>	2.42 <sup>c</sup>	0.82 <sup>a</sup>
Partner effects by gender	0.51	0.68	0.69

<sup>a</sup>P < 0.05.

<sup>b</sup>P < 0.01.

<sup>c</sup>P < 0.001.

providing support that severe depressive symptoms are significantly associated with personal, marital and social infertility-related distress at the individual and partner level. Although there are studies that have examined the dyadic impact of depression in couples pursuing infertility treatments (Berghuis and Stanton, 2002; Knoll *et al.*, 2009), to our knowledge, this is the first study to demonstrate that severe depressive symptoms are significantly associated with individual and partner infertility distress.

The current study used severe depressive symptoms as the independent variable in the study analysis. Although we cannot draw predictive conclusions relative to severe depressive symptoms and infertility-related distress, the purpose of the current study was to examine if such an association exists so that baseline data can lay the groundwork for future longitudinal studies. In our sample, 11.6% of women and 4.3% of men reported severe depressive symptoms; these rates compared favourably with a large sample of infertility patients reporting depression in Sweden (10.9% women, 5.1%, men) (Volgsten *et al.*, 2008). The fact that two studies found such high rates of depressive symptoms in men and women prior to pursuing infertility treatments illustrates the significance of studying the possible association between severe depressive symptoms and infertility-related distress. Furthermore, it is possible that these rates even underrepresent the actual percentage of depressed men and women experiencing infertility, as researchers have found that depression can act as a barrier to seeking out medical advice for infertility (Herbert *et al.*, 2010).

It has been well documented that infertility is commonly linked with depression, particularly in women (Domar *et al.*, 1992), and that an infertility diagnosis and the subsequent stress of treatments have been linked with increased infertility distress (Newton *et al.*, 1999; Greil *et al.*, 2010). In the current study, women reported higher levels of infertility distress when compared with men, a finding supported by a wide body of literature (Newton *et al.*, 1999; Greil *et al.*, 2010). In addition, a significantly higher percentage of women reported severe depressive symptoms when compared with men. This is consistent with depression rates in



the general population where women are two to three times as likely to be depressed as men (Kessler, 2003).

It is noteworthy that the current study used a sample of men and women that included people who reported severe depressive symptoms. A meta-analysis of 28 studies examining the relationship between depression and women experiencing polycystic ovary syndrome found that over 50% of the studies reported depression scores in the non-clinical range, while the remaining studies were in the mild depression range (Veltman-Verhulst *et al.*, 2012). Using a sample of couples with severe depressive symptoms helps give voice to an understudied and at-risk population of women and men. Furthermore, the current study answered calls of previous researchers to use multilevel models that enhance our understanding of the dyadic impact of an individual's severe depressive symptoms on one's partner (Lund *et al.*, 2009). The finding of the current study that an individual's severe depressive symptoms are related to increased infertility-related distress in the partner supports this call, and underscores the importance of conceptualizing infertility as a couples-level stressor.

A large number of studies examining the relationship between depression and infertility have done so by examining the impact of depression on pregnancy outcomes. While it is encouraging that recent meta-analyses and studies have found that depression prior to infertility treatment does not influence pregnancy rates, a finding that can reduce the amount of self-blame a woman may feel following unsuccessful treatment (Boivin *et al.*, 2011; Matthiesen *et al.*, 2011; Pasch *et al.*, 2012), the findings from this study underscore possible risk factors for depressed men and women pursuing infertility treatments. It has been shown that higher depression in women prior to IVF treatment was associated with higher depression following IVF treatment (Pasch *et al.*, 2012). This finding may be explained in part because men and women, who are depressed prior to treatments, are likely experiencing greater amounts of infertility distress compared with non-depressed couples. Because this distress increases at both the individual and partner level, and because depressed individuals have fewer emotional resources to cope with this distress, this group may be at particular risk of future depression following treatment failure.

The findings from the current study may have implications for medical and mental health professionals (Peterson *et al.*, 2012). Pasch *et al.* (2012) recommended that psychological interventions be focused on helping couples cope with the stress of infertility and treatment failure, as opposed to using psychological treatments to reduce stress in an attempt to become pregnant. This may be particularly true for men and women entering treatment with severe depressive symptoms, as their levels of infertility stress may be higher than those without depressive symptoms.

The findings from this study must be interpreted in the context of the study's limitations. First, due to the cross-sectional study design, we cannot make conclusions that depressive symptoms cause increased infertility distress in individuals or partners, or that infertility distress causes an increase in an individual's or partner's depressive symptoms. These findings only represent the association between severe depressive symptoms and infertility distress, and therefore cannot be used to infer any causality or directionality of this relationship. Second, the COMPI scales used in this study have not yet been validated in large-scale psychometric studies. The fertility problem stress scales were adopted from an existing scale (Abbey *et al.*, 1991) and further developed based on

findings from in-depth detailed qualitative research and interviews with Danish fertility patients (Schmidt, 1996). Explanatory factor analyses showed infertility-specific distress in three different domains (personal, marital, social) (Schmidt *et al.*, 2003), and the infertility-specific scales are being used in several other studies in different countries, with a cross-cultural validation study currently being carried out. Third, the multilevel analyses are unadjusted, although the findings show that the couples are intertwined and that the dyadic analyses add information about couples and their influence on each other. Fourth, the MHI-5 was developed to assess mental health in general and was not designed to assess severe depressive symptoms. However, a study comparing clinical diagnosis with MHI-5 found good agreement for mood disorders and the MHI-5 (Rumpf *et al.*, 2001), which indicates that it is plausible to use the MHI-5 as a proxy for severe depressive symptoms. Finally, the cut-point of the MHI-5 could have been higher (e.g. 56 or 60), hence identifying more individuals with severe depressive symptoms. However, because the MHI-5 is not a clinical instrument, the lowest cut-point identified was used. This is also in accordance with other studies (Holmes, 1998; Strand *et al.*, 2003; Rugulies *et al.*, 2012) that found  $\leq 52$  as the best cut-point. Given these limitations, additional studies using a longitudinal study design to track the impact of depression on distress over the course of the infertility treatment cycle would be valuable in increasing our understanding of the complex relationship that exists between these variables.

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## Authors' roles

All authors contributed substantially to the concept and the design of the study. L.S. obtained the data. C.S.S. and M.P. performed the data analysis. B.D.P. drafted the article. All authors contributed to the data interpretation, critical and substantial revisions of the paper and final approval of the manuscript.

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## Conflict of interest

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