

# The association between female-factor infertility and depression and anxiety

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## Abstract

**Background** Female-factor infertility is diagnosed when women of reproductive age are unable to conceive a pregnancy within 12 months of unprotected, frequent intercourse. Infertility affects between 11.5% and 15.7% of Canadian couples. The process of receiving a diagnosis and seeking treatment is often described as a devastating experience, which leads to psychological distress.

**Objective** A review of the literature was conducted to assess the association between an infertility diagnosis and the subsequent development of depression and anxiety symptoms among women.

**Methods** PubMed, PsycINFO, ClinicalKey, and Google Scholar databases were searched using the following MeSH terms and keywords: female-factor infertility, infertility, mental health, depression, and anxiety. Inclusion and exclusion criteria were established to identify pertinent articles for full-text review.

**Results** The majority of infertility research has been conducted in Europe and Asia using self-report questionnaires. The main finding from the research was that women experienced increased levels of infertility-related depression and anxiety, particularly with longer durations of infertility.

**Conclusion** Existing literature demonstrates an association between a diagnosis of female-factor infertility and the risk of development of depression and anxiety. Future research should focus on complementary qualitative research and quantitative research.

## Introduction

Most women of reproductive age are able to conceive a pregnancy within 12 months of unprotected, frequent intercourse. However, for up to one in four women, conceiving and carrying a fetus is difficult and often unattainable, leading to an eventual diagnosis of infertility.<sup>1,2</sup> Female-factor infertility, infertility specifically related to the female reproductive tract, has been identified worldwide.<sup>1-3</sup> For example, 15.4% of Norwegian and 17.3% of Australian women experience infertility.<sup>2,4</sup> Among Americans, prevalence rates are as high as 24.3% of nulliparous women.<sup>3</sup> In Canada, infertility affects between 11.5% and 15.7% of couples, with an increased risk among women aged 35 to 44 years or who have given birth to less than two children.<sup>1</sup> The inability for a woman to become pregnant or have a live birth is commonly described as a devastating experience, which leads to psychological distress.<sup>5,6</sup> Therefore, the purpose of this literature review was to assess the relationship between female-factor infertility and mental health concerns. Specifically, the goal of this review was to examine the association between an infertility diagnosis and subsequent development of depression and anxiety symptoms among women.

## Methods

The identification and review of articles that met inclusion criteria involved two phases. The initial search yielded 81 articles in PubMed, using the following medical subject heading (MeSH) terms: female infertility, psychology, depression, and anxiety. The search was limited to English language articles that included human subjects, adults between the ages of 19 and 44 years old, and female sex. The second review phase involved an expanded search of articles using PsycINFO, ClinicalKey, and Google Scholar. Keywords used in these searches included female-factor infertility, infertility, mental health, depression, and anxiety. Articles were selected based on inclusion and exclusion criteria. Articles were included in the review if they examined the effect

of infertility on women's mental health and wellbeing. Articles were excluded if a mental illness diagnosis preceded an infertility diagnosis or was not directly related to infertility, if psychological factors were used as a predictor of treatment outcome, if modulating factors were assessed in relation to infertility and mental health, if only male infertility was assessed, and if only male responses to an infertility diagnosis were assessed. Additionally, articles were excluded if they were not original research that were peer-reviewed and published in research journals. Of a total of 92 articles, 12 studies met the established criteria and were selected for full-text review.

## Results/Discussion

### Study characteristics

Of the 12 articles reviewed, nine originated in Europe or Asia; the remainder were from Africa (n=2) or the United States (n=1) (Table 1). The majority of studies were published within the last seven years (n=8) and the remainder were published over ten years ago (n=4). The studies were predominantly cross-sectional with comparison groups (Table 1). Infertile patients were the focus participants in 11 of the 12 studies and were recruited from fertility treatment centres, hospitals, and physician clinics. Comparison groups were recruited from outpatient departments, physician clinics, or survey agencies and included healthy fertile women, pregnant women, or males within the same age ranges. The majority of studies assessed participants between 20 and 35 years of age. Participants were excluded if they had prior mental health concerns or remarkable past medical histories. Sample sizes ranged from 100 to 9200 participants, with the majority of studies assessing approximately 200 participants. All participants were assessed using self-reported questionnaires. Depression and anxiety were measured using various validated measurement tools (Table 1). Increased levels of infertility-related depression and anxiety were found in 11 out of 12 studies and 9 out of 12 studies, respectively (Table 2). Infertile women had clinically significant levels of depression and/or anxiety in over half of the studies (n=7; Table 2).

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**Depression**

Researchers suggest that women having difficulty conceiving are at a marked risk of developing depression after a diagnosis of infertility.<sup>7</sup> The majority of patients (62%) attending fertility clinics had some form of depression, with 40% reaching mild levels and 22% reaching moderate levels of depression.<sup>8</sup> In a similar demographic, only 10% of infertile women exhibited elevated depression scores; however, this was statistically greater than their male counterparts (1%).<sup>9</sup> Compared to fertile participants, infertile patients were more likely to exhibit a greater number of depression symptoms and score significantly higher on depression scales.<sup>7,10-15</sup> Researchers found that women with infertility exhibit a two-fold increase of depression scores compared to their fertile counterparts.<sup>12</sup> Prevalence rates of severe depression following an infertility diagnosis are as high as 35.4%, compared to the prevalence of severe depression among fertile women within the same age group (19.4%).<sup>7</sup> An additional study supports this finding, as more infertile patients (24.9%) demonstrated clinically significant depression symptoms than controls (6.8%).<sup>13</sup> Conversely, Rostad and colleagues found no significant differences between the prevalence of depression among infertile women without a child (6.1%), infertile women with a child

**Table 1** | Characteristics and overall profile of the 12 studies included in the literature review.

Overall Profile	# of Reviewed Studies
<i>Study Design</i>	
Cross sectional	8
Unidentified cross sectional	2
Longitudinal	2
<i>Measurement tool used for assessing depression/ anxiety</i>	
Beck Depression Inventory/Beck Anxiety Inventory	5
Hospital Anxiety and Depression Scale	3
State-Trait Anxiety Inventory	3
Symptom Checklist-90	2
Other *	5
<i>Response rate reported</i>	8
<i>Control/ comparison group</i>	
Fertile/non-fertile/pregnant females	7
Males	2
Other (unspecified, female fertility preservation patients)	3
<i>Assisted reproductive technology treatment planned or pursued by patients</i>	10
<i>Location</i>	
Europe	6
Asia	3
Africa	2
America	1

\*Institute for Personality and Aptitude Testing, Zung Depression Scale /Zung Anxiety Scale, Profile Of Mood States, Women's Health Questionnaire, Center for Epidemiologic Studies Depression Scale

**Table 2** | The number of reviewed studies with and without statistically significant findings as they relate to their categorized main results.

Results of Study	# of studies reporting statistically significant findings	# of studies reporting non-significant findings	N/A
Increased depression scores among infertile patients	11	1*	
Significantly high depression scores compared to comparison group	9	2*/**	1
Increased anxiety scores among infertile patients	9	2***	1
Significantly high anxiety scores compared to comparison group	8	3*	1
Increased symptomology with duration of infertility diagnosis	6	2	4
Clinically significant levels or diagnosis of depression/anxiety	7	3	2

\* Comparison group was between infertile and non-infertile participants; however, further analysis compared infertile patients with and without children.

\*\* Comparison group was recovering cancer patients who had undergone fertility preservation.

\*\*\* One study found a trend toward high anxiety scores.

(6.5%), and fertile women (6.9%), in a similar European population.<sup>2</sup> While depression did not appear to be a factor among the studied infertile Norwegian population, childless infertile women were significantly more likely to experience life dissatisfaction and poor health compared to their fertile counterparts.<sup>2</sup> Therefore, the impact of infertility may manifest in forms similar to depression in this subset of infertile women. Limitations in the study may have led to the differences in the association of infertility and depression between articles. The study had a higher response rate from middle aged women compared to younger women.<sup>2</sup> Older women may have accepted their infertility diagnosis, whereas, younger women may have refused to participate due to the sensitive and emotional nature of the study. In addition to differing ages between participants, the data were antecedent. Therefore, confounding variables, time, and recall bias are of concern. Rostad and colleagues suggest that the impact of infertility may be stressor-specific, manifesting as a range of psychological symptoms, and recommend that stressor-specific measurements are employed when assessing infertile women.<sup>2</sup>

**Anxiety**

Researchers suggest that infertile women are in jeopardy of developing anxiety.<sup>7</sup> For example, anxiety cases were identified among 38% of infertile females awaiting assisted reproductive technology (ART), which was significantly greater than the 12% anxiety prevalence in the comparison group.<sup>9</sup> In another study, a greater proportion of female infertile patients were diagnosed with moderate anxiety (15.5%) compared to fertile participants (7.9%).<sup>7</sup> Only one study failed to find a significant difference between the prevalence of depression and anxiety in the treatment and control group; nevertheless, a trend toward increased anxiety was noted in women undergoing ART compared to age-matched, fertile women.<sup>15</sup> This study also showed that childless infertile women were at a significant risk of suffering from phobic anxiety. These studies support the notion that infertile patients may experience increased anxiety compared to fertile women.<sup>2,7,11-15</sup>

**Duration of infertility**

The duration of infertility may be an important risk factor for the development of depression and anxiety among women (Table 2).<sup>8</sup> In

one study, 43.4% of women experienced both depression and anxiety symptoms before beginning fertility treatment, with an additional 18.9% developing symptoms of depression and anxiety between the commencement and the conclusion of treatment.<sup>16</sup> Moreover, the symptoms worsened over the duration of treatment.<sup>17</sup> Drosdzol and Skrzypulec suggest that women struggling with infertility for three to six years were at a higher risk of developing mood and emotional disorders.<sup>7</sup> Chiaffarino *et al.*<sup>16</sup> demonstrated a positive association between a minimum four year diagnosis of infertility and depression or anxiety. Verhaak and colleagues found that infertile women experienced a significant increase in depression and anxiety between the first and second visits, with a significant increase in depression by the third visit.<sup>14</sup> Conversely, Kee *et al.* found more severe depression symptoms at the first visit compared to subsequent visits.<sup>11</sup> Further, some researchers have not found an association between infertility, depression, and anxiety at the five year mark.<sup>12</sup> The inconsistencies between studies may be a function of culture or geography, as both articles with contradictory evidence showing decreased depression with longer periods of diagnosis assessed women from Asian populations.<sup>11,12</sup> Infertility-associated depression and anxiety may be increased initially and taper with acceptance of the diagnosis or desensitization to the distress, allowing women to cope with prolonged emotional turmoil.<sup>11</sup> It is conceivable that infertile women from Asian populations, who initially experience depression and anxiety with infertility, will experience resolution due to cultural influences and supports. Therefore, it is possible that women living outside Japan or Korea tend to experience a greater increase of depression and anxiety symptoms when nearing the end of infertility treatment/the longer they are infertile.

### Limitations

A major limitation of the reviewed research articles is the self-report, survey study design. Infertility and mental health cannot be randomly assigned or investigated through quasi-experimental research; therefore, researchers ask participants to provide their subjective self-perceptions regarding their health and illness. Questionnaires are often designed with a few answer choices to each question; therefore, with limited options for answers, the data may be distorted and unrepresentative. Future research should include continuous scales, open-ended questions, and qualitative methods in adjunct to quantitative measurements.

The majority of articles reviewed were cross-sectional studies. This poses a limitation, as cause-and-effect inferences cannot be established. While researchers took precautions to exclude participants with a pre-existing history of mental illness, it is possible that the participants' symptoms preceded their infertility diagnosis. Future research should implement a longitudinal design, with baseline depression and anxiety scores for comparisons. Moreover, numerous studies recruited participants from patient populations attending fertility treatment clinics and experienced low response rates. This may lead to a misrepresentation of the demographic and psychological wellbeing of infertile patients. Future research should aim to recruit patients from numerous different specialists and other resources within the population.

Additionally, there were limitations to the literature review.

Survey tools to measure mental health and definitions of fertility differed across studies. Differences across studies complicate and impede comparisons of results across study samples. Moreover, recent research that met the inclusion and exclusion criteria was limited. Older articles may not be relevant to today's population. Therefore, research on infertility is required globally, to address potential risk factors and associated psychological disorders among those who have difficulty conceiving.

### Conclusion

The goal of the present literature review was to explore the relationship between female-factor infertility and depression and anxiety symptoms. The majority of the findings suggest that women may have an increased risk of developing depression and/or anxiety following a diagnosis of infertility.<sup>7-16</sup> In particular, women who experienced a longer duration of infertility were more likely to experience greater levels of depression and anxiety.<sup>7,8,16</sup> Duration of infertility, along with other potentially associated variables, should be considered or explored in future research, as possible risk factors may confound infertility-related findings. The impact of infertility on women's lives is profound, as it influences their overall wellbeing. Mental health and counseling services are important services to consider when assisting women with infertility.

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